Interventional procedure overview of percutaneous thrombectomy for intermediate-risk or high-risk pulmonary embolism

Contents

Table 1 Abbreviations

Abbreviation	Definition
CDT	Catheter-directed thrombolysis
CTPA	CT pulmonary angiogram
DVT	Deep vein thrombosis
ECMO	Extracorporeal membrane oxygenation
ICU	Intensive care unit
LBAT	Large bore aspiration thrombectomy
LV	Left ventricular
MAE	Major adverse event
mMRC	modified Medical Research Council
mPAP	Mean pulmonary artery pressure
MT	Mechanical thrombectomy
PE	Pulmonary embolism
PT	Pulmonary thrombectomy
RC	Routine care
RV	Right ventricular
RV:LV diameter ratio	Right ventricular (RV) to left ventricular (LV) diameter ratio
SAE	Serious adverse event
TTE	Transthoracic echocardiogram

Indications and current treatment

A pulmonary embolism (PE) is when a pulmonary artery is obstructed, usually by an embolus (blood clot) that travels to the lungs from deep veins in the leg or pelvis. PE often causes shortness of breath, chest pain and cough. The symptoms and severity vary from no symptoms to cardiovascular collapse and death. A high-risk PE (also known as massive PE) is defined by sustained systemic hypotension or shock. An intermediate-risk PE (also known as submassive PE) involves right ventricular dysfunction or myocardial injury without haemodynamic compromise.

The first-line treatment for PE is systemic or oral anticoagulants. For high-risk or intermediate-risk PE with haemodynamic compromise, systemic thrombolysis may be used or, rarely, open surgical embolectomy. Catheter-directed therapies may be used which include catheter-directed thrombolysis (CDT) and percutaneous thrombectomy. Catheter-directed therapies are usually used if someone has high-risk PE and they cannot have surgery, or when systemic thrombolysis is contraindicated or has failed.

What the procedure involves

In this endovascular procedure, a catheter is inserted percutaneously into the peripheral vasculature (usually via a common femoral vein) and advanced through the right side of the heart into the pulmonary arteries under image guidance. This procedure is usually done by interventional radiologists and interventional cardiologists. It is usually done using local anaesthesia with or without sedation.

There are several thrombectomy devices available with some variation in their mechanism of action. The thrombus may be fragmented before removal or not. There are several methods by which the thrombus can be removed: vacuum suction, aspiration with a syringe, mechanical removal with a clot removal device, or a combination of methods. It is a minimally invasive procedure that may be used alone or in combination with other treatment options for PE.

The aim of the procedure is to rapidly remove the obstruction and restore pulmonary circulation, reducing right ventricular strain, while avoiding the bleeding risks associated with thrombolysis.

Outcome measures

The main outcome measures included right ventricular (RV) to left ventricular (LV) diameter ratio, pulmonary artery pressure, modified Miller score, cardiac

index, RV systolic pressure, and CT obstruction index. The measures used are detailed in the following paragraphs.

RV:LV diameter ratio

RV:LV diameter ratio can be measured by CT scan, echocardiography or as a composite measure. A meta-analysis found that, across all CT parameters reviewed as potential predictors of outcome in acute PE, RV:LV diameter ratio had the strongest predictive value for adverse clinical outcomes and mortality (Meinel 2015). It has also been used in multiple studies of various PE treatments as a marker of treatment effectiveness. For comparison, a meta-analysis of CDT reported a mean reduction of RV:LV diameter ratio of 0.34 (Bloomer 2017).

Pulmonary artery pressure

Usually reported as mean pulmonary artery pressure (mPAP), this outcome measure is used by multiple studies of the effectiveness of treatment in acute PE. Echocardiography is generally used to measure systolic pulmonary artery pressure and raised mPAP is a key feature of acute PE. Pre- and post-procedure mPAP is commonly reported, and some studies include later follow-up of this outcome measure.

Modified Miller score

The modified Miller score is a measure of thrombus burden according to CT pulmonary angiogram (CTPA) imaging which is used in acute PE. The extent of thrombus in each part of the pulmonary arteries is scored from 0 (none) to total occlusion (3), out of a maximum of 16. There is also a refined modified Miller score which has a maximum score of 40.

CT obstruction index

The CT obstruction index is another scoring system for thrombus burden on CT imaging (Qanadli 2001). The system assigns a heavier weighting to full vessel

occlusion than to partial occlusion. However, there have been conflicting results on the ability of this scoring system to predict mortality in acute PE (Vedovati 2013).

Cardiac index

The cardiac index is a haemodynamic parameter that is a measure of cardiac function. Specifically, it is a measure of cardiac output that normalises the cardiac output value according to body size. The normal range for this measure is 2.6 to 4.2 litres/min/m^2. The equation for calculating this measure is:

Cardiac index = cardiac output/body surface area = (stroke volume x heart rate)/body surface area

Major adverse event rate

The major adverse event (MAE) rate is a composite measure used in studies to detail the rate of MAE, the components of which vary by study.

Evidence summary

Population and studies description

This interventional procedures overview is based on 2483 patients and 67 'events' from 2 meta-analyses, 3 single-arm trials (1 trial included with its sub-study), 1 safety database review, 2 retrospective comparative studies, 1 prospective non-randomised study, 1 prospective registry, 1 sub-set of the prospective registry and 1 case report. In the Manufacturer and User Facility Device Experience (MAUDE) database, 67 events referred to this procedure. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 12 studies as the key evidence in table 2 and table 3, and lists 33 other relevant studies in table 5.

Of the 12 included studies, all were from the USA, and all reported follow-up outcomes of various durations except the MAUDE database review. Six studies reported 30-day follow-up periods, and 1 reported 45 days follow-up.

All studies reported inclusion criteria, but these varied, as did terminology for the level of risk of PE in participants. Excluding the MAUDE database review which did not specify, 2 studies included patients with high-risk PE, 3 studies referred to intermediate or submassive PEs only and 6 studies included both intermediate and high-risk PEs. Across the 10 studies reporting age of participants, the average age ranged from 55.6 to 73.8 with a slight majority of male patients. Table 2 presents study details.

Figure 1 Flow chart of study selection

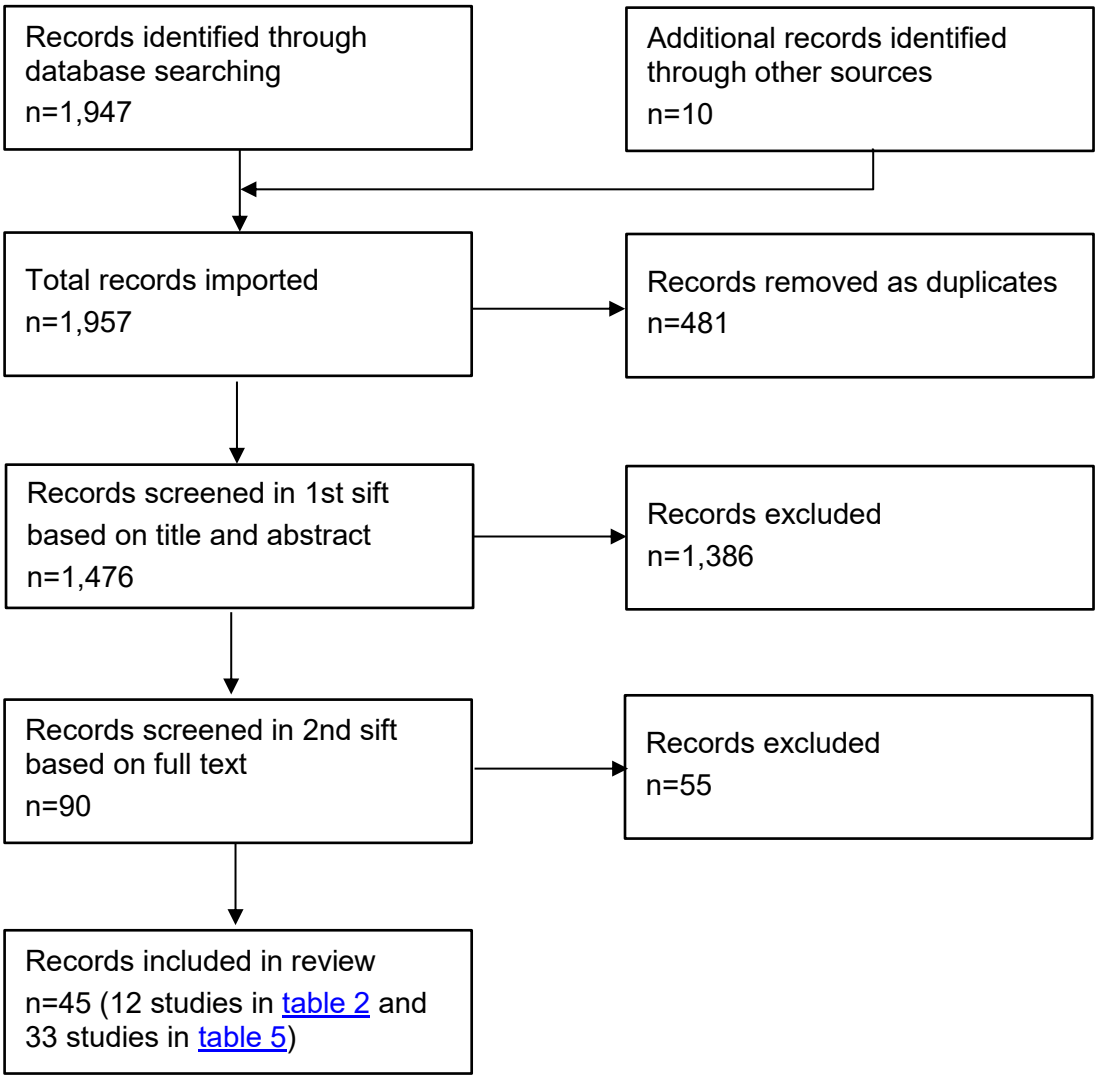

Table 2 Study details

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
1	Toma 2022 USA FLASH registry NCT03761173	N=800 US cohort 2018 to 2021 54% [431/798] were male. 8% (n=63) of patients had high-risk (massive) PE, and 92% (n=734) had intermediate-risk (submassive) PE, with most (83%) being categorised as intermediate-high risk. 32% had thrombolytic contraindications.	Mean 61.2±14.6 years	Prospective multicentre prospective registry in real-world population (single-arm, at 50 US sites)	Patients ≥18 years old with acute intermediate or high-risk PE (per European Society of Cardiology [ESC] guidelines) who underwent mechanical thrombectomy (MT) at the discretion of the treating physician or local PE response team.	FlowTriever System (Inari Medical) – percutaneous MT 86% had local anaesthesia with sedation. Access site: femoral vein.	48 hours, 30 days.
2	Chandra M 2022 USA	14 case series (516 patients with pulmonary embolism) 4 prospective case series and 10 retrospective case series were included.	Mean 58.4 years (299 men and 217 women)	Systematic review and meta-analysis Databases searched include PubMed, EMBASE, Web of	Studies reporting more than 5 patients, involving mechanical aspiration thrombectomy, and reported clinical outcomes and pulmonary artery pressures. Studies were excluded if they failed to separate thrombectomy data from catheter-	Mechanical aspiration thrombectomy for PE Inari FlowTriever device – 6 studies, Aspiration system – 5	Varied across studies.

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
		3 studies had only high-risk PE, 2 studies had only intermediate-risk PE, and 9 studies had a combination of both high-risk and intermediate-risk PE patients.		Science until April, 2021.	directed thrombolysis data.	studies, Rotarex or Aspirex suction thrombectomy system – 3 studies. 4 studies used concomitant intraprocedural thrombolysis in some patients.	
3	Milioglou I 2023	17 prospective studies (n=455 patients with acute PE, intermediate-to high risk in 13 studies and intermediate risk in 4 studies).	Mean 58.6 years 50.4% female.	Systematic review and meta-analysis Databases searched MEDLINE, Cochrane, Scopus and the Web of Science from inception to March 2022.	Included RCTs, non-randomised studies on percutaneous thrombectomy, patients with acute PE, intermediate- and high-risk PE with contraindications to thrombolysis; excluded patients who received systematic or local thrombolysis, case reports and other studies.	Percutaneous thrombectomy (including rheolytic, mechanical aspiration, and large-bore suction thrombectomy) in patients with contraindications to systemic and local thrombolysis.	Varied across studies.

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
4	Sista A 2021 USA	N=119 (66:53)	Mean 59.8 years	Prospective, single-arm, multicentre investigational device exemption trial	Submassive PE 1. Clinical signs and symptoms consistent with acute PE with duration of 14 days or less. Evidence of PE must be from CTPA 2. Systolic BP ≥90 mmHg with evidence of dilated RV with an RV:LV diameter ratio >0.9 3. 18 years of age or older	Penumbra Indigo aspiration system- suction embolectomy device	Intraprocedural, at 48 hours, at discharge, and at 30 days
5	Tu T 2019 USA FLARE study	N=104 (56:48)	Mean 55.6 years	Prospective single-arm multicentre investigational device exemption trial	Intermediate-risk patients. Ages 18 to 75, PE symptoms ≤14 days, symptomatic, CT-documented proximal PE, haemodynamically stable (no vasopressor requirement, heart rate <130, systolic blood pressure ≥90 mmHg at baseline assessment)	FlowTriever System (Inari Medical)- percutaneous MT	48 hours and 30 days

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
					and RV:LV diameter ratios ≥0.9 (on basis of CT). Acute intermediate-risk PE.		
6	Buckley J 2022 USA	N=58: MT N=28 (46% female) Routine care (RC) N=30 (67% female)	MT 68.8±14.3 years RC 73.8±12.7 years	Retrospective single-centre comparative study	Pulmonary Embolism Severity Index (PESI) score of 4 or 5 and ESC classification of intermediate-high or high risk; acute, central PE (defined as thrombus in pulmonary trunk, left/right main pulmonary artery, truncus anterior, or interlobar pulmonary artery); RV:LV diameter ratio >1; and treated as inpatients. Technical success (delivery of device to the pulmonary arteries with extraction of clot) for the MT group. 80% of RC group treated with anticoagulation alone, 13% with systemic thrombolysis and 7% with anticoagulation and CDT.	FlowTriever System (Inari Medical)-percutaneous MT	30 days

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
7	Inci EK 2023 USA	N=458 patients with acute PE (266:192)	MT 59 years CDT 56 years	Retrospective multicentre cohort study	18 years of age, with acute PE (intermediate or high-risk) that was clinically assessed, treated with either MT or CDT between February 2014 and 2021.	MT with the FlowTriever Retrieval/Aspiration System (Inari Medical), n=192 or CDT (n=266)	30 days
8	Jaber W 2020 USA (sub-study of Tu 2019)	N=76 (44:32)	Median 56 years	Multicentre single arm prospective trial: sub-study	Acute intermediate-risk PE. Emergency department (ED) patients with acute PE (that is diagnosed with PE in ED) and RV:LV diameter ratio ≥0.9 enrolled in the FLARE study (Inclusion criteria for this study seen listed in Tu, 2019).	FlowTriever System (Inari Medical)- percutaneous MT	48 hours, 30 days
9	Sedhom R 2021 USA	N=67 events (over 20 months)	Not documented	Manufacturer and User Facility Device Experience (MAUDE) FDA database review (real world data)	Reports related to the use of the device in the pulmonary vasculature. MAUDE database reporting is either mandatory (for manufacturers and device user facilities) or voluntary (for healthcare professionals, patients, and consumers)	Penumbra Indigo aspiration system- suction embolectomy device	No follow-up

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
10	Silver M, 2023 US NCT04795167	n=115 54:61	PT: 64.8 years Context arm: 61.6 years	Prospective multicentre non-randomised comparative study (FLAME study) March 2021 to November 2022	High-risk PE Systolic blood pressure less than 90 mmHg or systolic blood pressure decrease of 40 mmHg or more for longer than 15 minutes, need for vasopressor support, or resuscitation after cardiac arrest with less than 30 minutes of CPR and Glasgow Coma scale 8 or below.	• MT (FlowTriever, Inari Medical, US); n=53 • Context arm (other non-FlowTriever therapies; mostly systemic thrombolysis or anticoagulation alone); n=61 Prior therapy (Low or intermediate-risk PE progressed to high-risk after therapy); n=1	45 days
11	Horowitz J, 2023 US	n=63 29:34	59.4	Subset of prospective multicentre registry (FLASH NCT03761173)	High-risk PE Age 18 or over, cardiac arrest with CPR, obstructive shock with systolic blood pressure less than 90 mmHg or vasopressors needed to	MT with the FlowTriever system (Inari Medical) Most procedures	30 days

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow-up
					achieve a systolic blood pressure 90 mmHg or above and evidence of end-organ hypoperfusion, or persistent hypotension with systolic blood pressure less than 90 mmHg or 40 mmHg drop lasting longer than 15 minutes not caused by new-onset arrhythmia, hypovolemia or sepsis. Patients with life expectancy less than 30 days or inability to have anticoagulation were excluded.	were done using local anaesthesia, with or without sedation. The most common access site (98%) was a femoral or common femoral vein. 3 patients had adjuvant CDT.	
12	Taveer Ud Din M 2022 USA	N=1 woman with intermediate- to high-risk PE.	45 years	Case report	extensive PE involving all lobes of both lungs, including saddle embolus with right heart strain.	Percutaneous pulmonary MT using the FlowTriever Retrieval/Aspiration System	Post procedure

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Toma C 2022	**Secondary endpoints: intra-procedural changes in haemodynamics, cardiac function, dyspnoea, thrombectomy time and blood loss.** **Thrombectomy time** median 43 minutes (range 29 to 63 minutes). **Estimated blood loss** 225 ml (range 95 to 400 ml) **Hospital stay after thrombectomy** Mean 3 days; no post procedural hospital stay in 63% patients. **Haemodynamic assessments** **mPAP:** decreased from baseline 32.6 to 24.9 mmHg post procedure; statistically significant reduction of 7.6 mmHg (-23%, p<0.001). **Cardiac index:** there was a statistically significant change in the low baseline cardiac index group (<2.0 litres/min/m^2) from 1.64 to 1.93 litres/min/m^2 (p<0.0001). **Heart rate:** decreased from baseline 101.5 to 89.5 beats per minute (bpm) post procedure, statistically significantly reduction by 12 bpm (p<0.0001).	**Primary endpoint**: **Major adverse event rate (MAE) – composite of MAE within 48 hours of the index procedure consisting of device-related death, major bleeding, and device- or procedure-related adverse events: 1.8% (14/788)** Device-related death: n=0 Major bleeding: 1.4% (11/788) All-cause mortality at 48 hours: 0.3% (2/794) both unrelated to device;1 died of cardiopulmonary arrest and 1 as a result of new PE **Intraprocedural device- or procedure-related major adverse events: 0.4% (3/788;** 1 from cardiac injury due to ECMO and 1 from hypotension, 1 cardiac injury involving the tricuspid valve) No access-site complications. No intraprocedural deaths. Vascular injuries none Cardiac injuries 0.1% (1/788) Clinical deteriorations 0.3% (2/788) Serious adverse event 4.3% (34/791, none related to the device).

First author, date	Efficacy outcomes	Safety outcomes
	Mean RV:LV diameter ratio: statistically significantly decreased from 1.23±0.36 at baseline to 0.98±0.31 post procedure (p<0.0001). **RV systolic pressure:** statistically significantly decreased from baseline 48.9 to 38.8 mmHg post procedure (-13.4 mmHg, mean change [-22.9%]; p<0.0001). **RV function from baseline to 48 hours** RV function improved significantly from baseline to 48 hours, with the proportion of patients with severe dysfunction decreasing from 29% to 5%, and the proportion with no or mild dysfunction increasing from 34% to 75% (p<0.0001). **Dyspnoea** (self-reported using the modified Medical Research Council [mMRC] dyspnoea scale from 0 (breathless only on strenuous exercise) to 4 (too breathless to leave house, or breathless when dressing/undressing): dyspnoea significantly improved after thrombectomy, mMRC score improved from 2.7 at baseline to 1.1 at 48 hours (-1.7 point mean change [-61.2%]; p<0.0001). The proportion of patients with severe dyspnoea (mMRC score 3 or 4) decreased from 67% at baseline to 16% at 48 hours (p<0.0001). Supplemental oxygen use at 48 hours improved for 88% of patients, and the proportion of patients on room air increased significantly from 11% at baseline to 71% at 48 hours (p<0.0001).	**Secondary endpoints: individual components of the MAE composite, major access-site complications requiring open surgical repair, endovascular intervention, or blood transfusion, and device-related SAEs:** All-cause mortality was 0.8% (6/734) at 30 days (no device related death, all 4 were due to pre-existing conditions). 30-day all-cause readmission rate was 6.2% (46/734) (1.4% related to PE treatment and 4.8% unrelated).

First author, date	Efficacy outcomes	Safety outcomes
Chandra M 2022	**Technical success** (defined as successful delivery to the pulmonary artery, operation of the device, and removal of the device without complication) 97.1% (510/516), [95% CI: 94.8%, 98.4%], p=0.91, I2=0%. Subgroup and meta-regression analysis showed that none of the variables were associated with technical success. **Clinical success** (defined as stabilisation of haemodynamic parameters and survival to hospital discharge) 90.8% (483/516), [95% CI: 85.5%, 94.3%]; p=0.04, I2=44%.. Subgroup and meta-regression analysis showed that none of the variables were associated with clinical success. **Mean PAP** (13 studies, n=397) Mean pre-PAP changed from 35.1±7.7 to a mean post-PAP 25.7±7.5. **RV:LV diameter ratio** (5 studies, n=293) A mean pre-RV:LV diameter ratio of 1.44 improved to a post-RV:LV diameter ratio of 1.04. **Miller indices** (7 studies, n=228) The Miller index improved from 20.6±3.2 to 14.1±3.4 following intervention.	**Random effects meta-analysis** **In hospital mortality** (n=14 studies) 3.6% (22/516), [95% CI: 0.7%, 7.9%], (p <0.01, I2=65%). Subgroup and meta-regression analysis showed that the percentage of patients with high-risk PE within a study was associated with higher in-hospital mortality (p=0.0032). Studies with only high-risk PE had an estimate mortality of 8.7% [95% CI: 3.2%, 16.1%] (n=3 studies, 84 patients) compared to 0.1% [0%, 1.4%] (n=2 studies, 223 patients) in studies with only intermediate-risk PE (p=0.0005). The type of device used (p=0.20), use of intraprocedural thrombolysis (p=0.08), and mean age of patients in the study (p=0.1040) were not associated with in-hospital mortality. **Major bleeding** 0.5% (10/516), [95% CI: 0.0%, 1.8%], (p=0.577, I2=0%) Subgroup and meta-regression analysis showed that none of the variables were associated with major bleeding. **Major bleeding events (n=10)** 3 access site haematomas requiring intervention 1 retroperitoneal/rectus sheath haematomas 3 intracranial haemorrhage 2 episodes of severe haemoptysis

First author, date	Efficacy outcomes	Safety outcomes
	Days to discharge (7 studies, n=232) The median (IQR) days to discharge was 6 days (5.4 to 10.3) among these patients.	1 pulmonary bleed requiring lobectomy. **Major non-bleeding complications: n=4** 2 cerebral ischemic infarct 1 sustained ventricular tachycardia 1 ventricular fibrillation requiring emergency coronary angioplasty and stenting. **Overall major complication 2.7% (14/516).**
Milioglou I 2023	**Haemodynamic changes** **Mean PAP** Pooled analysis of 9 studies (n=213) showed that mean PAP decreased by 10.3 mmHg (95% CI 3.1 to 17.5, I2=96%, p<0.01). **Systolic PAP** Pooled analysis of 10 studies (n=121) showed that systolic PAP decreased by 15.4 mmHg (95% CI 7 to 23.7, I2=78%, p<0.01) after PT. This was not associated with in-hospital mortality (p=0.7). **Radiographic changes** **RV:LV diameter ratio** Pooled analysis of 6 studies (n=299) showed that RV:LV diameter ratio reduced by 0.42 (95% CI 0.38 to 46, I2=90%, p=0.47). **Miller Index** Pooled analysis of 10 studies (n=217) showed that Miller index reduced by 7.8 (95% CI 5.2 to 10.5, I2=0%, p=0.47).	**In-hospital mortality** Pooled analysis of 17 studies (n=455) showed that incidence of in hospital mortality was 4% (18/455), (95% CI 3 to 6, p=0.26, I2=17%). **30-day mortality** Pooled analysis of 14 studies (n=328) showed that incidence of 30-day hospital mortality was 5% (18/328), (95% CI 3 to 9, p=0.08, I2=37%). Subgroup analyses performed for studies including only intermediate-high-risk and high-risk patients, showed increased in-hospital mortality at 7% (95% CI 2 to 20) and 30-day mortality at 7% (95% CI 2 to 21). **Major bleeding** Pooled analysis of 17 studies (n=455) showed major bleeding at 3% (18/455), (95% CI 1 to 8, I2=2%, p=0.43). Meta-regression showed no

First author, date	Efficacy outcomes	Safety outcomes
	Heart rate Pooled analysis of 7 studies (n=221) showed a mean heart rate reduction of 20 bpm (95% CI 8.8 to 31.5, I2=95%, p<0.01) after PT. **O_2 saturation on pulse oximetry** Pooled analysis of 8 studies (n=234) showed O_2 saturation on pulse oximetry increased by 9.2% (95% CI 3.7 to 14.6%, I2=98%, p<0.01) after PT. **Systolic blood pressure** Pooled analysis of 5 studies (n=199) showed that systolic blood pressure increased by 15.7 mmHg (95% CI 3.4 to 28 mmHg, I2=94%, p<0.01) after PT. **Average procedure time** was 67 minutes (95% CI 42 to 92) **Average length of stay** was 7.3 days (95% CI 5.5 to 8.8).	association between catheter size and major bleeding (R −0.03, p=0.59).
Sista A 2021	**Primary endpoint: change in RV:LV diameter ratio from baseline to 48 h post-procedure (computed tomography angiography)** Mean RV:LV diameter ratio reduction 0.43 (95% CI 0.38 to 0.47; p<0.0001), representing 27.3% reduction (95% CI 24.83 to 29.67%). **Secondary endpoints:** Intraprocedural thrombolytics used in 2 patients (1.7%)	**Primary endpoint: composite of 48-hour MAEs: device-related death, major bleeding, and device-related serious adverse events (clinical deterioration, pulmonary vascular, or cardiac injury)** 2 (1.7%, 95% CI 0.0 to 4.0) patients experienced 3 MAEs: 1 patient experienced haemoptysis and access-site bleed, post-procedure death (ventricular tachycardia likely related to RV ischaemia from RV overload and haemorrhage). 1 patient experienced access-site bleeding only.

First author, date	Efficacy outcomes	Safety outcomes
	73 required ICU stay (61%) and median stay was 1.0 day mPAP reduction post-aspiration: 4.3 mmHg (95% CI: 2.6 to 5.9 mm Hg; 7.9% reduction; p<0.0001) mPAP reduction post-procedure: 4.7 mmHg (95% CI: 3.0 to 6.4 mmHg; 8.7% reduction; p<0.0001) Mean reduction in CT obstruction index from pre-procedure to 48-hour follow-up was 11.3% (p<0.0001).	**Primary endpoint:** Device-related SAEs within 48 hours = 0.8% (95% CI 0.0 to 2.5), a composite of: device-related clinical deterioration within 48 hours 0.8% (1/119), device-related pulmonary vascular injury within 48 hours 0.8% (1/119), device-related cardiac injury within 48 hours 0%. **Secondary safety endpoints:** **At 48 hours rates of:** cardiac injury 0%, pulmonary vascular injury 1.7%, clinical deterioration 0.8%, major bleeding 1.7%, and device-related death 0.8%. **At 30 days rates of:** Any cause-mortality 2.5% (95% CI 0.0 to 5.3), device-related SAEs 1.7%, symptomatic recurrence of PE 0%. 73.1% of patients had an estimated overall blood loss <400ml, 26.9% had >400ml but none required transfusion. 3 (2.5%) patients required transfusion related to the procedure
Tu A 2019	**Primary effectiveness endpoint: change in RV:LV diameter ratio from baseline to 48 hours** (±8 hours or discharge):	**Primary safety endpoint: composite MAE rate (any of following within 48 hours: device-related death, major bleeding,**

First author, date	Efficacy outcomes	Safety outcomes
	RV:LV diameter ratio 1.56 at baseline, 1.15 at 48 hours, average reduction of 0.38 (p<0.0001) that is 25.1%. **Mean pulmonary artery pressure (mPAP):** 29.8 mmHg pre-procedure vs 27.8 post-procedure (p=0.001). Effect driven by patients with pulmonary hypertension on presentation (n=70): 3.2 mmHg reduction (p<0.0001). **Refined modified Miller score (thrombus burden):** Pre-procedural score 20.8±2.4 vs 18.9±2.9 at post-procedure; p<0.001. **Length of ICU stay** 1.5±2.1 days Forty-three patients (41.3%) did not require any ICU stay. **Length of hospital stay** 4.1±3.5 days	**treatment-related clinical deterioration, treatment-related pulmonary vascular injury, and treatment-related cardiac injury):** Composite MAE rate within 48 hours 3.8% (n=4 patients experiencing 6 MAEs): • Clinical deterioration n=4 • Major bleeding event n=1 • Pulmonary vascular injury n=1 Major bleeding rate 0.9%. **Secondary safety endpoint: All primary safety events as well as mortality, device-related SAEs and symptomatic recurrence of embolism within 30 days:** An additional 10 patients experienced SAEs within 30 days. Total = 14 patients experienced 26 SAEs within 30 days, 5 experienced multiple SAEs. 1 death at 23 days (respiratory failure from undiagnosed cancer).
Buckley J 2022	**Secondary endpoints: ICU length of stay, total hospital length of stay:** Average ICU length of stay statistically significantly lower for mechanical thrombectomy (MT) group vs routine care (RC) (2.1 ±1.2 vs 6.1±8.6 days, p<0.05).	**Primary endpoint: in-hospital mortality:** In-hospital mortality was statistically significantly lower for MT group vs RC (3.6% vs 23.3%, p<0.05). **Secondary endpoints: 30-day readmission rate:**

First author, date	Efficacy outcomes	Safety outcomes
	No statistically significant difference in total hospital length of stay (7.7±6.9 days in MT, 6.8±6.9 in RC).	No statistically significant difference (11% in MT, 13% in RC, p>0.05). RC group: 3 self-limited bleeding complications not requiring transfusion (10%) and 1 case of haemodynamically significant bleeding requiring transfusion and endoscopy (3.3%). MT group: 3 procedure-related complications (10.7%; 1 self-limited haemoptysis, 2 post-procedure transfusions due to aspiration-related blood loss).
Inci EK 2023	**Need for ICU stay** MT 69% versus CDT 100% (p<0.0001) **ICU length of stay (days)** MT 2.8±0.3 versus CDT 3.8±0.2 (p=0.009) **Mean PAP** **Baseline** MT 33±0.7 versus CDT 35±0.6, p=0.008 **Post-procedure** MT 26±0.7 versus CDT 28±0.8, p=0.2	**primary outcome: composite of in-hospital death, significant bleed, vascular complication, access site complications and need for mechanical support** (combined adverse events) MT 11% versus CDT 12% (p=0.5) **In-hospital mortality** MT 0.8% versus CDT 2.1% (p=0.4) **Vascular complication** MT 1.0% versus CDT 1.5% (p=0.6) **Access site complication** MT 3.6% versus CDT 5.3% (p=0.4) **Significant bleeding** MT 4.7% versus CDT 4.2% (p=0.8) **Intracranial bleeding** MT 0 versus CDT 1.1% (p=0.1) **Need for mechanical support**

First author, date	Efficacy outcomes	Safety outcomes
		MT 2.1% versus CDT 2.2% (p=0.9)
Jaber W 2020	**Primary endpoint: change in the RV:LV diameter ratio from baseline to 48 hours post-procedure** Reduction in median RV:LV diameter ratio of 0.37 from 1.50 pre-procedure (range 0.88 to 2.52) to 1.13 post-procedure (range, 0.66 to 1.81), (p<0.001). **Secondary endpoints:** **Change in RV:LV diameter ratio of patients with non-elevated cardiac troponin and zero simplified PE Severity Index (sPESI) score, for example normal cTn-sPESI: intermediate-low risk (n=17, 22.4%)** Reduction in mean RV:LV diameter ratio of 0.27 (p<0.001) **ICU stay:** 53% admitted to ICU post-procedure, median length of stay 1 day (range 0 to 11 days). **Heart rate:** median 91 bpm (55 to 123) to 89 (62 to 118) at 48 hours. **Median PAP:** 30 mmHg (range, 7 to 57 mmHg) at presentation and 27 mmHg (range, 9 to 50 mmHg) after the procedure (p=0.533, NS). In 52 patients with elevated PAP (68.4%): statistically significant reduction in median PAP (34 to 31 mmHg, p=0.003).	**Primary endpoint: composite MAEs including major bleeding, device-related death or clinical deterioration, and vascular or cardiac injury within 48 hours.** 3 MAEs (4%): 2 periprocedural respiratory deterioration requiring intubation, 1 major bleeding (leading to lobectomy), 1 patient experienced pulmonary vascular injury. All adjudicated as procedure-related rather than device-related. **Secondary endpoints:** **All-cause mortality** 100% survival to 30 days **Symptomatic recurrence PE within 30 days** None

First author, date	Efficacy outcomes	Safety outcomes
Sedhom R 2021	**None reported**	**Primary outcome: mechanisms of failure of Penumbra Indigo aspiration system** Most common failure mode: Lightning Unit malfunction (35.8%, n=24) (tubing with dual pressure sensors with a built-in microprocessor for real-time blood flow monitoring). Rotating haemostasis valve malfunction (31.3%, n=21) Resistance during use (15%, n=10) Aspiration failure (11.9%, n=8) Engine malfunction (9%, n=6) Catheter clogging with thrombi (7.5%, n=5) Catheter kinking (6%, n=4) Engine canister malfunction (4.5%, n=3) Catheter broken (4.5%, n=3). **Secondary outcome: clinical consequences of device failure** Death (4.5%, n=3); 2 from fatal pulmonary vessel perforation (3%) and 1 from fatal right-sided heart failure (1.5%). Pericardial effusion (1.5%, n=1) Procedure aborted (6%, n=4) No need for ECMO, no haemoptysis, no intracranial bleeding and no blood transfusions.
Silver, 2023	Median length of hospital stay after treatment (nights)	**Primary endpoint (in-hospital composite of all-cause mortality, bailout to an alternate**

First author, date	Efficacy outcomes	Safety outcomes
	• PT=7.0 (IQR 3.0 to 12.5; 95% CI 7.5 to 14.3), n=52 • Context arm=8.0 (IQR 6.0 to 15.0; 95% CI 9.0 to 14.2), n=43 Median length of ICU stay after treatment (nights) • PT=2.0 (IQR 1.0 to 4.0; 95% CI 2.9 to 8.1), n=52 • Context arm=3.0 (IQR 1.0 to 7.0; 95% CI 3.4 to 7.2), n=43	**thrombus removal strategy, clinical deterioration, and major bleeding)** • PT=17.0% (9/53; 95% CI 8.1 to 29.8) • Context arm=63.9% (39/61; 95% CI 50.6 to 75.8), p=0.0169 In-hospital mortality • PT=1.9% (1/53; 95% CI 0 to 10.1) • Context arm=29.5% (18/61; 95% CI 18.5 to 42.6) Clinical deterioration • PT=15.1% (8/53; 95% CI 6.7 to 27.6) • Context arm=21.3% (13/61; 95% CI 11.9 to 33.7) Major bleeding • PT=11.3% (6/53; 95% CI 4.3 to 23.0) • Context arm=24.6% (15/61; 14.5 to 37.5) There were 2 intracranial haemorrhage major bleeding events in the context arm, both in patients who had systemic thrombolysis. **Serious adverse events related to the device or therapy** • PT=18.9% (10/53)

First author, date	Efficacy outcomes	Safety outcomes
		• Context arm=37.7% (23/61) **Device-related complications** • PT=22.6% (12/53; 95% CI 12.3 to 36.2), most commonly haemoglobin decrease or anaemia • Context arm=16.4% (10/61; 95% CI 8.2 to 28.1).
Horowitz, 2023	Median length of hospital stay after procedure=4.0 nights (IQR 2 to 7). Median length of ICU stay after procedure=1.0 nights (IQR 0 to 2). 25 (42.4%) patients had no overnight ICU stay. Immediately after thrombectomy, mean mPAP decreased from 31.5 to 24.3 mmHg (mean change -7.2, n=60), p<0.0001. Mean sPAP decreased from 50.7 to 38.3 mmHg (mean change -12.3, n=61), p<0.0001. Mean right atrial pressure decreased from 12.8 to 10.6 mmHg (mean change -2.3, n=48), p<0.0001. Systolic blood pressure increased from 116.8 to 121.3 mmHg (mean change 4.5, n=60), p=0.1302.	No patients met the primary endpoint (composite of major adverse events within 48 hours of thrombectomy, consisting of device-related mortality, major bleeding, and intraprocedural device or procedure-related adverse events) Mortality at 48 hours=0% (0/63) Mortality at 30 days=0% (0/61) Serious adverse events at 48 hours=6.3% (4/63), none were adjudicated to be device-related; there were 2 subsequent PEs, 1 pelvic retroperitoneal haematoma and 1 right groin haematoma.

First author, date	Efficacy outcomes	Safety outcomes
	Heart rate decreased from 98.4 to 93.5 beats per minute (mean change -4.8, n=61), p=0.0091. Among the 42.9% of patients with depressed baseline cardiac index <2 L/min/m2, CI increased from 1.54±0.21 to 1.91±0.56 L/min/m2 (mean change, 0.41 L/min/m2 [26.5%], p<0.0001). RV/LV ratio decreasing from 1.5±0.7 at baseline (n=43) to 1.1±0.4 at 48 hours (n=22; p <0.0001) and 0.9 at 30 days (n=24; p<0.0001).	
Taveer Ud Din M 2022	Mean PAP decreased from 42 mmHg to 19 mmHg and patient admitted to ICU.	**Cardiac tamponade** The device caused micro-perforation of the right ventricle resulting in tamponade and required pericardiocentesis of pericardial effusion after the procedure. Post procedure TTE showed resolution of the pericardial effusion. After 8 hours, patient experienced cardiac arrest and TTE showed pericardial effusion, right ventricle collapse and haemorrhagic shock. The patient was extubated after haemodynamic stabilisation.

Procedure technique

Of the 12 studies, all detailed the devices used and 5 detailed the procedure technique. Eight studies used the Inari FlowTriever device for MT (Tu 2019, Toma 2022, Buckley 2022, Jaber 2020, Inci 2023, Silver 2023, Horowitz 2023 and Taveer 2022). Two studies used the Penumbra Indigo aspiration system for aspiration thrombectomy (Sedhom 2021, Sista 2021). Studies included in the systematic reviews and meta-analyses used various devices (Inari FlowTriever device, Penumbra device, Apsirex device, Rotarex device, Angiojet device, Amplatz device).

Aspiration thrombectomy involves the aspiration of thrombus through an aspiration catheter. MT involves mechanical engagement of the thrombus and removal. Rheolytic thrombectomy includes the use of high-pressure jets of saline to disperse the thrombus followed by aspiration. The jets can consist of saline, but local thrombolytic agents can also be used. There are multiple different devices with other mechanisms associated with this procedure, some of which are no longer in use.

Efficacy

RV:LV diameter ratio

This outcome was reported in 7 studies. Four studies found a statistically significant reduction in mean RV:LV diameter ratio from baseline to follow-up. With the FlowTriever, Tu (2019) found a mean reduction of 0.38 ($p<0.0001$) at 48 hours and Toma (2022) found that mean RV: LV diameter ratio statistically significantly reduced from 1.23 at baseline to 0.98 post procedure ($p<0.0001$). In the Jaber (2020) sub-study of the FLARE population, reduction was 0.37 at 48 hours ($p<0.001$). Jaber (2020) also reported the change in RV:LV diameter ratio for the intermediate-low risk sub-group of the study (n=17) and found a smaller but still statistically significant reduction of 0.27 ($p<0.001$). Sista (2021) reported a reduction of 0.43 ($p<0.0001$) at 48 hours with the Indigo system. A

meta-analysis of 14 studies reported that in 5 studies (n=293), the mean pre-RV:LV diameter ratio of 1.44 improved to a post-RV:LV diameter ratio of 1.04 (Chandra 2022). In a meta-analysis of 17 studies, pooled analysis of 6 studies (n=299) showed that RV:LV diameter ratio reduced by 0.42 (95% CI 0.38 to 46, I2=90%, p=0.47; Milioglou 2023). A sub-study of the US FLASH registry (Horowitz 2023) with 63 high-risk PE patients treated with MT reported that the RV/LV ratio decreased from 1.5 at baseline (n=43) to 1.1 at 48 hours (n=22; p<0.0001) and 0.9 at 30 days (n=24; p<0.0001).

Pulmonary artery pressure

This outcome was reported in 8 studies. Tu (2019) reported a statistically significant reduction in mPAP (29.8 to 27.8 mmHg), p=0.001. The effect was driven by patients with raised mPAP on presentation in which subgroup there was a 3.2 mmHg reduction (p<0.0001). Toma (2022) reported a statistically significant reduction of 7.6 mmHg (p<0.001) post procedure. In the Jaber (2020) sub-study, the median PAP demonstrated a statistically non-significant reduction of 3 mmHg (from 30 to 27 mmHg, p=0.533), although in the 52 patients with elevated PAP on presentation, there was a statistically significant reduction of 3 mmHg (34 to 31 mmHg, p=0.003). Sista (2021) reported a reduction in mPAP of 4.3 mmHg post-aspiration (p<0.0001) and of 4.7 mmHg post-procedure (p<0.0001), both statistically significant. The meta-analysis of 14 studies reported that in 13 studies (n=397) the mean pre-PAP changed from 35.1±7.7 mmHg to a mean post-PAP 25.7±7.5 mmHg (Chandra 2022). In the meta-analysis of 17 studies, pooled analysis of 9 studies (n=213) showed that mean PAP decreased by 10.3 mmHg (95% CI 3.1 to 17.5, I2=96%, p<0.01). Pooled analysis of 10 studies (n=121) showed that systolic PAP decreased by 15.4 mmHg (95% CI 7 to 23.7, I2=78%, p<0.01) after PT. This was not associated with in-hospital mortality (p=0.7; Milioglou 2023). The sub-study of the US FLASH registry (Horowitz 2023) with 63 high-risk PE patients treated with MT reported that immediately after thrombectomy, mean PAP decreased from 31.5 to 24.3 mmHg

(mean change, -7.2 mmHg; n=60, p<0.0001). Mean systolic PAP decreased from 50.7 to 38.3 mmHg (mean change -12.3, n=61, p<0.0001). A retrospective cohort study (Inci 2023) of patients undergoing MT or CDT for acute PE reported a decrease in mean PAP from baseline in both the groups. However, there was no difference in mean PAP between the 2 groups after the procedure (MT 26±0.7 versus CDT 28±0.8, p=0.2).

Length of stay

This outcome was reported in 10 studies. Tu (2019) reported an average length of ICU stay of 1.5±2.1 days, and hospital stay of 4.1±3.5 days. Toma (2022) reported a mean length of hospital stay of 3 days post-procedure and in the Jaber 2020 sub-study, a median length of ICU stay of 1 day was reported. In Sista (2021), 61% required ICU care and the median stay was 1.0 day. A study on patients with high-risk PE (Horowitz 2023) reported that after MT, the median length of hospital stay was 4.0 nights (IQR 2 to 7) and median length of ICU stay was 1.0 night (IQR 0 to 2). 42% (n=25) patients had no overnight ICU stay.

Buckley (2022) reported an average length of ICU stay of 2.1±1.2 days which is statistically significantly lower than the ICU length of stay for the routine care group (vs 6.1±8.6 days, p<0.05). There was, however, no statistically significant difference in hospital stay between the 2 groups, with the MT group staying in hospital on average 7.7±6.9 days overall. These hospital length of stay figures are higher than reported by the other studies. A retrospective cohort study (Inci 2023) of 458 patients reported that there was a statistically significant difference between the groups in the need for ICU stay (MT 69% versus CDT 100%, p<0.0001) and length of ICU stay (MT 2.8±0.3 versus CDT 3.8±0.2 days, p=0.009). Another non-randomised study (Silver 2023) of 115 patients with high-risk PE reported that the median length of hospital stay after treatment was 7 days (IQR 3.0 to 12.5; 95% CI 7.5 to 14.3) in the thrombectomy group and 8 days (IQR 6.0 to 15.0; 95% CI 9.0 to 14.2) in the systemic thrombolysis and anti-coagulation alone group.

The meta-analysis of 14 studies reported that in 7 studies (n=232), the median days to discharge was 6 days (range 5.4 to 10.3 days) among these patients (Chandra 2022). In the meta-analysis of 17 studies, average length of stay was 7.3 days (95% CI 5.5 to 8.8; Milioglou 2023).

Modified Miller score

This outcome was reported in 3 studies. Tu (2019) use the refined modified Miller score and reported a pre-procedural score of 20.8±2.4 versus a post-procedural score of 18.9±2.9, representing an average reduction of 1.9 ($p<0.001$). The meta-analysis of 14 studies reported that in 7 studies (n=228), the Miller index improved from 20.6±3.2 to 14.1±3.4 following intervention (Chandra 2022). In the meta-analysis of 17 studies, pooled analysis of 10 studies (n=217) showed that Miller index reduced by 7.8 (95% CI 5.2 to 10.5, I2=0%, p=0.47; Milioglou 2023).

CT obstruction index

This outcome was reported in 1 study. Sista (2021) reported a mean reduction in CT obstruction index of 11% at 48 hours ($p<0.0001$).

Cardiac index

This outcome was reported in 2 studies. Toma (2022) reported that there was a statistically significant improvement in cardiac index in the subgroup with low baseline cardiac index. The cardiac index increased from 1.64±0.26 to 1.93±0.58 litres/min/m^2 (0.29 litres/min/m^2 mean change [18.9%]; $p<0.0001$). Horowitz (2023) reported that in 43% of patients with baseline cardiac index <2 L/min/m2, cardiac index increased from 1.54 to 1.91 L/min/m2 (mean change, 0.41 L/min/m2, $p<0.0001$).

Technical success (defined as successful delivery to the pulmonary artery, operation of the device, and removal of the device without complication)

A meta-analysis of 14 case series (n=516 patients with high-risk or intermediate-risk pulmonary embolism) treated with mechanical aspiration thrombectomy (MAT) showed a technical success of 97.1% (510/516), 95% CI: 94.8% to 98.4%; p=0.91, I2=0% (Chandra 2022).

Clinical success (defined as stabilisation of hemodynamic parameters and survival to hospital discharge)

A meta-analysis of 14 case series (n=516 patients) showed a clinical success of 90.8% (483/516), 95% CI 85.5% to 94.3%; p=0.04, I2=44% (Chandra 2022).

Safety

Major adverse event rate

Seven studies reported a composite MAE rate as their primary safety endpoint. The composition of this MAE rate varied by study but was similar, usually including major bleeding, device-related death or clinical deterioration and injury to vessels/the heart/the lungs. The composite measure is discussed followed by the individual measures.

Tu (2019) reported a composite MAE rate (device-related death, major bleeding, treatment-related clinical deterioration, treatment-related pulmonary vascular injury, and treatment-related cardiac injury) of 4% (n=4) at 48 hours. Toma (2022) reported an MAE rate (device-related death, major bleeding, and device- or procedure-related adverse events) of 1.8% (14/788) at 48 hours, all major bleeding events but with no device-related injuries, clinical deteriorations or deaths at 48 hours. Jaber (2020), in their sub-study of the FLARE population (Tu 2019), reported an MAE rate (major bleeding, device-related death or clinical deterioration, and vascular or cardiac injury) of 4% (n=3) at 48 hours. Sista (2021) reported an MAE rate (device-related death, major bleeding, and device-related serious adverse events [clinical deterioration, pulmonary vascular, or cardiac injury]) of 3 MAEs in 2 patients (2%) at 48 hours.

A retrospective cohort study (Inci 2023) of 458 patients with acute intermediate- or high-risk PE treated with MT (n=192) or CDT (n=266) reported that the primary composite endpoint (in-hospital death, significant bleed, vascular complication, access site complications, and need for mechanical support) was not statistically significantly different between the 2 groups with MT 11% versus CDT 12% (p=0.5).

A non-randomised study of 115 patients with high-risk PE reported that the primary endpoint (in-hospital composite of all-cause mortality, bailout to an alternate thrombus removal strategy, clinical deterioration, and major bleeding) was reached in 17% (9/53) of patients who had thrombectomy, statistically significantly lower than the prespecified 32% performance goal (p<0.01) and 64% (39/61) in patients who had systemic thrombolysis or anticoagulation alone. Serious adverse events related to the primary treatment occurred in 19% (10/53) of patients in the thrombectomy arm and 38% (23/61) of patients in the systemic thrombolysis or anticoagulation alone arm (Silver 2023).

A sub-study of the US FLASH registry with 63 high-risk PE patients treated with MT reported that no patients met the primary endpoint (composite of major adverse events within 48 hours of thrombectomy, consisting of device-related mortality, major bleeding, and intraprocedural device or procedure-related adverse events) (Horowitz 2023). 6.3% (4/63) of serious adverse events were reported at 48 hours and these included 2 subsequent PEs, 1 pelvic retroperitoneal haematoma and 1 right groin haematoma. None were adjudicated to be device-related.

Major bleeding

Ten studies reported on bleeding-related complications. Tu (2019) reported 1 major bleeding event in 104 patients at 48 hours. Toma (2022) reported a 1.4% major bleeding rate (11/788). Buckley (2022) did not classify bleeding complications by severity but reported 3 procedure-related complications in the

MT group (11%): 1 self-limited haemoptysis and 2 post-procedure transfusions due to aspiration-related blood loss. In the routine care group the rate was similar with 3 self-limited bleeding complications not requiring transfusion (10%) and 1 significant bleed requiring transfusion (3%). Jaber (2020) reported 1 major bleeding event which was procedure-related at 48 hours in a study of 76 patients. Sista (2021) reported 2 instances of major bleeding (2%) and 3 patients requiring transfusion related to the procedure (3%). Sedhom (2021) reported no haemoptysis episodes, no intracranial bleeding and no episodes requiring blood transfusion. The meta-analysis of 14 studies showed major bleeding of 0.5% (10/516), 95% CI 0.0% to 1.8%, p=0.577, I2=0%). Subgroup and meta-regression analysis showed that none of the variables (type of device, mean age of patients, use of thrombolysis) were associated with major bleeding (Chandra 2022). In the meta-analysis of 17 studies, pooled analysis of 17 studies (n=455) showed that the incidence of major bleeding was 3% (18/455), 95% CI 1% to 8%, I2=2%, p=0.43. Meta-regression showed no association between catheter size and major bleeding (R -0.03, p=0.59) (Milioglou 2023).

The retrospective cohort study (Inci 2023) of 458 patients with acute intermediate or high-risk PE treated with MT (n=192) or CDT (n=266) reported no statistically significant difference in significant bleeding (MT 4.7% versus CDT 4.2%, p=0.8) and intracranial bleeding (MT 0 versus 1.1%, p=0.1) between the groups.

The non-randomised study of 115 patients with high-risk PE reported that bleeding occurred in 11% (6/53; 95% CI 4.3 to 23.0) patients in the thrombectomy group and in 25% (15/61; 14.5 to 37.5) patients in the systemic thrombolysis or anticoagulation alone group (Silver 2023).

Clinical deterioration

Five studies specifically reported a clinical deterioration rate. Tu (2019) reported a clinical deterioration rate of 4% (n=4) at 48 hours and the sub-study, Jaber (2020), reported 4% (n=3) at 48 hours. Toma (2022) reported a clinical

deterioration rate of 0.3% (2/788) at 48 hours. Sista (2021) reported 1 episode of clinical deterioration at 48 hours in 119 patients.

The non-randomised study of 115 patients with high-risk PE reported that clinical deterioration occurred in 15% (8/53; 95% CI 6.7 to 27.6) of patients in the thrombectomy group and in 21% (13/61; 95% CI 11.9 to 33.7) of patients in the systemic thrombolysis or anticoagulation alone group (Silver 2023).

Pulmonary vascular injury

Six studies reported on instances of pulmonary vascular injury. Tu (2019) reported 1 pulmonary vascular injury in 104 patients at 48 hours and Jaber (2020) also reported 1 pulmonary vascular injury in their sub-study of 76 patients, which likely represents the same patient. Sedhom (2021) reported 2 pulmonary vessel perforations (3%). Sista (2021) reported 2 instances of pulmonary vascular injury (2%) at 48 hours, 1 of which (1%) was device-related. Toma (2022) reported zero device-related pulmonary vascular injuries.

A retrospective cohort study (Inci 2023) showed no statistically significant difference in vascular complications between the MT and CDT groups (MT 1.0% versus CDT 1.5%, p=0.6).

Cardiac injury

Five studies reported on cardiac injury. Toma (2022) reported 1 cardiac injury at 48 hours follow-up. Tu (2019), Jaber (2020), Sista (2021) and Sedhom (2021) all reported no episodes of cardiac injury.

Mortality

Apart from the case report, all studies reported measures of mortality. Tu (2019) reported 1 death during follow-up (1%) at 23 days post-procedure, attributed to respiratory failure from undiagnosed cancer and so unrelated to the procedure. Toma (2022) reported 0.3% (2/794) deaths at 48 hours and 0.8% (6/734) deaths

at 30 days follow-up, all of which were unrelated to the procedure. Buckley (2022) reported in-hospital mortality of 4% for the MT group, which was statistically significantly lower than the routine care group (23%, p<0.05). Sedhom (2021) reported 3 deaths (5%), 2 from pulmonary vessel perforation (3%) and 1 from right-sided heart failure (2%). Jaber (2020) reported 100% survival at 30 days. Sista (2021) reported 1 post-procedure device-related death (1%) related to haemorrhage and right ventricular overload at 48 hours and a 3% rate of any cause mortality at 30 days (n=3). A retrospective cohort study (Inci 2023) showed no statistically significant difference in in-hospital mortality between the MT and CDT groups (MT 0.8% versus CDT 2.1%, p=0.4).

The meta-analysis of 14 studies (n=556) showed in-hospital mortality of 3.6% (22/516), 95% CI 0.7% to 7.9%, p<0.01, I2=65%. Subgroup and meta-regression analysis showed that the percentage of patients with high-risk PE within a study was associated with higher in-hospital mortality (p=0.0032). Studies with only high-risk PE had an estimate mortality of 8.7% [95% CI 3.2%, 16.1%] (n=3 studies, 84 patients) compared with 0.1% [95% CI 0%, 1.4%] (n=2 studies, 223 patients) in studies with only intermediate-risk PE (p=0.0005). The type of device used (p=0.20), use of intraprocedural thrombolysis (p=0.08), and mean age of patients in the study (p=0.1040) were not associated with in-hospital mortality (Chandra 2022).

In the meta-analysis of 17 studies, pooled analysis of 17 studies (n=455) showed that incidence of in hospital mortality was 4% (18/455), 95% CI 3% to 6%, p=0.26, I2=17%. Pooled analysis of 14 studies (n=328) showed that incidence of 30-day hospital mortality was 5% (18/328), 95% CI 3% to 9%, p=0.08, I2=37%. Subgroup analyses performed for studies including only intermediate-high-risk and high-risk patients showed increased in-hospital mortality at 7% (95% CI 2% to 20%) and 30-day mortality at 7% (95% CI 2% to 21%; Milioglou 2023).

The non-randomised study of 115 patients with high-risk PE reported that in-hospital mortality occurred in 2% (1/53) of patients in the thrombectomy group

and in 30% (18/61) of patients in the systemic thrombolysis or anticoagulation alone group (Silver 2023). A sub-study of the US FLASH registry with 63 high-risk PE patients treated with MT reported no mortality within 48 hours (0/63) and at 30 days (0/61) follow-up (Horowitz 2023).

Access-site complications

Access-site complications may include bleeding, nerve injury and damage to other structures, for example arteries. Sista (2021) reported 2 patients (2%) experiencing access-site bleeding. A retrospective cohort study (Inci 2023) showed no statistically significant difference in access site complications between the MT and CDT groups (MT 3.6% versus CDT 5.3%, p=0.4).

30-day readmission rate

Three studies discussed 30-day readmission rates. Toma (2022) reported a 30-day readmission rate of 6.2% (1.4% was related to PE treatment and 4.5% unrelated). When comparing with other treatments, Buckley (2022) found no statistically significant difference in 30-day readmission rate between the MT group (11%) and the routine care group (13%), (p>0.05). Horowitz (2023) reported 8.5% (5/63) all-cause readmission at 30 days. One (1.7%) readmission was related to the PE treatment, 5 days post procedure for a groin haematoma and discharged the following day.

Device failure

One study, Sedhom 2021, specifically reviewed device failure reports for the Indigo aspiration system used for aspiration thrombectomy. It found that the most common failure mode was a lightning unit malfunction (36%, n=24) followed by rotating haemostasis valve malfunction (31%, n=21), resistance during use (15%, n=10) and aspiration failure (12%, n=8).

Device-related complications

The non-randomised study of 115 patients with high-risk PE reported that device-related complications occurred in 23% (12/53; 95% CI 12.3 to 36.2) of patients in the thrombectomy arm and in 16% (10/61; 95% CI 8.2 to 28.1) of patients in the systemic thrombolysis or anticoagulation alone arm (Silver 2023).

Cardiac tamponade

Cardiac tamponade was reported in a patient with intermediate- to high-risk PE after percutaneous pulmonary MT in a case report (Taveer Ud Din 2022). This was as a result of micro-perforation of the right ventricle. The patient experienced several cardiac arrests from pericardial tamponade and required pericardiocentesis, leading to haemodynamic stabilisation.

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who were nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they have never happened (theoretical).

They listed the following anecdotal or theoretical adverse events not reported in the literature:

- deep vein thrombosis
- infection
- cardiac complications; tamponade, myocardial infarction, valvular dysfunction
- iodine anaphylaxis
- contrast nephropathy
- haemothorax
- puncture site pseudoaneurysm
- stroke (clot transit through patent foramen ovale).

Three professional expert questionnaires were submitted for this procedure. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

The main evidence summary included 12 studies, including 2 systematic reviews and meta-analyses, 5 prospective single-arm studies (3 trials,1 registry and 1 sub-study of the registry), 2 retrospective comparative studies, 1 prospective non-randomised study, 1 database review and 1 case report. All 12 studies were in US populations, the majority of studies included small sample sizes and had 30 days follow-up. The largest study had 800 participants. Variable inclusion criteria were used and many of the studies included intermediate-risk or submassive PEs either solely or in combination with high-risk or massive PEs. Two studies solely included patients with high-risk PE. All of these factors may impact on the outcomes and on the generalisability to the UK population. The FLARE-ED sub-study by Jaber (2020) is less generalisable as it has a smaller sample of patients presenting via the emergency department only. The longest follow-up period was 45 days so there is a lack of data on long-term outcomes in this group. The included studies generally reported fairly consistent outcomes, with statistically significant improvements in markers of right ventricular function and low MAE and mortality rates in the short-term follow-up.

The 2 meta-analyses included prospective or retrospective case series that are prone to bias (because of heterogeneity in data, varied short-term follow-up, and being funded through industry). Two studies contributed most patients in the meta-analysis (Milioglou 2023). There is an overlap of studies between the 2 meta-analyses.

Various techniques and devices are used for MT. The main evidence summary includes 8 studies which use the FlowTriever device and 2 which use the Indigo aspiration system. The systematic reviews and meta-analyses included studies

which used various devices. There are other devices with varying techniques available for this procedure, some of which are covered in the additional studies in table 5. This variability means that the outcomes may not be generalisable to other techniques and devices, and caution should be taken in interpreting outcomes for this procedure.

Due to the non-randomised nature of the studies and lack of comparator, the study samples may be subject to selection bias as those included are not randomly selected. Buckley (2022) included a comparator arm but was performed retrospectively and was not randomised. The comparator of routine care was heterogenous in terms of treatments used and the study did not include any measures of right ventricular function. Inci (2023) retrospectively compared invasive treatments (MT versus CDT) and there was a larger proportion of patients who had contraindications to thrombolysis in the thrombectomy group. There may be selection bias, information bias in terms of the way the cases are managed and outcomes recorded. Loss to follow-up may also introduce bias in the outcome reporting. FLAME study (Silver 2023) was a prospective non-randomised study using parallel registries in high-risk PE and a haemodynamically unstable population. The study was stopped early after a pre-specified interim analysis was done at enrolment of 50 patients in the PT arm and the primary endpoint results met established criteria for early stoppage.
The sub-group analysis of all high-risk patients in the US cohort of the FLASH registry may be prone to selection bias as it excluded patients with life expectancy less than 30 days from the study. Outcome measurements were individually assessed by site, which is also a potential source of bias. More than 50% of patients consented to participate in the registry after the procedure was completed, which could have also led to selection bias. (Horowitz 2023).
Sedhom (2021) was a review of the MAUDE safety database which relies on voluntary reporting of events, it therefore would not capture all events so introduces selection bias. It also would not capture all MT events being performed so an incidence rate cannot be calculated as there is no denominator

available. The review was retrospective in nature and does not correlate device failure to clinical outcomes.

The FLASH registry was funded by Inari Medical. The FLARE study and FLARE-ED sub-study were sponsored by Inari Medical, the manufacturers of the FlowTriever device, and they were involved in study design and data collection. Various authors of Toma (2022), Inci (2023), Silver (2023) and Horowitz (2023) are consultants for Inari Medical and various other manufacturers including Penumbra. Two authors for Sedhom (2021) are consultants for various manufacturers including Inari Medical. Sista (2021) was funded by Penumbra and the authors have consultant roles for various companies including Penumbra and Inari Medical.

There are gaps in the evidence overall and for particular patient populations such as those with patent foramen ovale. Further evidence is needed from randomised controlled trials with larger populations and longer-term follow-up. There are some ongoing trials which may help to address some of the evidence gaps:

- STRIKE-PE: A Prospective, Multicentre Study of the Indigo™ Aspiration System Seeking to Evaluate the Long-Term Safety and Outcomes of Treating Pulmonary Embolism NCT04798261. N=600, prospective cohort study. Completion date March 2026.
- The PEERLESS Study. NCT05111613. N=550, Prospective, multicentre, RCT of the FlowTriever System compared to Catheter-Directed Thrombolysis (CDT) for acute intermediate-high-risk pulmonary embolism (PE). Completion date October 2023.
- Evaluating the Safety and Efficacy of the AlphaVac Multipurpose Mechanical Aspiration (MMA) F1885 PE for Treatment of Acute Pulmonary Embolism. NCT05318092. N=122, single arm trial. Completion date November 2023.
- FlowTriever All-Comer Registry for Patient Safety and Hemodynamics (FLASH). Observational (patient registry), n=1300. Completion date July 2023.

Existing assessments

A clinical consensus statement on treatment options for acute PE by the European Society of Cardiology (ESC) Working Group on Pulmonary Circulation and Right Ventricular Function and the European Association of Percutaneous Cardiovascular Interventions concludes that:

1. Various CDT techniques and systems are available, although a lack of large randomised trials prevents strong recommendations on their use, both with regard to optimal patient selection as well as choice of technique/system.

2. Because high-risk PE is associated with a high risk of mortality, urgent reperfusion therapy, preferably systemic full-dose thrombolysis, is recommended.

3. Patients with high-risk PE and a contraindication to systemic full-dose thrombolysis may be considered for surgical embolectomy or CDT should be considered.

4. Rescue reperfusion including CDT should be considered in patients with failure of the initial therapy, i.e., lack of improvement or haemodynamic deterioration.

5. It is recommended to set up a local multidisciplinary team of specialists (PERT) to optimise and standardise treatment decisions for patients with severe or otherwise complex acute PE.

6. The aim of reperfusion therapy by CDT is to stabilise the patient haemodynamically (decrease in heart rate, increase in systemic blood pressure, reduction of vasopressor doses). For this purpose, only a partial reduction of the thrombotic burden may be required.

7. During percutaneous therapy of acute PE patients require continuous monitoring of systemic blood pressure, heart rate. This should be continued until haemodynamic stabilisation is achieved and the catheter is removed.

8. Continue full-dose parenteral anticoagulation after completion of the CDT procedure, unless strictly contraindicated. Most patients can be directly switched to low molecular-weight heparin (LMWH) or direct oral anticoagulants at the time of stopping the heparin infusion (Pruszczyk 2022).

Related NICE guidance

Interventional procedures

- NICE interventional procedures guidance 651 on Percutaneous mechanical thrombectomy for acute deep vein thrombosis of the leg (2019).
  Recommendation: special arrangements for acute iliofemoral DVT, research only for distal DVT.
- NICE interventional procedures guidance 524 on Ultrasound-enhanced, catheter-directed thrombolysis for pulmonary embolism (2015).
  Recommendation: special arrangements.
- NICE interventional procedures guidance 523 on Ultrasound-enhanced, catheter-directed thrombolysis for deep vein thrombosis (2015).
  Recommendation: special arrangements.

Technology appraisals

- Technology appraisal guidance 341 on Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism (2015).
- Technology appraisal guidance 327 on Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism (2014).
- Technology appraisal guidance 287 on Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism (2013).
- Technology appraisal guidance 261 on Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism (2012).

Medical technologies

- None.

NICE guidelines

NICE guideline 158 on Venous thromboembolic diseases: diagnosis, management and thrombophilia testing (2020).

Professional societies

- British Thoracic Society
- British Society of Interventional Radiologists
- The Vascular Society of Great Britain & Ireland
- British Society of Endovascular Therapy
- Society for Acute Medicine
- Royal College of Physicians of London
- Royal College of Physicians of Edinburgh
- Royal College of Physicians and Surgeons of Glasgow
- Society of Vascular Nurses
- Association of Surgeons of Great Britain and Ireland
- Society of Academic and Research Surgery
- Society for Vascular Technology of Great Britain and Ireland

- Vascular Anaesthesia Society of Great Britain & Ireland

Evidence from patients and patient organisations

NICE received one submission from a patient organisation about percutaneous thrombectomy for massive and submassive pulmonary embolus.

NICE received one patient commentary as part of consultation comments from a patient who had the procedure. Patients' views on the procedure were consistent with the published evidence and the opinions of the professional experts.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 3 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

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Methods

NICE identified studies and reviews relevant to percutaneous thrombectomy for massive and submassive pulmonary embolus from the medical literature. The following databases were searched between the date they started to 10th July 2023: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with massive and submassive pulmonary embolism.
- Intervention or test: percutaneous mechanical thrombectomy.

- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts, the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	10/07/2023	1946 to July 07, 2023
MEDLINE In-Process (Ovid)	10/07/2023	1946 to July 07, 2023
MEDLINE Epubs ahead of print (Ovid)	10/07/2023	July 07, 2023
EMBASE (Ovid)	10/07/2023	1974 to 2023 July 07
EMBASE Conference (Ovid)	10/07/2023	1974 to 2023 July 07
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	10/07/2023	Issue 7 of 12, July 2023
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	10/07/2023	Issue 7 of 12, July 2023
International HTA database (INAHTA)	10/07/2023	-

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

Ovid MEDLINE(R) <1946 to July 07, 2023>

1 Thrombectomy/ 10401
2 percutaneous.tw. 144796
3 1 and 2 1225
4 (percutaneous adj4 thrombectom*).tw. 601
5 3 or 4 1333
6 catheter*.tw. 203950
7 Catheters/ 7686
8 (mechanical* adj4 thrombectom*).tw. 4013
9 or/6-8 208788
10 5 and 9 667
11 Venous Thromboembolism/ 15677
12 ((Venous adj4 (thrombo-embolism* or thromboembolism*)) or VTE).ti,ab. 24921
13 Pulmonary Embolism/ 43272
14 (((Pulmonary or lung*) adj4 embol*) or PE).ti,ab. 88511
15 Venous Thrombosis/ 29524
16 (((vein* or ven*) adj4 thromb*) or DVT).ti,ab. 86771
17 (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or embol*).ti,ab. 343254
18 (blood adj4 clot*).ti,ab. 12191
19 or/11-18 412904
20 10 and 19 583
21 EKOS.tw. 74
22 21 and 19 65
23 (Indigo adj4 Aspiration).tw. 25
24 FlowTriever*.tw. 39
25 AlphaVac.tw. 1
26 or/20,22-25 696
27 Animals/ not Humans/ 5103420
28 26 not 27 681
29 limit 28 to english language 633
30 limit 29 to ed=20230316-20230731 14

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (table 2 and table 3) are listed in table 5 below. Case reports, case series ≤20 without unique safety/efficacy outcomes and non-systematic narrative reviews have not been included in table 5.

Table 5 additional studies identified

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Akbarshakh Akhmerov, Heidi Reich, James Mirocha, Danny Ramzy; Effect of Percutaneous Suction Thromboembolectomy on Improved Right Ventricular Function. Tex Heart Inst J 1 April 2019; 46 (2): 115–119. doi: https://doi.org/10.14503/THIJ-17-6551	N=13, AngioVac, median follow-up 74 days	77% survival to hospital discharge. Pre-procedure 8 (62%) had severe right ventricular dysfunction, post procedure this was 2 (17%) (p=0.031). 3 patients had intraprocedural haemodynamic instability leading to conversion to open surgery and standard cardiopulmonary bypass. Three in-hospital deaths, unrelated to procedure.	Small sample, short follow-up
Al-Hakim R, Park J, Bansal A, Genshaft S, Moriarty JM. Early Experience with AngioVac Aspiration in the Pulmonary Arteries. J Vasc Interv Radiol. 2016 May;27(5):730-4. doi: 10.1016/j.jvir.2016.01.012. PMID: 27106647.	N=5: 4 massive PE AngioVac	2/5 (40%) technical success (reduction in Miller Index ≥5). 4/5 deaths (80%) at mean of 7.3 days post procedure, of which 1 related to right ventricular free wall perforation.	Small sample, retrospective
Bangalore S, Horowitz JM, Beam D et al (2023). Prevalence and Predictors of Cardiogenic Shock in Intermediate-Risk Pulmonary	Registry analysis N=131 intermediate-risk PE patients in the	Although haemodynamically stable, over one-third of intermediate-risk FLASH patients were in normotensive shock with a depressed cardiac index. A	More comprehensive studies included in summary of evidence.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Embolism: Insights From the FLASH Registry. JACC. Cardiovascular interventions; 2023; vol. 16 (no. 8); 958-972	FLASH registry undergoing mechanical thrombectomy with the FlowTriever System.	composite shock score effectively further risk stratified these patients. Mechanical thrombectomy improved haemodynamics and functional outcomes at the 30-day follow-up.	
Bonvini RF, Roffi M, Bounameaux H, Noble S, Müller H, Keller PF, Jolliet P, Sarasin FP, Rutschmann OT, Bendjelid K, Righini M. AngioJet rheolytic thrombectomy in patients presenting with high-risk pulmonary embolism and cardiogenic shock: a feasibility pilot study. EuroIntervention. 2013 Apr 22;8(12):1419-27. doi: 10.4244/EIJV8I12A215. PMID: 23680957.	N=10 (high risk PE and cardiogenic shock). Angiojet Follow-up to 3 months	In 2, IV thrombolysis given due to progressive haemodynamic deterioration following procedure. 7/10 patients died in the first 12 hours post-procedure (4 refractory right heart failure). 3/10 patients favourable outcomes and normalisation of RV function, no PE recurrence at 1 year.	Small sample, short follow-up, single centre.
Bunc M, Steblovnik K, Zorman S, Popovic P. Percutaneous mechanical thrombectomy in patients with high-risk pulmonary embolism and contraindications for thrombolytic therapy. Radiol Oncol. 2020 Feb 14;54(1):62-67. doi: 10.2478/raon-2020-0006. PMID: 32061168; PMCID: PMC7087421.	N=25 (high-risk PE) Follow-up to hospital discharge. 56%: pigtail catheter 44%: Aspirex device	Non-significant improvements in systemic blood pressure and heart rate. Statistically significant reduction in peak systolic tricuspid pressure gradient (57±14 mm Hg vs 31±3 mm Hg; p = 0.018). Technical success in 80% Salvage thrombolytic therapy in 8/25 (32%). 68% survival to hospital discharge. No statistically significant difference in technical success, survival or any other parameters between subgroups receiving	Small sample, retrospective

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
		thrombolysis and PMT and those who only received PMT apart from transfusion requirement (50% vs 12%, p=0.04). Major complications: 1 significant puncture site bleeding Minor complications: 6/25 (24%), 5 transient bradycardia during catheterisation and 1 groin haematoma.	
Bunwaree, S., Roffi, M., Bonvini, J.M., et al. (2013). AngioJet® rheolytic thrombectomy: a new treatment option in cases of massive pulmonary embolism. Interventional Cardiology, 5, 71-87.	N=197 Group A (massive PE) = 76 Group B (massive + submassive PE) = 121 Systematic review of Angiojet rheolytic thrombectomy. Variable follow-up. 14 studies included: 9 (Group A) massive PE only 5 (Group B) massive and submassive PE combined population	Successful procedure (including clinical success/ technical success/ procedural success) reported in 66/76 (86.8%) in group A, 99/105 (94.3%) group B. In Group A (reported in 5 studies) systolic PAP was reduced from pre-procedure: 55 ± 9.9 to post-procedure: 37.3 ± 18.8 and mPAP was reduced from pre-procedure: 37.8 ± 5.8 to post-procedure: 33.9 ± 8.2. In group B (reported in 4 studies) systolic PAP: pre-procedure, 48.7 ± 0.4 vs post-procedure, 37.9 ± 0.8; mPAP: pre-procedure 34.3 ± 4.9 vs post-procedure, 27.3 ± 1.2. Significance not reported. There were 31/197 (15.7%) major periprocedural events including 23 (11.6%) episodes of bradyarrhythmia and 2 (1%) transient asystole, out of which 18 (9.1%) required temporary pacemaker	Older systematic review referencing solely the Angiojet device. Country of origin not detailed for studies. All but 2 of the studies included fewer than 20 participants each and most were retrospective case series lacking comparator arms. Many of the studies did not report the clinical outcomes studied and in more than 40% of the patients included, thrombolysis was given which makes interpretation of the efficacy and safety of thrombectomy difficult. Three of the included studies (Bonvini, 2013; Margheri, 2008; Chechi, 2009) are also discussed separately.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
		implantation. The review reported 6 (3%) intraprocedural deaths (all in group A), 1 prior to device activation. The in-hospital mortality rate was 29/197 (14.7%): 13/76 (17.1%) in group A and 16/121 (13.2%) in group B. After discharge, no further deaths to 30 days. Major post-procedural events in 61/197 (30.1%) patients including 6 (3.0%) episodes of haemoptysis, 13 (6.6%) major inguinal haematomas, 2 (1%) episodes of melaena, 5 (2.5%) macro-haematuria, 2 (1%) retroperitoneal bleeding, 4 (2%) cerebral haemorrhage, 23 (11.7%) impaired renal function, 3 (1.5%) multiorgan failure and 7 (3.5%) significant thrombocytopaenia.	
Chechi T, Vecchio S, Spaziani G, Giuliani G, Giannotti F, Arcangeli C, Rubboli A, Margheri M. Rheolytic thrombectomy in patients with massive and submassive acute pulmonary embolism. Catheter Cardiovasc Interv. 2009 Mar 1;73(4):506-13. doi: 10.1002/ccd.21858. PMID: 19235240.	N=51 Angiojet Massive and submassive PE Average follow-up 35.5 ± 21.7 months	Technical success in 92.2% Statistically significant improvement in obstruction, perfusion and Miller index in all subgroups of severity ($p<0.0001$) and in systolic PAP ($p<0.05$). 4/51 major bleeding events (7.8%) 8/51 (15.7%) in-hospital mortality (6 due to persistent/refractory shock) 3 further deaths at long term follow-up unrelated to procedure/PE.	Small sample, retrospective.
Cherfan P, Abou Ali AN, Zaghloul MS, Yuo TH, Phillips DP, Chaer RA,	N=340 Of which:	36 patients (10.6%) received propofol; 304 patients (89.4%) received	Majority of patients had catheter thrombolysis, only

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Avgerinos ED. Propofol administration during catheter-directed interventions for intermediate-risk pulmonary embolism is associated with major adverse events. J Vasc Surg Venous Lymphat Disord. 2021 May;9(3):621-626. doi: 10.1016/j.jvsv.2020.08.026. Epub 2020 Aug 26. PMID: 32858244.	85 catheter directed thrombolysis, 229 ultrasound-assisted thrombolysis, 26 suction thrombectomy.	midazolam plus fentanyl, morphine, or hydromorphone. Overall, 18 patients had ≥1 MAE (10 intubations, 11 decompensations, 2 surgical conversions, 3 deaths). Propofol group had a statistically significantly greater adverse event rate (13.8%) vs no-propofol group (4.2%; p=0.015). 16 patients experienced major bleeding or other procedure-related events (stroke in 4 (1.17%), coronary sinus perforation in 1, tricuspid valve rupture in 1, and the need for transfusion in 10 patients). Type of intervention was not a predictive factor for any outcome.	26 suction thrombectomy. Reviewing effect of anaesthetic rather than intervention directly. Retrospective.
Ciampi-Dopazo JJ, Romeu-Prieto JM, Sánchez-Casado M, Romerosa B, Canabal A, Rodríguez-Blanco ML, Lanciego C. Aspiration Thrombectomy for Treatment of Acute Massive and Submassive Pulmonary Embolism: Initial Single-Center Prospective Experience. J Vasc Interv Radiol. 2018 Jan;29(1):101-106. doi: 10.1016/j.jvir.2017.08.010. Epub 2017 Nov 6. PMID: 29102272.	N=18 Indigo Aspiration System Follow-up to discharge (median hospital stay 10 days)	Technical success in 17/18 (94.4%) and clinical success in 15/18 (83.3%). Statistically significant improvement in right ventricle size (46.36 mm ± 2.2 before treatment vs 41.79 mm ± 7.4 after; p=0.041). Two patients died with massive PE and one patient died with submassive PE. Mortality= 16.7%. Of the 4 patients who received thrombolysis, 2 experienced intracranial bleeding and 1 abdominal bleeding.	Small sample, short follow-up.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Donaldson, C.W., Baker, J.N., Narayan, R.L., Provias, T.S., Rassi, A.N., Giri, J.S., Sakhuja, R., Weinberg, I., Jaff, M.R. and Rosenfield, K. (2015), Thrombectomy using suction filtration and veno-venous bypass: Single center experience with a novel device. Cathet. Cardiovasc. Intervent., 86: E81-E87	N=14, AngioVac Mean follow-up 23 days	Indications included intracardiac mass (73%), acute PE (33%), and caval thrombus (73%). Four patients (27%) were in shock at the start of the procedure. Successful evacuation of mass in 73%. Peri-procedure mortality was 0% and in-hospital mortality 13% at a mean follow-up of 23 days. No pulmonary haemorrhages, strokes or myocardial infarctions. 73% had a post procedural drop in haematocrit with 6 of these 11 requiring transfusion. Two patients required subsequent embolectomy (one open).	Small sample, short follow-up, focuses more on right heart thrombi.
Dukkipati, R., Yang, E., Adler, S. et al. Acute kidney injury caused by intravascular hemolysis after mechanical thrombectomy. Nat Rev Nephrol 5, 112–116 (2009). https://doi.org/10.1038/ncpneph1019	N=1 Case report Angiojet	43F, 8 weeks pregnant Bilateral PE treated with Angiojet system. Intraprocedural bradycardia. Post-procedural massive intravascular haemolysis and acute kidney injury. 48 hours in ICU, haemodialysis until day 21. Fetal loss on day 7. Renal function returned to normal on day 25.	Case report.
Dumantepe, M., Teymen, B., Akturk, U. and Seren, M. (2015), The Efficacy of Rotational Thrombectomy on the Mortality of Patients with Massive and Submassive Pulmonary Embolism. J Card Surg, 30: 324-332.	N=36 Massive and submassive PE Aspirex percutaneous aspiration device.	Complete thrombus clearance (≥90%) in 83.3% and near-complete (50% to 90%) clearance in 13.8%. Statistically significant decrease (56%) in mean PAP post-procedure. Major complication rate 6.3%. Two in-hospital deaths (one from refractory shock). Two	Small sample, retrospective case series

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
https://doi.org/10.1111/jocs.12521	Mean follow-up 14.3±5.8 months.	patients had a significant bradycardic episode. No major bleeding events. Total 360-day survival was 88.8%.	
Eid-Lidt G, Gaspar J, Sandoval J, de los Santos FD, Pulido T, González Pacheco H, Martínez-Sánchez C. Combined clot fragmentation and aspiration in patients with acute pulmonary embolism. Chest. 2008 Jul;134(1):54-60. doi: 10.1378/chest.07-2656. Epub 2008 Jan 15. PMID: 18198243.	N=18, follow-up 12.3 ± 9.4 months. Massive PE.	Statistically significant increase in systolic blood pressure post-procedure and statistically significant decrease in mean PAP (37.1 ± 8.5 mmHg vs 32.3 ± 10.5 mmHg, p = 0.0001). In-hospital major complication rate 11.1%, one death from refractory shock. One patient had intracerebral haemorrhage with minor neurologic sequelae (deemed to be secondary to local fibrinolytic therapy). Two transitory decreases in oxygen saturation during procedure (Aspirex device) without haemodynamic instability.	Small sample
Eid-Lidt G, Gaspar J, Sandoval J, et al. Persistent pulmonary hypertension and right ventricular function after percutaneous mechanical thrombectomy in severe acute pulmonary embolism. Eur Respir J 2017; 49: 1600910 [https://doi.org/10.1183/13993003.00910-2016]	N=52 Mean follow-up 40.2 ± 16.7 months. Excluded 8 for prior pulmonary artery hypertension, 8 for right ventricular hypertrophy and 5 for follow-up < 6 months. 7 patients died in hospital and were not	After the procedure, the shock index (1.1±0.23 vs 0.7±0.1; p=0.019), heart rate (113±14 vs post-86±13 bpm; p=0.005) and systolic systemic arterial pressure (100±14 vs 124±13 mmHg; p=0.005) improved. No recurrence of pulmonary embolism in-hospital. Four patients were re-admitted to hospital, two patients for recurrence of severe pulmonary embolism (4.1%) and two for complicated pneumonia. Overall survival (extra-hospital phase) at 5 years	Small sample

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
	included in analysis.	was 96.2%. Improvements in right ventricular function were mainly in the first 6 months with a 24% reduction in PAP.	
Escobar GA, Burks D, Abate MR, Faramawi MF, Ali AT, Lyons LC, Moursi MM, Smeds MR. Risk of Acute Kidney Injury after Percutaneous Pharmacomechanical Thrombectomy Using AngioJet in Venous and Arterial Thrombosis. Ann Vasc Surg. 2017 Jul;42:238-245. doi: 10.1016/j.avsg.2016.12.018. Epub 2017 Apr 13. PMID: 28412100.	N=102 (n=52 Angiojet, n=50 catheter-directed thrombolysis) Follow-up 3 days	Acute kidney injury (AKI) occurred in 29% of patients treated with Angiojet vs 8% of catheter-directed thrombolysis. Odds for AKI increased by Angiojet (OR 8.2, 95% CI 1.98-34.17, p=0.004). Concomitant open surgery and drop in haematocrit also raise the odds of AKI.	Includes use of Angiojet catheter with thrombolytic drugs, includes various arterial and venous thromboses so not specific to PE.
Gayen S, Upadhyay V, Kumaran M, Bashir R, Lakhter V, Panaro J, Criner G, Dadparvar S, Rali P. Changes in Lung Perfusion in Patients Treated with Percutaneous Mechanical Thrombectomy for Intermediate-Risk Pulmonary Embolism. Am J Med. 2022 Aug;135(8):1016-1020. doi: 10.1016/j.amjmed.2022.03.028. Epub 2022 Apr 22. PMID: 35469736.	N=3 Intermediate risk PE. FlowTriever Use of imaging for perfusion tracking	Pre-procedure and post-procedure perfusion estimation: Case 1: perfusion score improved from 5/15 pre-procedure to 12/15 within 48 hours and 13/15 at 3 months. Case 2: 7/15 pre-procedure to 8/15 within 72h, 10.5/15 at 3 months and 12/15 at 9 months. Case 3: 6/15 pre-procedure to 7/5/15 within 72h and 9/15 at 3 months. Overall, average lung perfusion score increased from 6/15 (40%) pre-procedure to 9.17/15 (61.1%) immediately post-procedure and 11.33/15 (75.6%) at last follow-up.	Small sample

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
		No PE-related readmission within 30 days or PE-related complications.	
Graif A, Patel KD, Wimmer NJ, Kimbiris G, Grilli CJ, Upparapalli D, Kaneria AR, Leung DA. Large-Bore Aspiration Thrombectomy versus Catheter-Directed Thrombolysis for Acute Pulmonary Embolism: A Propensity Score-Matched Comparison. J Vasc Interv Radiol. 2020 Dec;31(12):2052-2059. doi: 10.1016/j.jvir.2020.08.028. Epub 2020 Nov 9. PMID: 33183975.	N=52 CDT group=26 Large-bore aspiration thrombectomy (LBAT)=26 (FlowTriever for majority)	Statistically significant decrease in systolic PAP, diastolic PAP, mean PAP, HR, and Miller score in both groups. Systolic PAP: Baseline and final systolic PAP was similar between the two groups (LBAT: 54.5 mm Hg ± 12.9 vs CDT: 54.5 mm Hg ± 16.3 at baseline, P=0.8; and LBAT: 42.5 mm Hg ± 14.1 vs CDT: 42.6 mm Hg ± 12.1, P =0.8, respectively). Heart rate: reductions not statistically significantly different between the 2 groups: (LBAT: -5.4 bpm ± 19.2 vs CDT: -9.6 bpm ± 15.8, P=0.4). Miller score: CDT demonstrated a higher reduction (-10.1 ± 3.9 vs -7.5 ± 3.8, P=0.02). Complications: LBAT had 1 minor haemorrhagic complication and 2 procedure-related deaths vs CDT resulted in 1 minor and 1 major haemorrhagic complication. ICU stay: 18/26 LBAT group and 26/26 CDT, p=0.004. Similar hospital length of stay.	Small sample, retrospective, propensity matched, non-randomised.
Kumar N, Janjigian Y, Schwartz DR. Paradoxical worsening of shock after the use of a percutaneous	Case report, unique safety information. Angiojet	31F, onset 1h post-caesarean section. Obstructive shock due to PE. Rheolytic thrombectomy removed	Small sample, older report.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
mechanical thrombectomy device in a postpartum patient with a massive pulmonary embolism. Chest. 2007 Aug;132(2):677-9. doi: 10.1378/chest.06-1082. PMID: 17699140.		obstruction and restoration of PA flow. Immediately post procedure refractory shock, cor pulmonale, gross haematuria and drop in haemoglobin secondary to fragmentary haemolysis. Haemolysis and shock resolved within 24h, remaining hospital course uneventful, and the patient discharged on day 7. An outpatient echocardiogram shortly after discharge revealed normal biventricular function and PAP.	
Kumar G, Jaber W, Sachdeva R. Intravascular ultrasound guidance in percutaneous mechani cal thrombectomy: A single-center experience from the FLASH registry Cardiovascular Revascularization Medicine; 2023.	Retrospective study Intravascular ultrasound (IVUS)-guided mechanical thrombectomy in PE from the FLASH registry 26 subset patients (96.2 %) had intermediate-risk PE and 3.8 % had high-risk PE.	The use of IVUS guidance with minimal or no angiographic contrast during mechanical thrombectomy for acute PE is technically feasible.	More comprehensive studies included in table 2.
Leong, DW.; Ayadi, B; Dexter, DJ (2023) Continuous mechanical aspiration thrombectomy performs equally well in main versus branch pulmonary emboli: A subgroup analysis of the EXTRACT-PE trial. Catheterization and Cardiovascular	Prospective study. N= 119 patients with acute submassive PE-with main pulmonary artery (PA, n=45) emboli versus discrete	No significant difference was observed between these groups for 30-day mortality, procedural device time, changes in RV:LV diameter ratio, reduction in CT Obstruction Index, or for systolic PA pressure from pre-and posttreatment. The mean absolute reduction in clot burden was significant	More comprehensive studies included in table 2.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Interventions; 2023; vol. 101 (no. 2); 468-475.	unilateral or bilateral PA emboli without main PA involvement (branch emboli n=73). Indigo Aspiration System for PE	in both groups. Continuous mechanical aspiration thrombectomy with the 8F Indigo Aspiration System was effective at improving clinical outcomes for submassive PE patients regardless of emboli location, and clot burden was significantly reduced in both groups.	
Luedemann WM, Zickler D, Kruse J et al (2023) Percutaneous Large-Bore Pulmonary Thrombectomy with the FlowTriever Device: Initial Experience in Intermediate-High and High-Risk patients. Cardiovascular and interventional radiology; 46 (1); 35-42.	Retrospective cohort study N= 27 patients with intermediate-high and high-risk (n=18) pulmonary embolism (PE) who were treated with transfemoral mechanical thrombectomy (MT) using the large-bore Inari FlowTriever aspiration catheter system.	After MT, a statistically significant reduction in mean pulmonary artery pressures from 35.9 +/- 9.6 to 26.1 +/- 9.0 mmHg (p = 0.002) and heart rates from 109.4 +/- 22.5 to 82.8 +/- 13.8 beats per minute (p < 0.001) was achieved. Two patients died of prolonged cardiogenic shock. Three patients died of post-interventional complications of which a paradoxical embolism can be considered related to MT. One patient needed short cardiopulmonary resuscitation during the procedure due to clot displacement. Patients with PE as primary driver of clinical instability had a median intensive care unit (ICU) stay of 2 days (0.5-3.5 days). Patients who developed PE as a complication of an underlying medical condition spent 11 days (9.5-12.5 days) in the ICU.	Larger studies included in table 2.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Margheri M, Vittori G, Vecchio S, Chechi T, Falchetti E, Spaziani G, Giuliani G, Rovelli S, Consoli L, Biondi Zoccai GG. Early and long-term clinical results of AngioJet rheolytic thrombectomy in patients with acute pulmonary embolism. Am J Cardiol. 2008 Jan 15;101(2):252-8. doi: 10.1016/j.amjcard.2007.07.087. PMID: 18178417.	N=25 (8 severe haemodynamic compromise, 12 moderate, 5 mild) Angiojet Median follow-up 61 months.	Technical and procedural success 100% Statistically significant improvement in obstruction, perfusion and Miller indexes overall, and in each subgroup (all p values <0.001). Statistically significant improvement in all above seen in patients given local fibrinolysis (n=8) and in those not given local fibrinolysis (n=17, p<0.05). 4/25 (16%) in-hospital mortality (2 persistent shock, 1 cerebral haemorrhage, 1 recurrence of embolism). All others alive at long-term follow-up except 1 noncardiopulmonary cause. Temporary transvenous pacing in 3 (12%) for bradycardia. 10 major haematomas requiring transfusion (40%). 7 post-procedural worsening of renal function (28%)	Small sample, retrospective, no comparator.
Martillotti, G, Boehlen, F, Robert-Ebadi, H, Jastrow, N, Righini, M, Blondon, M. Treatment options for severe pulmonary embolism during pregnancy and the postpartum period: a systematic review. J Thromb Haemost 2017; 15: 1942– 50.	Systematic review N=7 for percutaneous thrombectomy	Maternal survival 100% Two cases went on to further treatments. Risk of fetal death 25% Risk of major bleeding 20% All reported good angiographic results without procedure-related complications. One case, a rheolytic thrombolysis complicated by severe haemolysis (paper included separately).	Different modalities used in different cases (systematic review including a number of case reports). Small sample size.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Morrow KL, Kim AH, Plato SA 2nd, Shevitz AJ, Goldstone J, Baele H, Kashyap VS. Increased risk of renal dysfunction with percutaneous mechanical thrombectomy compared with catheter-directed thrombolysis. J Vasc Surg. 2017 May;65(5):1460-1466. doi: 10.1016/j.jvs.2016.09.047. Epub 2016 Nov 19. PMID: 27876521.	N=145 Retrospective comparative review, single centre. 4 groups: Percutaneous mechanical thrombectomy (PMT) alone (n=15), PMT with tissue-plasminogen activator (tPA) pulse-spray, PMT (n=42) with catheter directed thrombolysis (CDT) (n=70), or CDT only (n=18). Follow-up to 6 months.	The overall incidence of renal dysfunction was 15%. The incidence was highest in the PMT/tPA pulse group (21%), followed by the PMT group (20%) and the PMT/CDT group (14%). CDT was not associated with renal dysfunction (0%). PMT (p=0.046), and PMT/tPA pulse (p=0.033) were associated with higher rates of renal dysfunction than the CDT controls. Renal dysfunction was higher in the arterial thrombus (21%) than venous thrombus (12%) groups. Stratified by the RIFLE (Risk, Injury, Failure, Loss, and End-stage renal disease) criteria, 13 (9%) patients progressed to the risk category, 6 (4%) progressed to the injury category, and 3 (2%) progressed to the failure category. None of the patients progressed to dialysis within the same admission period. The average length of time for creatinine values to return to baseline was 5.1 ± 5.2 days. No difference in 6-month outcomes between procedural groups.	Assesses catheter therapies in all vasculature locations with only 11 in pulmonary vasculature. Retrospective, small sample.
Mously H, Hajjari J, Chami T, Hammad T, Schilz R, Carman T, Elgudin Y, Abu-Omar Y, Pelletier MP, Shishehbor	N=9 Follow-up 90 days	2/9 minimal thrombus retrieval (1 given salvage systemic thrombolysis, 1 converted to surgical embolectomy)	Small sample, combined treatment with ECMO.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
MH, Li J. Percutaneous mechanical thrombectomy and extracorporeal membranous oxygenation: A case series. Catheter Cardiovasc Interv. 2022 Aug;100(2):274-278. doi: 10.1002/ccd.30295. Epub 2022 Jun 10. PMID: 35686535.	Large bore thrombectomy and ECMO	Median ECMO duration 5 days (2.3-11.6) Median ICU stay 10 days (1.5-25.5) Median hospitalisation 16.1 days (1.5-30.9) 90 day mortality 22%	Results reporting limited.
Pelliccia F, De Luca A, Pasceri V, Tanzilli G, Speciale G, Gaudio C. Safety and Outcome of Rheolytic Thrombectomy for the Treatment of Acute Massive Pulmonary Embolism. J Invasive Cardiol. 2020 Nov;32(11):412-416. PMID: 33130592.	N=33 patients contraindicated to thrombolysis. Angiojet rheolytic thrombectomy. Follow-up 1 year	Angiographic improvement 32/33 (96%) Rapid improvement in functional class (3.3 ± 0.9 to 2.1 ± 0.7; P<0.001) Increase in oxygen saturation (71 ± 15% to 92 ± 17%; P<0.001) No deaths, no major bleeding, no renal failure. Post procedure anaemia in 4/33 (12.1%) Periprocedural side effects: Transient heart block (n=1, 3%) Hypotension (n=3, 9%) Bradycardia (n=5, 15.1%) At 1 year follow-up (n=30): PAP statistically significantly lower than baseline (65 ± 31 mm Hg vs 31 ± 19 mm Hg; P<0.001).	Small sample, no comparator.
Qureshi AM, Petit CJ, Crystal MA, Liou A, Khan A, Justino H. Efficacy and safety of catheter-based rheolytic and aspiration thrombectomy in children. Catheter Cardiovasc Interv. 2016 Jun;87(7):1273-80. doi:	Included for consideration of paediatric population. Median age 1.9 months. Median follow-up 10 months.	Thrombectomy was performed in 50 vessels in 21 patients. Thrombectomy successful in 47/50 (94%) vessels in 18/21 (86%) patients. Additional balloon/stent therapy or tPA administration performed in	Only 4/21 patients had PE. The rest had thrombosis in other vessels. Small sample, retrospective.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
10.1002/ccd.26399. Epub 2016 Feb 1. PMID: 26833887.	N=21 Rheolytic and aspiration thrombectomy.	16/18 (89%) of these patients. 2 (9.5%) major complications (both with AngioJet): asystole when using activation times of >5 sec. At median follow-up 10 months: all 47 treated vessels patent and 8/18 (44%) required reintervention. Of the 4 pulmonary vessel patients, 2/4 (50%) thrombectomy successful, 3/4 Angiojet and1/4 pronto catheter.	
Nakazawa K, Tajima H, Murata S, Kumita S-I, Yamamoto T, And Tanaka K. Catheter fragmentation of acute massive pulmonary thromboembolism: distal embolisation and pulmonary arterial pressure elevation The British Journal of Radiology 2008 81:971, 848-854	Case series Rotating pigtail catheter N=25	Decrease in mPAP after thrombus fragmentation (34.2mmHg to 30.8mmHg, $p<0.05$) and after thrombolysis and thrombus aspiration (24.0 mmHg, $p<0.01$). Distal embolization occurred in 7/25 cases, in this group mPAP statistically significantly increased after thrombus fragmentation (34.1 to 37.9 mmHg, $p<0.05$) before statistically significantly decreasing after thrombolysis and aspiration (25.7mmHg, $p<0.05$). Statistically significant decrease in Miller Score after fragmentation (21.2 to 18.5, $p<0.01$) and aspiration (to 14.1, $p<0.01$). No recurrences observed. Continuous monitoring of mPAP can predict distal	Small sample All cases received local thrombolytic therapy as well.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
		embolization and may improve safety.	
Nezami N, Chockalingam A, Cornman-Homonoff J, Marino A, Pollak J, Mojibian H. Mechanical thrombectomy for pulmonary embolism in patients with patent foramen Ovale. CVIR Endovasc. 2020 Nov 28;3(1):89. doi: 10.1186/s42155-020-00180-9. PMID: 33247349; PMCID: PMC7695793.	Case series N=9 (3 high-risk and 6 intermediate/high risk) FlowTriever	Included for unique patient group (PFO). Technical success rate 100% Clinical success rate 77.8% Right heart-strain improved in 6/8 mPAP statistically significantly decreased (36.0 ± 15.2 vs 23.4 ± 8.4 mmHg, p<0.012) 1 patient developed middle cerebral artery embolic stoke 1 day post-procedure (unclear if related to procedure). No in-hospital mortality	Small sample, retrospective
Toma, C, Khandhar, S, Zalewski, AM, D'Auria, SJ, Tu, TM, Jaber, WA. Percutaneous thrombectomy in patients with massive and very high-risk submassive acute pulmonary embolism. Catheter Cardiovasc Interv. 2020; 96: 1465– 1470. https://doi.org/10.1002/ccd.29246	Multi-centre case series N=34 Massive and very high-risk submassive PE. FlowTriever Mean follow-up 205 days.	Clot removal successful in 32/34 (94.1%). Procedural failure 2/34, both deteriorated during procedure and one died (2.9%). Decompensation following intubation (known profound negative haemodynamic effect in large PEs). Cardiac index improved from 2.0 ± 0.1 L/min/m2 before thrombectomy to 2.4 ± 0.1 L/min/m2 after (p = 0.01). The mPAP decreased from 33.2 ± 1.6 mmHg to 25.0 ± 1.5 mmHg (p = 0.01). Procedure. In 6 patients, cardiac index decreased post-procedure but additional vasopressors not required.	Small sample, no comparator.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
		At 24 hr blood pressures and heart rates statistically significantly improved. No complications directly attributable to device. No major treatment-related bleeding events. Statistically significant drop in haemoglobin was noted at 24 hr (12.2 ± 0.5 g/dL to 10.5 ± 2.2 g/dL, p = 0.007). The average length of stay was 9.8 ± 1.6 days. 33/34 (97%) survival to 205 days.	
Toma C, Bunte MC, Cho KH, et al. Percutaneous mechanical thrombectomy in a real-world pulmonary embolism population: Interim results of the FLASH registry. Catheter Cardiovasc Interv. 2022 Mar;99(4):1345-1355. doi: 10.1002/ccd.30091. Epub 2022 Feb 3. PMID: 35114059; PMCID: PMC9542558. NCT03761173	FLASH registry interim analysis N=250 high- and intermediate-risk Pes had mechanical thrombectomy. 30 days follow-up.	There were three MAEs (1.2%), all of which were major bleeds that resolved without sequelae, with no device-related injuries, clinical deteriorations, or deaths at 48 h. All-cause mortality was 0.4% at 30 days, with a single death that was unrelated to PE. Significant on-table improvements in hemodynamics were noted, including an average reduction in mean pulmonary artery pressure of 7.1 mmHg (22.2%, p < 0.001). Patient symptoms and cardiac function improved through follow-up.	More recent comprehensive study included in table 2.
Uecker NA, Rosenkranz S, Bunck A et al. (2023) Unexpected paradoxical embolization following catheter-directed thrombectomy with the FlowTrieverTM system in a patient	Case report Percutaneous mechanical thrombectomy for a patient with intermediate high-risk PE	Patient presented neurologic deficits and embolic stroke. Transesophageal echocardiography revealed a patent foramen ovale (PFO) as the origin of paradoxical embolism and	Adverse event reported in the evidence summary.

Article	Number of patients and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
with pulmonary embolism: A case report European Heart Journal - Case Reports; 7 (3); 74	using the FlowTrieverTM system.	thus mechanism of both ischemic lesions. PFO closure was performed. Patient recovered properly without any sequelae.	
Wible BC, Buckley JR, Cho KH, Bunte MC, Saucier NA, Borsa JJ. Safety and Efficacy of Acute Pulmonary Embolism Treated via Large-Bore Aspiration Mechanical Thrombectomy Using the Inari FlowTriever Device. J Vasc Interv Radiol. 2019 Sep;30(9):1370-1375. doi: 10.1016/j.jvir.2019.05.024. Epub 2019 Jul 30. PMID: 31375449.	N=46 (8 massive, 38 submassive). Retrospective case series. FlowTriever Follow-up 30 days post discharge.	Technical success 100% mPAP improved statistically significantly for all (33.9 ± 8.9 mm Hg before, 27.0 ± 9.0 mm Hg after; P < 0.0001) Intraprocedural reduction in mPAP in 88%. Survival to discharge 100% 2 MAEs (4.6%): haemoptysis requiring intubation, procedure-related blood loss requiring transfusion. No procedure-related deaths within 30d of discharge.	Small sample, single-centre, no comparator.

