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Multicentre, real-world data of next-generation computer-assisted vacuum aspiration thrombectomy in acute pulmonary embolism

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Abstract

Background Data on interventional treatment of intermediate-high (and high-risk pulmonary embolism (PE) are limited. The authors sought to evaluate the safety and efficacy of catheter-directed mechanical aspiration thrombectomy (CDMT) in a real-world PE patient population.

Methods This multicenter, prospective registry enrolled PE patients treated with CDMT using the Lightning 12 System. The primary safety endpoints included in-hospital all-cause mortality, procedure-related major bleeding, clinical deterioration, or bailout to another strategy. The primary efficacy outcomes included the reduction of pulmonary arterial pressures and change in the right-to-left ventricular (RV/LV) ratio 48 h after the CDMT. Multivariate regression analyzed characteristics associated with RV/LV improvement.

Results Our analysis included 150 patients, 72% with intermediate-high PE and 28% with high-risk PE. Systemic thrombolysis was contraindicated in 33.3%, whereas in 4% it failed. There were 2% intraprocedural deaths (1.3% due to RV failure and 0.7% due to massive interstitial bleeding), with no more deaths during follow-up. In 0.7%, CDMT was converted to open surgery, and in 0.7%, bailout systemic thrombolysis and extracorporeal oxygenation support. Major bleedings occurred in 1.3% within 48 h post CDMT. Immediate hemodynamic improvements included a mean 11.3±10 mmHg (22.1%) drop in systolic pulmonary arterial pressure ($p < 0.0001$) and a median 0.33 (0.25–0.45), (25.2%) drop in RV/LV ratio ($p < 0.0001$ for paired values),

Conclusions Aspiration thrombectomy with the Lightning 12 system characterizes an acceptable safety profile, substantial improvements in hemodynamic outcomes, and low mortality for patients with intermediate-high and high-risk PE.

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Keywords Pulmonary embolism, Intermediate-high risk, High-risk catheter-directed mechanical thrombectomy, Percutaneous thrombectomy

Background

Acute pulmonary embolism (PE) encompasses a heterogeneous spectrum of disease manifestation and severity with considerable mortality rates and unsatisfactory long-term outcomes of advanced stages. Hemodynamic deterioration in PE results from right ventricular pressure overload, leading to progressive RV failure and subsequently to the development of the spiral of cardiogenic shock and death [1–3]. The estimated early mortality is up to 30% in high-risk (HR) PE and up to 15% in intermediate-risk (IHR) PE [4].

For this population, interventionalists can offer catheter-based therapies (CBT), including catheter-directed fibrinolysis (CDF) or mechanical thrombectomy (CDMT), using a variety of newly emerging tools designed to address the risk of bleeding associated with systemic thrombolysis [5–12].

Despite the role of endovascular therapies in managing IHR and HR PE is constantly growing, evidence of its safety and efficacy is limited and impacts their implementation by societas guidelines (2, 3, 4, 5, 7–8, 12–13). In face of the increasing application of CDMT worldwide, there is a lack of data regarding European experience with different devices, especially non-industry-supported observational real-world outcomes.

Methods

The purpose of this report is to evaluate the effects of the new Lightning 12 computer-assisted aspiration system, including immediate changes in pulmonary hemodynamics, safety, and efficacy, as well as clinical outcomes during a 90-day follow-up.

This prospective multicenter registry study enrolled 150 consecutive unselected patients treated with the Lightning12 System in 9 centers in central Europe. The centers were selected to participate if the operator had performed at least 10 CDMT. The bioethics committee of the coordinating center approved the study protocol (Bioethics Committee of Poznan University of Medical Sciences; consent number 271/2021). The study was also registered at ClinicalTrials.gov (NCT04879069). All patients signed informed consent (if they were unconscious, close relatives approved the treatment). The study followed the principles established by the Declaration of Helsinki and Good Clinical Practice guidelines. Patients were eligible for enrollment if they had intermediate-high- or high-risk PE as specified by the European Society of Cardiology (ESC) guidelines and qualified for CDMT by the institutional PE response team (PERT) discretion [3, 5, 12]. In all patients, PE symptoms duration was less than 14 days, and clots were in at least one main or lobar pulmonary artery (PA), as demonstrated by computed tomography pulmonary angiography (CTPA) and conventional pulmonary angiography. There was no defined duration from the administration of parenteral anticoagulation to the thrombectomy initiation. The procedure was carried out promptly after the qualification by PERT. All patients underwent the procedure under parenteral anticoagulation (constant infusion of unfractionated heparin [UFH] or no longer than 4 h after the last dose of low-molecular-weight heparin).

The exclusion criteria were express refusal of the patient to participate in the study, life expectancy < 1 month due to severe comorbidities (according to the attending physician), platelets count below 20 000/ μL, known uncontrolled sensitivity to radiographic medium or active major bleeding as determined with the Bleeding Academic Research Consortium (BARC) score [14]. The follow-up assessments were performed at 48 h (± 8 h), 30 days (± 7 days), and 90 days (± 7 days) after the procedure. Demographic, vital, imaging, laboratory, and hemodynamic data were collected.

Catheter-directed mechanical aspiration thrombectomy

The Lightning 12 Intelligent aspiration system (Penumbra, Inc., Alameda, CA, US) consists of the engine pump, the Lightning control unit, the CAT 12 HTORQ or XTORQ Tips 12 F catheter, and the separator SEP 12. CDMT procedures were predominantly performed by puncturing the common femoral vein under ultrasound guidance. At the beginning and the end of the CDMT procedure, right heart catheterization was performed with a Swan-Ganz catheter and Fick method implementation for cardiac output (CO), pulmonary vascular resistance (PVR), and systemic vascular resistance (SVR) calculation along with pulmonary angiography (through a 6 F pigtail catheter) for detailed clot burden assessment, respectively. Thrombi load was evaluated with the Miller Index (15–16). Procedural anticoagulation was obtained with UFH under activated clotting time control (therapeutic range: 200–300 s.; in patients with absolute contraindications to anticoagulation, the target was 200 s).

The CAT 12 catheter was introduced over a preplaced 0.035" guidewire into the pulmonary arteries in the proximal thrombi, and aspiration was started to remove the thrombus. Optionally, the separator wire was applied to facilitate clot fragmentation. The CDMT procedure was terminated at the operator's discretion based on a careful assessment of the patient's hemodynamic status, residual thrombus load, and the total amount of aspirated blood

(typically below 350 ml). The postprocedural anticoagulation was managed with UFH or low molecular weight heparin (LMWH) in a weight-adjusted dose, and switching to oral anticoagulant was performed after 24–48 h, depending on the patient's clinical condition and comorbidities at the treating physician discretion.

Hemodynamic assessment

As per protocol, pre-procedural vital signs, including blood pressure (taken after administering vasopressors if necessary), heart rate (HR), respiratory rate (RR), and oxygen saturation, were measured 5 min after the patient was transferred to the hemodynamic table. Invasive hemodynamics were measured immediately before thrombectomy and again 5 min after the procedure completion, including mean right atrial pressure (mRAP), systolic, mean, and diastolic pulmonary arterial pressures (s/m/d PAPs), pulmonary arterial wedge pressure (PAWP), mixed venous oxygen saturation (SvO_2) and arterial oxygen saturation (SaO_2). Calculated hemodynamic variables included CO, cardiac index (CI), PVR, SVR, and PA pulsatility index (PAPI). The normotensive shock was defined as systolic blood pressure ≥ 90 mm Hg and CI ≤ 2.2 L/min/m^2 [1].

Study endpoints

The primary endpoint was defined as an in-hospital composite of PE-related mortality, bailout to an alternative clot debulking modality (including systemic thrombolysis, surgical embolectomy (SE), CDMT supplementation with CDF), clinical deterioration, and procedure-related major bleeding (defined as BARC type 3b or greater) [14]. The procedure or device-related adverse events were characterized as cardiac injury, cardiac tamponade, sustained ventricular rhythm disorders, PA injury, access-site pseudoaneurysm, arteriovenous fistula, peripheral ischemia, or nerve injury. Clinical deterioration was specified as hemodynamic or respiratory worsening meeting specific thresholds. Secondary safety outcomes were all-cause mortality during the index hospitalization or follow-up period and PE recurrence. Independent physician reviewers (not involved in the procedure) evaluated clinical safety outcomes.

The primary efficacy outcomes were the reduction of PAPs (sPAP and mPAP) and a change in the RV/LV ratio 48 h after the CDMT was assessed in echocardiography (using the four-chamber view) and/or CTPA (using the reformatted four-chamber view). The same modality was used for both measures in all cases, and an independent imaging specialist revised all measurements. CTPA was performed in accordance with the protocol in cases of a lack of an initial echocardiographic assessment, poor-quality images, or clinical indications for assessing the chest organs or pelvic veins, etc. Echocardiographic measurements of RV function and systolic pressure were collected using the standard practice at each site.

Secondary efficacy outcomes included the change in RV strain (change in the echocardiographic parameter TAPSE assessed 48 h after the CDMT and change in concentration of troponin I and terminal pro-brain natriuretic peptide [NT-proBNP]), reduction of HR, oxygen support (FiO_2), and symptom relief. All echo or CTPA images were of high quality for analysis.

Statistical analysis

Patient's characteristics are shown as absolute and percentage frequencies for categorical variables and as the mean with standard deviation (SD) for continuous variables that follow a normal distribution or median with interquartile range (IQR) for skewed distribution. The normality distribution was assessed with the Shapiro-Wilk test. A significance level was set at 0.05. The differences between the variables at baseline, after CDMT, and/or on discharge were analyzed using the paired Student's t-test, Wilcoxon signed-rank test, or Friedman Anova test, when appropriate. The post hoc pairwise Wilcoxon tests and Conover-Iman tests were applied. Multiple linear regression models were applied to evaluate associations between baseline characteristics and right-to-left ventricle ratio (RV/LV) reduction 48 h after the procedure. Statistical analysis was conducted using STATISTICA 13.7 software (TIBCO Software, Palo Alto, CA, US).

Results

Baseline patients' characteristics

A total of 150 (of all 500) IHR and HR PE patients were enrolled between June 2022 and June 2024. The median age was 68 years, and 45.3% were women. According to the current ESC guidelines, risk stratification designated 72% to have intermediate-high-risk (IHR) PE and 28% of patients to have high-risk (HR) PE. Importantly, 32.6% of patients were in normotensive shock. Among the study population, 33.3% had absolute contraindications to systemic thrombolysis, and 3.9% had contraindications to therapeutic anticoagulation. Systemic thrombolysis in the first line failed in 4% of patients. Most patients had at least comorbidity, and the median Charlson comorbidity index was 3 [IQR: 1–4].

High-sensitive (hs) troponin I and NT-proBNP were significantly elevated in the whole study group. The baseline median composite RV/LV ratio was 1.4 [IQR: 1.2–1.6], while the median tricuspid annular plane excursion (TAPSE) at presentation was 14 mm [IQR:11–16 mm]. Deep vein thrombosis coexisted in 66.7% of cases. Detailed patients' baseline characteristics are presented in Table 1.

Table 1 Baseline patients' characteristics

Characteristic	Baseline, *n* (%) or median [IQR], or mean ± SD
Demographics	
Female/ Male sex	68 (45.3) /82 (54.7)
Age, years	68 [52–76]
BMI, kg/m^2	28.7 [25.8–32.6]
Co-morbidities	
Arterial hypertension	74 (49.3)
Congestive heart failure	4 (2.7)
Diabetes mellitus	34 (22.6)
Concomitant deep vein thrombosis	100 (66.7)
Proximal	74 (49.3)
Distal	26 (17.3)
Coronary artery disease	8 (5.3)
Chronic obstructive pulmonary disease	8 (5.3)
Cerebrovascular accident	14 (9.3)
Ischemic stroke	11 (11.7)
Hemorrhagic stroke	3 (2)
COVID-19	2 (1.3)
Chronic kidney disease	19 (12.7)
Charlson Comorbidity Index	3 [1–4]
Risk factors for PE	
Obesity, BMI ≥ 30 kg/m^2	56 (37.3)
Overweight, 25 ≥ BMI < 30 kg/m^2	57 (38)
Malignancy	27 (18)
Surgery within last two weeks	26 (17.3)
Polytrauma	3 (2)
Immobilization	19 (12.7)
Thrombophilia	13 (8.7)
History of PE	30 (20)
Oral contraceptive	6 (4)
PE clinical presentation	
Syncope	21 (14)
Dyspnea at rest	144 (96)
Chest pain	15 (10)
Cardiac arrest	3 (2)
Hemoptysis	3 (2)
Symptoms duration, days	3 [1–4]
PE severity	
Intermediate-high risk	108 (72)
High risk	42 (28)
PESI score, points	111.5 [96.5–131]
PESI class	
PESI class	
I-II	14 (9.3)
III	29 (19.3)
IV	35 (23.3)
V	30 (20)
Normotensive shock, CI < 2.2 L/min/m^2	49 (32.6)
Vasopressor support at presentation	36 (24)
Obstructive shock on arrival refractory to catecholamine support	6 (4)
Systolic blood pressure, mmHg	121 ± 23.2
Diastolic blood pressure, mmHg	75.6 ± 9.7
Tachycardia on arrival	126 (84)
Heart rate, bpm	110 [97–120]
Tachypnoe on arrival	69 (46)
Respiratory rate, pm	26 [22–30]
Oxygen supplementation (to keep SaO_2 > 90%)	138 (92)
Arterial oxyhemoglobin saturation,	90.3 [88–95]
Arterial pO_2,	62.7 [55.8–80.8]
FiO_2	0.4 [0.32-1.0]
Oxygenation index (pO_2/FiO_2)	178.2 ± 82.3
Biomarkers	
hs Troponin I level, ng/ml (normal value < 0.005 ng/ml)	0.24 [0.07–0.65]
NT-proBNP level, pg/ml (normal value < 125 pg/ml)	3922 [1229–7623]
Lactate level, mmol/l (normal value < 2.2 mmo/l)	2.5 [2.0-3.3]
RV dysfunction	
RV/LV ratio, mm/mm (CTPA)	1.4 [1.2–1.6]
RV/LV ratio, mm/mm (echo)	1.3 [1.18–1.47]
RV/LV ratio, mm/mm (composite)	1.4 [1.2–1.6]
TAPSE, mm	14 [11–16]
TAPSE/sPAP, mm/mmHg	0.28 [0.22–0.34]
S' wave, cm/s	11 [9–13]
mRAP, mmHg	8.5 [5–11]
sPAP, mmHg	51.1 ± 14.2
Cardiac Output, L/min (echo)	4.8 [3.8–5.4]
Cardiac Output, L/min (Fick)	4.5 [3.7–5.4]
Failed therapy prior CDMT	
Systemic thrombolysis	6 (4)
Anticoagulation	103 (68.7)
Clinical deterioration during therapy	71 (47.3)
Lack of improvement	32 (21.3)
Absolute contraindication to thrombolysis	50 (33.3)
Absolute contraindication to therapeutic anticoagulation	6 (4)
Acute phase of hemorrhagic stroke	3 (2)
Active gastrointestinal bleeding	2 (1.3)
Active massive urinary tract bleeding	1 (0.7)

Composite used CTPA or echo measurements, prioritizing CTPA if both were available (follow-up CTPA was performed in 50 patients [33.3%]). BMI: body mass index; bpm: beats per minute; CDMT: catheter-directed mechanical thrombectomy; CI: cardiac index; CTPA: computed tomography pulmonary angiography; echo: echocardiogram; FiO_2: fraction of inspired oxygen; hs: high sensitive; mRAP: mean atrial pressure; NT-proBNP: N-terminal pro-brain natriuretic peptide; PE: pulmonary embolism; PESI: Pulmonary Embolism Severity Index; pO_2: partial pressure of oxygen; pm; per minute; RV/LV right-to-left ventricle ratio; SD: standard deviation; sPAP: systolic pulmonary artery pressure; TAPSE: tricuspid annular plane systolic excursion

Thrombectomy procedural characteristics

All patients had bilateral proximal emboli, with main PA involvement in 78 (52%) patients and lobar arteries occlusion in 72 (48%) patients. Most access sites

(98.7%) utilized the common femoral vein, whereas internal jugular vein access was utilized by only 1.3%. The median CDMT time (in-out) was 37.5 [IQR: 27–53] minutes, with the median estimated blood loss of 350 [IQR: 250–400] mL without the need for transfusion. Fourteen (9.3%) patients received adjunctive CDF due to unsatisfactory clot clearance and the need for CDMT completion due to high blood loss, and one patient (0.7%) needed escalation to rescue SE just after CDMT, and extracorporeal membrane oxygenation (ECMO) support was utilized in 3 (2%) patients. Two (1.3%) patients had CDMT performed on ECMO support, and one (0.7%) patient received ECMO support post-procedure. Six patients (4%) received a temporary inferior vena cava filter due to absolute contraindications to anticoagulation. The median time from parenteral anticoagulation initiation to CDMT was 1 [IQR: 0–7] days, whereas the median hospital stay after CDMT was 4 [IQR: 3–7] days. Most patients (72%) were discharged on direct oral anticoagulants, following LMWHs (15.3%), and vitamin K antagonists (6.7%). Details are presented in Table 2.

Table 2 Procedural characteristics and outcomes

Characteristic	*n* (%) or median [IQR]
Access site	148
Common femoral vein	(98.7)
Internal jugular vein	2 (1.3)
Access site complications	0
Major [&]	7 (4.7)
Minor	
Time from parenteral anticoagulation initiation to CDMT	1 [0–7]
PE location	150 (100)
Bilateral	78 (52)
Saddle and main arteries	72 (48)
Lobar	
Initial anticoagulant	40 (26.7)
Unfractionated heparin	110
Low-molecular-weight heparin	(73.3)
Thrombectomy time, min	37.5 [27–53]
Estimated blood loss, mL	350 [250–400]
Post-procedure vasopressor use	9 (6)
Post-procedure hospital stay, days	4 [3–7]
Periprocedural ECMO utilization	3 (2)
Conversion to open surgery	1 (0.67)
Supplementation with CDF	14 (9.3)
Vena cava filter implantation	6 (4)
Anticoagulation at discharge	106
Direct oral anticoagulant	(70.7)
Vitamin K antagonist	10 (6.7)
Low-molecular-weight heparin	23 (15.3)
None	3 (2)

CDMT: catheter-directed mechanical thrombectomy; CDF: catheter-directed fibrinolysis; ECMO: extracorporeal membrane oxygenation

Immediate post-thrombectomy hemodynamic outcomes

The was an early improvement of hemodynamic parameters after the CDMT procedure with a significant reduction of sPAP from 51.1±14.2 mmHg to 40.4±12.2 mmHg (-11.3±10 mmHg [22.1%] mean change, $p<0.0001$) and mPAP from 30.1±8.3 mmHg to 23.6 ±7.3 mmHg (-7.8±7.1 mmHg [35.9%] mean change, $p<0.0001$). Cardiac Index increased significantly from 2.2 [IQR:2.0-2.6] L/min/m^2 to 2.4 [IQR:2.0–3.0] L/min/m^2 (0.3 [IQR:0.04–0.5] L/min/m2 median change [15%]; $p<0.0001$). Immediately after thrombectomy, the PVR decreased from 4.8 ± 2.4 Wood Units to 2.9 ± 2.1 (–2.7 ± 2.0 Wood Units mean change [–58.3%]; $p<0.0001$). There were no significant differences in hemodynamic parameters improvement for patients with HR PE and IHR PE. Hemodynamic outcomes are presented in Fig. 1.

Right ventricular function and clinical outcomes

The median composite RV/LV ratio dropped from 1.4 [IQR:1.2–1.6] to 1.0 [IQR:0.85–1.2] (The median echocardiographic RV/LV ratio decreased from baseline 1.31 [IQR:1.18–1.47] to 0.98 48-h post-procedure (median change 25.2%) and then to 0.86 [IQR:0.73-1.0] (median change 12.5%) at the discharge ($p<0.0001$). TAPSE/sPAP values also significantly increased from baseline 0.28 [IQR:0.22–0.34] to 0.47 [IQR:0.38–0.63] at 48-h post-procedure (median change 67.9%) and up to 0.6 [IQR:0.49–0.74] at the discharge (median change 27.7%), ($p<0.0001$). Notably, RV strain markers levels reduced significantly, hs troponin I dropped from baseline 0.21 [IQR:0.07–0.46] to 0.16 [IQR:0.06–0.32] 48-h post-CDMT (median change 23.8%), and then to 0.05 [IQR:0.02–0.09] at the discharge (median change 68.8%), ($p<0.0001$). There was also a significant drop in NT-proBNP and lactate levels 48-h post-CDMT and then at the discharge. Moreover, there was a significant oxygen requirement (FiO_2) reduction from baseline 0.4 [IQR:0.32-1.0] to 0.25 [IQR:0.21–0.36] 48-h post-procedure (median change 37.5%), and then to 0.21 [IQR:0.21–0.21] at the discharge (median change 16%), ($p<0.0001$). Details are displayed in Table 3. No significant differences were between patients with HR PE and IHR PE. None of the patients showed echocardiographic signs of moderate or severe RV dysfunction, while seven patients (4.7%) exhibited only mild RV dysfunction at discharge. In the 90-day follow-up echocardiogram, 3 patients (2.0%) exhibited mild RV dysfunction, while the remaining patients showed normal RV function.

Safety outcomes

There were 3 (2%) procedure-related deaths, 2 (1.3%) caused by RV failure decompensation, and 1 (0.7%) caused by pulmonary infarction and reperfusion injury

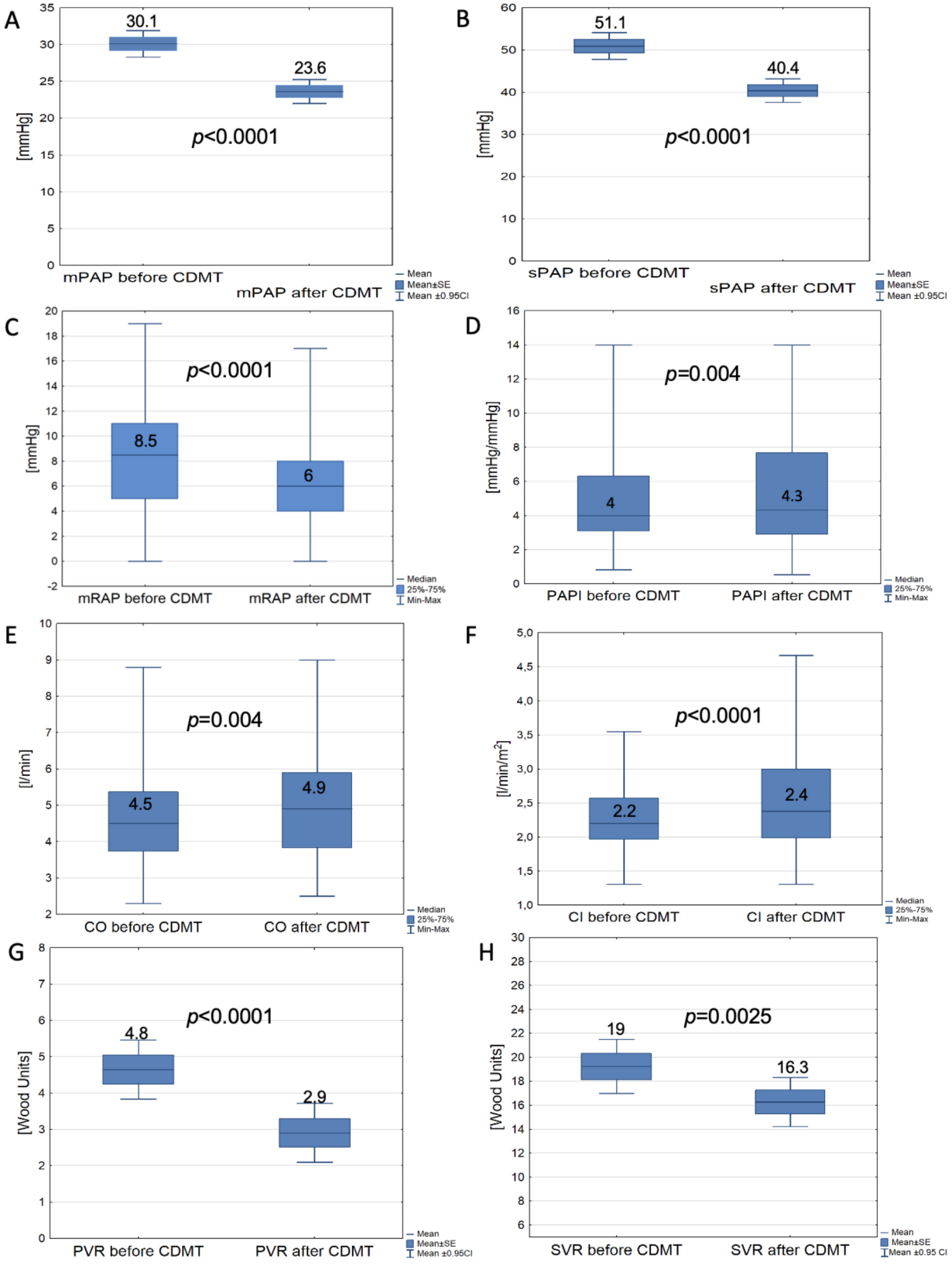


Fig. 1 Key hemodynamic outcomes. [#]Values are expressed as mean ± SD, or median [IQR]. CDMT: catheter-directed mechanical thrombectomy; CI: cardiac index; CO: cardiac output; mPAP: mean pulmonary artery pressure; mRAP: mean right atrial pressure; PAPI: pulmonary artery pulsatility index; PVR: pulmonary vascular resistance; sPAP: systolic pulmonary artery pressure; SVR: systemic vascular resistance

Table 3 Right ventricular function and clinical outcomes

	Initial mean ± SD or median [IQR]	48 h after CDMT mean ± SD or median [IQR]	At discharge mean ± SD or median [IQR]	*p* value
RV/LV ratio (echo)	1.31 (1.18–1.47) *	0.98 (0.85–1.11) *^	0.86 (0.73-1.0) *^	< 0.0001
TAPSE	14 (11–16) *	19 (17–22) *^	21 (19–24) *^	< 0.0001
TAPSE/sPAP, mm/mmHg	0.28 (0.22–0.34) *	0.47 (0.38–0.63) *^	0.6 (0.49–0.74) *^	< 0.0001
sPAP, mmHg[&]	50 (44–60) *	38.3 (30–50) *^	35 (30–43) *^	< 0.0001
Heart rate, bpm	110 (97–120) *	89 (80–95) *^	80.5 (78–88) *^	< 0.0001
Systolic blood pressure, mmHg	121±23.2	122±14.9	128±11	0.12
Diastolic blood pressure, mmHg	78.3±16.5	76.5±10.9	75.6±9.7	0.57
Arterial pO_2, mmHg	63 (56–83) *	71.4 (62–89) *^	75.4 (66–93) *^	< 0.0001
FiO_2	0.4 (0.32-1.0) *	0.25 (0.21–0.36) *^	0.21 (0.21–0.21) *^	< 0.0001
hs Troponin I, ng/ml	0.21 (0.07–0.46) *	0.16 (0.06–0.32) ^	0.05 (0.02–0.09) *^	< 0.0001
NT-proBNP, pg/ml	3922 (1229–7623) *	1702 (569–4142) *^	742 (281–1519) *^	< 0.0001
Lactate, mmol/l	2.5 (2-3.2) *	1.6 (1.1–1.9) *^	1.4 (1.1.-2.0) *^	< 0.0001
Hemoglobin concentration, mmol/l	7.9 (6.9–8.8) *	7.2 (6.3–7.7) *	7.4 (6.5–7.8) *	< 0.0001

*- significant differences in baseline value

^- significant differences to 48-h post thrombectomy

&- echocardiographic estimation

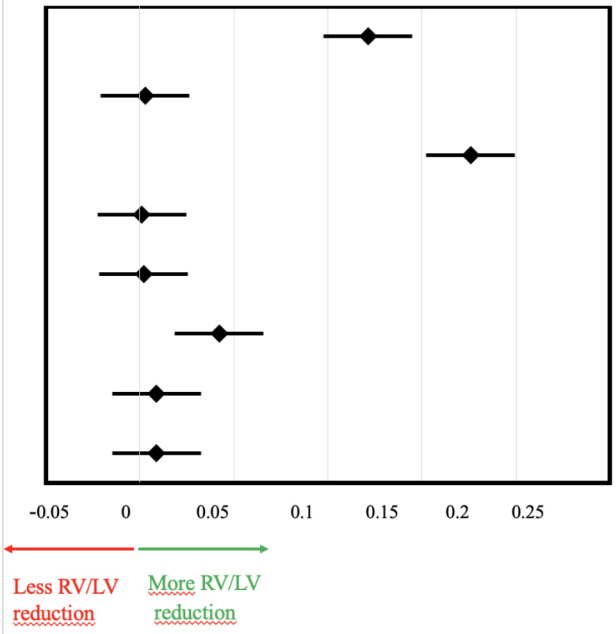
CDMT: catheter-directed mechanical thrombectomy; FiO_2: fraction of inspired oxygen; hs: high sensitive; NT-proBNP: N-terminal pro-brain natriuretic peptide; pO_2: partial pressure of oxygen; pm; per minute; RV/LV right-to-left ventricle ratio; sPAP: systolic pulmonary artery pressure; TAPSE: tricuspid annular plane systolic excursion

with massive intraprocedural interstitial bleeding, confirmed by pathological examination. Four (2.7%) patients deteriorated during the thrombectomy due to the progression of RV and respiratory failure, and 1 (0.7%) of them had a sudden cardiac arrest in the catheterization suite with successful cardiopulmonary resuscitation. One (0.7%) patient needed conversion to open surgery due to unsuccessful percutaneous massive saddle embolism debulking. One (0.7%) patient deteriorated within 48 h after CDMT due to recurrent PE and received bailout ST and ECMO support. One patient (0.7%) had a hemorrhagic transformation of ischemic stroke immediately after CDMT despite therapeutic ranges (220–260 s) of activated clotting time during the procedure. There were no major access site complications. One patient (0.7%) with a history of pacemaker implantation one week before HR PE occurrence and failed ST as a first-line therapy developed significant pocket hematoma requiring a transfusion of four red blood cell packs within 48 h post-intervention. One patient (0.7%) developed atrial fibrillation during the CDMT treated with the intravenous bolus and subsequent infusion of amiodarone. In contrast, the other 4 (2.7%) patients had episodes of atrial fibrillation within the first 48 h post-thrombectomy and were also treated with intravenous amiodarone infusion. Of note, 19 (12.7%) developed pneumonia or sepsis secondary to pneumonia during hospital stay. There were no all-cause readmissions within 30 days or 90 days, and no additional complications occurred. Details are presented in Table 4.

Table 4 Safety and mortality outcomes

Safety outcomes	*N*, (%)
Major bleeding during procedure	1 (0.67)
Pulmonary artery injury during procedure	0 (0)
Cardiac tamponade during procedure	0 (0)
Clinical deterioration during the procedure	4 (2.7)
Cardiac arrest during the procedure with successful CPR	1 (0.7)
PE-related death during the procedure	3 (2)
Conversion to open surgery	1 (0.7)
Sustained ventricular tachycardia during the procedure	0 (0)
Sustained supraventricular tachycardia during the procedure	1 (0.67)
Procedure-related death	3 (2)
Major bleeding within 48 h post procedure	2 (1.3)
Hemorrhagic stroke	1 (0.7)
Pulmonary artery injury within 48 h post procedure	0 (0)
Cardiac tamponade within 48 h post procedure	0 (0)
Clinical deterioration within 48 h post procedure	1 (0.7)
PE-related death within 48 h post procedure	0 (0)
All-cause death within 48 h post procedure	0 (0)
Infection (pneumonia/sepsis)	19 (12.7)
Stroke (ischemic/hemorrhagic)	0/1 (0/0.7)
Sustained ventricular tachycardia within 48 h post procedure	0 (0)
Sustained supraventricular tachycardia within 48 h post procedure	4 (2.7)
PE- related mortality within 30 days post procedure	0 (0)
All-cause mortality within 30 days post-procedure	0 (0)
Major bleeding within 30 days post procedure	0 (0)
PE recurrence	0 (0)
PE- related mortality within 90 days post procedure	0 (0)
All-cause mortality within 90 days post procedure	0 (0)
PE recurrence	0 (0)
Major bleeding within 90 days post procedure	0 (0)

PE: pulmonary embolism



Variable	Effect estimate	95% CI	P value
baseline RV/LV (per 0.1 mm/mm)	0.12	(-0.4– 0.12)	0.27
baseline sPAP (per 1 mmHg)	0.003	(-0.003-0.01)	0.29
delta sPAP (per 1 mmHg)	0.18	(0.55-1.32)	<0.0001*
delta NT-proBNP level (per 100 pg/mL)	0.001	(-0.002–0.003)	0.59
delta heart rate (per 1 bpm)	0.002	(-0.005–0.003)	0.59
delta hs Troponin I level (per 0.01 ng/mL)	0.042	(-0.05–0.14)	0.29
delta FiO_2 (per 0.1)	0.009	(-0.02–0.017)	0.83
delta TAPSE (per 1 mm)	0.01	(-0.015–0.023)	0.69

Fig. 2 Multiple linear regression model of absolute reduction in RV/LV ratio. # Composite used CTPA or echo measurements, prioritizing CTPA if both were available. * statistically significant. FiO_2: fraction of inspired oxygen; hs: high sensitive; NT-proBNP: N-terminal pro-brain natriuretic peptide; RV/LV right-to-left ventricle ratio; sPAP: systolic pulmonary artery pressure; TAPSE: tricuspid annular plane systolic excursion

Factors associated with post-thrombectomy RV/LV ratio reduction

Multiple linear regression model application indicated that only a higher reduction of sPAP immediately after thrombectomy was associated with a greater improvement in RV/LV ratio 48 h post-procedure ($P<0.0001$) with a multivariable model adjusted R^2 of 0.71 (see Fig. 2).

Discussion

This is the first prospective multicenter study reporting the outcomes of the next-generation CDMT with a Lightning 12 system performed in Europe. Our study showed that percutaneous thrombectomy with the Lightning 12 catheter resulted in a substantial debulking of thromboembolic pulmonary vascular bed obstruction and significant functional and hemodynamic improvement in patients with PE with relatively low periprocedural risk.

RV failure and hemodynamic instability due to acute RV pressure overload are powerful predictors of poor prognosis in advanced PE [11, 17]. Increased RV/LV ratio assessed by imaging studies (echo or CTPA) is a simply renowned prognostic indicator of early mortality in PE, which depends less on imaging quality or the physician's experience [18]. RV failure and hemodynamic instability caused by acute RV pressure overload are strong predictors of poor prognosis in advanced PE. An increased RV/LV ratio assessed through imaging studies (echo or CTPA) serves as a widely recognized prognostic indicator of early mortality in PE, relying less on imaging quality or the physician's experience. Consequently, a reduction in the RV/LV ratio indicates early improvement in RV function and significantly serves as a marker of therapeutic effectiveness in trials and studies (7–8, 16–17, 19, 20, 21).

The median reduction of echocardiographic RV/LV ratio during the first 48 h post-thrombectomy was 0.33 (25.2%), and then up to discharge, there was a further RV/LV reduction of 0.12 (12.5%), while the CT-based RV/LV 48-hour change was 0.4. Our results are in line with the previous studies assessing the efficacy of different catheter-based therapies, which showed a mean RV/LV ratio drop from 0.25 to 0.56 (7–8, 10, 17, 19, 21). In the EXTRACT-PE study assessing the previous generation of the 8 F Indigo catheter (Penumbra Inc, Alameda, CA, US), the 48-hour mean reduction of RV/LV diameter ratio was 0.43 [7]. Our previous study with the same 8 F catheter showed a mean RV/LV change of 0.48 at 48 h post-procedure [21]. In the largest registry evaluating the large-bore device FlowTriever system (FLASH registry), the mean RV/LV ratio drop was 0.25 [8]. The ultrasound-assisted catheter-directed thrombolysis (USAT) with EkoSonic System (EKOS, Boston Scientific,

Marlborough, US) led to RV/LV ratio change from 0.3 to 0.46 [19, 22–24]. The results of the RESCUE study with Bashir catheter application for pharmacomechanical thrombectomy showed a 0.56 reduction in RV/LV ratio [25]. Initial data on the effectiveness of mechanical-electric thrombectomy with Magneto 20 F device demonstrated a mean RV/LV change of 0.45 [10].

As mentioned above, an increased RV/LV ratio has been independently associated with 30-day mortality; therefore, identifying factors associated with a reduction of RV dilation may guide better outcomes. We found none of the baseline parameters of PE severity to be associated with the RV/LV reduction within the first 48 h. Notably, even the baseline RV/LV ratio did not correlate with the degree of improvement. Similar results were obtained in the FLASH registry [8]. Importantly, when evaluating the change in the main PE severity markers only immediate sPAP reduction significantly correlated with RV/LV ratio change. Prior analyses of CDF also proved similar correlations [19].

The present study demonstrated an immediate improvement in hemodynamic parameters, including a significant decrease in PA and RA pressures, an increase in CI, and a substantial drop in PVR. The mean on-table drop in sPAP (-11.3 mmHg) was comparable with those in the FLASH registry (-12.8 mmHg) and our real-world data with previous generation Indigo 8 F catheter (-10.4 mmHg), but favorable than the EXTRACT-PE Indigo 8 F approval study results (only −4.3 mmHg) (7–8, 21). The mean reduction of mPAP (-7.8 mmHg) was also comparable with previous reports [8, 21]. Direct comparisons with studies assessing CDF are pointless because these treatment modalities need more time to reduce clot load, contrary to CDMT with fast clot removal.

The increasing applicability of CDMT is based on the growing studies indicating the potential reduction of PE-related mortality [8, 26]. The all-cause mortality in our study population was 2% at 48-hour follow-up, without more deaths at 30-day day follow-up. The reported all-cause mortality in other studies on CDMT devices ranged from 0.8 to 5.5% [7, 8, 17, 21]. This is significantly lower than the recently reported 13.6–28.3% at 30 days despite ST, catheter-directed thrombolysis, or surgical embolectomy [27]. The FLAME study focused on outcomes in high-risk PE treated with a large-bore thrombectomy and other contemporary therapies (ST, anticoagulation) and showed only 1.9% in-hospital mortality in the CDMT arm, while 29.5% in the context arm [26]. The low mortality of patients treated with percutaneous thrombectomy seems to be related to the rapid effect of clot debulking, which promptly reverses RV strain and might shift the risk-benefit estimation towards intervention for PE management.

Concerning safety, in our cohort, serious bleeds occurred in 1.3% within the first 48 h post-thrombectomy in two elderly patients with HR PE. Our results are in line with the studies assessing the safety of the previous generation 8 F catheter with a 1.7–1.8% serious bleeding rate [7, 21]. The safety profile of large-bore CDMT was comparable to our results with a 1.4% major bleeding rate despite FlowSaver blood return use [8]. On the other hand, the catheter can be advanced through the clot multiple times, permitting more extensive removal, whereas the smaller caliber and flexibility improve maneuverability and access more distal clots, compared to the larger profile of the FlowTriever system [11, 13]. In the studies on the safety of CDF (total dose of alteplase ≤ 20 mg), the overall major bleeding rate was also low ranging from 0 to 4.0% [16, 23, 25, 28].

Importantly, our study population was older (median age 68 years) than the patient populations included in previous CDMT registries and the major bleeding occurred in patients ≥ 75 years old, in whom the probability of bleeding outcomes is expected to be higher up to 9% (1, 7–8, 11, 29). Notably, age > 75 years old is often mentioned as a relative contraindication for ST due to the high extracranial bleeding risk [30]. However, patients with advanced age and frailty have also increased surgical risk [29]. Therefore, these patients require alternative reperfusion strategies.

The median procedure blood loss was 350 mL and decreased with the operators' experience. The amount of aspirated blood must be closely monitored to avoid excessive acute blood loss during the procedure because the system cannot recycle aspirated blood, contrary to the FlowSaver blood return system utilized in large-bore CDMT with FlowTriever [8]. Lightning 12 is an intelligent computer-assisted vacuum aspiration system that includes innovative mechanisms with auditory and visual feedback from the control unit, regulates aspiration and enables aspiration of larger clots as compared to the previous generation device [7, 13, 21]. Furthermore, the next-generation highly torqueable Lightning Flash 16 system (Penumbra Inc, Alameda, CA, US) with dual clot detection algorithms and no necessity for separator use has been available in the US market since 2023. The ongoing multicenter STRIKE-PE study results will demonstrate whether Lightning technology ultimately improves PE patients' short- and long-term clinical outcomes [31]. Also, the ongoing randomized clinical trials (PEERLESS II, STORM _PE, HI-PEITHO, PE-TRACT), the results of which we are awaiting, will provide an answer about the effectiveness of different types of transcatheter therapies for PE treatment and may and may inform future guideline recommendations [20].

Limitations

Several limitations need to be addressed. First, our study has an observational character, which may also be considered a strong point and reflects the real-life nature of our cohort. Second, our patient population was relatively small and heterogeneous. Third, this was a single-arm study without a comparative arm with any other interventional modalities or a matched control group on anticoagulation alone that did not undergo intervention which would allow an evaluation of mortality outcomes with conservative therapies. Fourth, treatment indications were quite heterogeneous, as the local PERT made decisions to perform the CDMT. Fifth, a detailed treatment protocol was not established. As a result, thrombectomy procedures and lab testing were not standardized. Despite the limited number of study patients, we believe that the consistency of the results validates our observations and helps to improve the understanding of the role of CDMT in IHR and HR PE management. Doubtless, future studies would have to identify, among IHR PE patients, the subgroup of patients with a higher risk of deterioration who most likely benefit from urgent catheter-based therapy.

Conclusions

In our real-world multicentre observational registry of patients treated with the Lightning 12 system, we observed substantial improvements in RV strain and pulmonary hemodynamics with low observed major bleeding and early mortality rates. Currently, societies have no consensus about the optimal time and method for catheter-based therapy of PE. Future prospective studies and randomized trials are needed to evaluate different catheter-directed and pharmacological approaches in advanced forms of PE.

Abbreviations

CDMT	Catheter-directed mechanical thrombectomy
IHR	Intermediate-high risk
HR	High risk
PAP	Pulmonary arterial pressure
IL	Individualistic Learning
PE	Pulmonary embolism
PRISMA	Prepared Items for Systematic Reviews and Meta-Analysis
RV/LV	Right-to-left ventricle ratio

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Author contributions

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the bioethics committee of the coordinating center (Poznan University of Medical Sciences Bioethics Committee; approval number 271/2021). The study was also registered at ClinicalTrials.gov (NCT04879069). All patients signed informed consent.

Consent for publication

The authors affirm that human research participants provided informed consent for the anonymized data publication.

Competing interests

The authors declare no competing interests.

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References

1. Bangalore S, Horowitz JM, Beam D, Jaber WA, Khandhar S, Toma C, Weinberg MD, Mina B. Prevalence and predictors of cardiogenic shock in Intermediate-Risk pulmonary embolism: insights from the FLASH registry. JACC Cardiovasc Interv. 2023;16:958–72.
2. Pruszczyk P, Klok FA, Kucher N, et al. Percutaneous treatment options for acute pulmonary embolism: a clinical consensus statement by the ESC working group on pulmonary circulation and right ventricular function and the European association of percutaneous cardiovascular interventions. EuroIntervention. 2022;18:e623–38.
3. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European respiratory society (ERS). Eur Heart J. 2020;41:543–603.
4. Lauder L, Pérez Navarro P, Götzinger F, Ewen S, Al Ghorani H, Haring B, et al. Mechanical thrombectomy in intermediate- and high-risk acute pulmonary embolism: hemodynamic outcomes at three months. Respir Res. 2023;24(1):257.
5. Kopeć G, Araszkiewicz A, Kurzyna M, et al. Role of catheter-directed therapies in the treatment of acute pulmonary embolism. Expert opinion of the Polish PERT initiative, working group on pulmonary circulation, association of cardiovascular interventions, and association of intensive cardiac care of the Polish cardiac society. Kardiol Pol. 2023;81:423–40.
6. Araszkiewicz A, Sławek-Szmyt S, Jankiewicz S, et al. Continuous aspiration thrombectomy in High- and Intermediate-High-Risk pulmonary embolism in Real-World clinical practice. J Interv Cardiol. 2020;2020:4191079.

7. Sista AK, Horowitz JM, Tapson VF, et al. Indigo aspiration system for treatment of pulmonary embolism: results of the EXTRACT-PE trial. JACC Cardiovasc Interv. 2021;14:319–29.
8. Toma C, Jaber WA, Weinberg MD, et al. Acute outcomes for the full US cohort of the FLASH mechanical thrombectomy registry in pulmonary embolism. EuroIntervention. 2022;18:1201–12.
9. Pasha AK, Siddiqui MU, Siddiqui MD. et. Catheter directed compared to systemically delivered thrombolysis for pulmonary embolism: a systematic review and meta-analysis. J Thromb Thrombolysis. 2022;53:454–66.
10. Andersen A, Musialek P, Araszkiewicz A, et al. First-in-Human trial of Mechanical-Electric thrombectomy in acute pulmonary embolism. JACC Cardiovasc Interv. 2023;16:623–25.
11. Finocchiaro S, Mauro MS, Rochira C, et al. Percutaneous interventions for pulmonary embolism. EuroIntervention. 2024;20:e408–24.
12. Sławek-Szmyt S, Jankiewicz S, Smukowska-Gorynia A, et al. Implementation of a regional multidisciplinary pulmonary embolism response team: PERT-POZ initial 1-year experience. Kardiol Pol. 2020;78:300–10.
13. Araszkiewicz A, Sławek-Szmyt S, Jankiewicz S, Grygier M, Lesiak M. Lightning 12 - an intelligent computer-assisted vacuum aspiration thrombectomy system in the treatment of pulmonary embolism: an initial experience. Kardiol Pol. 2024;82:543–46.
14. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research consortium. Circulation. 2011;123:2736–47.
15. Miller GA, Sutton GC, Kerr IH, Gibson RV, Honey M. Comparison of streptokinase and heparin in treatment of isolated acute massive pulmonary embolism. Br Med J. 1971;2:681–84.
16. Sławek-Szmyt S, Araszkiewicz A, Jankiewicz S, Grygier M, Mularek-Kubzdela T, Lesiak M. Outcomes with hybrid Catheter-Directed therapy compared with aspiration thrombectomy for patients with Intermediate-High risk pulmonary embolism. Cardiovasc Drugs Ther. 2024. https://doi.org/10.1007/s10557-024-07562-4.
17. Tu T, Toma C, Tapson VF, et al. A prospective, Single-Arm, multicenter trial of Catheter-Directed mechanical thrombectomy for Intermediate-Risk acute pulmonary embolism: the FLARE study. JACC Cardiovasc Interv. 2019;12:859–69.
18. Meinel FG, Nance JW Jr, Schoepf UJ, et al. Predictive value of computed tomography in acute pulmonary embolism: systematic review and meta-analysis. Am J Med. 2015;128:747–59.
19. Piazza G, Hohlfelder B, Jaff MR, et al. A prospective, Single-Arm, multicenter trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose fibrinolysis for acute massive and submassive pulmonary embolism: the SEATTLE II study. JACC Cardiovasc Interv. 2015;8:1382–92.
20. Klok FA, Piazza G, Sharp ASP, et al. Ultrasound-facilitated, catheter-directed thrombolysis vs anticoagulation alone for acute intermediate-high-risk pulmonary embolism: rationale and design of the HI-PEITHO study. Am Heart J. 2022;251:43–53.
21. Sławek-Szmyt S, Stępniewski J, Kurzyna M, et al. Catheter-directed mechanical aspiration thrombectomy in a real-world pulmonary embolism population: a multicenter registry. Eur Heart J Acute Cardiovasc Care. 2023;12:584–93.
22. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014;129:479–86.
23. Tapson VF, Sterling K, Jones N, et al. A randomized trial of the optimum duration of acoustic pulse thrombolysis procedure in acute Intermediate-Risk pulmonary embolism: the OPTALYSE PE trial. JACC Cardiovasc Interv. 2018;11:1401–10.
24. Avgerinos ED, Jaber W, Lacomis J, et al. Randomized trial comparing standard versus Ultrasound-Assisted thrombolysis for submassive pulmonary embolism: the SUNSET sPE trial. JACC Cardiovasc Interv. 2021;14:1364–73.
25. Bashir R, Foster M, Iskander A, et al. Pharmacomechanical catheter-Directed thrombolysis with the Bashir endovascular catheter for acute pulmonary embolism: the RESCUE study. JACC Cardiovasc Interv. 2022;15:2427–36.
26. Silver MJ, Gibson CM, Giri J, et al. Outcomes in High-Risk pulmonary embolism patients undergoing flowtriever mechanical thrombectomy or other contemporary therapies: results from the FLAME study. Circ Cardiovasc Interv. 2023;16:e013406.
27. Silver M, Giri J, Duffy A, et al. Incidence of mortality and complications in high-risk pulmonary embolism: a systematic review and meta-analysis. JSCAI. 2023;2:100548.
28. Sadeghipour P, Jenab Y, Moosavi J, et al. Catheter-Directed thrombolysis vs anticoagulation in patients with acute Intermediate-High-risk pulmonary embolism: the CANARY randomized clinical trial. JAMA Cardiol. 2022;7:1189–97.
29. Farmakis IT, Barco S, Giannakoulas G, et al. A nationwide analysis of reperfusion therapies for pulmonary embolism in older patients with frailty. EuroIntervention. 2023;19:772–81.
30. Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med. 2014;370:1402–11.
31. Moriarty JM, Dohad SY, Schiro BJ et al. Clinical, functional, and quality of life outcomes after computer assisted vacuum thrombectomy for pulmonary embolism: interim analysis of the STRIKE-PE study. J Vasc Interv Radiol. 2024: S1051-0443(24)00335-X.

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