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CONTENTS

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Letters to the Editor

Research letters

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Clinical Research

Catheter-directed versus standard therapy in intermediate–high-risk pulmonary embolism: A retrospective cohort study

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ABSTRACT

Background: Interventional techniques for managing acute-phase pulmonary embolism (PE) are under investigation, but their efficacy compared with anticoagulant alone remains uncertain.
Aim: To assess the efficacy and safety of catheter-directed interventions (CDI) compared with standard anticoagulation management in patients with intermediate–high-risk pulmonary embolism.
Methods: We conducted a large-scale, retrospective, multicentre cohort study of patients hospitalized with intermediate–high-risk PE between 2017 and 2024 in three intensive care units (ICU) and two cardiac ICUs. Patients were stratified based on the use of CDI versus standard anticoagulation. Data on demographics, clinical characteristics and outcomes were collected and analysed.
Results: Among 1637 patients admitted for PE, 549 met the inclusion criteria. Of these, 258 patients (47%) received CDI, including 213 (83%) undergoing catheter-directed thrombolysis and 45 (17%) underwent thromboaspiration. The primary composite outcome of in-hospital mortality or systemic thrombolysis was significantly lower in the CDI group versus the standard-treatment group (3.1% vs. 7.2%; $P = 0.031$); multivariable analysis demonstrated a 65% risk reduction (adjusted odds ratio 0.35, 95% confidence interval 0.14–0.80). Minor bleeding events were more frequent with CDI whereas major bleeding complications were similar between groups. Echocardiographic evaluations showed no significant differences in the incidence of pulmonary hypertension, but demonstrated a significant reduction in early and late systolic pulmonary artery pressure in the CDI group.
Conclusion: CDI appears to provide potential benefits in the management of intermediate–high-risk PE, including a reduction in the composite outcome of in-hospital mortality or systemic thrombolysis.

1. Abbreviations

BARC	Bleeding Academic Research Consortium
CDI	Catheter-directed intervention
ESC	European Society of Cardiology

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ICU	Intensive care unit
IPTW	Inverse probability of treatment weighting
LV	Left ventricle
PE	Pulmonary embolism
PH	Pulmonary hypertension
RV	Right ventricle
sPAP	Systolic pulmonary artery pressure
sPESI	Simplified Pulmonary Embolism Severity Index

2. Background

Pulmonary embolism (PE) is a prevalent and serious condition affecting between 39 and 115 individuals per 100,000 per year in Europe [1–6]. In the absence of haemodynamic instability, risk stratification for PE is guided by the Simplified Pulmonary Embolism Severity Index (sPESI) score, which differentiates low-risk from intermediate-risk PE [7]. Intermediate-risk PE encompasses a broad spectrum, with significant heterogeneity that greatly affects prognosis [8–10]. Intermediate–high-risk PE, characterized by echocardiographic or imaging evidence of right ventricular (RV) dilatation and elevated blood troponin levels, requires hospitalization in an intensive care unit (ICU) [7]. A large-scale randomized controlled trial has established the role of thrombolysis in this situation, recommending it only for patients who exhibit haemodynamic deterioration despite anticoagulation [11]. Standard treatment involves the initiation of therapeutic anticoagulation, typically with unfractionated heparin or low-molecular-weight heparin. Despite early initiation of anticoagulation, the risk of haemodynamic deterioration, which may lead to the need for systemic thrombolysis or result in death, remains significant, with mortality rates ranging from 3% to 7% [12–14].

In this context, several interventional techniques are being investigated for managing high-intermediate-risk PE. These techniques, known as catheter-directed interventions (CDI), primarily include catheter-directed thrombectomy or thromboaspiration and catheter-directed thrombolysis. The role of CDI in managing intermediate–high-risk PE is not well-defined. Only a limited number of studies have evaluated these techniques, most of which were prospective cohort studies or randomized controlled trials with small sample sizes [15–19]. Although CDI appear to be beneficial in terms of imaging parameters, few studies have evaluated their effect on strong clinical criteria. Furthermore, comparisons of these techniques with a control group receiving anticoagulation alone are still needed [18,20–22].

This large-scale, comprehensive, retrospective cohort study aimed to compare catheter-directed management (thrombolysis or thromboaspiration) associated with curative anticoagulation with standard management (curative anticoagulation alone) in patients with intermediate–high-risk PE. Our primary hypothesis was that CDI reduces the incidence of in-hospital mortality and the need for systemic thrombolysis without increasing the incidence of major complications. Additionally, we hypothesized that interventional management improves clinical parameters at 48 hours post-ICU admission and reduces the incidence of pulmonary hypertension (PH) during follow-up.

3. Methods

3.1. Study design and patient population

This retrospective cohort study was conducted at Marseille University Hospitals, which include three ICU and two cardiac ICU. We identified all patients hospitalized in these units between January 2017 and April 2024 with a primary or secondary diagnosis of PE according to French CMI-10 codes I26.0 or I26.9. Subsequently, an experienced physician thoroughly reviewed each patient's medical records to specifically assess the inclusion and exclusion criteria and collected the data if the study criteria were met. Patient presenting characteristics of intermediate–high-risk PE according to the 2019 European Society of Cardiology (ESC) recommendations [7] diagnosed via thoracic computed tomography were included. We then excluded patients presenting any of the following criteria: age < 18 years or legal incapacitation, participation in another clinical trial, presentation with high-risk PE criteria upon admission (haemodynamic instability defined by cardiac arrest, obstructive shock or persistent hypotension) or who received systemic thrombolysis < 12 hours after admission for intermediate–high-risk PE, contraindications to interventional techniques or systemic thrombolysis as described in 2019 ESC recommendations (including limitation of life-sustaining treatment), cardiogenic shock with associated pulmonary embolism, septic PE due to infective endocarditis or known chronic PH.

3.2. Reperfusion strategy and anticoagulation

Patients received intravenous or oral anticoagulation according to the 2019 ESC guidelines [7]. For patients undergoing CDI, the choice and duration of technique was left to the discretion of the clinician and interventions were performed by an experienced operator. For catheter-directed thrombolysis, the EKOS® Endovascular System (Boston Scientific, Marlborough, MA, USA) was left in one or two pulmonary arteries for 6–24 h, depending on clinical judgment, with standardized delivery of in-situ thrombolysis at 1 mg/h. For patients receiving thromboaspiration, the single-use FlowTriever Retrieval/Aspiration System (Inari® Medical, Irvine, CA, USA) was used.

3.3. Data collection

Upon ICU admission, we collected demographic data (including age, sex, period of admission), medical history data (risk factors for venous thromboembolic: history of cancer or venous thromboembolism and trauma or surgery in previous month, chronic pulmonary disease, coronary disease, diabetes and antithrombotic treatment), clinical data for sPESI calculation (e.g. haemodynamic and respiratory parameters), echocardiographic data (including left ventricular ejection fraction, RV dilatation, presence of flattened septum) and laboratory data (N-terminal pro-B-type natriuretic peptide, troponin and creatinine). At day two after ICU admission, we collected haemodynamic and respiratory parameters.

3.4. Outcomes

3.4.1. Primary outcome

The primary outcome variable was a composite measure of in-hospital death or the use of systemic thrombolysis.

3.4.2. Clinical secondary outcomes

We compared patients' clinical characteristics at 48 h, including respiratory and haemodynamic parameters. We also studied overall and ICU length of stay, and the occurrence of pulmonary infarction. Diagnosis of pulmonary infarction was established by the clinician, essentially by the presence of pulmonary consolidation on diagnostic computed tomography scan or chest X-ray during hospitalization, associated with fever and/or elevated inflammatory markers.

3.4.3. Safety outcomes

Bleeding complications were reported using the Bleeding Academic Research Consortium (BARC) classification. Major haemorrhage was defined as a decrease in haemoglobin of 3–5 g/dL or any transfusion (type 3a), bleeding requiring surgical intervention

or intravenous vasoactive drugs (type 3b), intracerebral bleeding (type 3c) or fatal bleeding (type 5). Minor haemorrhage was defined as BARC type 1 or 2.

3.4.4. Echocardiographic secondary outcomes

Follow-up echocardiographic evaluation was performed using transthoracic examination at our institution between 1 and 12 months after the PE episode, according to each department's follow-up protocol for intermediate–high-risk PE. All echocardiography examinations were performed in each department by an experienced cardiologist specifically looking for chronic complications of pulmonary embolism, including signs of PH. For patients unable to attend follow-up visits, data were collected from medical records, and additional information was obtained from the patient, their cardiologist or general practitioner.

Intermediate or high probability of PH was defined according to the ESC recommendations for PH [23] as the presence of tricuspid insufficiency flow > 2.8 m/s or other signs suggestive of PH, such as septal flattening, RV/LV ratio > 1, or pulmonary ejection flow acceleration time < 105 m/s and/or "notch". Normal systolic pulmonary artery pressure (sPAP) was defined as < 35 mmHg.

3.4.5. Exploratory outcomes

The primary outcome was included in multivariable analysis with variables identified in a univariate model. As a sensitivity analysis, to limit the risk of confounding bias inherent to the retrospective and non-randomized design of the study, we applied an inverse probability of treatment weighting (IPTW) method to compare the two groups on primary outcome. As an exploratory analysis, we also compared the main, safety and long-term outcomes between the two techniques (catheter-directed thrombolysis and thromboaspiration) in the subgroup receiving CDI.

3.5. Statistical analysis

This study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) recommendations for cohort studies [24]. No prior power calculation or sample size computation was performed. Continuous variables are summarized as median (interquartile range) or mean (standard deviation), and comparisons were conducted using Student's *t*-test or Wilcoxon's test, as appropriate. Categorical variables are presented as count (%) and were compared using the χ^2 or Fisher's exact test, as appropriate. For the multivariable analysis, variables with a *P*-value < 0.2 in the univariate model were included. Similar variables were excluded based on collinearity assessment using two correlation matrices (one for continuous variables and one for binary variables), applying a threshold of $r > 0.7$. Collinearity between continuous and binary variables (e.g., BMI and obesity) was evaluated using clinical judgment. For IPTW, a propensity-score–based method, we first identified potential confounding factors that could influence both treatment allocation and outcomes. The following baseline variables were included in the propensity score model: sex, age, body mass index, history of venous thromboembolism, cancer or recent trauma or surgery (< 1 month), sPESI score and elevated troponin levels (> 3 times the 99th percentile upper reference limit). Propensity scores were estimated using a multivariable logistic regression model. Stabilized weights were applied to reduce variance and improve the precision of the estimates. Covariate balance between groups after weighting was assessed using standardized mean differences, with values < 0.1 considered indicative of adequate balance. All statistical analyses were computed at a 2-sided α-level of 5% with R software (version 4.3.2) and validated by an experienced statistician.

The study protocol was approved by the ethical committee of *Société de Réanimation de Langue Française* (CE-SRLF-24-065). In agreement with French regulations, written informed consent was not required for this observational retrospective study, but patients and/or their relatives were informed about the study and the use of their data. The study is registered on the *Assistance Publique–Hôpitaux de Marseille* Health Data Access Portal under number PADS24-2.

4. Results

4.1. Study population

During the 8-year study period, 1637 patients were admitted to the five units with a primary or secondary diagnosis of PE (Fig. 1). Among these, 851 met the criteria for intermediate–high-risk PE. After excluding 302 patients, 549 were included in the main analysis, of whom 291 (53%) received standard therapy and 258 (47%) underwent CDI. In the CDI group, 213 patients (83%) underwent catheter-directed thrombolysis with the EKOS® device and 45 patients (17%) received thromboaspiration therapy using the FlowTriever® system.

Patient characteristics at admission are summarized in Table 1. The mean (SD) patient age was 67 ± 16 years and 49% were female (54% in the standard therapy group vs. 44% in the CDI group; $P = 0.014$). The distribution of venous thromboembolic risk factors was similar between the two groups: 22% of the overall population had a history of venous thromboembolism and 21% had a history of cancer. History of recent trauma or surgery was more frequent in the CDI group versus the standard therapy group (18% vs. 8.2%; $P < 0.001$). There were no significant differences between groups for the prevalence of chronic pulmonary disease (7.5%), diabetes (17%) or coronary artery disease (4.7%).

Clinical parameters on admission were similar between the two groups, with a median (interquartile range) heart rate of 98 (87–109) beats/min, systolic blood pressure of 131 (118–146) mmHg and oxygen flow rate of 4 ± 7 L/min. The mean sPESI score was 1 in the CDI group and 2 in the standard-therapy group ($P = 0.2$). Echocardiographic parameters also showed no significant differences between groups; only 2.4% of the overall population had a left ventricular ejection fraction < 50% and 98% presented with RV dilatation. Finally, elevated troponin levels exceeding 3 times the 99th percentile were more frequently observed in the CDI group (76% vs. 69%; $P = 0.046$).

4.2. Primary outcome

The primary outcome occurred in 3.1% of patients in the CDI group and 7.2% in the standard group ($P = 0.031$) (Fig. 2, Table 2). Specific assessment of the two components revealed a significant reduction in the use of systemic thrombolysis (0.4% vs. 4.8%; $P = 0.002$) and a moderate but non-significant decrease in hospital mortality (2.7 vs. 3.8%; $P = 0.50$).

4.3. Clinical secondary outcomes

Although the ICU length of stay was similar in both groups, total length of stay was shorter in the CDI group than the standard group (median 5 vs. 7 days, respectively; $P = 0.038$) (Table 2). On day 2, CDI was associated with improved respiratory and haemodynamic parameters, including a lower heart rate (81 vs. 85 bpm; $P = 0.034$), higher systolic blood pressure (128 vs. 125 mmHg; $P = 0.04$) and reduced oxygen flow requirements (1.5 vs. 2.5 L/min; $P < 0.001$).

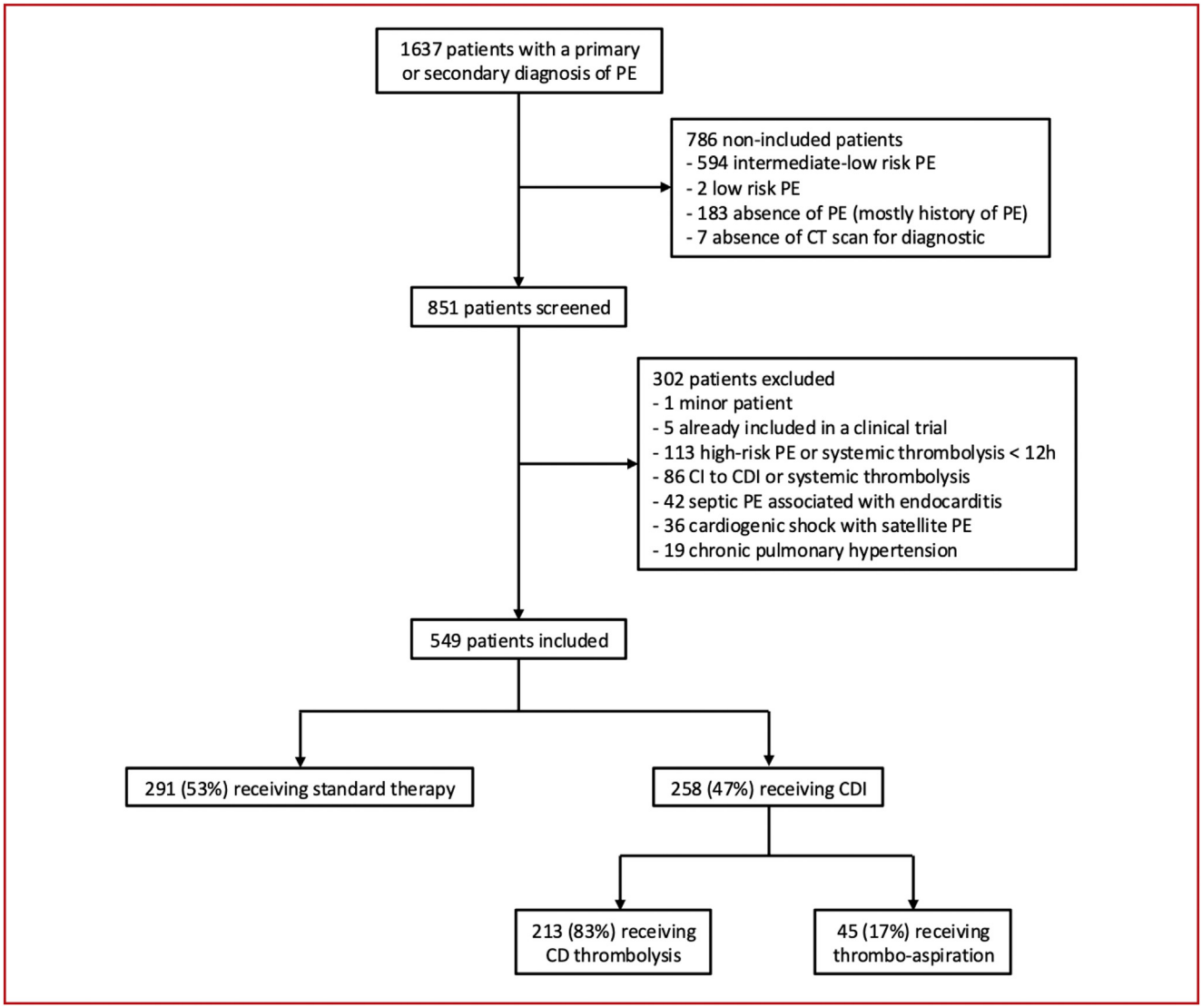


Fig. 1. Study flowchart. CI: contraindication; CDI: catheter-directed intervention; CD: catheter-directed; CT: computed tomography; PE: pulmonary embolism.

4.4. Safety outcomes

Global bleeding complications reported using the BARC classification were higher in the CDI group versus the standard group (13% vs. 3.8% respectively; $P < 0.001$). A more detailed analysis of bleeding types showed a higher incidence of minor (8.9% vs. 1.7%; $P < 0.001$) and puncture site (7.4% vs. 0.3%; $P < 0.001$) bleeding but no significant difference in major bleeding (4.7% vs. 2.1%; $P = 0.09$), intracranial haemorrhage (1.2% vs. 0%; $P = 0.1$) or transfusion (3.9% vs. 2.4%; $P = 0.3$).

We also assessed changes in sPAP in both groups from admission through 1–5 days post-admission and during long-term follow-up. This analysis included 513 patients who had at least one sPAP measurement: 271 in the standard-therapy group and 242 in the CDI group. Our findings indicate that the average reduction in sPAP from baseline to early evaluation was higher in the CDI group (–13.1 vs.–6.9 mmHg, respectively; $P = 0.001$), and for average reduction from baseline to late evaluation (–28.1 vs.–21.7 mmHg, respectively; $P = 0.01$) (Fig. 3).

4.5. Echocardiographic secondary outcomes

Among the 295 patients who underwent long-term echocardiographic evaluation by transthoracic examination 1–12 months after the PE episode (169 in standard-therapy group and 126 in the CDI group), there was no difference in the incidence of criteria for intermediate or high probability of chronic thromboembolic PH (17% vs. 13%, respectively; $P = 0.4$). Normal sPAP, defined as sPAP estimated < 35 mmHg by echocardiography, was reached in 66% of patients (67% in standard therapy group and 64% in CDI group; $P = 0.8$).

4.6. Multivariable analysis

Using univariate analysis, we analysed typical risk factors associated with poor outcomes in intermediate-risk PE (Table 3). Apart from CDI, the analysis revealed a significant effect of history of chronic pulmonary disease, sPESI score, treatment with unfractionated heparin and transfusion on the incidence of the composite primary outcome. All these parameters were included in the multivariable analysis, which showed a 65% reduction in risk of in-hospital mortality or thrombolysis (adjusted odds ratio 0.35, 95% CI 0.14–0.80).

Table 1
Patient characteristics according to therapy.

Characteristic	Overall population (n = 549)	Standard therapy (n = 291)	CDI (n = 258)	P
Age	67 ± 16	67 ± 17	67 ± 14	> 0.9
Female sex	271 (49)	158 (54)	113 (44)	0.014
VTE risk factors				
Obesity	183 (34)	86 (30)	97 (38)	0.053
History of VTE	119 (22)	61 (21)	58 (22)	0.7
History of cancer	118 (21)	58 (20)	60 (23)	0.3
Trauma/surgery < 1 month	70 (13)	24 (8.2)	46 (18)	< 0.001
Other chronic condition				
Chronic pulmonary disease	41 (7.5)	20 (6.9)	21 (8.1)	0.6
Diabetes	92 (17)	48 (16)	44 (17)	0.9
Coronary artery disease	26 (4.7)	11 (3.8)	15 (5.8)	0.3
Treatment				
Antiplatelet	82 (15)	42 (14)	40 (16)	0.7
Anticoagulant	15 (2.7)	11 (3.8)	4 (1.6)	0.11
Oral contraception	10 (1.8)	8 (2.7)	2 (0.8)	0.11
Period of admission				
2017–2019	164 (30)	108 (37)	56 (22)	< 0.001
2020–2022	250 (46)	113 (39)	137 (53)	
2023–2024	135 (25)	70 (24)	65 (25)	
Clinical variables				
Heart rate (bpm)	98 (87–109)	99 (87–112)	98 (87–108)	0.2
Systolic BP (mmHg)	131 (118–146)	130 (117–145)	133 (120–147)	0.3
Oxygen flow (L/min)	4 ± 7	4 ± 7	4 ± 6	0.2
High flow oxygen	13 (2.4)	6 (2.1)	7 (2.7)	0.6
sPESI score	2 ± 1	2 ± 1	1 ± 1	0.2
Echographic variables				
LVEF < 50%	13 (2.4)	8 (2.8)	5 (2)	0.5
RV dilatation	532 (98)	281 (98)	251 (98)	0.8
Flattened septum	367 (84)	198 (83)	169 (86)	0.3
Troponin > 3 times 99th percentile	397 (72)	200 (69)	197 (76)	0.046
CDI type				
Catheter-directed thrombolysis (EKOS® therapy)	213 (39)	0 (0)	213 (83)	–
Thromboaspiration therapy (FlowTriever®)	45 (8.2)	0 (0)	45 (17)	–

Data are expressed as number (%), median (interquartile range) or mean ± SD. BP: blood pressure; CDI: catheter-directed intervention; LVEF: left ventricular ejection fraction; RV: right ventricle; sPESI: Simplified Pulmonary Embolism Severity Index; VTE: venous thromboembolism.

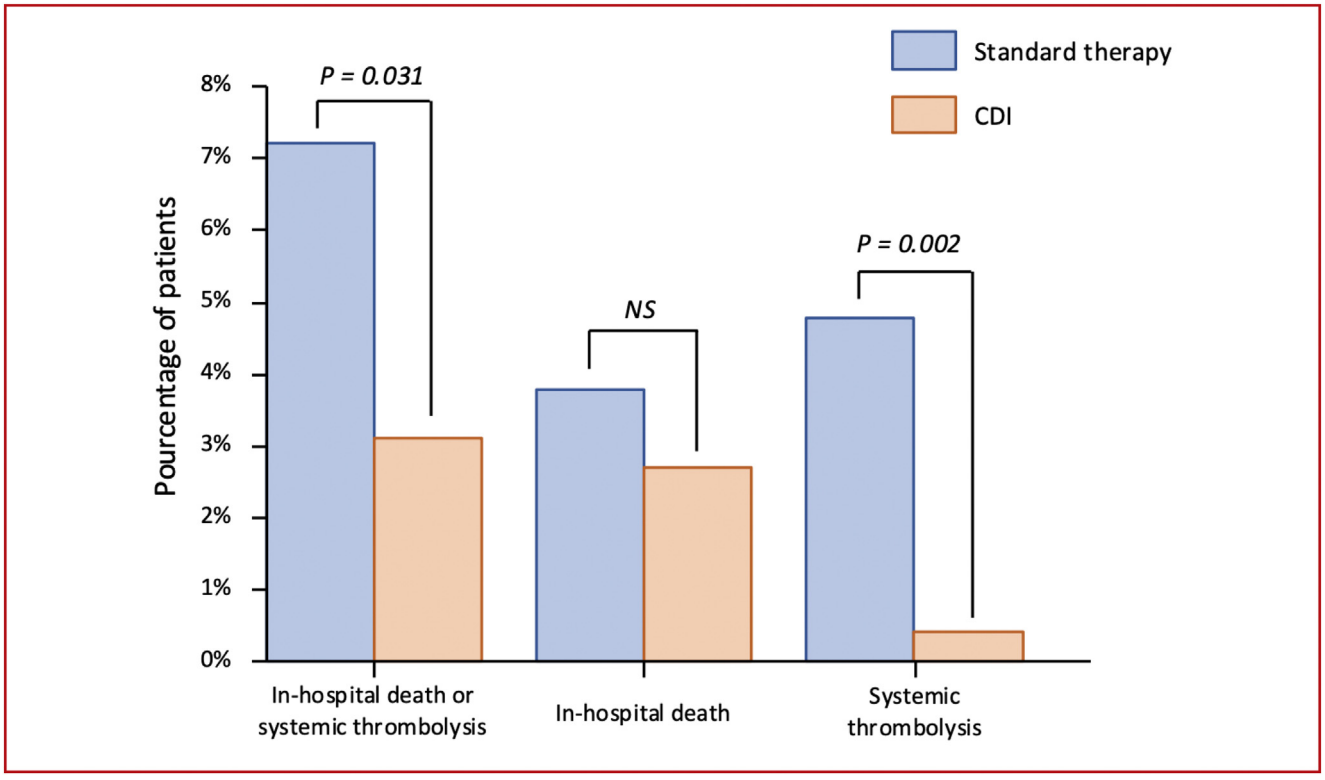


Fig. 2. Proportion of patients presenting composite primary outcome (in-hospital death or systemic thrombolysis) according to therapy. CDI: catheter-directed intervention.

Table 2
Outcomes according to therapy.

Outcomes	Overall population (*n* = 549)	Standard therapy (*n* = 291)	CDI (*n* = 258)	*P*
Primary outcome	29 (5.3)	21 (7.2)	8 (3.1)	0.031
In-hospital death	18 (3.3)	11 (3.8)	7 (2.7)	0.5
Systemic thrombolysis	15 (2.7)	14 (4.8)	1 (0.4)	0.002
Clinical secondary outcomes				
Length of ICU stay (days)	2 (1–3)	2 (1–3)	2 (2–3)	0.4
Total length of stay (days)	6 (4–9)	7 (4–10)	5 (4–8)	0.038
Pulmonary infarction	116 (21)	65 (23)	51 (20)	0.4
Heart rate at day 2 (beats/min)	84 (74–93)	85 (75–95)	81 (73–91)	0.034
Systolic BP at day 2 (mmHg)	126 (115–140)	125 (112–138)	128 (117–141)	0.04
Oxygen flow at day 2 (L/min)	2 ± 5.5	2.5 ± 6	1.5 ± 5	< 0.001
Safety outcomes				
Any bleeding	45 (8.2)	11 (3.8)	34 (13)	< 0.001
Minor bleeding	28 (5.1)	5 (1.7)	23 (8.9)	< 0.001
Puncture site bleeding	20 (3.7)	1 (0.3)	19 (7.4)	< 0.001
Major bleeding	18 (3.3)	6 (2.1)	12 (4.7)	0.09
Intracranial haemorrhage	3 (0.5)	0 (0)	3 (1.2)	0.1
Transfusion	17 (3.1)	7 (2.4)	10 (3.9)	0.3

Data are expressed as number (%), median (interquartile range) or mean ± SD. CDI: catheter-directed intervention; ICU: intensive care unit; BP: blood pressure.

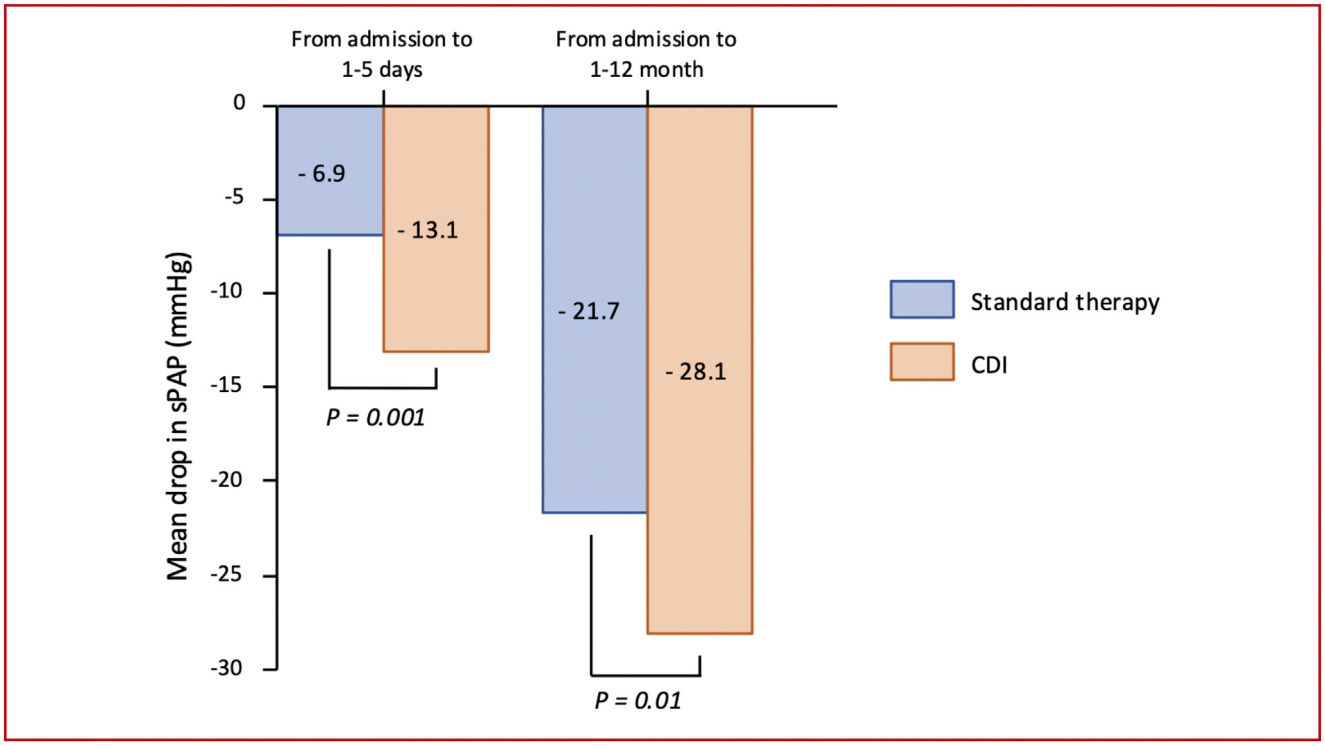


Fig. 3. Mean drop in systolic pulmonary artery pressure (sPAP) evaluated by echocardiography, from admission to 1–5 days and from admission to 1–12 months, according to therapy. CDI: catheter-directed intervention.

Table 3
Predictive factors associated with in-hospital mortality or use of systemic thrombolysis in intermediate–high-risk PE.

Predictive factors	*n*	Univariate		Multivariable	
		OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Treatment					
Standard therapy	549	1	–	1	–
Catheter-directed intervention		0.41 (0.17–0.91)	0.036	0.35 (0.14–0.80)	0.017
Chronic pulmonary disease	549	3.61 (1.27–8.97)	0.018	3.20 (0.98–9.46)	0.055
sPESI score	549	1.67 (1.12–2.49)	0.012	1.40 (0.90–2.20)	0.14
Unfractionated heparin treatment	549	4.41 (1.3–27.6)	0.014	4.02 (1.15–25.5)	0.027
Transfusion	546	6.20 (1.66–19.0)	0.01	8.16 (2.06–27.6)	0.005

CI: confidence interval; OR: odds ratio; sPESI: Simplified Pulmonary Embolism Severity Index.

Table 4
Outcomes according to therapy type in CDI subgroup.

Outcomes	Total (n = 258)	Catheter-directed thrombolysis (n = 213)	Thromboaspiration therapy (n = 45)	P-value
In-hospital death or systemic thrombolysis	8 (3.1)	8 (3.8)	0 (0)	0.4
In-hospital death	7 (2.7)	7 (3.3)	0 (0)	0.6
Systemic thrombolysis	1 (0.4)	1 (0.5)	0 (0)	>0.9
Any bleeding	34 (13)	32 (15)	2 (4.4)	0.057
Minor bleeding	23 (8.9)	21 (9.9)	2 (4.4)	0.4
Punction point bleeding	19 (7.4)	17 (8.0)	2 (4.4)	0.5
Major bleeding	12 (4.7)	12 (5.6)	0 (0)	0.13
Intracranial haemorrhage	3 (1.2)	3 (1.4)	0 (0)	>0.9
Transfusion	10 (3.9)	9 (4.2)	1 (2.2)	>0.9
Intermediate or high probability of pulmonary hypertension at echocardiography follow-up	16 (13)	13 (13)	3 (13)	>0.9

Data are expressed as number (%).

4.7. Propensity-score based method

In the IPTW-adjusted analysis, baseline characteristics were well balanced between treatment groups (Tables A.1 and A.2, Fig. A.1). The association between CDI and the primary outcome was no longer statistically significant (weighted odds ratio 0.40, 95% CI 0.15–1.07; P = 0.07), although the point estimate remained consistent with the direction of the main analysis (Table A.3).

4.8. Comparison between the two techniques

As part of the exploratory analysis, we compared the primary outcome, safety outcomes and long-term outcomes between the two techniques in the subgroup of patients who underwent CDI (Table 4). While no in-hospital deaths or need for systemic thrombolysis was reported in the thromboaspiration group, the difference in the primary outcome between the two techniques was not statistically significant (0% in the thromboaspiration group vs. 3.8% in the catheter-directed thrombolysis group; P = 0.4).

Regarding the safety outcomes, thromboaspiration demonstrated a marked, although not statistically significant, reduction in the incidence of any bleeding events (4.4% vs. 15% in the catheter-directed thrombolysis group; P = 0.057). There were no significant differences in the rates of major bleeding between the two groups (0% in the thromboaspiration group vs. 5.6% in the catheter-directed thrombolysis group; P = 0.13).

5. Discussion

This large, retrospective, multicentre cohort study aimed to evaluate the efficacy and safety of CDI compared with standard anticoagulation alone in patients with intermediate–high-risk PE. Our findings suggest that CDI, including both catheter-directed thrombolysis and thromboaspiration, reduces the composite outcome of systemic thrombolysis or in-hospital mortality. This result is further supported by improvements in secondary clinical criteria, such as haemodynamic stabilization and a reduction in oxygen requirements by day 2 in the CDI group. In addition, our study provided valuable insights into the safety profile of CDI: while minor bleeding and puncture site complications were more common in the CDI group, the incidence of major bleeding was similar, indicating that CDI is a safe procedure. Finally, although CDI did not change the incidence of an intermediate or high probability of PH at follow-up ultrasound, it did appear to increase the drop in sPAP, suggesting an effect on the consequences of PE on pulmonary vascularization.

This finding aligns with several randomized controlled trials and observational studies suggesting that CDI can be effective in improving outcomes for patients with intermediate–high-risk PE. The ULTIMA trial demonstrated that catheter-directed thrombolysis led to a greater reduction in RV/LV ratio at 24 h compared with anticoagulation alone [15]. Similarly, the SEATTLE II study reported significant improvements in RV function and pulmonary artery pressure following catheter-directed thrombolysis [20]. More recently, the FLARE trial reported that thromboaspiration could improve the RV/LV ratio by 25% and decrease sPAP [18]. However, these studies primarily assessed imaging and haemodynamic-based surrogate endpoints rather than robust clinical outcomes. Our study builds on this evidence by suggesting that CDI may reduce the composite outcome of systemic thrombolysis or in-hospital mortality, supporting its potential role in improving hard clinical endpoints. Our results are consistent with earlier findings, which indicate a hospital mortality rate of approximately 3% for intermediate–high-risk PE [12,25]. Although the difference in hospital mortality between CDI and standard treatment was not statistically significant in our study, the trend towards a lower mortality rate in the CDI group warrants further investigation. Finally, our study complements other larger-scale observational studies by providing additional information on the potential mechanism for reducing mortality through CDI [26].

From a safety perspective, our findings align with many previous studies on both catheter-directed thrombolysis and thromboaspiration. The rate of major bleeding events, which was 4.7% in the CDI group, was similar to previous data on interventional techniques showing major bleeding rates of between 2% and 5% [17,21,22]. However, it is important to note the occurrence of three intracranial haemorrhages in the CDI group, in patients treated with catheter-directed thrombolysis. The increase in minor bleeding events in the CDI group is an expected result, especially given the high proportion of bleeding at the puncture site, representing 19 of the 23 minor events.

Our exploratory analysis of catheter-directed thrombolysis versus thromboaspiration did not reveal significant differences in the primary outcome, potentially due to the small sample size of the thromboaspiration group. Nevertheless, the reduced incidence of bleeding complications with thromboaspiration suggests it may be a preferable option in certain scenarios. Future research is needed to identify the optimal CDI technique based on patient characteristics and clinical context.

5.1. Study limitations

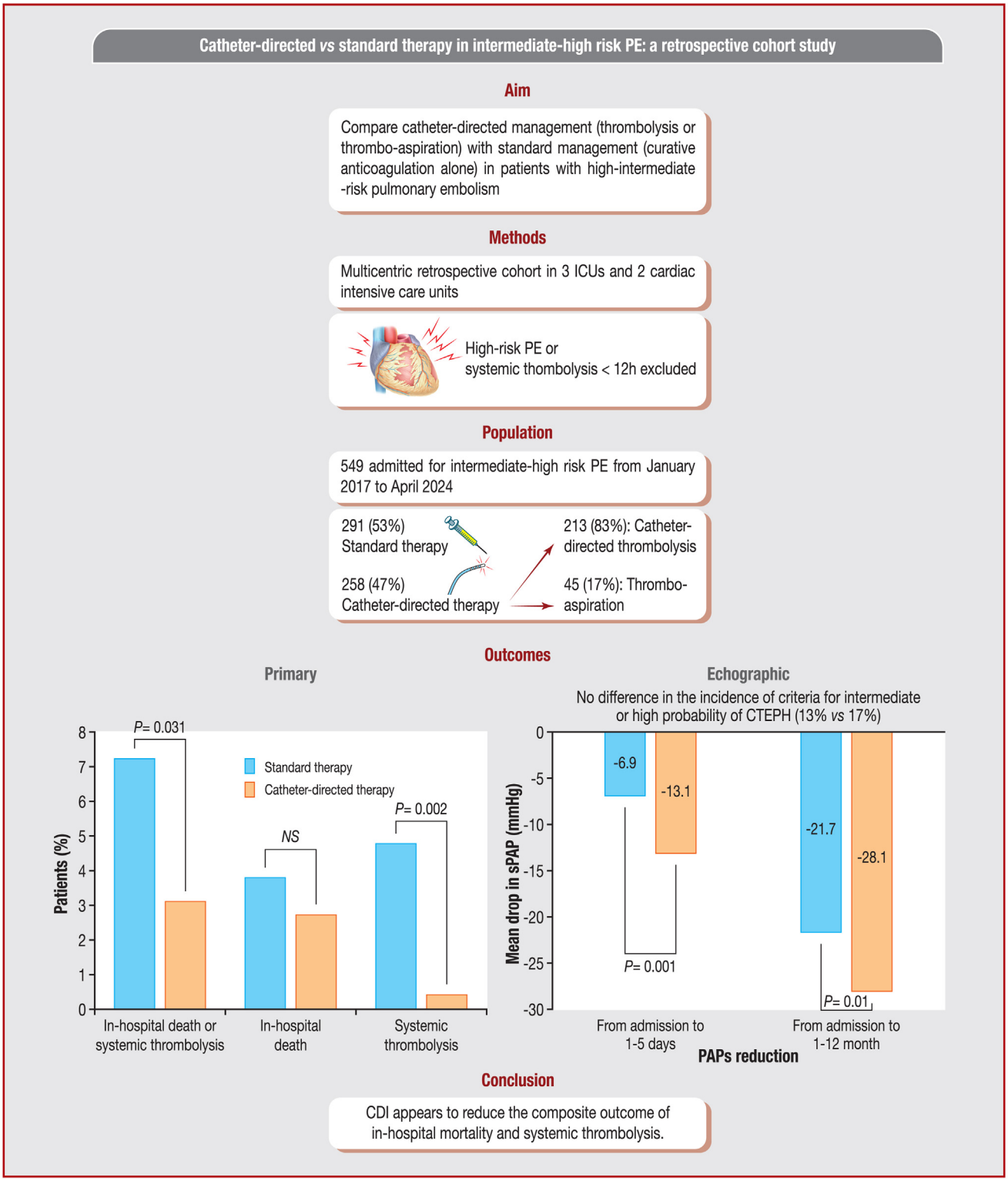
Our study has several limitations. Despite the large sample size and objective nature of our primary outcome, the retrospective design introduces the possibility of bias. In the IPTW-adjusted sensitivity analysis, the association between CDI and the primary outcome was attenuated and no longer reached statistical significance, although the effect estimate remained consistent with the

direction observed in the multivariable model. This finding suggests that the benefit of CDI may be partly explained by baseline differences between groups but also supports the robustness of our main analysis. Additionally, the inclusion of all patients managed with catheterization led to some heterogeneity in the CDI group with an over-representation of catheter-directed thrombolysis. The lack of computed tomography scan data also means we cannot definitively confirm that all patients treated for PE would have benefited from catheter-based procedures, especially in cases where proximal pulmonary artery involvement is required, such as with thromboaspiration. Moreover, the inclusion of systemic thrombolysis as a component of the composite primary outcome may introduce a potential bias. Given that the CDI group mainly underwent catheter-directed thrombolysis, clinicians may have been inclined to consider alternative rescue therapies rather than administering a second thrombolytic treatment. However, no patient in the CDI group underwent a repeat catheter-based intervention or any other form of life-saving therapy in the event of haemodynamic deterioration. Therefore, it appears unlikely that clinicians deliberately withheld rescue therapy, including systemic thrombolysis, in such situations. Concerning echocardiographic data, because of the low incidence of PH after intermediate–high-risk PE [27–29], we focused on the probability of PH, which is an intermediate outcome. To demonstrate the effect of catheter intervention on the occurrence of PH, it would be interesting to measure the precise incidence of this disease in the at-risk population with a more specific haemodynamic assessment by right heart catheterization.

Our study provides valuable insights into the role of CDI compared with anticoagulation alone in the management of intermediate–high-risk PE. While current evidence remains limited, ongoing large-scale randomized controlled trials – such as the HI-PEITHO trial (NCT04790370), evaluating catheter-directed thrombolysis, and the PEERLESS II study (NCT06055920), evaluating catheter-directed thrombectomy – are expected to offer more definitive answers. Their results may significantly influence future guidelines and clarify the role of these techniques in clinical practice.

6. Conclusion

Or work suggests that CDI, composed of catheter-directed thrombolysis and thromboaspiration, reduces the composite outcome of rescue systemic thrombolysis or in-hospital mortality. Moreover, the increased risk of bleeding complications associated with CDI seems to concern only minor events. Future research should focus on larger, multicentre randomized controlled trials to further elucidate the benefits and risks of CDI compared with standard treatment. Finally, dedicated studies are needed to identify the most appropriate technique for this indication (Central Illustration).



Central Illustration. Catheter-directed vs. standard therapy in intermediate–high-risk PE: a retrospective cohort study. CTEPH: chronic thromboembolic pulmonary hypertension; ICU: intensive care unit; OR: odds ratio; PAP: pulmonary artery pressure; PE: pulmonary embolism; spap: systolic pulmonary artery pressure.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2025.08.014.

Disclosure of interest

The authors declare that they have no competing interest.

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