SYSTEMATIC REVIEW

Outcome Analysis of Catheter-Directed Thrombolysis and Mechanical Thrombectomy in Intermediate- and High-Risk Pulmonary Embolism: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction: Pulmonary embolism (PE) is a severe condition associated with high morbidity and mortality, particularly in intermediate- and high-risk patients. Catheter-directed thrombolysis (CDT) and mechanical thrombectomy (MT) have emerged as advanced treatment modalities. This study aimed to systematically compare clinical outcomes between CDT and MT in this population. **Materials and Methods:** This systematic review and meta-analysis was registered in PROSPERO (CRD42023460836) and conducted according to PRISMA guidelines. A comprehensive literature search was performed in PubMed, Scopus, ProQuest, SAGE Journals, and Cochrane up to January 6, 2025. Study quality was assessed using the Newcastle-Ottawa Scale, and statistical analyses were performed using Review Manager 5.4.1. **Results:** Eight studies involving 5,438 patients were included. In-hospital mortality was similar between groups (CDT: 2.31%; MT: 2.96%; RR 0.82, 95% CI: 0.48–1.38; p = 0.45). MT was associated with a significantly reduced ICU length of stay (SMD 0.38, 95% CI: 0.15–0.62; p = 0.001). Rates of significant bleeding (RR 1.02, 95% CI: 0.70–1.47; p = 0.93) and major complications (RR 0.73, 95% CI: 0.36–1.45; p = 0.37) were comparable between groups. Post-procedural pulmonary artery pressure improved in both groups, with a slight advantage toward MT (SMD −0.17, 95% CI: −0.29 to −0.05; p = 0.006). **Conclusion:** CDT and MT demonstrate favorable outcomes in intermediate- and high-risk PE. MT may offer shorter ICU stays and improved pulmonary artery pressure, whereas other clinical outcomes appear comparable. Treatment should be individualized according to patient condition, bleeding risk, and institutional expertise.
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Keywords: Pulmonary Embolism, Catheter-Directed Thrombolysis, Mechanical Thrombectomy, Thrombectomy, Treatment Outcomes

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INTRODUCTION

Pulmonary embolism (PE) is a leading global cause of morbidity and mortality, with intermediate- and high-risk cases posing major clinical challenges [1]. These cases, characterized by right ventricular (RV) dysfunction, elevated cardiac biomarkers, and hemodynamic instability, require interventions beyond standard anticoagulation. Despite advances in care, PE is the third leading cause of cardiovascular death, with intermediate-risk patients experiencing early mortality rates of 3–15% and clinical deterioration in 5–18% of cases. The rising incidence of PE, driven by improved diagnostic capabilities and an aging population, has further underscored the need for effective management strategies [2,3].

The use of catheter-based therapies has been increasing significantly in intermediate- and high-risk acute PE patients, with catheter-directed thrombolysis (CDT) and mechanical thrombectomy (MT) being the most prominent [4]. CDT involves the delivery of thrombolytic agents, such as recombinant tissue plasminogen activator (rTPA), directly to the thrombus via a catheter. This approach provides targeted therapy but carries a

4.5% risk of non-intracranial major hemorrhage and a 0.7% risk of intracranial hemorrhage [5]. In contrast, MT utilized large-bore catheters to mechanically extract the thrombus, providing immediate hemodynamic relief without the need for thrombolytics. While MT avoids the bleeding risks associated with rTPA, it requires greater technical expertise and carries its own risks, such as vascular complications [6]. Both approaches aim to alleviate RV strain and restore pulmonary circulation but differ in procedural risks and resource demands [7].

Despite the growing adoption of advanced therapies for PE, evidence remains fragmented, with no prior randomized controlled trials (RCTs) directly comparing these modalities [8]. This systematic review and meta-analysis aim to synthesize existing evidence on CDT and MT, offering clinicians critical insights into their relative efficacy, safety, and optimal application in intermediate- and high-risk PE management.

MATERIALS AND METHODS

Search Strategy and Selection Criteria

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023460836). A systematic literature search was conducted across PubMed, SCOPUS, ProQuest, Sage Journals, and The Cochrane Database to identify studies comparing CDT) and MT) in PE) patients up to January 6 2025. Keywords included "Pulmonary Embolism OR PE OR Emboly Pulmonal," "Catheter-directed thrombolysis OR CDT OR catheter-directed intervention," and "Mechanical Aspiration Thrombectomy OR suction thrombectomy OR mechanical thrombectomy". Manual and bibliographical searches were also conducted to obtain additional evidence and cover grey literature. Studies were excluded if they fell into any of the following categories: reviews, case-control studies, case reports, case series, unpublished records such as conference papers, theses, patents), or lacked full-text availability. Additionally, studies not reported in English were also excluded to ensure clarity and comprehensibility. These selection criterias ensured the inclusion of high-quality primary research to facilitate a robust comparison of CDT and MT.

Data Extraction

Two authors independently screened all articles obtained from the database searches to assess their relevance for inclusion. Any disagreements were resolved by reviewing the full text and discussing with the senior authors. The study selection process is depicted in a PRISMA diagram (Fig 1). Data from eligible studies were also independently extracted using a standardized data extraction form. Extracted data included: author and year of the study; number of participants; study design; primary and secondary outcome measures. All data were organized using Microsoft Excel 2019. The primary endpoint was the post-procedural clinical outcomes, including in-hospital mortality, Intensive Care Unit (ICU) length of stay (LOS), major complications and bleeding as defined by Society of Interventional Radiology [SIR] criteria [9]. Secondary endpoints include the need for blood transfusion, overall hospital length of stay, and post-procedural pulmonary arterial pressure (PAP) reduction.

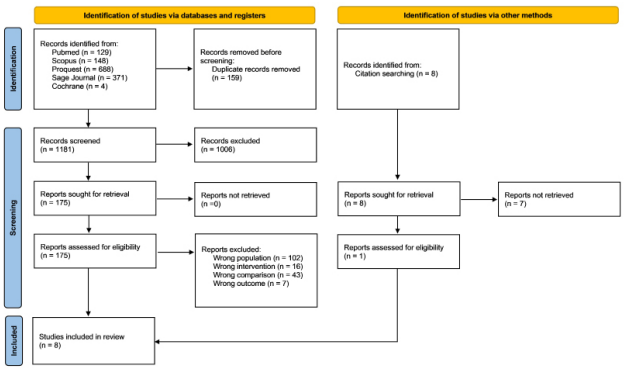


Figure 1: PRISMA Flow Diagram for Study Selection
This figure illustrates the process of identifying, screening, and selecting studies for the systematic review and meta-analysis. Records were sourced from multiple scientific databases and citation searching. Duplicates were removed, and studies were excluded based on eligibility criteria, leading to the final inclusion of eight studies.

Quality assessment

Three authors independently evaluated the quality of the included studies using the Newcastle-Ottawa Quality Assessment Scale (NOS), a validated tool for assessing non-randomized studies in meta-analyses [10]. Each study was scored out of a maximum of 9 points: up to 4 points for participant selection and exposure measurement, 2 points for cohort comparability based on design or analysis, and 3 points for outcome assessment and adequate follow-up. Studies were categorized as poor quality (0–3 points), moderate quality (4–6 points), or high quality (7–9 points). For studies with multiple adjustment models, only those accurately accounting for potential confounding factors were retained. Funnel plots were used to assess the symmetry of effect size distribution, while forest plots were employed to illustrate variations in clinical outcomes.

Data analysis

The binary random-effects model was used to calculate the pooled prevalence and 95% confidence intervals (CI) for each study's weighted effect size. For binary outcomes, effect sizes were expressed as risk ratios (RR). For continuous outcomes, standardized mean differences (SMD) were used. When heterogeneity was indicated by the X test (p-value ≤ 0.10) and I > 50%, the random-effects model was applied. Otherwise, the fixed-effects Mantel-Haenszel model was used. P-values ≤ 0.05 were considered statistically significant. Data analysis was conducted using Cochrane Review Manager version 5.4.1. Any continuous outcomes that

were reported as medians and interquartile ranges, were converted to means and standard deviations (SD) using mean variance estimation formulas [11,12].

RESULTS

Study Selection and Quality assessment

A preliminary search in scientific databases yielded 1,340 records (Fig 1). After removing duplicates, 1,181 records remained. During title and abstract screening, 1,006 records were excluded due to ineligible publication types (e.g., case reports, reviews, or editorials) or study designs (e.g., descriptive studies, case-control studies, or propensity score-matched analyses). A total of 175 full-text articles were assessed for eligibility, resulting in the exclusion of 102 articles for incorrect patient populations, 16 for incorrect interventions, 43 for irrelevant comparisons, and 7 for lacking relevant outcomes. Ultimately, eight retrospective cohort studies comprising 5,438 patients were included in the analysis [13–20]. Quality assessment using the Newcastle-Ottawa Scale (NOS) indicated that all studies were of acceptable quality (Supplementary Table S1). However, Tran et al., 2023 [19] received the lowest NOS score, although it still qualified as moderate quality.

Table I: Baseline characteristics of Included Studies

Baseline characteristics of the included studies, detailing study design, patient demographics, inclusion criteria, catheter-directed thrombolysis (CDT) agents, and thrombolytic infusion rates where applicable.

Author, Year Published (Follow up)	Patient (n)	Study Design	Inclusion Criteria	CDT drug/agent	Mean Rate of thrombolytic agent infuse
Avgerinos et al., 2019 (3 months and 12 months)	72 patients (54 CDT vs 18 ST)	Retrospective Cohort	Patients who received CDT or ST (Suction Thrombectomy) for acute high-risk (massive) and intermediate-risk (submassive) PE	tissue plasminogen activator (r-tPA)	N/A
Feroze et al., 2023 (median follow-up: 284 days)	147 patients (50 CDT vs 97 LBT)	Retrospective Cohort	Patients who received CDT using the EKOSonic (Boston Scientific) or LBT using the Inari FlowTriever thrombectomy catheter (Inari Medical)	tissue plasminogen activator (r-tPA)	N/A
Graif et al., 2020 (30 days)	168 patients (41 LBAT vs 27 CDT) 52 matched patients (from total patients) (26 LBAT vs 26 CDT)	Retrospective Cohort with Propensity Score Matching	Patients presented with acute submassive or massive PE, underwent pulmonary artery CDT with recombinant tissue plasminogen activator (tPA) (Alteplase; Genentech Inc, San Francisco, California) or LBAT using the Flow-Triever device	recombinant tissue plasminogen activator (r-tPA) (Alteplase)	0.57 mg/h ± 0.17
Inci et al., 2023 (30 days)	458 patients (266 CDT vs 192 MT)	Retrospective Cohort	Patients with acute intermediate or high-risk PE that were treated with either MT with the FlowTriever Retrieval/Aspiration System (Inari Medical) or CDT.	tissue plasminogen activator (r-tPA)	tPA infusion was variable and dependent on individual practices
Jaber et al., 2024 (30 days)	349 patients (171 CDT vs 178 LBMT)	Prospective, multicenter, RCT	Intermediate-risk PE patients with right ventricular dilatation and additional clinical risk factors who received CDT using ultrasound-facilitated CDT (EKOS Endovascular System; Boston), standard side-hole CDT (Cragg-McNamara Micro Therapeutics Infusion Catheter; Medtronic), standard side-slit CDT (Uni-FuseTM Infusion Catheter; AngioDynamics), pharmacomechanical CDT (BASHIR Endovascular Catheter; Thrombolex), and gradient side-hole CDT (Fountain Infusion Systems; Merit Medical); or LBMT using the Inari FlowTriever thrombectomy catheter (Inari Medical)	tissue plasminogen activator (r-tPA)	Most tPA infusions were administered at a rate of 0.5–1.0 mg/hour per lung (95.9%) for a duration of 6–24 hours (90.8%).

CONTINUE

Table I: Baseline characteristics of Included Studies. (CONT.)
Baseline characteristics of the included studies, detailing study design, patient demographics, inclusion criteria, catheter-directed thrombolysis (CDT) agents, and thrombolytic infusion rates where applicable.

Author, Year Published (Follow up)	Patient (n)	Study Design	Inclusion Criteria	CDT drug/agent	Mean Rate of thrombolytic agent infuse
Sedhom et al., 2023 (30 days)	2732 (1864 CDT vs 868 CDE); 1583 matched patients (809 CDT vs 774 CDE)	Retrospective Cohort with Propensity Score Matching	High-risk PE patients underwent CDT or CDE	N/A	N/A
Tran et al., 2023	372 patients (226 CDT vs 146 MT)	Retrospective Cohort	Intermediate risk PE patients who received MT using the FlowTriever (FT) Aspiration System (Inari Medical) or CDT using either a Cragg–McNamara (CM) perfusion catheter (Medtronic) or EKOS ultrasound-facilitated thrombolysis system (Boston Scientific)	tissue plasminogen activator (r-tPA)	r-tPA was infused 1 mg/hour either into 1 lung or divided between both lungs
Tsukagoshi et al., 2024 (30 days)	4115 patients (1137 CDT vs 2978 PMT); 2204 matched patients (1102 CDT vs 1102 PMT)	Retrospective Cohort with Propensity Score Matching	Acute PE patients who received CDT or PMT	N/A	N/A

Table I: (CONT.)

Author, Year Published (Follow up)	Thrombectomy Method	Thrombectomy Aspiration Catheter	Anticoagulant administration (%)	High Bleeding Risk Criteria	End Points
Avgerinos et al., 2019 (no follow up)	Contemporary Suction Thrombectomy	Devices used in this series were: AngioVac (Angiodynam- ics), Arrow-Trerotola (PTD; Arrow, Reading, Pa), Indigo (Penumbra, Alameda, Calif), and FlowTriever (INARI Med- ical, Irvine, Calif).	Patients not on heparin at the time of admission were given a bolus of 80 IU/kg, fol- lowed by an infusion of 18 IU/kg/h intravenously. If on heparin at admission, an infusion was continued to maintain an activated partial thromboplastin time of 68 to 106 seconds per institutional protocol	Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) classification	Clinical success : survival to hospital discharge without major bleeding, perioperative stroke, or other major procedure-related adverse event (eg, heart or valve injury) and without decompensation or persistent shock for the submassive and massive PE groups,

CONTINUE

Table I: Baseline characteristics of Included Studies (CONT.)

Baseline characteristics of the included studies, detailing study design, patient demographics, inclusion criteria, catheter-directed thrombolysis (CDT) agents, and thrombolytic infusion rates where applicable.

Author, Year Published (Follow up)	Thrombectomy Method	Thrombectomy Aspiration Catheter	Anticoagulant administration (%)	High Bleeding Risk Criteria	End Points
Feroze et al., 2023 (median follow-up: 284 days)	Large-bore thrombectomy (LBT)	Inari FlowTriever thrombectomy catheter (Inari Medical)	Direct oral anticoagulant: CDT: 38 (76.0%) LBT: 61 (62.8%) Vitamin K antagonist: CDT: 11 (22.0%) LBT: 24 (24.7%)	Major bleeding as defined by the development of intracranial hemorrhage, a hemoglobin drop of 3 g/dL, and/or need for blood transfusion.	The primary outcome was all-cause mortality; The secondary outcomes were all-cause readmission, readmission for PE, and length of stay in the intensive care unit and hospital. The safety outcome of procedure-related bleeding was evaluated. Kaplan-Meier curves were used to estimate the cumulative event rate. Multivariate Cox-proportional hazard regression and inverse propensity weighting were used to adjust for confounders.
Graif et al., 2020 (30 days)	Large-bore Aspiration Thrombectomy (LBAT)	Flow-Triever device (20-F Triever20 (Inari Medical) aspiration catheter, adjunctive coaxial placement of the 16-F Triever16 aspiration catheter, 24-F Triever24 device)	Unfractionated heparin infusion: LBAT cohort: 25.9% CDT cohort: 66% LBAT matched cases: 23.1% CDT matched cases: 84.6% Low-molecular-weight heparin: LBAT cohort: 70.4% CDT cohort: 34% LBAT matched cases: 73.1% CDT matched cases: 15.4%	Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) classification	- Technical end-points: total procedure time, total fluoroscopy time, and total contrast medium administered. - The primary clinical effectiveness end-points: change in invasive PAP; change in heart rate (HR), and change in pulmonary artery thrombus burden (quantified according to the Miller PE severity index (Miller score)). - Safety end-points: all 30-day complications (which were classified according to the Society of Interventional Radiology (SIR) reporting standards) and hemorrhagic complications (classified according to the Global Use of Strategies to Open Occluded Arteries (GUSTO) criteria).

CONTINUE

Table I: Baseline characteristics of Included Studies (CONT.)

Baseline characteristics of the included studies, detailing study design, patient demographics, inclusion criteria, catheter-directed thrombolysis (CDT) agents, and thrombolytic infusion rates where applicable.

Author, Year Published (Follow up)	Thrombectomy Method	Thrombectomy Aspiration Catheter	Anticoagulant administration (%)	High Bleeding Risk Criteria	End Points
Jaber et al., 2024 (30 days)	Large-bore mechanical thrombectomy (LBMT)	Inari FlowTriever thrombectomy catheter (Inari Medical)	Parenteral Heparin (85.5% Unfractionated heparin (UFH) vs 80.7% Low molecular weight Heparin (LMWH) CDT: 267 (96.7%) LBMT: 261 (95.3%)	Major bleeding per International Society for Thrombosis and Haemostasis (ISTH) definition	The primary endpoint was a hierarchal win ratio (WR) composite of the following: 1) all-cause mortality, 2) intracranial hemorrhage, 3) major bleeding, 4) clinical deterioration and/or escalation to bail-out, and 5) postprocedural intensive care unit (ICU) admission and length of stay, assessed at the sooner of hospital discharge or 7 days post-procedure. Assessments at the 24-hour visit included respiratory rate, mMRC dyspnea score, NYHA classification, right ventricle (RV)/left ventricle (LV) ratio reduction, and RV function. Endpoints through 30 days included total hospital stay, all-cause readmission, and all-cause mortality.
Inci et al., 2023	Mechanical Thrombectomy (MT)	Flow-Triever (20-26 F Sheats)	N/A	Significant bleed was defined as clinically evident bleeding requiring postprocedural transfusion, hematoma requiring surgical evacuation, fatal bleed, or intracranial bleed.	- Primary : the composite of in-hospital death, significant bleed, vascular complication, or need for mechanical support postprocedure. - Secondary : individual components of the composite outcome in addition to blood transfusions, invasive pulmonary artery pressures post-procedure, right ventricular function and estimated filling pressures by echo- cardiography, in-hospital mortality, and ICU length of stay.

CONTINUE

Table I: Baseline characteristics of Included Studies (CONT.)
Baseline characteristics of the included studies, detailing study design, patient demographics, inclusion criteria, catheter-directed thrombolysis (CDT) agents, and thrombolytic infusion rates where applicable.

Author, Year Published (Follow up)	Thrombectomy Method	Aspiration Catheter	Anticoagulant administration (%)	High Bleeding Risk Criteria	End Points
Sedhom et al., 2023 (30 days)	Catheter-directed embeolectomy (CDE)	N/A	N/A	Major bleeding included intracranial hemorrhage (ICH)	The primary outcome is the composite of all-cause mortality, ICH, or major bleeding at 7 days.
Tran et al., 2023	Mechanical Thrombectomy (MT)	FlowTriever (FT) Aspiration System (Inari Medical) or CDT using either a Cragg–McNamara (CM) perfusion catheter (Medtronic) or EKOS ultrasound-facilitated	Unfractioned heparin (UFH)	N/A	- Primary outcomes is the cost comparison between CDT and MT for intermediate-risk PE - Secondary outcomes includes LOS, complications, adjusted cost analysis, device & protocol variations
Tsukagoshi et al., 2024 (30 days)	Percutaneous Mechanical Thrombectomy (PMT)	N/A	N/A	N/A	- The primary outcomes of this study divided into perioperative outcomes (30-day outcome) such as all-cause mortality, bleeding complications, pulmonary outcomes, cardiac outcomes and long-term outcomes (5-year outcomes) such as all-cause mortality; chronic pulmonary hypertension; right heart failure, respiratory failure, and healthcare utilization - The secondary outcomes includes safety profile, hemodynamic outcomes, economic consideration, healthcare utilization, and technological & procedural comparisons.

Baseline Characteristics and Demographics

The included studies in the analysis examined a diverse spectrum of patient populations. The mean age of participants that were included ranged from 56-66 years, with various comorbidity profiles such as hypertension (48%-70%), diabetes mellitus (12%-32.6%), and cancer or malignancy (11%-49.2%) [14–16,18–20]. Notably, absolute contraindications to thrombolytics were present in up to 50% of patients in several included studies [13–18]. These variations in patient demographics and clinical risk factors contributed to the complexity of baseline risk assessment and outcomes.

Systemic anticoagulants used also varied across included studies, dominated by low-molecular-weight heparin (LMWH) use ranged from 15.4% to 73.1% of participants [13–15,17,19]. of participants. In terms of thrombolytic administration, both the type and rate of infusion varied. Jaber et al., 2024 [17] reported that 95.9% of patients in their cohort received tissue plasminogen activator (tPA) at rates of 0.5–1.0 mg/hour per lung, over 6–24 hours in the majority of cases. In contrast, other studies employed variable or less clearly defined infusion protocols, such as a dose of 1 mg/hour divided between lungs in the Tran et al. (2023) cohort or practice-dependent regimens in Inci et al., 2023 [16]. Several thrombectomy and thrombolysis devices were reported across studies, highlighting variability in procedural strategies[13–20]. Notably, Inari's FlowTriever system was used in included studies [14,16], while EKOS ultrasound-assisted catheters were the predominant devices in CDT arms, underscoring differences in device selection, operator preference, and institutional protocols for patient management. Baseline characteristics of the included studies are detailed in Tables 1 and 2.

Table II: Clinical characteristics of Participants in the Included Studies

Clinical characteristics of participants across included studies, summarizing key patient demographics, comorbidities, history of thrombotic events, malignancy rates, and contraindications to thrombolytic therapy.

Study Author	Mean age (years)	HTN (%)	DM (%)	CKD (%)	History of Surgery (%)	History of ACS/ MI (%)	History of CVA (%)	History of DVT (%)	Cancer/ Malignancy (%)	Absolute Contraindication to Lytics (%)
Avgerinos et al., 2019	CDT : 63.5±14.2 ST : 64.1±14.1	N/A	N/A	N/A	N/A	N/A	N/A	CDT : 79.6% ST : 66.7%	CDT : 20.4% ST : 38.9%	CDT : 37.1% ST : 66.7%
Feroze et al., 2023	CDT: 61 (48-68) LBT: 65 (53-74)	CDT: 35 (70%) LBT: 72 (74.2%)	N/A	N/A	N/A	CDT: 49 (98%) LBT: 96 (99%)	N/A	N/A	CDT: 3 (6%) LBT: 22 (22.7%)	13 (8.84%)
Graif et al., 2020	Total cohort: 56.7±15.5 Patient matched: 59.9±15.6	LBAT cohort: 51.9% CDT cohort: 57.4% LBAT matched cases: 50% CDT matched cases: 61.5%	LBAT cohort: 25.9% CDT cohort: 22.7% LBAT matched cases: 26.9% CDT matched cases: 19.2%	LBAT cohort: 0% CDT cohort: 0% LBAT matched cases: 0% CDT matched cases: 0%	Surgery within 30-days: LBAT cohort: 18.5% CDT cohort: 10.6% LBAT matched cases: 42.3% CDT matched cases: 30.8%	LBAT cohort: 14.8% CDT cohort: 5% LBAT matched cases: 15.4% CDT matched cases: 11.5%	LBAT cohort: 0% CDT cohort: 0% LBAT matched cases: 0% CDT matched cases: 0%	LBAT cohort: 92.3% CDT cohort: 85.7% LBAT matched cases: 92% CDT matched cases: 88.5%	LBAT cohort: 3.7% CDT cohort: 7.8% LBAT matched cases: 3.8% CDT matched cases: 0%	LBAT cohort: 18.5% CDT cohort: 0% LBAT matched cases: 15.4% CDT matched cases: 0%
Inci et al., 2023	CDL : 56±0.9 Thrombectomy : 59±1.1	CDL : 48% Thrombectomy : 56%	CDL : 19% Thrombectomy : 22%	CDL : 16% Thrombectomy : 12%	CDL : 11% Thrombectomy : 16%	CDL : 7% Thrombectomy : 9%	CDL : 3% Thrombectomy : 6%	N/A	CDL : 11% Thrombectomy : 16%	CDL : 2% Thrombectomy : 23%
Jaber et al., 2024	CDT: 61.2 ± 14.8 LMBT: 63.7 ± 13.0	N/A	N/A	N/A	N/A	N/A	N/A	CDT: 60 (21.9%) LBMT: 58 (21.0%)	CDT: 56 (20.3%) LBMT: 56 (20.4%)	CDT: 11 (4.0%) LBMT: 12 (4.4%)
Sedhom et al., 2023	Total cohort: CDT: 65 (54–73) CDE: 66 (54–74) Patient matched: CDT: 66 (55–74) CDE: 66 (54–74)	Total cohort: CDT: 1148 (61.5%) CDE: 517 (59.6%) Patient matched: CDT: 507 (62.7%) CDE: 474 (61.3%)	Total cohort: CDT: 608 (32.6%) CDE: 211 (24.4%) Patient matched: CDT: 198 (24.5%) CDE: 196 (25.3%)	Total cohort: CDT: 273 (14.6%) CDE: 111 (12.8%) Patient matched: CDT: 128 (15.8%) CDE: 107 (13.9%)	N/A	Total cohort: CDT: 66 (3.5%) CDE: 38 (4.4%) Patient matched: CDT: 35 (4.4%) CDE: 36 (4.7%)	Total cohort: CDT: 63 (3.4%) CDE: 40 (4.6%) Patient matched: CDT: 34 (4.2%) CDE: 39 (5.0%)	Total cohort: CDT: 849 (45.5%) CDE: 422 (48.7%) Patient matched: CDT: 392 (48.5%) CDE: 381 (49.2%)	Total cohort: CDT: 248 (13.3%) CDE: 137 (14.8%) Patient matched: CDT: 126 (15.6%) CDE: 125 (16.2%)	CDT: 2% CDE: 50%
Tran et al., 2023	CDT: 57 [21] MT: 59.5 [21]	CDT: 107 (47%) MT: 81 (55%)	CDT: 41 (19%) MT: 30 (21%)	CDT: 34 (15%) MT: 17 (12%)	N/A	N/A	CDT: 4 (2%) MT: 7 (5%)	N/A	Active cancer CDT: 25 (11%) MT: 20 (14%)	N/A

CONTINUE

Table II: Clinical characteristics of Participants in the Included Studies (CONT.)

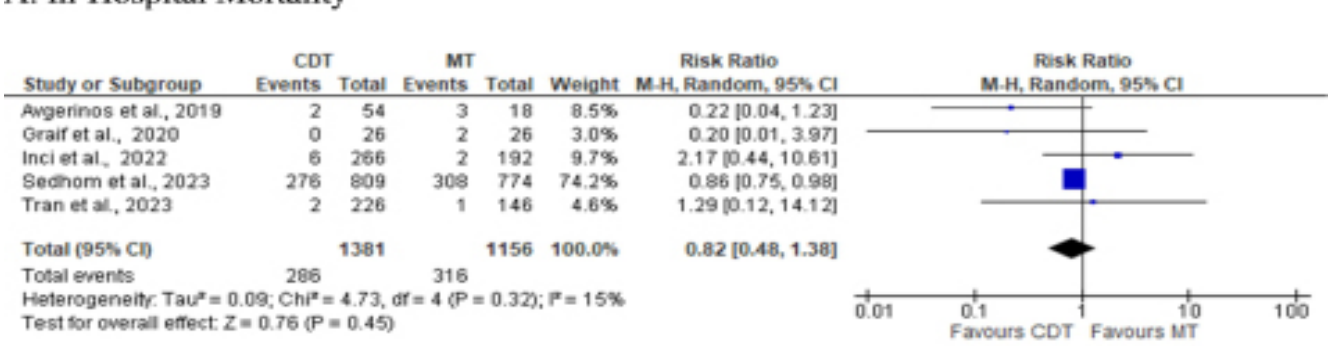
Clinical characteristics of participants across included studies, summarizing key patient demographics, comorbidities, history of thrombotic events, malignancy rates, and contraindications to thrombolytic therapy.

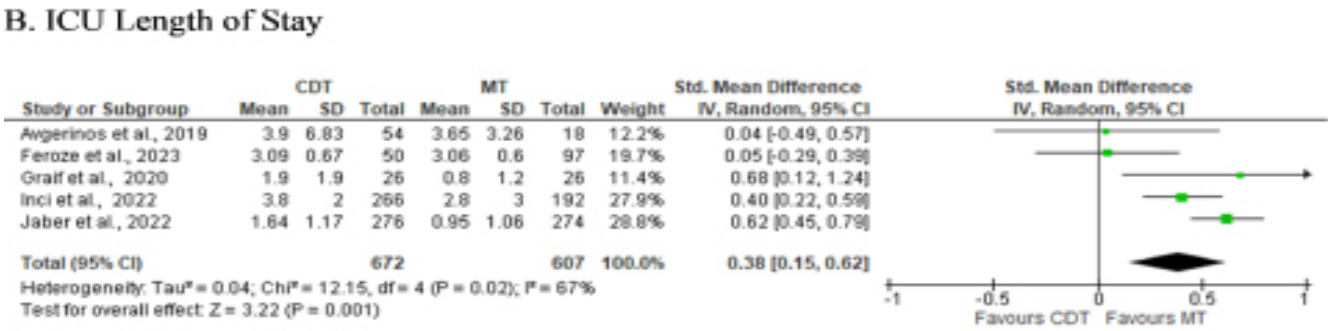
Study Author	Mean age (years)	HTN (%)	DM (%)	CKD (%)	History of Surgery (%)	History of ACS/ MI (%)	History of CVA (%)	History of DVT (%)	Cancer/ Malignancy (%)	Absolute Contraindication to Lytics (%)
Tsukagoshi et al., 2024	Total cohort: CDT: 58.5±15.0 PMT: 60.0 ±15.7 Patient matched: CDT 58.5±15.1 PMT 59.1±15.2	Total cohort: CDT: 568 (50.0%) PMT: 1467 (49.3%) Patient matched: CDT: 539 (48.9%) PMT: 516 (46.8%)	Total cohort: CDT: 317 (27.9%) PMT: 671 (22.5%) Patient matched: CDT: 288 (26.1%) PMT: 297 (27.0%)	Total cohort: CDT: 78 (6.9%) PMT: 77 (2.6%) Patient matched: CDT: 54 (4.9%) PMT: 58 (5.3%)	N/A	N/A	N/A	Acute lower extremity DVT Total cohort: CDT: 493 (43.4%) PMT: 1267 (42.5%) Patient matched: CDT: 466 (42.3%) PMT: 452 (41.0%) Chronic lower extremity DVT Total cohort: CDT: 48 (4.2%) PMT: 131 (4.4%) Patient matched: CDT: 46 (4.2%) PMT: 35 (3.2%)	Total cohort: CDT: 81 (7.1%) PMT: 123 (4.1%) Patient matched: CDT: 68 (6.2%) PMT: 63 (5.7%)	N/A

Follow-up durations also varied widely. Most studies reported short-term results with 30-day follow-ups [15–18], focusing on immediate safety and effectiveness outcomes such as mortality and major bleeding. Feroze et al. (2023) [14] incorporated a median follow-up of 284 days, offering intermediate-term insights into readmission rates and procedural safety [14]. Avgerinos et al., (2019) [13] also performed follow-up at 3 months and 12 months after the procedure. On the other hand, Tsukagoshi et al. (2024) [20] uniquely extended the follow-up to 5 years, documenting long-term outcomes.

In-Hospital Mortality

For in-hospital mortality, five studies [13,15,16,18,19] with a total of 2537 participants were analyzed. The in-hospital mortality rate was numerically lower in the CDT group compared to the MT group, but the pooled risk ratio (RR) is 0.82 (95% CI: 0.48–1.38, p = 0.45; I2=15%), indicating that there was no statistically significant difference, with low heterogeneity (Fig 2A)





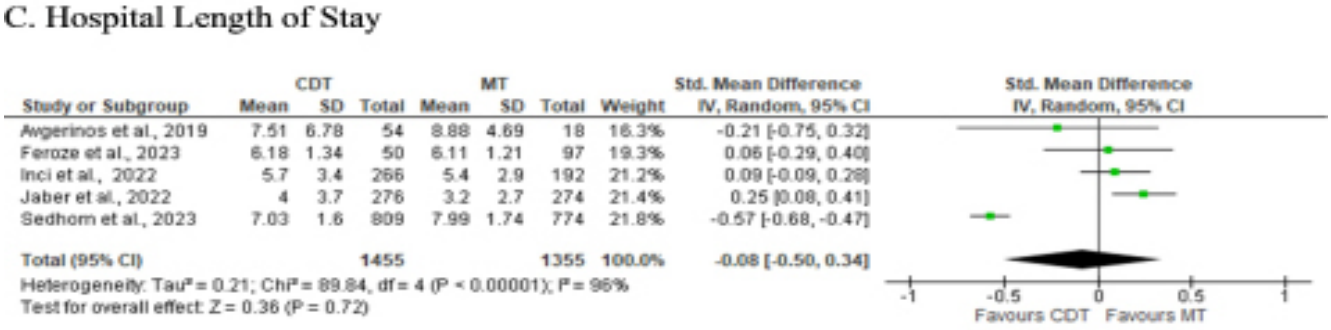


Figure 2A: Forest Plot Comparing In-Hospital Mortality Between CDT and MT
This meta-analysis forest plot presents the comparison of in-hospital mortality between catheter-directed thrombolysis (CDT) and mechanical thrombectomy (MT). The pooled relative risk (RR) is 0.82 (95% CI 0.48–1.38, p = 0.45), indicating no significant difference between the two treatment modalities.

Figure 2B: Forest Plot Comparing ICU Length of Stay Between CDT and MT
This forest plot shows the standardized mean difference (SMD) in ICU length of stay. MT significantly reduced ICU stay compared to CDT (SMD 0.38; 95% CI 0.15–0.62, p = 0.001), suggesting a potential benefit of MT in reducing ICU burden.

Figure 2C: Forest Plot for Hospital Length of Stay Between CDT and MT
This plot compares hospital length of stay between CDT and MT. The standardized mean difference (SMD) is -0.08 (95% CI -0.50 to 0.34, p = 0.72), indicating no significant difference in hospital length of stay.

ICU Length of Stay
Five studies [13–17] with a total of 1279 participants were included for the analysis. The pooled analysis revealed a statistically significant reduction in ICU LOS for patients treated with MT compared to CDT, with a standardized mean difference (SMD) of 0.38 (95% CI: 0.15–0.62, p = 0.001, I =67%) favoring MT, with moderate heterogeneity (Fig 2B).

Significant Bleeding
Seven studies [13–18,20] with 5438 participants were analyzed. The pooled RR for significant bleeding was 1.02 (95% CI: 0.70–1.47, p = 0.93; I =35%), indicating no statistically significant difference in the risk of bleeding between CDT and MT, with negligible heterogeneity (Supplementary Figure S1)). The included studies reported varying rates of significant bleeding, largely influenced by differences in procedural strategies and definitions of bleeding events. Factors such as the choice of thrombectomy devices, variations in adjunct anticoagulant regimens, and the use of different bleeding classification systems such as the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries (GUSTO) and International Society on Thrombosis and Haemostasis (ISTH) criteria, contributed to the observed heterogeneity in bleeding outcomes across studies.

Major Complications according to the SIR Criteria
Major complications, as defined by SIR, were infrequent but varied across studies. Four studies [13–16] with 729 participants were analyzed. The pooled risk ratio (RR) for major complications was 0.73 (95% CI: 0.36–1.45, p = 0.37; I =0%), indicating no statistically significant difference between CDT and MT, with low heterogeneity (Supplementary Figure S2). The differences in complication rates can be attributed to variations in procedural techniques, patient selection, and institutional expertise.

Blood Transfusion
Three studies [13,14,16] with 677 participants were analyzed. The pooled risk ratio (RR) for blood transfusion was 0.81 (95% CI: 0.48–1.35, p = 0.42; I =0%), indicating no statistically significant difference between CDT and MT, with low heterogeneity (Supplementary Figure S3). Blood transfusion rates were generally low but differed among studies. These differences may reflect varying thresholds for transfusion and procedural-related bleeding risks across institutions.

Hospital Length of Stay
Five studies [13,14,16–18] with a total of 2810 participants were analyzed. The pooled standardized mean difference (SMD) for hospital LOS was -0.08 (95% CI: -0.50 to 0.34, p = 0.72; I =98%), indicating no statistically significant difference in LOS between CDT and MT, with high heterogeneity (Fig 2C). While the point estimate was numerically lower for MT, this should be interpreted with caution given the lack of statistical significance and substantial heterogeneity across studies, likely reflecting differences in patient risk profiles and institutional management approaches.

Post-Procedural PAP Reduction
Three studies [13,16,17], with a total of 1080 participants were analyzed. The pooled SMD is -0.17 (95% CI: -0.29 to -0.05, p = 0.006; I =75%), suggesting a modest trend toward improved outcomes with MT, with moderate heterogeneity (Supplementary Figure S4).

DISCUSSION

General Findings
This meta-analysis provides a comprehensive evaluation of catheter-directed thrombolysis (CDT) and mechanical thrombectomy (MT) for the treatment of intermediate- and high-risk pulmonary embolism (PE). A key finding of this study is the statistically significant reduction in ICU length of stay associated with MT compared to CDT (SMD 0.38, p = 0.001). This result highlights the procedural efficiency of MT, which enables faster clot removal and minimizes the need for prolonged ICU monitoring. For other important outcomes, including in-hospital mortality, hospital length of stay, significant bleeding, blood transfusion, and major complications, no statistically significant differences were identified. Both therapies significantly improved pulmonary artery pressures (PAP) and RV function, with MT showing a slight advantage in the reduction of post-procedural PAP (SMD: -0.17; 95% CI: -0.29 to -0.05; p = 0.006; I = 75%). Notably, several outcomes including hospital length of stay and post-procedural PAP reduction demonstrated high heterogeneity. This may be attributed to differences in device types, operator experience, and patient profiles, including variations in thrombolytic protocols, comorbidities, and institutional management pathways. These factors likely contributed to the inconsistent outcomes and should be explored in future subgroup analyses to improve clinical interpretation and standardization. Despite variations in patient demographics, procedural strategies, and clinical settings, both CDT and MT are effective and safe interventions. This emphasizes the importance of tailoring treatment strategies based on patient characteristics and institutional resources.

Comparison between CDT vs MT
Mechanical thrombectomy (MT) demonstrated shorter ICU stays compared to catheter-directed thrombolysis (CDT), attributed to its ability to achieve rapid clot removal without prolonged thrombolytic infusion and monitoring. Hospital stays were similar between the two modalities, likely influenced by variations in patient risk profiles and institutional management practices. In-hospital mortality rates were also comparable, with MT offering rapid hemodynamic stabilization that supports low mortality rates observed in prior studies. These

findings align with the fact that MT provides immediate hemodynamic improvement compared to the delayed effects observed with CDT, making it a suitable choice for urgent revascularization.

Both CDT and MT exhibited low rates of significant bleeding and transfusion requirements, reflecting advancements in procedural safety and patient management. Major complications were infrequent and similar across both groups, underscoring the safety of these modalities when performed by skilled operators. While both therapies improved post-procedural PAP, MT showed a slight advantage, emphasizing its suitability for cases requiring immediate hemodynamic relief. This highlights the complementary roles of CDT and MT in the management of intermediate- and high-risk pulmonary embolism (PE) [21].

Clinical Implications and Recommendations for Daily Practice

In the field of peripheral vascular interventions, both CDT and MT are recognized as efficient therapies for addressing thrombosis. CDT is particularly indicated for intermediate-risk PE patients with RV dysfunction or elevated pulmonary pressures who are unsuitable for systemic thrombolysis due to bleeding risks or comorbidities. It provides a controlled and gradual thrombus dissolution, making it suitable for patients with a higher risk of complications from more invasive approaches. By contrast, MT is ideal for high-risk (massive) PE or intermediate-risk cases requiring immediate hemodynamic relief. Guidelines emphasize that the appropriateness of CDT is based on patient-specific factors, including clot characteristics, general health, and bleeding risk, while MT requires operator expertise and careful imaging guidance to ensure success. MT's ability to rapidly remove clots without thrombolytics makes it the preferred option in cases of contraindications to thrombolytic therapy or where urgent revascularization is necessary. MT uses advanced tools such as aspiration catheters and stent retrievers [22]. Feroze et al. (2023) [14] further highlighted that patients treated with MT often present with higher risk profiles, such as lower systolic blood pressure and elevated troponin levels, yet demonstrate outcomes comparable to CDT in terms of mortality and readmission. This suggests that MT is a robust option for hemodynamically compromised patients who might not tolerate thrombolysis. However, its higher procedural complexity and learning curve require experienced operators [23].

The choice between CDT and MT involves multiple factors, including the urgency of the situation, clot characteristics and burden, patient comorbidities, and institutional expertise. CDT offers a gradual, controlled clot dissolution, which can be particularly advantageous in patients with multiple comorbidities or compromised health. In such cases, CDT's progressive thrombolysis allows for close monitoring and swift intervention in case of complications. On the other hand, MT provides immediate clot removal, making it the preferred choice for urgent revascularization to preserve organ function and reduce long-term complications. Unfortunately, in the context of low- and middle-income countries (LMICs), the availability of MT may be limited due to its higher cost, technical requirements, and need for experienced operators. CDT, while requiring thrombolytics, may be more accessible in facilities with limited interventional infrastructure. To ensure optimal outcomes regardless of the chosen intervention,a multidisciplinary team approach is essential. Treatment decisions should be guided by a collaborative evaluation of clinical risks and benefits, patient-specific factors, and institutional capabilities, highlighting the need for tailored strategies [24,25].. Future research should focus on standardizing thrombolytic protocols in CDT to maximize efficacy while minimizing risks. Randomized controlled trials comparing CDT and MT are needed to provide definitive evidence on long-term outcomes.

Study Strengths and Limitations

This study has several strengths and limitations. One strength of this study is that , it provides a comprehensive comparison of CDT and MT in intermediate- and high-risk PE, addressing clinically relevant outcomes such as in-hospital mortality, ICU length of stay, significant bleeding, and major complications. By adhering to PRISMA guidelines and including high-quality studies assessed via the Newcastle-Ottawa Scale (NOS), it ensures methodological rigor and reliability. Additionally, the study focuses on emerging therapies, offering valuable insights to guide clinical decision-making. However, limitations include the small number of included studies, most of which were retrospective cohorts, and the absence of RCTs, which limits the strength of the conclusions. Heterogeneity in patient populations, intervention protocols, and outcome definitions introduces variability, particularly in mortality and ICU stay outcomes. Furthermore, the study lacked long-term outcome data, such as PE recurrence or quality-of-life assessments, and the small sample size constrained the ability to detect publication bias. Despite these limitations, this study provides a robust foundation for understanding the comparative efficacy of CDT and MT, highlighting the need for further research, particularly high-quality RCTs.

CONCLUSION

In conclusion, CDT and MT are both effective and safe therapeutic options for intermediate- and high-risk PE patients, with no significant differences in mortality or major complication rates. CDT offers gradual and controlled clot dissolution, making it a suitable choice for patients with significant comorbidities or contraindications to invasive procedures. MT may offer practical benefits in select clinical contexts,

such as potentially shorter ICU stays, though further research is needed to clarify the significance of these findings. These findings underscore the importance of individualized treatment strategies that consider patient-specific factors and institutional expertise. Future studies should aim to further optimize clinical decision-making and procedural standardization, ensuring enhanced outcomes for patients with PE.

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