Endovascular treatment of pulmonary embolism: a systematic review

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Abstract:

Objective: Pulmonary embolism (PE) is a serious cardiopulmonary condition associated with considerable morbidity and mortality, particularly among high-risk patients. The standard therapeutic approach relies on anticoagulation and, in selected cases, systemic thrombolysis. However, these strategies are accompanied by an increased risk of bleeding and may not always achieve rapid restoration of hemodynamic stability. The aim of this study is to conduct a systematic review of the international literature on endovascular techniques in the management of PE, with a focus on mechanical thrombectomy, catheter-directed thrombolysis, and the latest thrombectomy devices (e.g., FlowTriever, Indigo).

Methods: A comprehensive search was performed in PubMed and Google Scholar databases up to October 1st, 2025, to identify relevant studies. The analysis emphasizes effectiveness, safety, complications, and limitations of the available data, while also reviewing current guideline recommendations.

Results: The analysis of 11 studies (RCTs, prospective trials, and registries) demonstrated that endovascular techniques, including ultrasound-assisted thrombolysis (EKOS) and mechanical or pharmacomechanical thrombectomy (FlowTriever, Indigo), achieve rapid and significant improvement in RV/LV ratio and hemodynamic stabilization. In 9 out of 11 studies that used the RV/LV change as an endpoint, the results were particularly encouraging with a mean overall reduction of 0.389. Rates of major bleeding were lower compared with systemic thrombolysis in 8 out of 11 studies (mean rate 2.2%), and overall mortality remained low in most series. In one study (with a significant number of patients, n=800), it was reported that in 87.4% of patients who underwent percutaneous thrombectomy, oxygen requirements decreased within 48h and the percentage of patients with satisfactory oxygen saturation on room air increased from 10.5% to 71.2% postoperatively. However, the available evidence is mainly derived from non-randomized studies and registries, with limited clinical endpoints.

Conclusion: Endovascular techniques appear highly promising, achieving improvement in right ventricular function and hemodynamic stability with a lower risk of bleeding compared to systemic thrombolysis. Nevertheless, the lack of large randomized controlled trials limits the strength of the available evidence. The study highlights the need for further research and the integration of multidisciplinary Pulmonary Embolism Response Teams (PERT) into routine clinical practice.

INTRODUCTION

Pulmonary embolism (PE) remains a leading cause of cardiovascular morbidity and mortality worldwide, with an estimated annual incidence of 60-70 cases per 100,000 population[1]. It results from the obstruction of the pulmonary arteries by embolic material—most commonly thrombus—originating from the deep venous system of the lower extremities. The clinical spectrum ranges from mild dyspnea to hemodynamic collapse and sudden death, underscoring the importance of prompt diagnosis and appropriate management.

Anticoagulation remains the cornerstone of therapy, preventing thrombus propagation and facilitating endogenous fibrinolysis. In high-risk or massive PE, systemic thrombolysis can rapidly restore pulmonary perfusion but carries a considerable risk of major bleeding and is often contraindicated. Surgical embolectomy, although effective, is invasive and available only in specialized centers. These limitations have created a therapeutic gap that has spurred the development of minimally invasive endovascular approaches.

Over the past two decades, endovascular therapies have emerged as a promising alternative or adjunct to conventional treatment. Techniques such as catheter-directed thrombolysis (CDT), ultrasound-assisted CDT, pharmacomechanical interventions, and mechanical thrombectomy aim to achieve rapid thrombus reduction, relieve right ventricular (RV) strain, and restore pulmonary hemodynamics while minimizing systemic exposure to thrombolytic agents. New-generation devices like FlowTriever™ and Indigo™ have further expanded the scope of these interventions by enabling single-session mechanical thrombectomy without the need for thrombolytics.

Growing evidence from prospective trials and registries suggests that endovascular therapies offer significant hemodynamic improvement with lower bleeding risk compared to systemic thrombolysis[2,3]. Consequently, major societies—

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including the European Society of Cardiology (ESC) and the American Heart Association (AHA)—now recognize their role in selected high- or intermediate-risk patients, particularly when thrombolysis is contraindicated or ineffective[4,5]. Furthermore, the multidisciplinary Pulmonary Embolism Response Team (PERT) model has facilitated timely patient selection and improved outcomes[6].

This systematic review aims to summarize and critically evaluate the current evidence regarding endovascular treatment of acute pulmonary embolism, including the efficacy, safety, and clinical outcomes of available techniques, as well as existing gaps in knowledge and directions for future research.

METHODS

This study was designed as a systematic review of the literature following the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The objective was to systematically identify, select, and evaluate clinical studies addressing endovascular management of acute pulmonary embolism (PE).

Search Strategy

The systematic search was conducted in accordance with PRISMA recommendations. As this work forms part of a postgraduate thesis, no protocol was registered in PROSPERO. A structured search strategy was developed, and the PubMed and Google Scholar databases were explored up to **October 1, 2025**, to identify studies evaluating endovascular interventions for PE. Interventions of interest included catheter-directed thrombolysis (CDT), ultrasound-assisted thrombolysis (EKOS), and mechanical thrombectomy using devices such as FlowTriever and Indigo. Reference lists of all included studies were also screened manually for additional eligible publications.

The search strategy combined free-text terms and MeSH headings as follows:

("Pulmonary Embolism"[Mesh] OR "pulmonary embolism" OR "pulmonary thromboembolism")

AND ("Endovascular Procedures"[Mesh] OR "endovascular treatment" OR "endovascular management" OR "catheter-directed therapy" OR "catheter-directed thrombolysis" OR "percutaneous thrombectomy" OR "interventional radiology")

AND ("mechanical thrombectomy" OR "aspiration thrombectomy" OR "EKOS" OR "FlowTriever" OR "Indigo").

Inclusion Criteria

Study selection was based on the PICO framework (Population, Intervention, Comparison, Outcome). Eligible studies included peer-reviewed clinical investigations (randomized controlled trials, prospective and retrospective cohorts, and registries) enrolling adult patients (≥18 years) with **acute intermediate- or high-risk PE** treated with endovascular techniques. Interventions included CDT, ultrasound-assisted CDT (EKOS), and mechanical or pharmacomechanical thrombectomy (FlowTriever, Indigo).

Outcomes of interest comprised **hemodynamic improvement** (e.g., RV/LV ratio, mean pulmonary artery pressure) and **clinical outcomes** (mortality, major bleeding, procedural success). Only studies with ≥50 participants and published between **2000-2025** in English were included.

Exclusion Criteria

Exclusion criteria were:

- Case reports or series with <10 patients
- Animal or in vitro studies
- Narrative reviews, expert opinions, or editorials
- Articles lacking full-text data
- Duplicate publications

Study Selection

All retrieved citations were merged and screened for relevance by title and abstract. Irrelevant or duplicate records were excluded. Full texts of potentially eligible articles were reviewed, and those meeting the inclusion criteria were retained.

From an initial **414 unique studies**, after duplicate removal and screening, **63 full-text articles** were assessed. Of these, **11 studies** met all criteria and were included in this systematic review (e.g., *ULTIMA*, *FLARE*, *FLASH*, *EXTRACT-PE*, *EKOS-PE*).

The selection process is summarized in the **PRISMA flow diagram (Figure 1).**

Data Extraction

From each study, the following information was extracted: first author, publication year, country or study center, sample size, patient characteristics, type of endovascular intervention (CDT, EKOS, FlowTriever, Indigo), and key outcomes such as hemodynamic improvement, complication rates, major bleeding, and mortality. Data were organized into a summary table for comparison.

Data Synthesis

Given the heterogeneity of study designs and limited number of randomized controlled trials, no meta-analysis was performed. Results are presented descriptively in narrative and tabular form.

RESULTS

The database search yielded **421 publications**. After removal of duplicates (n = 7), **414 records** were screened. A total of **63 full-text studies** were reviewed, and **11** met all inclusion criteria. These comprised randomized trials, prospective multicenter studies, retrospective cohorts, and registries.

Key Findings

- **Ultrasound-assisted CDT (EKOS)** studies (*ULTIMA*, *SEATTLE II*, *OPTALYSE*) consistently demonstrated significant **reductions in RV/LV ratio within 24-48 hours**, with **major bleeding rates <5%** and no intracranial hemorrhage.

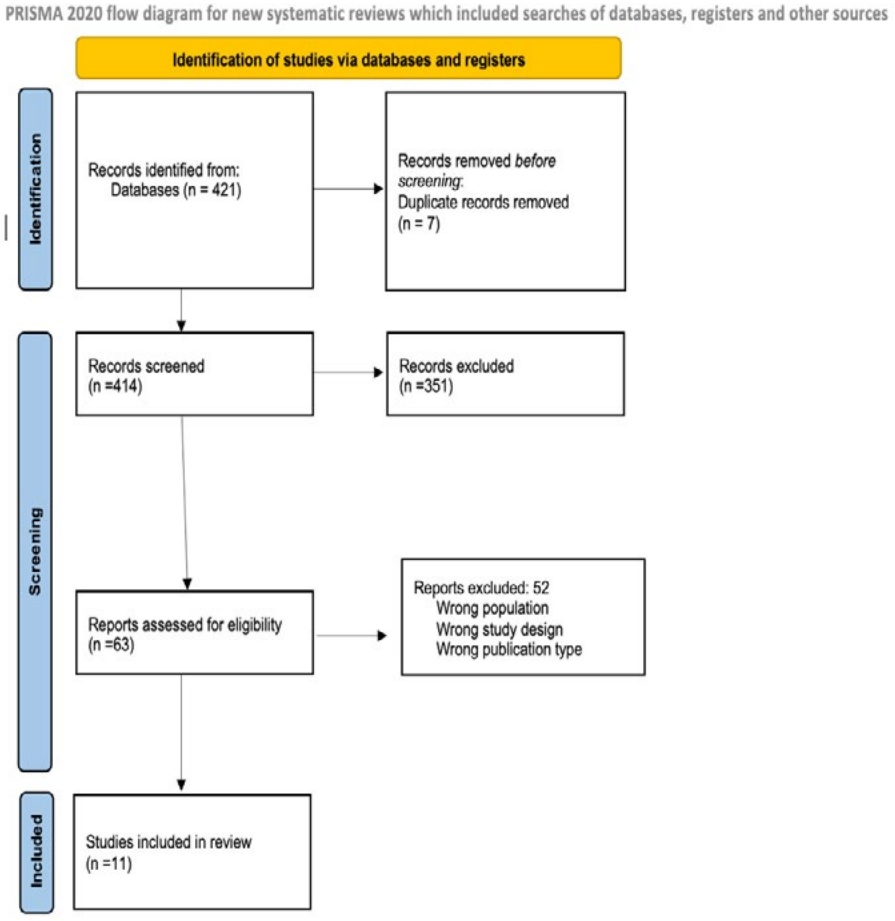

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Figure 1 PRISMA flow diagram

Table 1 Studies included in systematic review

STUDY	YEAR	METHOD USED	N	TYPE OF STUDY	MAIN OUTCOMES
ULTIMA trial – Kucher et al., Circulation[7]	2014	EKOS (US-CDT)	59	RCT (CDT+AC vs AC)	RV/LV ratio reduction (0.30 vs 0.03), no major bleeding
SEATTLE II – Piazza et al., JACC: Cardiovasc Interv[8]	2015	EKOS	150	Prospective multicenter	RV/LV 1.55→1.13. Major bleeding 10%, no ICH
OPTALYSE PE – Tapson et al., JACC[9]	2018	EKOS (dose-ranging)	101	Prospective multicenter	RV/LV -0.3 to -0.4 with low dose tPA, bleeding <4%
SUNSET sPE – Avgerinos et al., Circulation[10]	2021	EKOS vs CDT	82	RCT	No difference in clot burden, RV/LV improved, safe
FLARE trial – Tu et al., JACC: Cardiovasc Interv[11]	2019	FlowTriever	106	Prospective multicenter	RV/LV 1.53→1.15. 0% ICH, mortality 1%
FLASH registry – Toma et al., JACC[12]	2022	FlowTriever	>800	Real-world registry	Hemodynamic improvement, mortality 0.8%, bleeding <2%
EXTRACT-PE – Sista et al., JACC[13]	2021	Indigo	119	Prospective multicenter	RV/LV 1.47→1.04. Bleeding 1.7%, no ICH
Indigo multi-center study – Sylwia Sławek-Szmyt et al., JACC[3]	2023	Indigo	110	Multicenter prospective registry	RV/LV 0.48 benefit, bleeding low, procedural success >90%
PERFECT registry – Kuo et al., Chest[14]	2015	CDT & MT	101	Multicenter registry	Clinical success 86%, mortality 4%, no ICH
FLARE ED substudy – Jaber et al., JACC[15]	2023	FlowTriever	~100	Prospective substudy	Rapid stabilization, RV/LV improved, 0% ICH
PERT Consortium – Kattih et al., JACC[6]	2020-22	Mixed	~200–300	Registry	Mortality 2–4%, outcomes consistent

- **Mechanical thrombectomy with FlowTriever** (*FLARE trial*, *FLASH registry*) showed **rapid hemodynamic improvement**, **mortality <1%**, and **minimal bleeding risk**.
- **Aspiration thrombectomy using the Indigo system** (*EXTRACT-PE trial*, *Indigo registry*) achieved marked reductions in RV/LV ratio with **major bleeding <2%**.
- Large **multicenter registries** (*PERFECT*, *PERT Consortium*, *FLASH*) confirmed high procedural success (>85%) and low periprocedural mortality (2-4%) in real-world practice.
- Across studies, endovascular therapies achieved a **mean RV/LV reduction of 0.39** and an **average major bleeding rate of 2.2%**. In one large registry (>800 patients), oxygen requirements decreased markedly within 48 hours, with the proportion of patients maintaining room-air saturation rising from **10.5% pre-procedure to 71.2% post-procedure**.

Collectively, these data suggest that **endovascular interventions rapidly restore hemodynamics and right ventricular function while minimizing hemorrhagic complications** compared to systemic thrombolysis.

Ultrasound-Assisted Thrombolysis (EKOS)

ULTIMA (2014): RCT (n=59); RV/LV ratio decreased 1.28→0.99 (-23%); no major or intracranial bleeding; 0% mortality.

SEATTLE II (2015): Prospective multicenter study (n=150); RV/LV 1.55→1.13 in 48h; 10% major bleeding, no ICH; improved mPAP and cardiac index.

OPTALYSE-PE (2018): Multicenter (n=101); low-dose tPA (4-12 mg) infusions over 2-6h reduced RV/LV by 0.3-0.4; <4% major bleeding.

SUNSET sPE (2021): RCT (n=82); EKOS vs standard CDT; similar thrombus resolution and RV/LV improvement; no safety difference.

Mechanical Thrombectomy - FlowTriever

FLARE (2019): Prospective (n=106); RV/LV 1.53→1.15 in 48h; no ICH, minimal bleeding.

FLASH Registry (2022): >800 patients; reduced mPAP, improved cardiac output; 30-day mortality 0.8%, major bleeding <2%.

FLARE-ED (2023): Emergency department substudy; confirmed rapid RV/LV improvement and hemodynamic stabilization; 0% ICH.

Aspiration Thrombectomy - Indigo

EXTRACT-PE (2021): Prospective (n=119); RV/LV 1.47→1.04 in 48h; 1.7% major bleeding, no ICH.

Indigo Registry (2023): 110 patients; procedural success >90%, low complication rate.

COMBINED TECHNIQUES AND REGISTRIES

PERFECT Registry (2015): Multicenter CDT & mechanical thrombectomy (n=101); clinical success 86%, mortality ~4%, no ICH.

PERT Consortium Data (2020-2022): ~200-300 patients; mortality 2-4%, good safety profile despite procedural heterogeneity; highlights multidisciplinary PERT value.

Summary of Findings

Across 11 major studies, endovascular therapies (CDT, EKOS, FlowTriever, Indigo) consistently demonstrated **significant hemodynamic and clinical improvement** with **markedly lower bleeding risk** than systemic thrombolysis. Ultrasound-assisted thrombolysis appears safe, though its superiority over standard CDT remains uncertain. Mechanical thrombectomy with FlowTriever and Indigo shows excellent safety and efficacy **without the need for thrombolytics**. Registry data (PERFECT, FLASH, PERT) strengthen external validity and reflect real-world practice.

However, the **lack of large randomized trials** and **limited long-term follow-up** remain major limitations.

DISCUSSION

This systematic review highlights that **endovascular therapy represents a highly promising treatment option** for acute PE, especially in **intermediate- and high-risk patients** for whom systemic thrombolysis is contraindicated or carries excessive bleeding risk.

EKOS-based studies demonstrate that **low-dose local thrombolysis** can achieve rapid right ventricular unloading with minimal bleeding complications. **Mechanical thrombectomy systems** such as FlowTriever and Indigo further advance safety by eliminating thrombolytics altogether, providing immediate thrombus debulking and hemodynamic stabilization.

Nevertheless, several limitations temper the evidence:

- Most studies were **single-arm** and lacked control groups.
- The number of **large randomized trials** remains limited (e.g., *ULTIMA*, *SUNSET sPE*), with relatively small cohorts.
- **Follow-up periods** were short, with scarce data on chronic outcomes such as CTEPH.
- **Outcome heterogeneity** (RV/LV ratio, hemodynamic endpoints, mortality, complications) complicates direct comparison across studies.
- Reported improvements, though clinically meaningful, should be interpreted cautiously due to study variability.

Current **ESC (2019)** and **ATS** guidelines endorse endovascular therapies as **alternative options** in selected cases but emphasize the need for robust, well-designed randomized trials.

In conclusion, while the existing evidence strongly supports the **efficacy and safety** of endovascular approaches, their **definitive role** in the PE treatment algorithm requires further validation through large-scale, long-term randomized

studies. The establishment of **multidisciplinary Pulmonary Embolism Response Teams (PERTs)** is likely to enhance patient selection, streamline decision-making, and improve overall clinical outcomes.

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