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Epidemiology and management of massive, sub-massive, and non-massive pediatric pulmonary embolism: a systematic reviews

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Abstract

Objective To evaluate the current evidence on the diagnosis, management, and outcomes of pediatric pulmonary embolism (PE) across varying severity classifications, including massive, submassive, and non-massive presentations.

Methods A systematic review was conducted following PRISMA guidelines. Searches were performed in PubMed, Scopus, Web of Science, and Cochrane databases up to February 17, 2024. Eligible studies included pediatric and adolescent patients (≤ 21 years) with confirmed PE diagnoses. Risk of bias was assessed using the NIH tool.

Results Six studies involving 258 pediatric patients with massive, submassive, or non-massive PE were included. Most patients were adolescents, with a mean age of 14.1 years and a predominance of females (62–66%). Risk factors included obesity, oral contraceptive use, thrombophilia, and autoimmune conditions. Computed tomography pulmonary angiography (CTPA) was the most frequently used diagnostic modality, showing varied lobar, segmental, and subsegmental involvement. Management strategies ranged from anticoagulation to catheter-directed thrombolysis and surgical thrombectomy. Outcomes varied by severity, with massive PE cases showing higher mortality and complications compared to submassive and non-massive cases.

Conclusion Pediatric PE requires tailored risk stratification and management strategies to optimize outcomes. Delays in diagnosis and severe disease presentations contribute to higher morbidity and mortality. Future research should focus on standardized severity classifications, novel diagnostic modalities, and comparative assessments of therapeutic interventions to enhance outcomes in this population.

Keywords Pediatric pulmonary embolism, Severity classification, Massive pulmonary embolism, Submassive pulmonary embolism, Non-massive pulmonary embolism, Systematic review

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Background

Pediatric pulmonary embolism (PE) presents a rare but significant clinical challenge due to its potential for high morbidity and mortality. Unlike adults, children with PE often exhibit atypical symptoms and delayed diagnoses, complicating timely interventions. Risk stratification based on severity is essential for guiding appropriate management strategies. In this study, we categorized PE into three severity levels: massive, submassive, and non-massive. Massive PE is defined by hemodynamic instability, requiring immediate intervention due to its high mortality risk [1, 2]. Submassive PE, while lacking hemodynamic instability, is characterized by evidence of right ventricular dysfunction or pulmonary hypertension, necessitating close monitoring and tailored management [1, 3]. Non-massive PE cases lack these features but still require prompt diagnosis to avoid progression. Categorizing PE severity is crucial as studies suggest that outcomes differ significantly based on severity levels. Massive PE has been associated with higher mortality and complication rates, while submassive PE outcomes hinge on early recognition and intervention [1, 3, 4]. In the pediatric population, however, evidence on the prognostic impact of PE severity remains limited. This study hypothesizes that PE severity significantly influences outcomes and highlights the need for tailored management approaches. Recent literature underscores disparities in pediatric PE outcomes based on demographic factors such as age, gender, and comorbid conditions. For instance, adolescents with PE exhibit a higher incidence of mortality compared to younger children, while females are at greater risk due to hormonal influences, including oral contraceptive use [5–10]. Studies also report that racial disparities may affect recurrence rates and access to care, emphasizing the need for standardized diagnostic tools and equitable management strategies [6, 7]. Currently, diagnostic practices include computed tomography pulmonary angiography (CTPA), echocardiography, and D-dimer testing. Despite these modalities, variability in diagnostic accuracy and outcomes persists, particularly for massive and submassive PE [3, 4]. Emerging therapeutic interventions, such as catheter-directed thrombolysis, have shown promise for severe cases but require validation in pediatric settings [8–11]. These gaps in evidence necessitate comprehensive research to address the lack of standardized guidelines.

Therefore, this systematic review aims to summarize the literature on the epidemiology of PE in children and evaluate current management strategies for massive, submassive, and non-massive PE. Through this analysis, we seek to identify knowledge gaps and provide future directions for improving outcomes in pediatric PE.

Methods

We performed the current systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews of Interventions, version 6.3 [12]. The study protocol was registered in PROSPERO (ID: CRD42024517245).

Eligibility criteria

This review included studies involving pediatric and adolescent patients (≤ 21 years) with confirmed diagnoses of pulmonary embolism (PE), comparing different severities of the disease: massive, sub-massive, and non-massive PE. The inclusion criteria encompassed randomized control trial, retrospective and prospective cohort studies, case-control studies, and case series (defined as studies involving up to 8 patients). Non-English publications, grey literature, reviews, editorials, basic science research, abstracts, letters, and case reports were excluded.

The population of interest comprised pediatric and adolescent patients with confirmed PE. Studies were analyzed based on management strategies, including anticoagulation, thrombolysis, surgical interventions, and supportive treatments. Outcomes were compared across different PE severities. Primary outcomes included mortality rates, PICU admission, and recurrence of PE. Secondary outcomes focused on complications such as chronic thromboembolic pulmonary hypertension (CTEPH), minor bleeding events, and procedural outcomes like thrombus resolution.

Literature search

We conducted a comprehensive search of four electronic databases (PubMed, Scopus, Web of Science, and Cochrane) on February 17, 2024. The following search query was used: ("Pulmonary embolism" OR "Pulmonary Thromboembolism" OR "Lung embolism") AND (Children OR Child OR Pediatric* OR Adolescent* OR Young OR Infant* OR Neonate* OR Paediatric*) AND Massive AND (Submassive OR "Sub-massive" OR "Sub massive" OR "Non-massive" OR "non massive" OR "nonmassive"). No filters were applied to capture a broad range of studies.

Study selection

Duplicates were removed using Endnote software (Clarivate Analytics, PA, USA). Two independent authors screened the records for eligibility through a two-step process: title and abstract screening, followed by full-text screening. Any disagreements between reviewers were resolved through discussion or consultation with a third reviewer. References of the included studies were reviewed to identify additional relevant studies.

Data extraction

We extracted data using a standardized Excel spreadsheet, which included the following key information: (1) Characteristics of the included studies (2), Characteristics of the study population (age, sex, comorbidities, risk factors), and (3) Outcome measures such as mortality and complications. Data extraction was performed by two independent reviewers to ensure accuracy and minimize bias. Pulmonary embolism diagnosis was confirmed using imaging modalities, primarily computed tomography pulmonary angiography (CTPA), and laboratory markers such as D-dimer levels.

Quality assessment

The quality of the included studies was assessed using the NIH Study Quality Assessment Tools for both cohorts and case series [13]. This tool evaluates factors such as study design, risk of bias, and methodological rigor, with each study classified as good, fair, or poor quality. Although we used the NIH tool for individual study assessment, we acknowledge that the GRADE framework could be used in future studies to assess the cumulative strength of the body of evidence.

Outcome measures and data synthesis

Outcomes were synthesized narratively, given the heterogeneity of the included studies. Primary outcomes of interest were PICU admission rates and mortality rates (including all-cause mortality, in-hospital mortality, and PE-related mortality). Secondary outcomes included PE recurrence rates, complications such as minor bleeding events not requiring significant medical intervention, and chronic thromboembolic pulmonary hypertension (CTEPH).

For studies evaluating Catheter-Directed Thrombolysis (CDT), thrombus resolution (partial or complete) was assessed. All outcomes were reported as percentages relative to the total study population.

Results

Search results

We identified 82 potentially relevant studies from PubMed, Scopus, and Google Scholar. After removing duplicates ($n = 20$), 62 articles underwent abstract and title screening, with 51 excluded. A full-text review of 11 articles resulted in the inclusion of six studies that met eligibility criteria (PRISMA; Fig. 1).

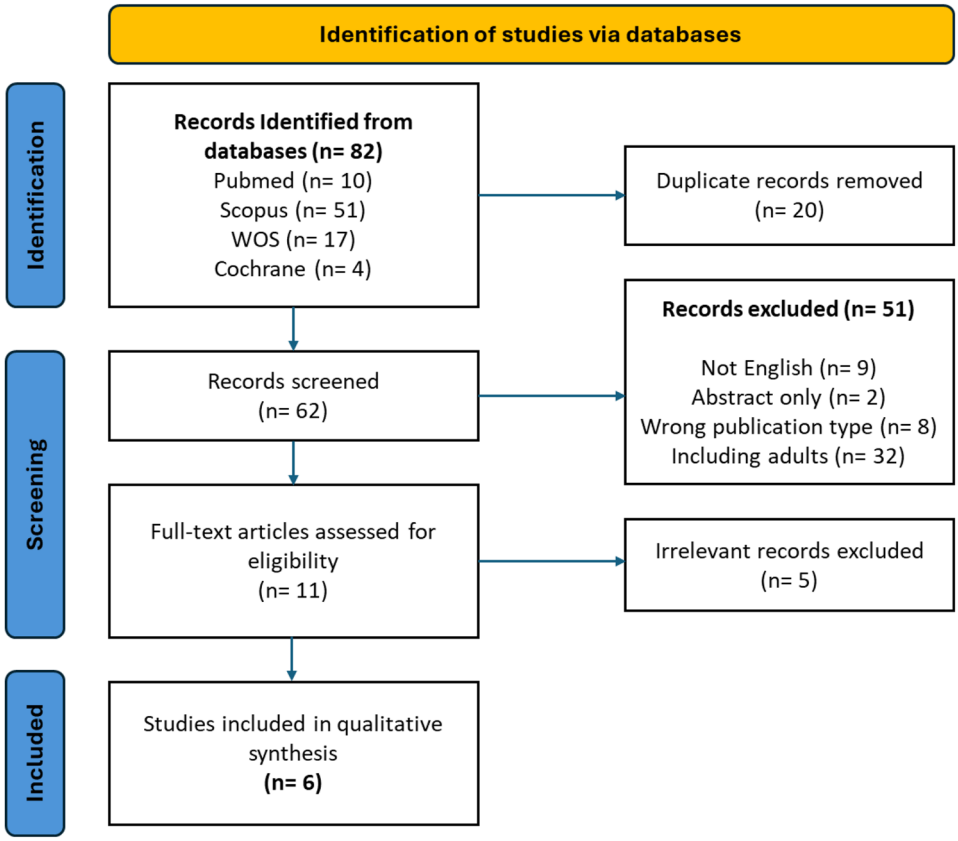

Fig. 1 The PRISMA flowchart summarizing the different stages of screening until the final inclusion of eligible studies

Baseline characteristics

The six studies included 258 pediatric patients with massive, submassive, or non-massive PE (Table 1). Three studies were retrospective cohort studies [3, 4, 11], and three were case series [8–10]. The age of the participant ranged from 12.5 to 16 years old.Common risk factors included oral contraceptive use, thrombophilia, obesity, autoimmune conditions, and positive family history are demonistrted in details in (Tables 2 and 3). Diagnostic criteria and sensitivity varied among studies. In Bragança et al. 2021, the patient cohort ranged from neonates to adolescents, with a mean age of 14.1 years [4]. Belsky 2019 and Akam-Venkata 2018 reported median ages of 15 and 16 years, respectively, for patients with submassive or massive PE [8, 9]. Younger patients and females were disproportionately represented in massive PE cases [3, 10].

Management strategies

Management strategies varied significantly by PE severity and institutional practices. The primary modalities included:

Anticoagulation Therapy: Used in nearly all patients, anticoagulation therapy involved low-molecular-weight heparin (LMWH), unfractionated heparin (UFH), and warfarin as first-line treatments [4, 11]. Patients were transitioned to direct oral anticoagulants (DOACs) in some cases for long-term management [4].

Catheter-Directed Thrombolysis (CDT): CDT was performed in submassive and massive PE cases, showing high thrombus resolution rates (85-92%) with minimal bleeding complications [8, 9]. For instance, in Belsky et al., CDT was initiated within a median of 6.8 h from diagnosis and resulted in complete or partial thrombus resolution in 83% of patients.

Surgical Interventions: Reserved for critical cases, surgical thrombectomy was performed in patients with hemodynamic instability or intracardiac thrombi [4, 11]. This modality was typically used when thrombolysis was contraindicated or unsuccessful.

Supportive Measures: Oxygen therapy, extracorporeal membrane oxygenation (ECMO), and inotropic support were utilized in critically ill patients with massive PE and cardiopulmonary compromise [3, 4, 8]. In Akam-Venkata et al., five patients received ultrasound-accelerated thrombolysis using.

Prognosis and outcomes

Patient outcomes were stratified by PE severity, revealing significant variability:

Massive PE: Associated with the highest mortality rates, reaching up to 22%, largely due to delayed diagnoses and treatment failures [8, 11]. Survivors often required prolonged hospitalization and faced higher rates of complications, such as chronic thromboembolic pulmonary hypertension (CTEPH).

Submassive PE: This cohort exhibited favorable survival rates with the use of CDT and anticoagulation therapy, though a small percentage (8%) progressed to massive PE. In Ross et al., right ventricular dysfunction was observed in all submassive PE cases but resolved with timely CDT [3, 9].

Non-Massive PE: Patients in this category had lower mortality (2%) and minimal long-term complications. Outcomes were generally favorable with anticoagulation alone, as reported in Bragança et al. [4].

During follow-up (median 11 months), Ji et al. reported sustained improvements in right ventricular function in all survivors, with no cases of PE recurrence [10]. However, Pelland-Marcotte et al. documented long-term complications, including CTEPH, in 12% of massive and submassive PE cases [11].

Symptoms and presentations

The clinical presentation of PE varied widely across studies:

Common Symptoms: Thoracalgia (42%), dyspnea (38%), hemoptysis (25%), syncope (18%), and deep vein thrombosis (15%) were frequently reported [4,8,9].

Submassive PE: Characterized by imaging findings of right ventricular dysfunction, with echocardiographic evidence of pulmonary hypertension in 85% of cases [12].

Massive PE: Often presented with hemodynamic instability and signs of severe cardiopulmonary compromise, including tachycardia, hypotension, and hypoxia [3, 10].

Quality assessment

We assessed the included cohort studies and case series using the NIH tool. The quality of the included cohorts ranged from fair to poor, whereas it ranged from fair to good in case series (Supplementary Table). This indicates the crucial need for large future studies to address PE in pediatric population.

Discussion

Key findings

This systematic review emphasizes the clinical variability, diagnostic challenges, and management strategies for pediatric pulmonary embolism (PE). Adolescents, particularly females, were disproportionately affected, with risk factors such as obesity, oral contraceptive use, and hereditary thrombophilia. Categorizing pulmonary embolism (PE) by severity—massive, submassive, and non-massive—provides a structured approach that guides treatment and predicts outcomes. Our findings reveal that massive PE cases are associated with the highest morbidity and mortality, often necessitating aggressive interventions such as catheter-directed thrombolysis

Table 1 Summary table of included studies

Study ID	Study design	Study Period	Country	Sample size	Inclusion Criteria	Exposure groups (MPE, SMPE, NMPE)	Main finding(s) of the study
Bragança et al., 2021	Retrospective cohort	2008–2020	Portugal	29	• Discharge diagnostic code "415.1-Pulmonary Embolism and infarction" (ICD-9CM) in the administrative database. • Length of stay > 24 h in the Pediatric Department or Intensive Care Unit. • Radiological reports reviewed to confirm diagnosis.	• NMPE: 13 patients (45%) • SMPE: 11 patients (38%) • MPE: 5 patients (17%)	• Risk Factors: Contraceptives (65%), thrombophilia (35%), obesity (20%), autoimmunity (20%), among eight inpatients, immobilization (87.5%), complex chronic diseases (75%), infections (75%), and central venous catheter use (62.5%) were associated.
Ross et al., 2020	Retrospective cohort	1997–2019	USA	33	• Patients < 19 years old with MPE or SMPE acutely managed at the institution. • Excluded patients with Glenn or Fontan procedures. • Pulmonary embolism (PE) confirmed by: o Computed tomography angiogram. o Fluoroscopic pulmonary angiogram. o Ventilation and/or perfusion scan. o Autopsy. • Cases identified through electronic medical record and autopsy reports using keyword searches (January 1, 1997– June 30, 2019).	• SMPE: 24 patients (73%) • MPE: 9 patients (27%)	• Risk Factors: Oral contraceptive pills (49%), major comorbidities (89% of MPE vs. 25% of SMPE, $p = 0.002$), critical illness (56% of MPE vs. 8% of SMPE, $p = 0.009$), immobility (67% of MPE vs. 13% of SMPE, $p = 0.005$), central venous catheters (67% of MPE vs. 17% of SMPE, $p = 0.01$), and postoperative status (44% of MPE vs. 4% of SMPE, $p = 0.01$). • Complications: Mortality rate of 18%, with 9% PE-related deaths. MPE patients had a higher likelihood of dying before discharge (56% vs. 4%, $p = 0.003$). • Treatment: Both groups had similar rates of primary reperfusion attempts (78% of MPE vs. 67% of SMPE, $p = 0.69$).
Pelland-Marcotte et al., 2019	Retrospective cohort	2000–2016	Canada	170	• Children aged 0–18 years with pulmonary embolism confirmed by imaging or pathology. • Excluded: o Sudden death without radiological or pathological confirmation of pulmonary embolism. o Non-thromboembolic pulmonary embolism (e.g., tumor thrombus or septic emboli).	o NMPE: 121 patients (71%) o SMPE + MPE: 49 patients (29%)	• Risk Factors: Patients with massive or submassive pulmonary embolism were younger (median age 12.5 years [IQR 0.6–15.1] vs. 14.4 years [9.3–16.1], $p < 0.0001$), more likely to have a cardiac condition (33% vs. 14%, $p = 0.009$), and had more central venous catheters (59% vs. 40%, $p = 0.027$). • Treatment: Aggressive treatment modalities were more commonly used in patients with massive or submassive pulmonary embolism (45% vs. 6%, $p < 0.0001$).
Belsky et al., 2019	Case series	2010–2018	USA	8	• Children (ages ≤ 21 years) diagnosed with pulmonary embolism between January 1, 2010, and June 31, 2018. • Submassive pulmonary embolism (SMPE) was defined per American Heart Association guidelines as acute PE without evidence of systemic hypotension but with echocardiographic evidence of right ventricular dysfunction. • Baseline demographic data were extracted for patients who received catheter-directed thrombolysis (CDT).	• SMPE: 6 patients (75%)	• Treatment: Five patients underwent six episodes of CDT. • Complications: No patient developed major or clinically relevant non-major bleeding. • Outcomes: Most patients had complete radiological thrombus resolution, and no patient showed evidence of chronic thromboembolic pulmonary hypertension.

Table 1 (continued)

Study ID	Study design	Study Period	Country	Sample size	Inclusion Criteria	Exposure groups (MPE, SMPE, NMPE)	Main finding(s) of the study
Akam-Venkata et al., 2018	Case series	2005–2017	USA	9	• Children aged ≤ 20 years with a structurally normal heart who underwent catheter-directed therapy for acute pulmonary embolism at Detroit Medical Center. • Exclusion criteria: Children with underlying congenital heart disease (CHD), except for patent foramen ovale. • Definitive diagnosis of acute pulmonary embolism was made based on chest CT angiography in all included cases.	• SMPE: 6 patients (67%) • MPE: 3 patients (33%)	• Treatment: Significant clinical improvement was noted within 24 h in four out of five patients treated with EkoSonic. • Complications: Among the seven patients who survived, two had minor gastrointestinal bleeding. • Outcomes: Median hospital stay was 8 days (range 5–24 days). Two patients with massive pulmonary embolism died, possibly due to delayed initiation of catheter-directed therapy.
Ji et al., 2019	Case series	2016–2018	USA	9	• Patients < 21 years old who presented with acute pulmonary embolism (PE) and associated cardiac arrest, sustained hypotension requiring vasopressor support, or normotensive shock with heart rate < 40 beats per minute. • Patients < 21 years old with acute PE without hypotension or shock but with evidence of right heart strain on imaging or evidence of myocardial necrosis. • All patients were primarily managed by the Pediatric Intensive Care Unit (PICU). • Hematology and interventional radiology consults were obtained for all patients.	• SMPE: 4 patients (44%) • MPE: 5 patients (56%)	

Abbreviations: CDT: Catheter-Directed Thrombolysis, CHD: Congenital Heart Disease, CT: Computed Tomography, MPE: Massive Pulmonary Embolism, NMPE: Non-Massive Pulmonary Embolism, PE: Pulmonary Embolism, PICU: Pediatric Intensive Care Unit, SMPE: Submassive Pulmonary Embolism, IQR: Interquartile Range

(CDT) or surgical thrombectomy. Delays in diagnosis were a significant contributor to adverse outcomes, highlighting the importance of heightened clinical suspicion in high-risk patients. Submassive PE cases generally show favorable outcomes with CDT and anticoagulation therapy, although some cases can progress to massive PE. Right ventricular dysfunction, which is observed in most submassive PE cases, serves as an important prognostic indicator. Although non-massive PE cases are less severe, they still require timely intervention to prevent complications. Anticoagulation alone was effective in most cases, but identifying and addressing underlying risk factors remains crucial to reducing recurrence.

Comparison to adult literature

The findings align with adult literature, where PE severity significantly influences clinical outcomes. In adults, massive PE carries a mortality rate exceeding 25% if untreated, a trend echoed in pediatric cases with delayed diagnoses [14]. However, differences in risk factors are evident; hormonal influences such as oral contraceptive use and genetic predispositions play a more prominent role in pediatric cases compared to the immobilization and malignancy frequently seen in adults [6]. In adults, CDT is well-documented for reducing thrombus burden and improving right ventricular function. Although pediatric studies demonstrate promising outcomes, including favorable thrombus resolution and minimal bleeding complications, robust data from randomized controlled trials remain lacking, limiting widespread adoption of CDT in pediatric PE management [3, 8, 9].

Diagnostic and therapeutic implications

Accurate and early diagnosis remains the cornerstone of improving outcomes in pediatric PE. CTPA is the most reliable imaging modality, though its use is often limited by concerns over radiation exposure, particularly in younger children. Echocardiography plays a complementary role, particularly in assessing right ventricular strain and pulmonary hypertension, both of which are critical indicators in submassive and massive PE. The findings highlight gaps in the utility of D-dimer in pediatrics. While sensitive in adults, its high false-positive rates in children—owing to concurrent inflammatory or

Table 2 Baseline characteristics of included studies

Study ID		Bragança et al., 2021			Ross et al., 2020		Pelland-Marcotte et al., 2019		Belsky et al., 2019	Akam-Venkata et al., 2018			Ji et al., 2019		
Sample size		29			33		170		8	9			9		
Exposure group		NMPE	SMPE	MPE	SMPE	MPE	NMPE	SMPE + MPE	SMPE	Total (SMPE + MPE)	SMPE	MPE	Total (SMPE + MPE)	SMPE	MPE
n (%)		13	11	5	24	9	121	49	6	9	6	3	9	4	5
Age Median (IQR)		-	-	-	15(15–16)	16(10–16)	14·5 (9·3–16·1)	12·5 (0·6–15·1)	15 (3–21)	16 (12–20)	-	-	13.9 (4.38)	-	-
Females n (%)		6(46.2%)	9(81.8%)	2(40%)	17(71)	5(56)	52 (43%)	29 (59%)	2 (30%)	6 (66.67%)	3 (50%)	3 (100%)	5 (55%)	-	-
PE location n (%)	Bilateral	-	-	-	-	-	46 (39%)	34 (69%)	-	-	-	-	-	-	-
	Lobar	-	-	-	-	-	63 (53%)	35 (71%)	-	-	-	-	-	-	-
	Segmental	-	-	-	-	-	43 (36%)	10 (20%)	-	-	-	-	-	-	-
	Subsegmental	-	-	-	-	-	13 (11%)	4 (8%)	-	-	-	-	-	-	-
Clinical presentation n (%)	None	-	-	-	-	-	21 (17%)	2 (4%)		-	-	-	-	-	-
	Dyspnoea (SOB)	-	-	-	-	-	64 (53%)	28 (57%)	3 (50%)	9 (100%)	-	-	1 (10%)	-	-
	Chest pain	-	-	-	-	-	63 (52%)	9 (18%)	6 (100%)	-	-	-	-	-	-
	Haemoptysis	-	-	-	-	-	7 (6%)	4 (8%)	-	-	-	-	-	-	-
	Cyanosis or hypoxemia	5(38.5%)	4(36.4%)	5(100%)			13 (11%)	33 (67%)	-	9 (100%)	-	-	-	-	-
	Shock or cardiac arrest	0	0	1(20%)	0	4(44)	4 (3%)	21 (43%)	-	-	-	-	-	-	-
	Syncope	2(15.4%)	3(27.3%)	1(20%)	-	-	-	-	2 (30%)	-	-	-	-	-	-
	Tachycardia/ palpitation	3(23.1%)	10(90.9%)	5(100%)	-	-	-	-	1 (16%)	-	-	-	-	-	-
	Leg pain or DVT	-	-	-	-	-	-	-	1 (16%)	5 (56%)	2 (33%)	2 (66%)	3 (33%)		
	Vasopressor requirement	-	-	-	1 (50)	5(56)	-	-	-	-	-	-	-	-	-
Major Comorbidities n (%)		-	-	-	6(25)	8(89)	-	-	-	-	-	-	-	-	-
D-dimer: Negative n (%)		2(15.4%)	-	0	-	-	-	-	-	-	-	-	-	-	-
Thrombophilia: Negative n (%)		-	-	-	-	-	53/90 (59%)	15/28 (53%)	4 (66%)	-	-	-	-	-	-
Diagnostic method n (%)	CT	-	-	-	23(96)	2(22)	-	-	6 (100%)	9 (100%)	6 (100%)	3 (100%)	-	-	-
	Angiography	-	-	-	0	5(56)	-	-	-	-	-	-	-	-	-
	Ventilation or perfusion scan	-	-	-	1(4)	0	-	-	-	-	-	-	-	-	-
	Autopsy	-	-	-	0	2(22)	-	-	-	-	-	-	-	-	-

Table 2 (continued)

Study ID		Bragança et al., 2021			Ross et al., 2020		Pelland-Marcotte et al., 2019		Belsky et al., 2019	Akam-Venkata et al., 2018			Ji et al., 2019			
Sample size		29			33		170		8	9			9			
Exposure group		NMPE	SMPE	MPE	SMPE	MPE	NMPE	SMPE+MPE	SMPE	Total (SMPE+MPE)	SMPE	MPE	Total (SMPE+MPE)	SMPE	MPE	
n (%)		13	11	5	24	9	121	49	6	9	6	3	9	4	5	
Management n (%)	Anticoagulation only	12(92.3%)	8(72.7%)	0	24(100)	7(78)	106 (88%)	23 (47%)	-	-	-	-	-	-	-	
	Any reperfusion (aggressive therapy)	-	-	-	16(67)	7(78)	7 (6%)	22 (45%)	-	-	-	-	-	-	-	
	Surgical embolectomy	-	-	-	2 (13)	3 (43)	-	-	-	-	-	-	-	-	-	
	Catheter-directed therapy	-	-	-	1 (6)	3 (43)	-	-	6 (100%)	9 (100%)	6 (100%)	3 (100%)	9 (100%)	6 (100%)	3 (100%)	
	Systemic thrombolysis	-	-	-	13 (81)	1 (14)	-	-	-	-	-	-	-	-	-	
	Observation	-	-	-	-	-	8 (7%)	4 (8%)	-	-	-	-	-	-	-	
PICU admission		2(15.4%)	2(18.2%)	4(100%)	-	-	-	-	-	-	-	-	-	-	-	

infectious conditions—limit its diagnostic specificity [4]. Future studies should explore advanced diagnostic tools, including biomarkers and low-radiation imaging modalities, tailored to pediatric needs.

Management strategies must be stratified by severity

Management strategies must be tailored according to the severity of PE. In cases of massive PE, early use of ECMO and systemic thrombolysis is essential for hemodynamic stabilization, though these interventions carry risks of major bleeding. Surgical thrombectomy, while infrequently used, remains a viable option in refractory cases. For submassive PE, CDT demonstrated high rates of thrombus resolution with minimal complications. Timely intervention, especially in cases with right ventricular strain, is critical to preventing progression to massive PE. In non-massive PE cases, anticoagulation alone is generally effective; however, it must be complemented by addressing underlying risk factors to minimize recurrence.

Future plans

Addressing the gaps identified in this review requires a multi-pronged research agenda. Future studies should establish standardized diagnostic criteria and risk stratification models for pediatric PE severity to improve inter-study comparability and clinical application. Collaboration across institutions is essential for conducting prospective multicenter studies that generate robust data on diagnostic accuracy, therapeutic efficacy, and long-term outcomes in children with PE. Additionally, comparative trials on CDT, ECMO, and novel anticoagulants in pediatric patients are needed, as well as studies exploring ultrasound-accelerated thrombolysis to refine protocols for submassive and massive PE. Furthermore, research should focus on addressing health equity by examining disparities in outcomes based on gender, race, and socioeconomic status, and developing targeted interventions to ensure equitable access to care. Lastly, prioritizing the validation of novel biomarkers and low-radiation imaging techniques tailored to pediatric patients will help improve early diagnosis while minimizing harm.

Limitations

This systematic review highlights several limitations. First, the heterogeneity of studies, including variations in diagnostic criteria, treatment protocols, and reporting standards, introduced significant variability, which prevented a quantitative synthesis of the data. Second, most studies relied on retrospective designs, which are prone to biases such as incomplete documentation of patient characteristics and outcomes. Third, the small sample sizes in many studies reduce the generalizability of the

Table 3 Risk factor characteristics of patients within the included studies

Study ID		Bragança et al., 2021			Ross et al., 2020		Pelland-Marcotte et al., 2019		Belsky et al., 2019	Akam-Venkata et al., 2018			Ji et al., 2019		
Sample size		29			33		170		8	9			9		
Exposure group		NMPE	SMPE	MPE	SMPE	MPE	NMPE	SMPE + MPE	SMPE	Total (SMPE + MPE)	SMPE	MPE	Total (SMPE + MPE)	SMPE	MPE
n (%)		13	11	5	24	9	121	49	5	9	6	3	9	4	5
Risk factors n (%)	OCP	-	-	-	15 (88)	1 (20)	-	-	1 (16%)	4 (67%)	2 (33%)	2 (66%)	3 (33%)	-	-
	Obesity	-	-	-	9(38)	2(22)	25 (21%)	10 (20%)	1 (16%)	6 (67%)			3 (33%)	-	-
	Cardiac disease	-	-	-	0	2(22)	17 (14%)	16 (33%)	-	-	-	-	-	-	-
	Central venous catheter	-	-	-	4(17)	6(67)	48 (40%)	29 (59%)	1 (16%)	-	-	-	-	-	-
	Immobility	-	-	-	3(13)	6(67)	-	-	-	5 (56%)	2 (33%)	3 (100%)			
	Malignancy	-	-	-	1 (4)	2 (22)	28 (23%)	5 (10%)	-	-	-	-	-	-	-
	Family history of VTE	-	-	-	8 (36)	0	30 (25%)	7 (14%)	-	-	-	-	-	-	-
	History of VTE	-	-	-	0	2 (22)	21 (17%)	14 (29%)	-	-	-	-	-	-	-
	Postoperative	-	-	-	1(4)	4(44)	12 (10%)	4 (8%)	-	-	-	-	-	-	-
	Vascular malformation	-	-	-	2 (8)	2 (22)	7 (6%)	6 (12%)	-	-	-	-	-	-	-
	Critical illness	-	-	-	2(8)	5(56)	-	-	-	-	-	-	-	-	-
	Infectious or inflammatory	-	-	-	-	-	22 (18%)	8 (16%)	-	-	-	-	-	-	-
	Psychiatric medications	-	-	-	7 (29)	1 (11)	-	-	-	-	-	-	-	-	-
	Pulmonary disease	-	-	-	1 (4)	2 (22)	-	-	1 (16%)	-	-	-	-	-	-
	Prothrombotic disorder	-	-	-	7 (39)	1 (100)	-	-	-	-	-	-	-	-	-
	SLE	-	-		-	-	-	-	-	2 (23%)					
	haematological diseases	-	-	-	-	-	-	-	-	3 (33%)	-	-	-	-	-

findings and underscore the rarity of pediatric PE. To address these limitations, future research should focus on standardized, prospective studies with larger sample sizes and extended follow-up periods.

Conclusion

This systematic review highlights the importance of classifying pediatric pulmonary embolism (PE) by severity to guide diagnosis and treatment. Adolescents, particularly females with risk factors like hormonal influences and thrombophilia, are at higher risk and require tailored management. Massive PE demands aggressive interventions such as catheter-directed thrombolysis (CDT) and ECMO, while submassive PE benefits from CDT and anticoagulation. Non-massive PE typically has favorable outcomes with timely anticoagulation.

Pediatric PE, though rare, carries significant morbidity and mortality, especially in severe cases. Delays in diagnosis, limited access to therapies, and inconsistent management protocols remain key challenges. Addressing these through large-scale, multicenter trials and novel therapeutic approaches is essential to improving outcomes.

Future research should focus on standardized severity classifications, comparative therapeutic assessments, and the development of diagnostic tools to enhance early detection and treatment, ultimately improving outcomes for affected children and adolescents.

Abbreviations

PE	Pulmonary Embolism
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
VTE	Venous Thromboembolism
CDT	Catheter-Directed Therapy
PROSPERO	International Prospective Register of Systematic Reviews
PICU	Pediatric Intensive Care Unit
NIH	National Institutes of Health
UFH	Unfractionated Heparin
LMWH	Low-Molecular-Weight Heparin
DOACs	Direct Oral Anticoagulants
CT	Computed Tomography
CTEPH	Chronic Thromboembolic Pulmonary Hypertension
PA	Pulmonary Artery
ECMO	Extracorporeal Membrane Oxygenation
tPA	Tissue Plasminogen Activator
SMPE	Submassive Pulmonary Embolism
MPE	Massive Pulmonary Embolism

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Author contributions

Mohammed Alsabri (MA) is the frist and corresponding author. He proposed the project, contributed to the conception, formulation, and drafting of the article, participated in and supervised the elaboration at every step of the paper writing process, and was responsible for coordination of the study and communication with all co-authors. Dina Essam (DA) and Mohammed Ayyad (MAA) also both contributed equally to the conception and drafting of the paper, as well as the revision of the whole paper. They are considered first authors. Mahmoud Shaban Abdelgalil (MS) helped with the revision of the whole paper. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

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Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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