

Pulmonary Embolism in the Pediatric Emergency Department

AUTHORS: Beesan Shalabi Agha, DO,^{a,b} Jesse J. Sturm, MD,^{a,b,c,d} Harold K. Simon, MD, MBA,^{a,b,c} and Daniel A. Hirsh, MD^{a,b,c,e}

Departments of ^aPediatrics, and ^cEmergency Medicine, Emory University, Atlanta, Georgia; ^bPediatric Emergency Medicine, Children's Healthcare of Atlanta, Atlanta, Georgia; ^dPediatric Emergency Medicine, Connecticut Children's Medical Center, University of Connecticut, Hartford, Connecticut; and ^ePediatric Emergency Medical Associates LLC, Atlanta, Georgia

KEY WORDS

pulmonary embolism, pediatric emergency department, Wells criteria, Pulmonary Embolism Rule-out Criteria (PERC)

ABBREVIATIONS

AHA—American Heart Association

DVT—deep venous thrombosis

ESI—Emergency Severity Index

ICD-9—International Classification of Diseases, Ninth Revision

OCP—oral contraceptive

PED—pediatric emergency department

PE—pulmonary embolism

PERC—Pulmonary Embolism Rule-out Criteria

Dr Agha carried out the initial analyses and drafted the initial manuscript; Drs Sturm and Simon critically reviewed and revised the manuscript; Dr Hirsh conceptualized and designed the study, designed the data collection instruments, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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Address correspondence to Beesan Shalabi Agha, DO, 1645 Tullie Circle, Atlanta, GA 30329. E-mail: bagha@emory.edu

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WHAT'S KNOWN ON THIS SUBJECT: Pulmonary embolism (PE) in the pediatric population is rare but does occur and is underrecognized. In adult emergency medicine, there are validated clinical decision rules derived to provide reliable and reproducible means of determining pretest probability of PE.



WHAT THIS STUDY ADDS: There are known risk factors, signs, and symptoms that should raise the clinician's suspicion of pulmonary embolism, even in the pediatric population.

abstract

OBJECTIVE: To describe patients who present to the pediatric emergency department (PED) and are subsequently diagnosed with pulmonary embolism (PE).

METHODS: Electronic medical records from 2003 to 2011 of a tertiary care pediatric health care system was retrospectively reviewed to identify patients <21 years who had a final *International Classification of Diseases, Ninth Revision* diagnosis of PE. Patient demographics, and hospital course were recorded. Adult validated clinical decision rules Wells criteria and Pulmonary Embolism Rule-out Criteria (PERC) were retrospectively applied. PERC identified 8 clinical criteria for adult patients using logistic regression modeling to exclude PE without additional diagnostic evaluation. If all criteria are met, further evaluation is not indicated.

RESULTS: Of 1 185 794 PED visits, 105 patients had an ultimate diagnosis of PE. Twenty-five met study criteria, and all were admitted. Forty percent of these patients had PE diagnosed in the PED. The most common risk factors were BMI ≥ 25 (50%, 10 of 20), oral contraceptive use (38% 5 of 13 female patients), and history of previous thrombus without PE (28%, 7 of 25). When the PERC rule was applied retrospectively, 84% of patients could not be ruled out, indicating additional evaluation for PE was needed.

CONCLUSIONS: Pulmonary embolism is rare in children but does occur. This study emphasizes risk factors among children that should raise the suspicion of PE. Additional studies are needed to further evaluate risk factors and signs and symptoms of PE to develop pediatric specific clinical decision rules to provide reliable and reproducible means of determining pretest probability of PE. *Pediatrics* 2013;132:663–667

Pulmonary embolism (PE) in the pediatric population is rare, but evidence suggests it is underrecognized and seldom considered by physicians.¹ National Hospital Discharge Survey has reported the annual incidence of childhood PE as 0.9 per 100 000 children per year.² Predisposing risk factors for PE in children include obesity, immobility, central venous catheter, malignancy, congenital heart disease, systemic lupus erythematosus, nephrotic syndrome, surgery, trauma, and prolonged total parenteral nutrition.^{2,3} Despite numerous predisposing risk factors and underlying disease states, a study that reviewed 23 years of admission and autopsy data in children found the incidence of clinically important PE to be 25 per 100 000 admissions.²

Despite known predisposing risk factors, signs, and symptoms, there is still often delay to diagnosis of PE because presenting concerns often overlap with other conditions. Prompt recognition and treatment of PE is crucial, failure to diagnose can have grave consequences. Mortality rates of PE in childhood are reported to be around 10%.^{3,4}

In adult emergency medicine, there are validated clinical decision rules derived to provide reliable and reproducible means of determining pretest probability of PE and prevent unnecessary diagnostic testing. Wells Criteria for pretest probability of PE consists of 7 weighted criteria: (1) clinical signs and symptoms of deep venous thrombosis (DVT; +3.0); (2) an alternative diagnosis that is less likely than PE (+3.0); (3) pulse rate >100 beats per minute (+1.5); (4) immobilization or surgery in the previous 4 weeks (+1.5); (5) previous DVT/pulmonary embolism (+1.5); (6) hemoptysis (+1.0); and (7) malignancy (on treatment, treated in the past 6 months, or palliative; +1.0). Summation of these point values can be categorized into low (<2), moderate (2–6), or high (>6) pretest probability with prevalence for

pulmonary embolism of 2% to 4%, 19% to 21%, and 50% to 67%, respectively.^{5,6}

The Pulmonary Embolism Rule-out Criteria (PERC) rule identified 8 clinical criteria for adult patients using logistic regression modeling to exclude PE without additional diagnostic evaluation, including the use of D-dimer. According to the rule, if all criteria are met, further evaluation is not indicated. The 8 variables were (1) age <50 years; (2) initial heart rate was <100 beats per minutes; (3) initial oxygen saturation was >94% in room air; (4) no asymmetric lower leg swelling was present; (5) no hemoptysis was reported; (6) no recent surgery was reported; (7) no previous PE or DVT; and (8) no hormone use.^{7,8}

There are no such tools for pediatric patients. Lack of similar validated criteria combined with lower clinical suspicion may be a partial explanation for the delay in diagnosis in pediatric patients. To our knowledge, no study to date has assessed time to diagnosis of PE in pediatric patients who present to the PED. The objective of this study was to describe patients who present to the PED and are subsequently diagnosed with PE. Additionally, the subsequent clinical course of patients diagnosed in the PED was compared with those who were diagnosed after subsequent admission to the hospital (delayed diagnosis group).

METHODS

The electronic medical record from a large tertiary care pediatric health care system was reviewed for patients treated from January 2003 to October 2011. Cases were identified of children <21 years who had a final emergency department or hospital discharge *International Classification of Diseases, Ninth Revision* diagnosis of pulmonary embolism (PE) and had initially presented to 1 of its 2 tertiary care pediatric emergency departments (PEDs; >120 000

combined annual visits). Patients were excluded if PE was diagnosed at an outside facility, were directly admitted, had a known history of PE, or had PE occur as a complication during hospitalization (but had no signs or symptoms of PE at onset of hospitalization). Patients with a known history of DVT without PE were included.

A standard data form was created before data extraction and was used to collect PED and subsequent hospital data. Patient demographics including age, gender, race, weight, and BMI were recorded as well as visit characteristic (Emergency Severity Index [ESI] triage level, disposition, and PED diagnosis).⁹ Charts were reviewed to determine morbidity and mortality from diagnosis of PE and time to delayed diagnosis of PE. Because PE is such a rare condition, charts with missing data were included in the study, and missing elements were excluded from individual analysis.

Records were reviewed to obtain D-dimer data, triage vital signs and presenting signs and symptoms such as chest pain, shortness of breath, cough, and hemoptysis. If a symptom was not noted in the medical record it was excluded from individual analysis. Age-based vital sign standards from American Heart Association (AHA) were used to define abnormal respiratory rate and heart rate. For study purposes, hypoxia was defined as room air saturations <95% measured via pulse oximetry.

Medical history and risk factors relevant for PE including malignancy, congenital heart disease, systemic lupus erythematosus, nephrotic syndrome, obesity, immobility, central venous catheter, oral contraceptive (OCP) use, previous thrombus, recent surgery, trauma, and prolonged total parenteral nutrition were recorded and summarized.

Time from PED encounter to diagnosis, length of stay, and previous and subsequent PED utilization after PE diagnosis were recorded.

The adult PE rules (Wells Criteria and PERC) were applied to the cases identified retrospectively. Of the 7 weighted criteria that make up Wells criteria, 6 could be applied retrospectively by looking at the medical records. Criteria number 2, an alternative diagnosis that is less likely than PE (+3.0), was excluded because this could not be ascertained from the medical records. Criteria 3, pulse rate >100 beats per minute (+1.5), was adjusted when applied to our population. Because a pulse >100 is considered abnormal in adults, we applied this same rule but used age-based vital sign standards from the AHA guidelines to define abnormal heart rate.

When applying the PERC rule retrospectively, all 8 criteria could be obtained from the medical records. Similarly to the Wells criteria, PERC rule 2, initial heart rate was <100 beats per minutes, was adjusted when applied to our population. Again, we applied this same rule but used age-based vital sign standards from the AHA guidelines to define abnormal heart rate.

Patient characteristics and clinical course of those patients with PE who were diagnosed in the PED were compared with those who were diagnosed after admission. Statistical tests were performed with SPSS 20.0 statistical analysis software (SPSS Inc, Chicago, IL). Categorical variables were compared by using the χ^2 test or by Fisher exact test when appropriate. Continuous variables were compared by using the paired and unpaired *t* test as appropriate.

RESULTS

From January 2003 through October 2011, there were 1 185 794 total PED visits and 105 patients with a final diagnosis of PE. Twenty-five cases met study inclusion criteria. Patients were excluded because they had their PE diagnosed at an outside facility (4%, 5

TABLE 1 Patient Demographics of Those Diagnosed in the PED Versus Those Diagnosed After Admission

	All Patients (<i>N</i> = 25)	In PED (<i>n</i> = 10)	After Admission (<i>n</i> = 15)	<i>P</i>
Median age (range)	15 y (26 d–18 y)	15.5 y	13.5 y	.03 ^a
Females, %	52%	50%	53%	1.0
African American, % (<i>N</i> = 24)	50%	20% (2/10)	71% (10/14)	.04 ^a
White, % (<i>N</i> = 24)	46%	80% (8/10)	21% (3/14)	.01 ^a
BMI >25, % patients (<i>N</i> = 20)	50%	63% (5/8)	42% (5/12)	.65

^a Significant *P* value.

of 105), were directly admitted (and thus did not present to the PED; 41%; (43 of 105), had a known history of PE (19%; 20/105), or had PE occur as a complication during a prolonged hospitalization (but did not have signs or symptoms of PE at onset of hospitalization; 11%; 12 of 105). The resulting incidence of patients presenting to the PED without a known diagnosis of PE on presentation in this study population was 2.1 cases per 100 000 visits.

Patient demographics are shown in Table 1. The median age was 15 years (range 26 days–18 years). Seventy-six percent of patients were given high-acuity ESI level 1 and 2. The remainder of patients were given an ESI level of 3. Forty percent (10 of 25) of patients diagnosed with PE were diagnosed in the PED during the index visit. All 25 patients with PE were admitted, regardless of whether their PE was diagnosed in the PED or during the hospitalization. Of the 25 patients with PE identified in this study, no patients died of a complication related to PE. Of those who did not have a diagnosis of PE at the time of admission, the top 3 PED diagnoses on admission were DVT, respiratory distress,

and pneumonia. Of those patients diagnosed with PE after admission, the mediantime to make the diagnosis was 2 days (range 0–11 days).

Signs and symptoms of patients diagnosed with PE both in the PED and after admission are shown in Table 2. Triage vital signs showed AHA age-based tachypnea in 75% (18 of 24) and tachycardia in 58% (14 of 24) of patients. Chest pain was reported in 52% (13 of 25) of patients, shortness of breath in 44% (11 of 25) and cough in 32% (8/25).

Eighty percent of all patients had 1 risk factor, and 48% had ≥ 2 risk factors as shown in Table 3. The risk factors for patients diagnosed with PE in our study are identified in Fig 1. The most common risk factors in our study was BMI ≥ 25 (50%, 10 of 20), OCP use (38% of female patients), and history of previous thrombus without PE (28%, 7 of 25).

For the 25 patients in this study, Wells criteria and PERC were retrospectively applied. Of our 25 patients, 48% (12/25) had a Wells score of <2, putting them into the low-risk group with a pretest probability of PE between 2% to 4%. Fifty-two percent of the patients (13 of

TABLE 2 Signs and Symptoms of Patients Diagnosed in the PED Versus After Admission

	All Patients (<i>N</i> = 25)	In PED (<i>n</i> = 10)	After Admission (<i>n</i> = 15)	<i>P</i>
Chest pain, %	52	80	33	.04 ^a
Shortness of breath, %	44	60	33	.24
Hemoptysis, %	4	10	0	.4
Tachycardia, % <i>N</i> = 24	58	70 (7/10)	50 (7/14)	.42
Tachypnea, % <i>N</i> = 24	75	70 (7/10)	79 (11/14)	.67
Hypoxia, % <i>N</i> = 23	17	0 (0/9)	29 (4/14)	.13

^a Significant *P* value.

TABLE 3 Risk Factors and D-Dimer Data of Patients Diagnosed in the PED Versus After Admission

	All Patients (N = 25)	In PED (n = 10)	After Admission (n = 15)	P
1 risk factor	80%	100%	67%	.06
≥2 risk factors	48%	60%	40%	.43
D-dimer obtained during hospitalization	84%	90%	80%	.63
D-dimer obtained in PED	44%	80%	20%	.005 ^a
Abnormal initial D-dimer, N = 21	90% (19/21)	100% (9/9)	83% (10/12)	.49

^a Significant P value.

25) had a Wells score between 2 and 6, putting them into the moderate risk group with a pretest probability of PE between 19% to 21%. None of our patients had a Wells score >6, which is the high-risk group with a pretest probability of PE between 50% to 67%. When applying the PERC rule, all 8 criteria could be obtained from the medical records. Eighty-four percent of patients (21 of 25) did not meet all 8 criteria, which would mean additional evaluation for PE was indicated. The most common PERC criteria not satisfied dealt with heart rate. Fifty-eight percent of patients (14 of 24) were tachycardic, indicating PE could not be excluded. The next most common PERC criteria not satisfied was clinical signs of DVT. Thirty-six percent of patients (9 of 25) had clinical signs of DVT at their ED visit. Twenty-eight percent of patients (7 of 25) had a previous history of DVT, and 20% of all patients (5 of 25; 38% of females, 5 of 13) had hormone use. These patients could not all have PE excluded by PERC, suggesting additional work-up was indicated.

DISCUSSION

PE in children is rare but underrecognized.² Studies have looked at various characteristics of pulmonary embolism in the pediatric population, but no study has looked at pulmonary embolism presenting to the PED.

We found the incidence of PE diagnosed within the PED and excluding those with a known diagnosis of PE, those diagnosed at outside hospitals, those directly admitted, or those that had PE occur as complication of hospitalization to be 2.1 cases per 100 000 visits.

Adult emergency medicine has clinical decision rules derived to provide reliable and reproducible means of determining pretest probability of PE. No such rules exist in pediatric emergency medicine. The PERC rule was established to exclude PE without further diagnostic evaluation. When PERC was applied to a pediatric population (adjusting for age-based vital signs), 84% of patients could not be ruled out with this rule, indicating additional evaluation for PE was needed.

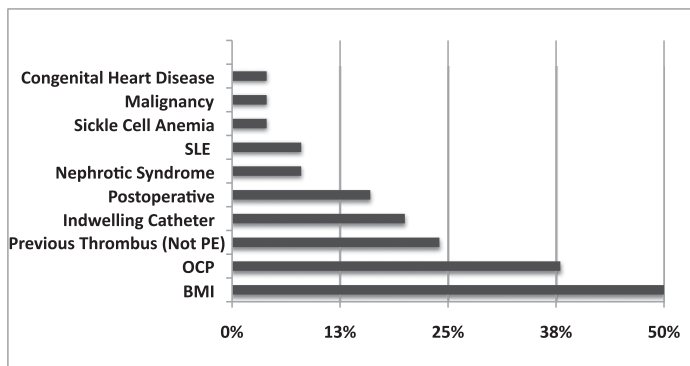


FIGURE 1 Risk factors for patients diagnosed with PE. SLE, systemic lupus erythematosus.

Although PERC and Wells do overlap in certain criteria (abnormal heart rate, clinical signs and symptoms of DVT, history of previous DVT or PE, hemoptysis, and recent surgery) there are some differences. Unlike PERC, Wells criteria looks into a patient's history of malignancy, specifically asking whether a patient is currently undergoing treatment, has in the past 6 months, or is receiving palliative treatments. None of the patients in this study met this criterion. Unlike Wells criteria, PERC looks into exogenous estrogen use as well as initial room air oxygen saturation >94%. Twenty percent (5 of 25) of overall patients (38% of females) were using OCP in this study. Seventeen percent (4 of 24) of patients had an initial room air oxygen saturation <95%. These patients would have been captured through PERC, indicating further studies were indicated and PE could not be ruled out. These rules were established for adult patients, and no such rules exist for pediatric patients. More studies need to be conducted in children with PE in an effort to develop pediatric clinical decision rules to help determine pretest probability of PE.

Pediatric PE studies have reported that chest pain, shortness of breath/dyspnea, and cough are the most common reported symptoms of PE.^{10,11} Our study confirmed this with 52% of our patients reporting chest pain, 44% reporting shortness of breath, and 32% reporting cough. An adult pulmonary embolism study consisting of 117 patients found that dyspnea, hemoptysis, or pleuritic pain was present in 107 of 117 patients (91%).¹² Only 1 of our patients (4%) reported hemoptysis.

Central venous line-related thrombosis has been reported to be the most common predisposing factor for PE in children and adolescents.^{3,13,14} This was not found in our study. We found the most common risk factor to be obesity. The Centers for Disease Control and Prevention reports that obesity affects 17%

of children and adolescents in the United States (triple the rate from 1 generation ago). Because obesity is a known risk factor of PE, this may contribute to an increased incidence of PE in the pediatric population.

In our study, the median time to make the accurate diagnosis of PE was 1 day (range 0–11 days). Our time to diagnose PE can be compared with another study that looked at inpatient and outpatient clinic charts of 14 patients with proven PE followed at a hemostasis and thrombosis center, which reported an average time to accurate diagnosis of 7 days with 4 of 14 (29%) patients diagnosed on the day of presentation.¹⁵

Because this study relies on diagnosis code to identify cases, it is possible that some cases of PE were not identified. The electronic medical record was reviewed

for admission diagnosis, PED discharge diagnosis, and hospital discharge diagnosis where PE was included in the *International Classification of Diseases, Ninth Revision* diagnosis. If a patient presented to the study institution and expired without a known diagnosis, those patients could have been missed. However, this number of patients would be expected to be low. Once identified in the study data set, if a patient expired, it would have been recorded. It is also unlikely that a patient would be diagnosed with pulmonary embolism (either in the PED or during admission) but not have record of that diagnosis in the electronic medical record.

CONCLUSIONS

PE does occur in the pediatric population. In this series, no patient died of

PE or from delayed care. Despite known risk factors and signs or symptoms of PE, it remains a challenge for clinicians to diagnose during the initial PED presentation. This study emphasizes risk factors that should raise the suspicion of PE, even among children. OCP use is part of PERC but not part of the Wells criteria and is a known risk factor of PE. A substantial portion of the female patients with PE in this study did report OCP use. Pediatric multicenter studies are needed to evaluate risk factors and signs and symptoms of PE to develop pediatric-specific clinical decision rules to provide reliable and reproducible means of determining pretest probability of PE. This is especially true because this is a rare but recognizable concern in the pediatric population.

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