

# Bringing PERT to Pediatrics



## Initial Experience and Outcomes of a Pediatric Multidisciplinary Pulmonary Embolism Response Team (PERT)

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**BACKGROUND:** Multidisciplinary pulmonary embolism response teams (PERTs) streamline care of adults with life-threatening pulmonary embolism (PE). Given rarity of pediatric PE, developing a clinical, educational, and research PERT paradigm is a novel and underused concept in pediatrics.

**RESEARCH QUESTION:** Is a PERT feasible in pediatrics, and does it improve PE care?

**STUDY DESIGN AND METHODS:** A strategy-to-execution proposal to launch a pediatric PERT was developed for institutional buy-in. Key stakeholders collectively implemented the PERT. Data were collected for the 2-year pre-PERT and post-PERT eras, and outcomes were compared.

**RESULTS:** PERT implementation took 12 months. Our PERT, led by hematology, is composed of pediatric experts in emergency medicine, critical care, interventional cardiology, anesthesiology, and interventional radiology. Data on 30 patients pre-PERT and 31 patients post-PERT were analyzed. Pre-PERT, 10% (3 of 30), 13% (4 of 30), 20% (6 of 30), and 57% (17 of 30), and post-PERT, 3% (1 of 31), 10% (3 of 31), 16% (5 of 31), and 71% (22 of 31) were categorized as high-risk, intermediate-low-risk, intermediate-high-risk, and low-risk PE, respectively. Post-PERT, there were 13 unique PERT activations. PERT was activated on all eligible patients with PE and, additionally, on four low-risk PEs. Time to echocardiogram was shorter post-PERT (4.7 vs 2 hours;  $P = .0147$ ). Anticoagulation was ordered (90 vs 54 min;  $P = .003$ ) and given sooner (154 vs 113 min;  $P = .049$ ) post-PERT. There were no differences in time to reperfusion therapies (12 hours pre-PERT vs 8.7 hours post-PERT,  $P = .10$ ). Five of six (83.3%) eligible (intermediate-high and high-risk) patients received reperfusion therapies in the post-PERT era compared to three of eight (37.5%) eligible patients in the pre-PERT era ( $P = .0001$ ). There were no differences in major bleeding, mortality, or length of stay in either era.

**INTERPRETATION:** The pediatric PERT paradigm was successfully created and adopted locally. Our PERT enhanced access to experts, facilitated timely advanced therapies, and held value for low-risk PE. The University of Texas Southwestern Medical Center and Children's Medical Center pediatric PERT may serve as a best practice model for streamlining care for pediatric PE.

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**KEY WORDS:** catheter-directed thrombolysis; pediatric pulmonary embolism; pediatrics; PERT; pulmonary embolism; pulmonary embolism response team; reperfusion therapies; venous thromboembolism

**ABBREVIATIONS:** CDT = catheter-directed thrombolysis; ECMO = extracorporeal membrane oxygenation; IQR = interquartile range; IR = interventional radiology; LMWH = low-molecular-weight heparin; LOS = length of stay; OSH = outside hospital; PE = pulmonary embolism; PERT = pulmonary embolism response team; tPA = tissue

plasminogen activator; UFH = unfractionated heparin; UTSW = University of Texas Southwestern Medical Center

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## Take-home Points

**Study Question:** Is a pulmonary embolism response team (PERT) feasible in pediatrics and does it improve pulmonary embolism (PE) care?

**Results:** PERT, activated on all eligible patients with PE, improved time to echocardiogram, time to anticoagulation administration, and access to reperfusion therapies when pre- and post-PERT eras were compared.

**Interpretations:** Pediatric PERT implementation was feasible, and a PERT should be considered by pediatric thrombosis programs to streamline PE care.

VTE affects approximately one in 200 hospitalized children.<sup>1,2</sup> The incidence of pulmonary embolism (PE), the most severe clinical presentation of VTE, has increased dramatically by approximately 200%, disproportionately affecting adolescents.<sup>3,4</sup> Despite markedly increased PE rates, pediatric PE remains infrequent, even at high-volume centers, and its

management is highly variable. A broad range of therapeutic options is available, including parenteral anticoagulation and advanced reperfusion therapies including systemic thrombolysis or tissue plasminogen activator (tPA), catheter-directed thrombolysis (CDT), thrombectomy, and surgical embolectomy. Physician and institutional expertise and available resources largely drive treatment. In adults with PE, implementing pulmonary embolism response teams (PERTs), modeled after hospital-based rapid response teams, has optimized the care of adults with PE.<sup>5-10</sup> We created a pediatric PERT to address institutional variation in PE management and rapidly initiate a management plan individually tailored to the degree of hemodynamic and cardiopulmonary instability in each patient. Herein, we describe the PERT creation and implementation process and compare clinical, process, and health care utilization outcomes before implementation and after implementation at our center. We hypothesized that multidisciplinary PE care will improve PE outcomes, enhance access to PE experts, and facilitate the receipt of appropriate advanced reperfusion therapies.

## Study Design and Methods

### *PERT Creation, Composition, and Activation*

We developed and implemented the PERT at The University of Texas Southwestern Medical Center (UTSW) and Children's Health System of Texas, comprising a large urban quaternary children's hospital and a second level II children's hospital campus. After introducing our concept, development phase, and institutional buy-in (collectively called strategy-to-execution proposal) at UTSW, we invited pediatric experts with a self-identified interest in PE to join the PERT. Core

members, led by hematology alongside a dedicated anticoagulation pharmacist, consisted of pediatric specialists in emergency medicine, critical care, interventional cardiology, anesthesiology, and interventional radiology (IR). All specialties, including an in-house intensivist and a cardiologist performing echocardiograms, are available 24/7 at both campuses. Our second campus does not offer CDT, embolectomy/thrombectomy, or extracorporeal membrane oxygenation (ECMO) because it does not have the resources for these modalities. Any patient with a PE necessitating reperfusion is transferred to the primary children's hospital on stabilization. Additional steps included developing institutional PE guidelines; setting up a PE activation pager, which simultaneously notifies all core PERT members; establishing PERT activation criteria; creating a standing PERT conference platform; and dispersing institutional education about the newly developed PERT. The PERT can be activated at any time via the PERT pager through an initial hematology consultation for any patient with confirmed intermediate- or high-risk PE or suspected PE with clinical instability, hemodynamic compromise, or collapse at either of our two hospitals or an outside hospital (OSH) without risk categorization. A diagnostic and treatment plan is developed in real-time at the multidisciplinary online meeting, and resources are mobilized (Fig 1). CDT is typically

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## A Schematic Flow Diagram of the Pediatric PERT Process

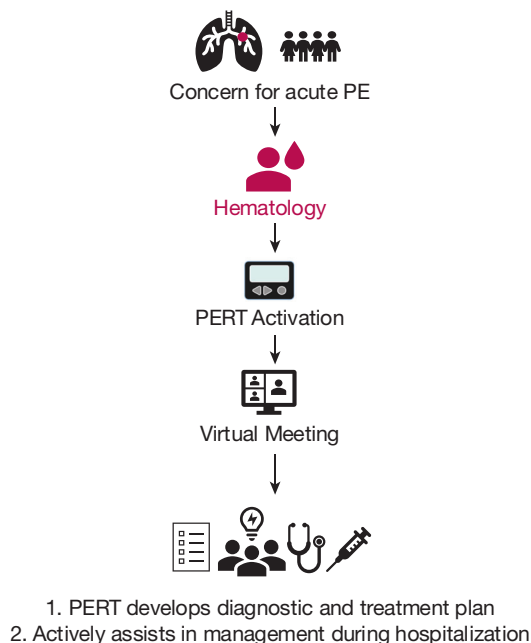


Figure 1 – Schematic flow diagram of the University of Texas Southwestern Medical Center Pediatric PERT process. PE = pulmonary embolism; PERT = pulmonary embolism response team.

performed by IR at our center, but interventional cardiology intervenes in PE cases associated with congenital heart disease or clot-in-transit. They do not alternate call. Patients are admitted to the pediatric ICU unless they have significant cardiac complexity requiring cardiac ICU admission. The PERT can also be activated before the interhospital transfer to facilitate a safe transfer and prevent clinical deterioration.

### Data Collection

We reviewed data between May 2019 and June 2023. The study received ethics approval from the UTSW institutional review board (STU No. 2021-0982). We defined the post-PERT era to include any patient with a PE after the first official PERT activation in May 2021 until June 2023. Because this included 2 years of data, we selected the pre-PERT era as the preceding 2 years to official PERT implementation. Data from consecutive patients with any acute PE were collected across both eras, including demographics, medical history, and details of their hospital course. The post-PERT era also included PERT-specific information (eg, activation time, consultation time, members present at each meeting).

**Study Definitions:** We categorized PE severity as high risk, intermediate risk, or low risk based on the European Society of Cardiology 2019 guidelines<sup>11</sup>;

intermediate risk was subcategorized into intermediate-low risk and intermediate-high risk. Our PE stratification excluded Pulmonary Embolism Severity Index/simplified Pulmonary Embolism Severity Index due to differences in disease presentation, physiological responses, clinical parameters, comorbidities, and incidence between children and adults; it is also not validated in children. We defined the time of PE diagnosis as the time a radiologist or cardiologist first documented an objective PE in the impression section of the relevant imaging (CT angiography, echocardiogram) report. Although echocardiograms are not the criterion standard or initial imaging modality for diagnosing PE, in a few cases, they detected PE or saddle emboli, prompting PE-directed intervention. The time to echocardiogram was calculated as the time taken from PE diagnosis to the time to echocardiogram completion. Echocardiogram completion time was selected because the official report in the electronic medical system lags behind when the echocardiogram results are verbally conveyed to treating physicians. For an OSH transfer with diagnosed PE, we measured the arrival time at our emergency department to the time of echocardiogram completion. We excluded patients with echocardiograms completed for an alternative diagnosis before PE workup. We curated our management approach based on European Society of Cardiology 2019 guidelines<sup>11</sup> and American College of Chest Physicians (CHEST) guidelines.<sup>12,13</sup> We have refined our approach based on literature by Ross et al<sup>14</sup> and subspecialty input. Time to anticoagulation order measured the time of PE diagnosis to when an anticoagulation (low-molecular-weight heparin [LMWH], unfractionated heparin [UFH]) was first ordered. Time to anticoagulation given measured the time of PE diagnosis to the time anticoagulation was first administered. If LMWH was administered at an OSH and continued at our facility after arrival, we used the OSH time to anticoagulation. If LMWH was given at an OSH, and the patient was transitioned to UFH at our hospital, then we measured arrival time at our hospital to the time UFH was started; LMWH in this case was considered a bolus. If a UFH bolus was given at an OSH and was continued at our hospital, then we used the first time that UFH was initiated. Time to reperfusion therapy was measured as the time of PE diagnosis to when any reperfusion therapy (CDT, systemic thrombolysis, or thrombectomy/embolectomy) was performed. Any patient with PE stratified as intermediate-high risk or high risk was deemed eligible for reperfusion therapy as part of our local treatment protocol. Hospital length of stay (LOS) was

counted from the day after hospital admission for PE diagnosis (the day of admission counted as day 0) and included the day of discharge in the total duration. ICU LOS was counted from the day the patient arrived at the ICU (the day of ICU admission counted as day 0) with a PE diagnosis or developed a PE while in the ICU and included the day of transfer if the patient stayed in the ICU until at least 12 PM. We excluded medically complex patients requiring prolonged ICU stays for diagnoses other than PE for LOS calculations. Major bleeding and clinically relevant nonmajor bleeding were defined using the International Society on Thrombosis and Hemostasis criteria before the updated International Society of Thrombosis and Hemostasis Scientific Standardization Committee guidance for efficacy and safety outcomes was published.<sup>15</sup> PE-related mortality was defined as death

within 30 days due to PE diagnosis. We used the 30-day period to better understand the acute impact of PE and to ensure consistent comparisons across other studies that have used a similar end point.<sup>5,6,8</sup>

### Statistical Analysis

We summarized continuous variables as medians with interquartile ranges (IQRs) and means  $\pm$  SDs, and categorical variables using frequencies and percentages. We compared pre- and post-PERT patients using Fisher exact and/or  $\chi^2$  tests for categorical variables and the Mann-Whitney *U* test for comparing nonnormally distributed variables. All analyses considered two-sided  $P < .05$  as statistically significant. The sample size was a convenience sample, including all consecutive patients with PE within our prespecified eras.

## Results

### PERT Implementation, Composition, and Activation

PERT implementation took 12 months (Fig 2). At UTSW, the pediatric PERT core faculty, spearheaded by hematology alongside a dedicated anticoagulation pharmacist, includes specialists in pediatric critical care, anesthesiology, interventional cardiology, emergency medicine, and IR (Fig 3, Table 1). Cardiothoracic surgery and ECMO experts do not convene at the initial PERT activation (Figs 3, 4) but are informed after multidisciplinary discussion by the intensivist, if appropriate for that patient.

### PE Cohorts

We identified 30 patients before PERT activation and 31 patients after PERT activation in the time periods examined (Table 2) at both campuses. A small number of PE cases ( $n = 5$ ) presented to our second campus, and all were transferred to the main campus for further management. The two cohorts were similar in age (16 [IQR, 14–17] vs 15 [IQR, 13–16] years). A higher proportion of young female patients were diagnosed with PE after PERT (73% vs 46%); otherwise, there were no differences in the demographics in either era. The comorbidities or predispositions to PE were similar in the two cohorts, except there were for more cases of active cancer in the post-PERT era. Before PERT, 10% (3 of 30), 13% (4 of 30), 20% (6 of 30), and 57% (17 of 30), and after PERT, 3% (1 of 31), 10% (3 of 31), 16% (5 of 31), and 71% (22 of 31) were categorized as high-risk, intermediate-low risk, intermediate-high risk, and low-risk PE, respectively. After PERT, low-risk PE comprised

the largest PE category (71% vs 57%). Although the PERT was primarily activated for PE stratified as intermediate- or high-risk PE, PERT was also activated for low-risk PE associated with significant morbidity and complexity.

### Outcomes

**Treatment Outcomes:** Post-PERT, there were 13 unique PERT activations: one (7.7%) for high-risk PE, eight (61%) for intermediate-risk PE, and four (30%) for low-risk PE; all were confirmed PE (Fig 5, Table 3). Hematology, critical care, IR, and anesthesia experts attended all PERT activations. The PERT was activated on all eligible patients with PE and, additionally, on four low-risk PEs. A total of 10% were started on LMWH and 90% on UFH before PERT and 5% on LMWH and 95% on UFH after PERT, respectively. The proportion of patients undergoing reperfusion therapies (3 [10%] vs 5 [16%]) was numerically higher in the post-PERT group ( $P = .48$ ). Five of six (83.3%) eligible (intermediate-high and high-risk) patients received reperfusion therapies in the post-PERT era compared to three of eight (37.5%) eligible patients in the pre-PERT era ( $P = .0001$ ). No eligible patients had contraindications to reperfusion therapies. Before PERT, all three patients received CDT. After PERT, reperfusion techniques included CDT ( $n = 3$  [10%]), systemic tPA ( $n = 3$  [10%]), and surgical embolectomy ( $n = 1$  [3%]); one patient received surgical embolectomy and systemic tPA; one patient received systemic tPA and CDT. In each era, there was one patient who was cannulated for ECMO.

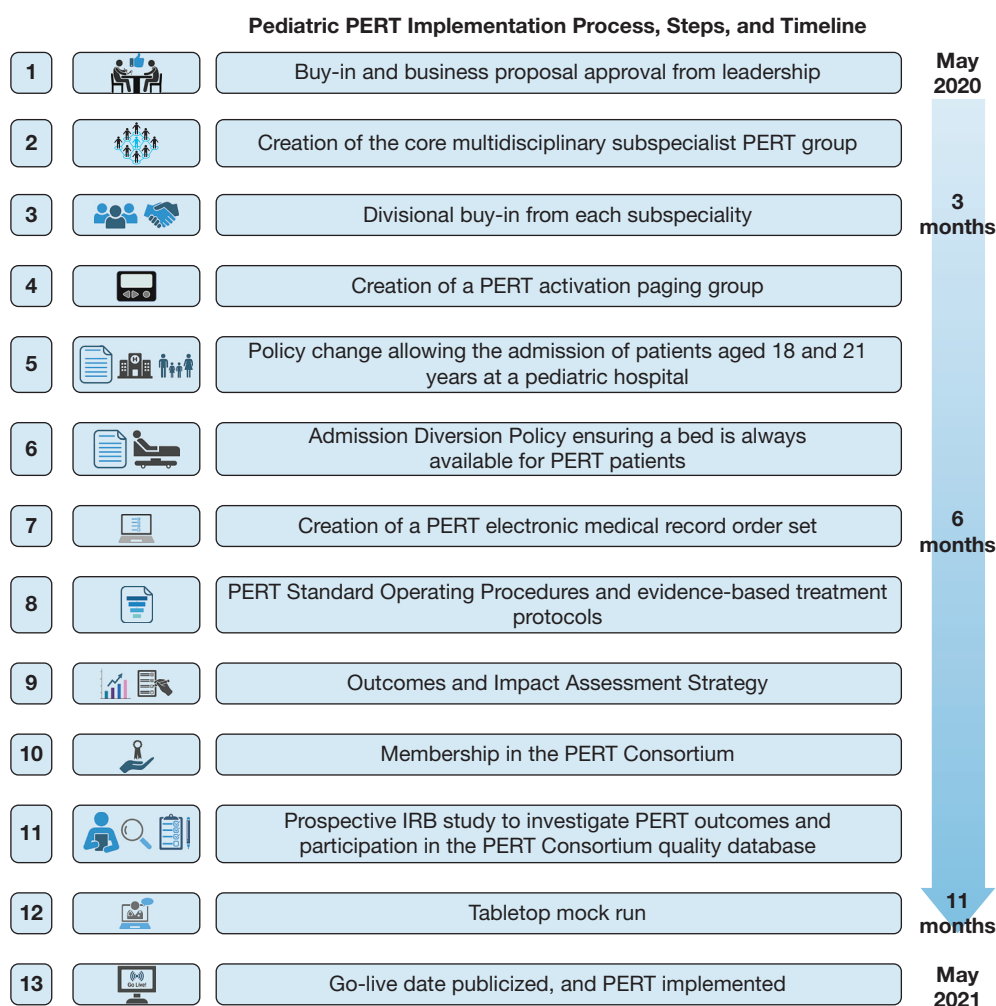


Figure 2 – Pediatric PERT implementation process, steps, and timeline. IRB = institutional review board; PERT = pulmonary embolism response team. Created with BioRender.com.

**Process Outcomes:** The median time to echocardiogram was shorter after PERT (4.7 [IQR, 1.8-11] vs 2 [IQR, 0.85-3.75] hours;  $P = .0147$ ). Anticoagulation was ordered and given sooner after PERT (time to anticoagulation order: 90 [IQR, 62-205] vs 54 [IQR, 31-82] min;  $P = .003$ ; time to anticoagulation given: 154 [IQR, 107-256] vs 113 [IQR, 62-170] min;  $P = .049$ ). There were no differences in time to reperfusion therapies (12 hours before PERT [IQR, 4.9-17.5] vs 8.75 hours after PERT [IQR, 5.7-14.1];  $P = .10$ ).

**Health Care Utilization Outcomes:** The median LOS was similar (6 [IQR, 3-15] vs 6 [IQR, 4-17] days;  $P = .72$ ), and the median ICU LOS was 1.5 days (IQR, 0-3) before PERT vs 1 day (IQR, 0-4.5) ( $P = .63$ ) after PERT. ICU LOS analysis included 27 patients before PERT and 31 patients after PERT. Patients with comorbidities requiring ICU for additional reasons were excluded.

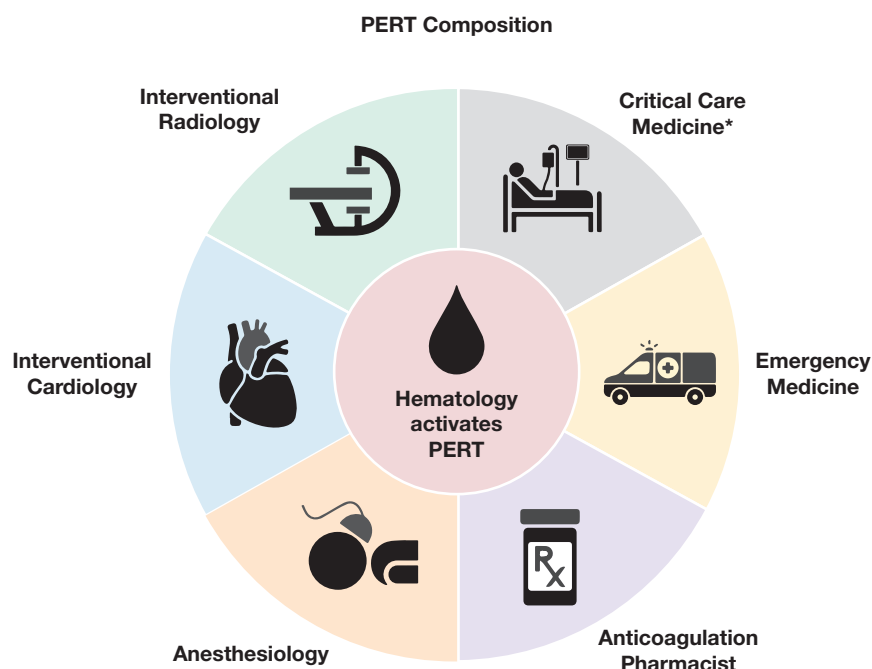
**Bleeding Outcomes and Mortality:** Major bleeding occurred in five of 30 patients (16.6%; 95% CI, 5.6%-34.7%) before PERT and two of 31 patients (6.4%; 95% CI, 0.79%-21.4%) after PERT ( $P = .21$ ). Clinically relevant nonmajor bleeding occurred in two of 30 patients (6.6%; 95% CI, 0.82%-22%) before PERT and two of 31 patients after PERT (6.4%; 95% CI, 0.79%-21%). Two patients died before PERT, and 1 died after PERT. All deaths were PE related.

## Discussion

We describe our entire process from concept to creation of a pediatric PERT program in the United States. Our institution's rapid adoption of the PERT paradigm facilitated timely medical consultations for pediatric patients with acute PE. The PERT process enhanced the time to echocardiogram and anticoagulation and improved access to reperfusion



Figure 3 – Composition of PERT. \*Critical care medicine includes pediatric intensivists and cardiac intensivists. PERT = pulmonary embolism response team. Created with BioRender.com.



therapies. Our pediatric PERT model may serve as a best practice model for other centers to unify and streamline care for pediatric patients with higher-risk PE and complex patients with low-risk PE. Pediatric PERT may enhance awareness of severe PE and provide access to PE experts.

We show improved process outcomes, particularly time to echocardiogram and anticoagulation ordered and

given after PERT. These data align with that of adult PERTs. Wiske et al<sup>16</sup> reported an average time from PERT activation to anticoagulation of 2.3 min. We chose to measure time from PE diagnosis to initial anticoagulation to understand the degree of reduction before and after PERT implementation, a metric also used by Wright et al,<sup>17</sup> where PE diagnosis to heparin time was reduced (182 vs 76 min, 58% decrease;  $P = .001$ ). Although we also found that anticoagulation

**TABLE 1 ]** Participation During PERT Activation Conference and PERT Monthly Meeting

Participant	PERT Activation Conference		Monthly PERT Meeting
	Core PERT Member	On-Call Member	
Hematology	+	+	
Interventional radiology	-	+	
Interventional cardiology	-	+	
Anesthesiology	+	+	
Pediatric critical care	+	+	All core members join
Cardiac critical care	+	+	
Anticoagulation pharmacist	+ <sup>a</sup>	+	
Emergency medicine	+	+	
Treating physician or outside referring physician	N/A	+ <sup>b</sup>	N/A
Family of patients	-	-	N/A

+ = core PERT member joins irrespective of being on-call, and on-call member joins only when scheduled to be on-call; - = does not join; N/A = not applicable; PERT = pulmonary embolism response team.

<sup>a</sup>During workday hours only.

<sup>b</sup>As applicable.

# Suggested Algorithm for PERT Activation in Management of Acute PE in Children

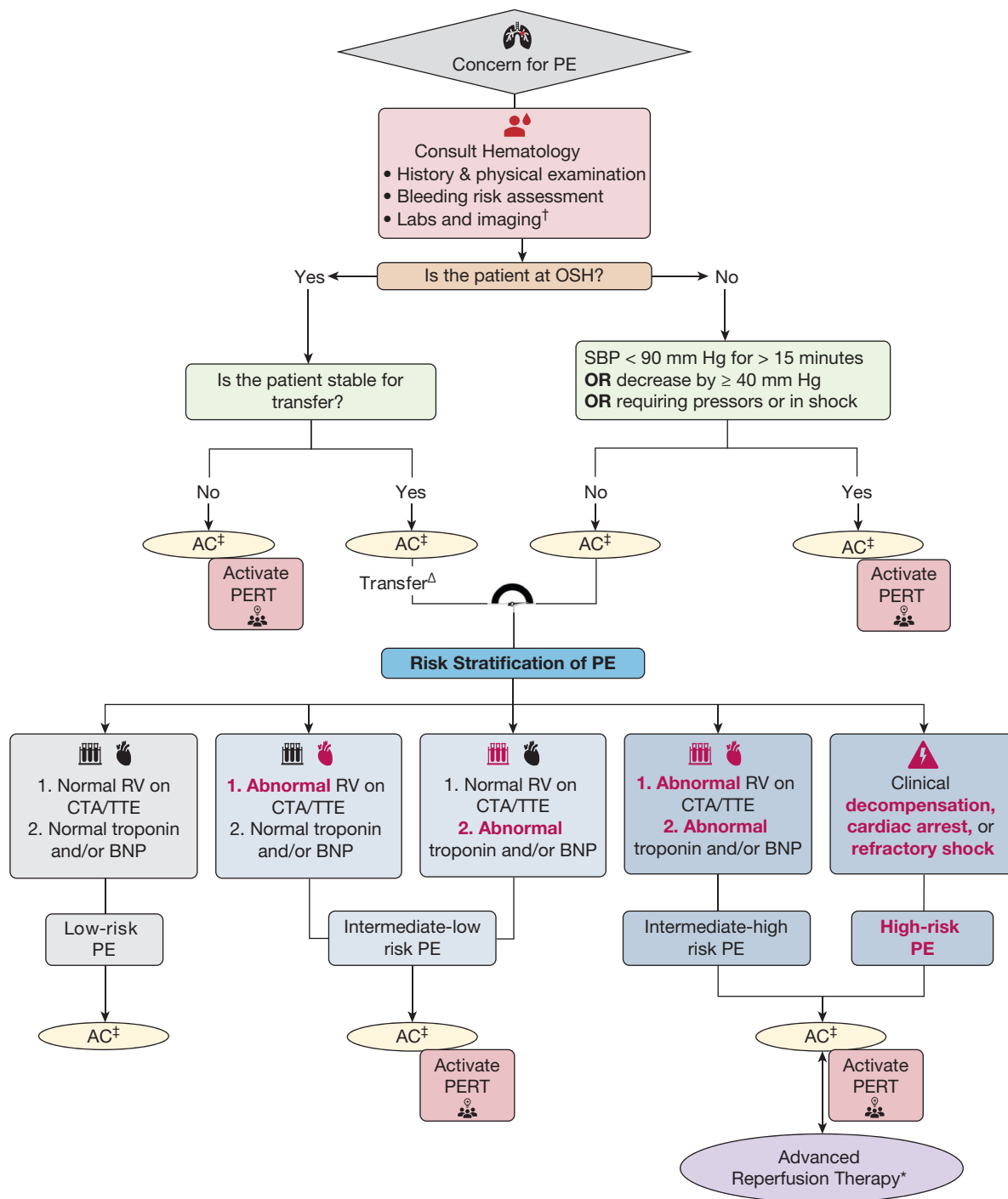


Figure 4 – Suggested algorithm for PERT activation in management of acute PE in children. †Laboratory tests: CBC count, PT/PTT/INR, fibrinogen, D-dimer, BNP, troponin, and creatinine; and imaging: CTA (or ventilation/perfusion scan if contraindications to CTA), and TTE. ‡AC: unfractionated heparin and low-molecular-weight heparin. Δ PE risk stratification may occur at OSHs prior to transfer based on local resources. \*Advanced reperfusion therapy: interventional radiology thrombectomy, surgical embolectomy, systemic thrombolysis, and catheter-directed thrombolysis. AC = anticoagulation; BNP = B-type natriuretic peptide; CTA = CT angiography; INR = international normalized ratio; OSH = outside hospital; PE = pulmonary embolism; PERT = pulmonary embolism response team; PT = prothrombin time; PTT = partial thromboplastin time; RV = right ventricle; SBP = systolic BP; TTE = transthoracic echocardiogram.

**TABLE 2 ] Characteristics of Patients With PE in the Pre- and Post-PERT Eras**

Variables	All (N = 61)	Pre-PERT (n = 30)	Post-PERT (n = 31)
Age at admission, y	61 (15, 17)	16 (14, 17)	15 (13, 16)
Sex			
Male	22 (36)	13 (43)	9 (29)
Female	39 (64)	17 (57)	22 (71)
Ethnicity			
Hispanic/Latino	12 (20)	4 (13)	8 (26)
Non-Hispanic	49 (80)	26 (87)	23 (74)
Race			
White	28 (46)	12 (40)	16 (52)
Asian	4 (7)	1 (3)	3 (10)
Black	28 (46)	17 (57)	11 (35)
American Indian/Native Alaskan	0 (0)	0 (0)	0 (0)
Presenting characteristics			
PE category risk			
Low risk	39 (64)	17 (57)	22 (71)
Intermediate-low risk	7 (11)	4 (13)	3 (10)
Intermediate-high risk	11 (18)	6 (20)	5 (16)
High risk	4 (7)	3 (10)	1 (3)
Concurrent VTE	12 (20)	4 (13)	8 (26)
Significant comorbidities			
Obesity (BMI > 95th percentile)	18 (29)	8 (26)	10 (32)
Inflammatory disorder/autoimmune disease	12 (19)	7 (23)	5 (16)
Congenital heart disease/ cardiac condition	4 (6)	3 (10)	1 (3)
Active malignancy	6 (10)	1 (3)	5 (15)

Values are median (25th percentile, 75th percentile) or No. (%). PE = pulmonary embolism; PERT = pulmonary embolism response team.

was given sooner before PERT, our time to anticoagulation was longer than the Wright et al<sup>17</sup> study, likely due to our smaller sample size and inclusion of low-risk PEs and those diagnosed outside our ED.<sup>17</sup>

Our concurrent improvement in anticoagulation order and administration time after PERT suggests the positive impact of order time on administration. After the PERT, our time to echocardiogram completion was also shorter. Improved time to echocardiogram, a metric not highlighted in adult literature, may facilitate rapid triage of intermediate- to high-risk children who may be eligible for early reperfusion. It can also help support the PE diagnosis in patients with high pretest probability in the absence of comorbid conditions. Although we were not able to find any studies investigating time from PE diagnosis to echocardiogram, echocardiogram and cardiac biomarker evaluation increased after PERT in adults.<sup>16,18-21</sup> A higher proportion of patients were diagnosed with intermediate-risk PE after PERT, attributing this change to increased assessment of right

ventricular strain on echocardiography.<sup>16,18</sup> Our study's shorter median time to echocardiogram after PERT may be related to increased PE awareness.

We report increased access to reperfusion therapies after PERT, which aligns with previous adult literature describing the association between PERT implementation and increased access to advanced reperfusion therapy in PE.<sup>5,8,18,20,22-26</sup> Rosovsky et al<sup>5</sup> showed that after PERT implementation, there was a significant increase in the proportion of patients receiving any advanced therapy (9% to 19%), including CDT (1% to 14%). The increased use of advanced therapies was notable among those with submassive PE.<sup>5</sup> All the patients eligible for advanced reperfusion received these interventions after PERT; not all eligible patients received reperfusion therapy before PERT. Time to reperfusion was not different for either era. The effect of CDT timing on PE outcomes remains unclear in existing guidelines and literature.<sup>11,13,27</sup> Wiske et al<sup>16</sup> was the only study (to our knowledge) that allowed for



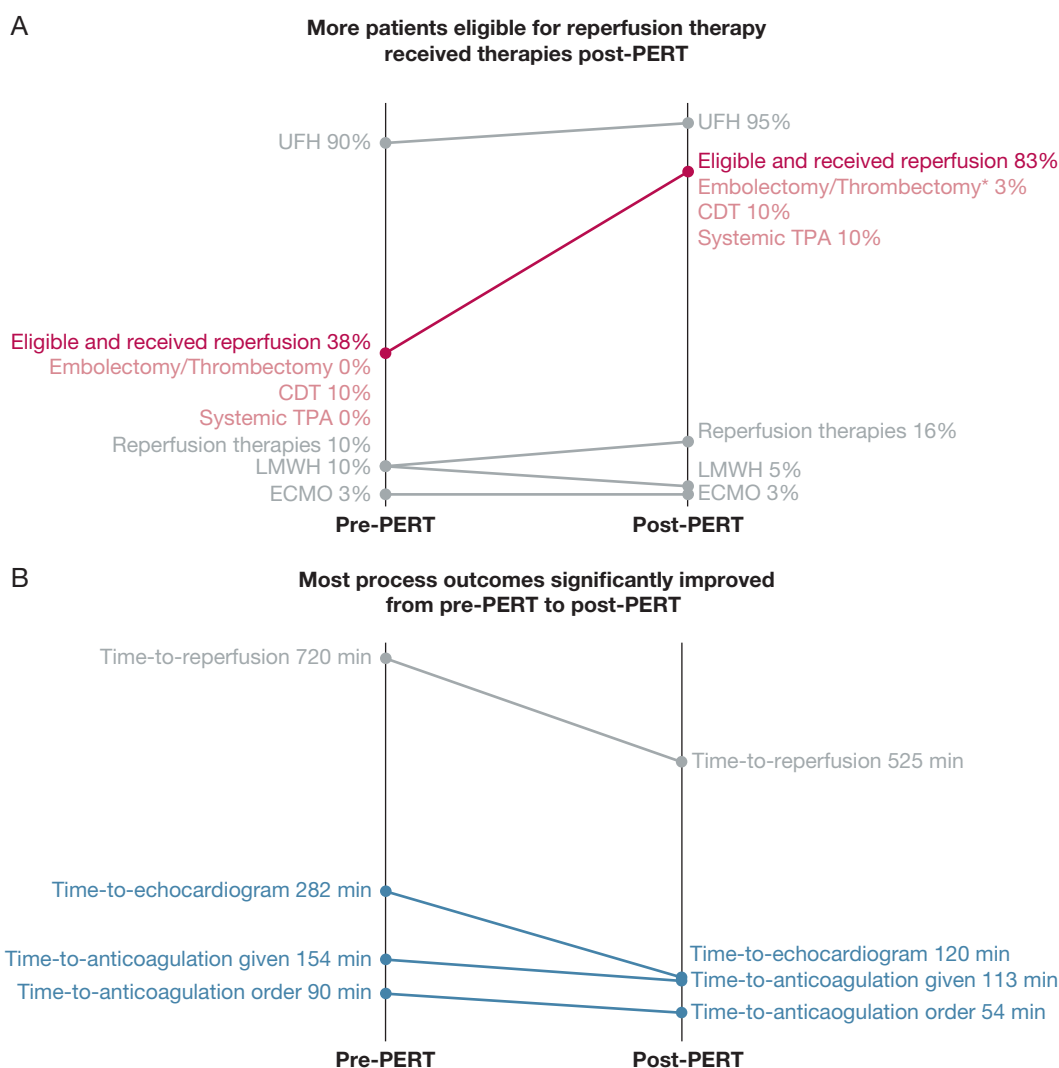


Figure 5 – A-D, Slopegraphs showing changes in process, treatment, and clinical outcomes in the pre- and post-PERT eras. A, More patients eligible for reperfusion therapy received therapies after PERT. \*Surgical embolectomy ( $n = 1$ ) and catheter-directed thrombectomy ( $n = 0$ ). B, Most process outcomes significantly improved from before PERT to after PERT. C, No difference in bleeding or mortality after PERT. D, No difference in LOS post-PERT. CDT = catheter-directed thrombolysis; ECMO = extracorporeal membrane oxygenation; LMWH = low-molecular-weight heparin; LOS = length of stay; PE = pulmonary embolism; PERT = pulmonary embolism response team; TPA = tissue plasminogen activator; UFH = unfractionated heparin.

comparison of similar metrics (time to treatment and in-hospital outcomes after PERT). Wiske et al<sup>16</sup> defined time to reperfusion differently, using the time of PERT activation as the initial time point instead of time of PE diagnosis; this may elucidate why we found their average time to intervention to be shorter than our study. Improved pulmonary hemodynamics and decreased hospital and ICU LOS have been shown in those that underwent CDT within 24 hours compared with 24 hours after admission.<sup>28</sup> Despite the rise in reperfusion therapy, our study and others did not note increased bleeding complications, worsened mortality, or increased LOS; however, that was not the focus of our study. Like the pediatric population reported here, LOS

after PE ranges from 5 to 11 days in adults.<sup>21,29</sup> Although we did not evaluate PE-related death > 30 days due to the small sample size, Wright et al<sup>21</sup> showed that PERT implementation was associated with a reduction in 6-month mortality (14% after PERT vs 24% before PERT), particularly in those with high-risk PE. Notably, Annabathula et al<sup>30</sup> found that hospital LOS significantly decreased post-PERT (7.7 vs 4.4 days;  $P < .05$ ), which they hypothesized was due to earlier intervention and streamlined decision-making. Our short-term early data fell within this range with no change pre- and post-PERT implementation. This may be explained by our institutional practice of initially managing pediatric PE in the ICU, subsequently

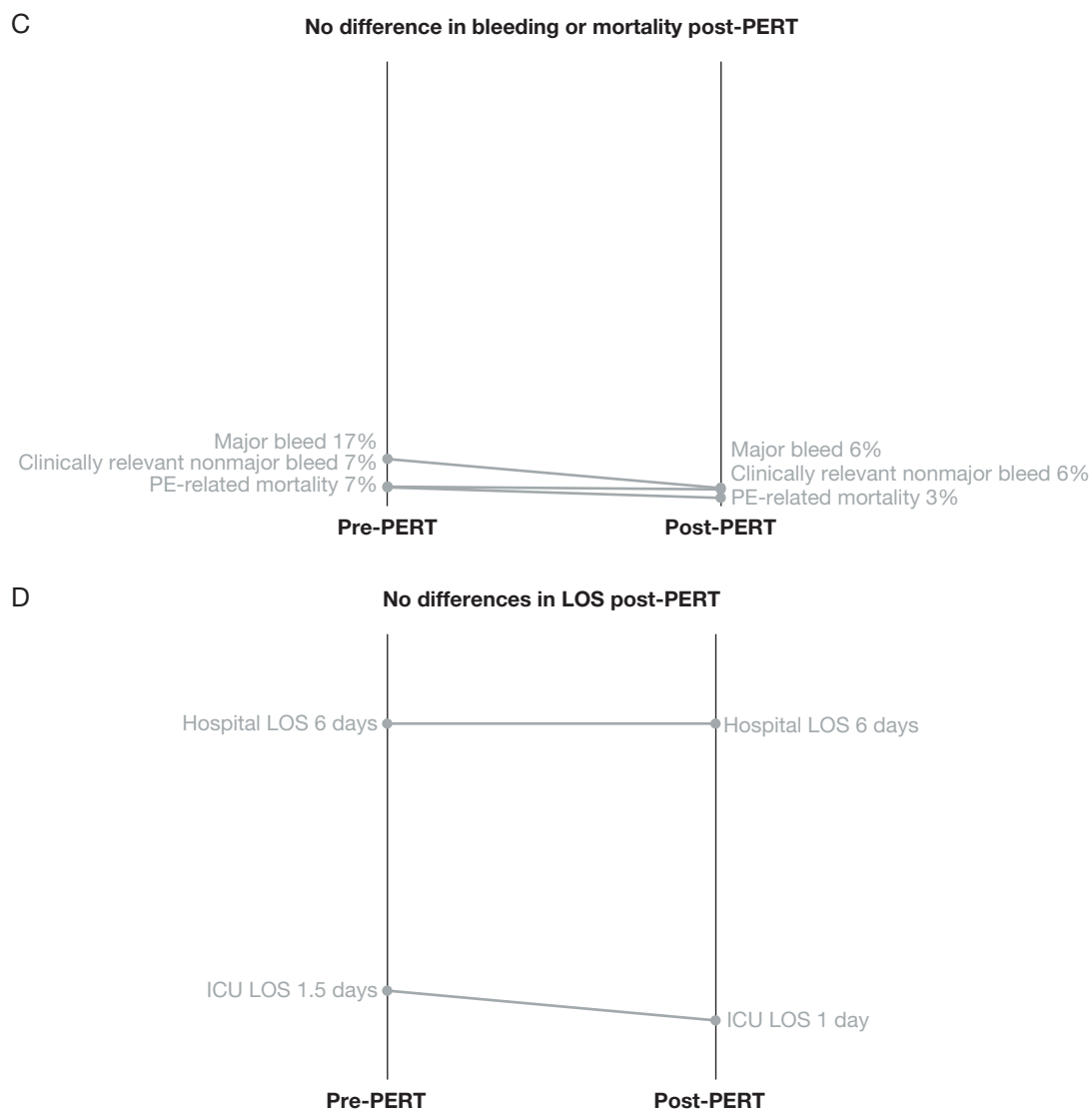


Figure 5 – Continued

**TABLE 3 ] Frequency of Advanced Reperfusion Therapies and Bleeding Rates Pre- and Post-PERT Eras**

Variable	Pre-PERT (n = 30)	Post-PERT (n = 31)
<b>Advanced reperfusion therapy</b>		
Embolectomy/thrombectomy <sup>a</sup>	0 (0)	1 (3)
CDT	3 (10)	3 (10)
Systemic tPA	0 (0)	3 (10)
Total recipients of reperfusion	3 (10)	5 (16) <sup>b</sup>
<b>Bleeding category</b>		
Major bleed	5 (17)	2 (6)
Clinically relevant non-major bleed	2 (7)	2 (6)

Values are No. (%). CDT = catheter-directed thrombolysis; PERT = pulmonary embolism response team; tPA = tissue plasminogen activator.

<sup>a</sup>Surgical embolectomy (n = 1) and CDT (n = 0).

<sup>b</sup>One patient received systemic tPA and CDT, and one patient received surgical embolectomy and systemic tPA.

transitioning care to the floor prior to discharge, and exclusively using UFH instead of LMWH. Although there is no difference currently, we hope to refine this metric with larger numbers in our ongoing model. The PERT has seemed to increase our entire team's overall awareness of PE diagnosis and management, underscoring the value of situational awareness in facilitating urgent and/or emergent care to patients eligible for advanced reperfusion. We recognize that increased use of reperfusion therapy in intermediate-high-risk PE, even if not associated with bleeding, does not necessarily equate with improved care.

The strength of our study includes the systematic examination of a large pediatric PE cohort, encompassing cases from both our quaternary and satellite hospital and OSHs. We included consecutive patients with PE over the study period to limit selection bias. Evaluating several time-sensitive metrics from the time of PE diagnosis, rather than from PERT activation, contributes to larger improvement in the PERT process, and by extension, improves treatment, clinical outcomes, and health care utilization. These time-based metrics are particularly well suited to pediatrics, where PE management and follow-up care is largely guided by hematology and can aid pediatric hematologists seeking to initiate PERT.

We acknowledge limitations related to our observational design and absence of a randomized controlled approach to PERT implementation. As acknowledged by several groups, these types of trials are challenging to conduct given a smaller sample size in pediatrics. We also did not exclude analysis of patients in the immediate pre-PERT and post-PERT eras, which may confound outcomes associated with behavior changes and practices surrounding efforts to launch and implement a new program.<sup>20</sup> Including time to therapeutic anticoagulation, a metric with implications for recurrent VTE and mortality in adult studies, may have strengthened our results.<sup>31-34</sup> Clarifying anticoagulation selection with respect to direct oral anticoagulation and/or warfarin duration of PE management may shed light on long-term outcomes. We also recognize that our institution's extensive experience with reperfusion modalities (eg, CDT) may limit generalizability to centers lacking access to similar

modalities. There were no differences in LOS and PE-associated mortality. Although not statistically significant, we observed fewer major bleeding events after PERT. We did not analyze bleeding risk factors, limiting our ability to fully explain the decrease in bleeding after PERT. It is possible that PERT implementation improved our ability to identify and monitor patients at high risk for bleeding through more streamlined discussion and enhanced PE management. Additionally, the PERT has highlighted opportunities to improve education for pediatric trainees and clinicians unfamiliar with PE. Given the infrequent and underreported nature of pediatric PE, understanding PERT's impact on long-term outcomes (mortality, LOS, health care utilization) will likely take years.

Future studies may consider exploring the PERT's impact on medical education, institutional perception of PE care, and hospital-related costs associated with PE management.<sup>19,20,30</sup> A separate analysis of outside transfers should also be evaluated because initial PE care varies across institutions (particularly when patients are first treated at an adult hospital and then transferred to our pediatric hospital). Comparing day vs night PERT metrics and evaluating the time from PERT activation to time of meeting could further illuminate the PERT's efficiency and impact on timely decision-making.

## Interpretation

We show that a PERT in pediatrics is a novel concept to enhance care for children with PE through facilitation of rapid consultation and expert consensus for coordinated care. Our study sets the precedence for future pediatric PERTs by outlining an implementation process and defining patient-centered metrics and methods. Long-term powered studies examining the impact of pediatric PERTs on morbidity and mortality and post-PE syndrome are essential.

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