Patient Outcomes After Implementation of Pulmonary Embolism Response Teams in the United States of America: A Review of the Literature

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Abstract

Introduction: Pulmonary embolism (PE) is the 3rd leading cause of cardiovascular death, with approximately 200,000 - 900,000 new cases annually in the United States of America (USA). PE is categorized into one of three categories (low, intermediate, and high risk) based on the severity of hemodynamic compromise, right ventricular (RV) enlargement, and laboratory values. Individuals with low-risk PE generally do well with anticoagulation alone. Those with intermediate-risk PE pose a challenge, and prior research has been inconsistent with treatment recommendations. Due to this challenge, the Pulmonary Embolism Response Team (PERT) was established in 2012 to provide a multidisciplinary approach for individualizing risk stratification and tailoring treatment plans. This literature review aims to analyze the effect of implementing PERT on patient outcomes, focusing on mortality rates and patient care efficiency metrics (time to diagnosis, time to anticoagulation and time to triage).
Methods: A systematic literature review using PubMed and Google Scholar was conducted to analyze mortality rate and patient outcomes, specifically time to diagnosis, time to triage and timing of initiation of anticoagulation after the implementation of the PERT.
Results: Six articles were analyzed and found to have inconsistent findings regarding mortality rate after the implementation of PERT. Of those that found statistically significant reductions in mortality rate, a correlation was noted with improved patient care efficiency metrics.
Conclusion: PERT provides individualized risk stratification and management of treatment decisions, which is particularly important for intermediate PE. Emphasis on the timing of diagnosis and initiation of anticoagulation is crucial in reducing mortality rates. Continued research is essential to evaluate the long-term effects of PERT on mortality rates.

Introduction

PE is potentially a life-threatening condition, dependent on the severity of RV enlargement and hemodynamic compromise.[1] PE is a blood clot that causes partial or complete blockage of an artery within the pulmonary system, often migrating from another source.[2] PE remains a leading cause of morbidity and mortality in the United States of America (USA), accounting for 200,000 – 900,000 cases annually.[3-5] The financial burden of PE is substantial, accounting for $2 – 10 billion in healthcare expenses in the USA annually.[5] PE is the third leading cause of cardiovascular death after myocardial infarction (MI) and cerebrovascular accident (CVA).[5-7] Research has demonstrated reduced mortality rates with early treatment, particularly anticoagulation, highlighting the importance of prompt diagnosis and treatment.[4,7,8]

PE is categorized into one of three categories based on hemodynamics, RV enlargement noted on echocardiogram, and biomarkers of RV strain (brain natriuretic peptide [BNP] and troponin).[5] Synonyms for PE categories are low-risk, intermediate (sub-massive), and high-risk (massive). For this literature review, the first terms will be used to ensure consistency. Low-risk PE is defined as the absence of hemodynamic instability and no evidence of RV enlargement.[3,9] Intermediate PE is defined as RV enlargement or strain found on echocardiogram and elevated biomarkers without hemodynamic compromise. [3,9] High-risk PE is defined as hemodynamic instability, RV enlargement noted on echocardiogram or computed tomography (CT), and elevated biomarkers.[3,9] See Appendix A for additional details.

30% of patients die within 30 days after diagnosis of PE, and one-third will develop long-term complications, such as pulmonary hypertension, recurrent venous thromboembolism and venous insufficiency.[3,5] Low-risk PE has a 1% 30-day mortality rate, and treatment with anticoagulation alone is sufficient.[5] High-risk PE is associated with the highest mortality rate of

approximately 50% in the first 72 hours after diagnosis.[5] High-risk PE requires more invasive treatment or procedures, such as catheter-directed thrombolysis, Tenecteplase, or extracorporeal membrane oxygenation (ECMO).[5] Despite the development of advanced therapies, the literature and consensus regarding treatment for intermediate PE are inconsistent. Intermediate PE poses a risk for decompensation 20-45% of the time, further emphasizing the importance of an individualized treatment approach for this category.[1]

To provide guidance on treatment decisions, the PERT was established. The first PERT was developed in 2012 in Boston, Massachusetts.[10] PERT is a multidisciplinary consult team that provides an individualized approach to management and treatment. PERT members vary from one hospital to another, as there is no universal outline, and their composition depends on the available resources.[10] Research in Canada is limited, as PERT is a novel concept. Therefore, this literature review focuses on studies completed in the USA. This literature review aims to analyze the impact of PERT on patient outcomes, focusing on mortality rates and patient care efficiency metrics, including time to triage, time to diagnosis, and time to anticoagulation.

Methods

A literature review was conducted to review the impact of patient outcomes after implementing PERT. PubMed and Google Scholar were the two search engines used. Search terms applied were: (PERT) AND (Mortality); (PERT) AND (Morality rate); (PERT) AND (Time to triage); (PERT) and (Time to anticoagulation); (Pulmonary embolism response team) AND (mortality rate); (Pulmonary embolism response team) AND (Time to triage); (Pulmonary embolism response team) AND (Time to anticoagulation); (PERT) and (Length of admission); (Pulmonary embolism response team) AND (Length of admission); (PERT) and (Hospital stay); and lastly (Pulmonary embolism response team) AND (Hospital stay).

An initial PubMed search was conducted on December 8, 2024, yielding 171 results for systematic reviews or meta-analyses. Repeating search terms on Google Scholar yielded similar results. The inclusion criteria used were English, published in the USA, and not limited to full text. No specific years were added to the inclusion criteria as PERT was only established in 2012; therefore, research is limited. Studies written in languages other than English were excluded due to the inability to translate them accurately. PERT is also an acronym for pancreatic enzyme replacement therapy, which had an impact on the number of yielded results. With PERT (Pulmonary Embolism Response Team) spelled out, this yielded additional journal articles. Ultimately, five articles were deemed suitable for this review. A further article was added after the initial search was completed, bringing the total to six articles analyzed in the literature review.

Results

Study 1: Wright et al (2021)

Wright et al. conducted an observational analysis of patients presenting to the emergency department (ED) who were diagnosed with intermediate or high-risk PE.[11] The authors hypothesized that implementing PERT would improve patient care for those diagnosed with high-risk PE. The primary outcome examined was the six-month mortality rate. Additional outcomes measured in this study included a comparison of efficiency metrics before and after the implementation of PERT. The efficiency metrics analyzed were the time from emergency triage to PE diagnosis, the time from diagnosis to anticoagulation, and the time from triage to hospital admission. Secondary measures included length of hospital stay, in-hospital or 30-day major bleeding events and hemodynamic compromise. This literature review will not discuss bleeding complications and hemodynamic compromise.[11]

Two groups were formed: the pre-PERT cohort included 137 patients and data collection occurred from 2014 to 2015; the post-PERT cohort included 231 patients and data collection occurred from 2016 to 2019.[11] Patients excluded from the study included those with low-risk PE, chronic venous thromboembolism, and patients transferred from another facility who were already diagnosed with PE. The emergency physician activates a PERT consultation if the patient meets the criteria for intermediate or high-risk PE (see Appendix A). The medical and cardiac intensive care physicians then complete a team assessment and risk stratification. A treatment plan is confirmed within a 30-minute timeframe. Unless contraindicated, low-molecular-weight heparin is the anticoagulation of choice. The risks and benefits of anticoagulation alone versus advanced therapies are discussed; experts in cardiac surgery, interventional radiology, or vascular medicine are available as part of PERT. All patients diagnosed with intermediate or high-risk PE had outpatient follow-up at the post-PERT clinic.[11]

The study found a reduction in six-month mortality in the PERT cohort (14% PERT vs. 24% pre-PERT, relative risk reduction [RRR] 43%, p=0.025).[11] A 4.6% decrease in six-month relative mortality was noted for each hour earlier the diagnosis of PE was made. The time from triage to diagnosis was an independent predictor of mortality (HR, 1.05; 95% CI, 1.00-1.09; p=0.034). All other efficiency metrics did not reach statistically significant results. Lastly, the PERT cohort was associated with a reduced length of hospital stay (6.5 ± 9.8 days post-PERT vs. 9.1 ± 10.8 days pre-PERT; p=0.007).[11]

Study 2: Russel et al. (2023)

Russel et al. completed a retrospective study at Baylor Scott and White Heart Hospital Plano, examining patients diagnosed with PE between July 2020 and April 2022.[3] The study analyzed the impact of PERT on patient outcomes and treatment. PERT was established at this

facility in 2017 and comprises 14 different specialists, including vascular surgery, cardiothoracic surgery, cardiology, and pulmonology. The decision to consult PERT is solely based on the admitting physician; no formal protocols activate PERT. Upon consultation, the PERT attending physician completes an initial assessment. Then, a conference call is held with the remaining PERT staff to aid in the final treatment decision.[3]

The total number of patients included in the study was 279 (n = 279), comprising low-risk (n = 79, 28%), intermediate-risk (n = 173, 62%), and high-risk (n = 27, 10%) groups.[3] This study compared two groups, non-PERT and those consulted by PERT. PERT was activated for consultation for 133 patients (47.7%). The inclusion criteria were all patients diagnosed with PE on CT pulmonary angiography and those transferred from another facility who had already been diagnosed with PE. Patients were excluded from the study if they were under 18 years of age, had subacute PE, had incomplete electronic records, or didn't have a confirmed PE diagnosis based on imaging. Primary outcomes measured were inpatient mortality, major bleeding, and use of catheter-directed interventions. Secondary outcomes measured included hospital and intensive care length of stay, 30-day and 12-month mortality rates, vasopressor requirements, and cardiac arrests. The results specific to treatments will not be discussed in this literature review. Upon discharge, PERT consults received outpatient follow-up at the pulmonary hypertension clinic.[3]

Results from this study showed a numerical trend of reduced in-hospital mortality (2% non-PERT vs. 5% PERT; P=0.2) and 30-day mortality (2% non-PERT vs. 8% PERT; P=0.06) but did not yield statistically significant results.[3] No difference was found when analyzing 12-month mortality (7% non-PERT vs 8% PERT, P=0.7). While the PERT cohort was associated with a decrease in the median number of admission days within the intensive care unit (ICU) by one-half (median 1.4 PERT vs 3 days non-PERT; P = 0.03), the overall total admission days were

unaffected. Lastly, the 30-day readmission rate was analyzed and did not yield statistically significant results (7% PERT vs non-PERT 5%; P=0.48).[3]

Study 3: Wright et al. (2019)

Wright et al. completed an observational study at the University of Rochester Medical Center/Strong Memorial Hospital comparing a baseline population to three-month post-PERT and 18-month post-PERT, focusing on intermediate and high-risk PE in the ED.[8] The pre-PERT cohort served as the control group (n = 159; 27% high-risk, 73% intermediate-risk), and the review of records was from May 22, 2014, to Dec 31, 2015. The authors hypothesized that implementing PERT would positively impact patient care efficiency metrics, focusing on time to diagnosis, treatment, and disposition. Patients excluded from the study were those with chronic deep venous thromboembolism, low-risk PE, and those with a confirmed PE transferred from another facility. The emergency physician activates PERT if the patient meets intermediate or high-risk PE criteria. A medical and cardiac intensive care physician completes a combined physical examination and risk stratification. The risks and benefits of treatment with anticoagulation alone versus advanced therapies are discussed. Unless contraindicated, the treatment of choice is low-molecular-weight heparin. Additional expertise regarding advanced treatment is evaluated by vascular surgery, interventional radiology, or cardiac surgery.[8]

The study found that patients in the pre-PERT cohort were treated more conservatively compared to those in the post-PERT cohort.[8] In the pre-PERT cohort, treatment with anticoagulation alone occurred 85% of the time, and 15% received advanced treatment. In comparison, the post-PERT cohort received anticoagulation alone 68% of the time, and 32% received advanced treatment. Advanced treatment included systemic thrombolysis, ECMO, surgical embolectomy, and catheter-directed procedures. Improvements in efficiency metrics were

observed in the post-PERT cohort. A 45% reduction in the median time from triage to diagnosis (384 minutes pre-PERT vs 212 minutes post-PERT, p=0.0001) and a 58% reduction in timing of administration of anticoagulation (384 minutes pre-PERT versus 212 minutes post-PERT, p=0.001). Lastly, a 26% reduction in disposition time was observed, from 392 minutes in the pre-PERT cohort to 290 minutes in the post-PERT cohort ($p < 0.0001$).[8]

Study 4: Gardner et al. (2024)

Gardner et al. conducted a retrospective study at a single tertiary center, utilizing a propensity-matched analysis that focused on patients with intermediate and high-risk PE.[1] The study assessed patient outcomes, comparing the two years preceding and two years following the implementation of PERT from April 2017 to April 2021. The outcomes measured included 30-day mortality, hospital length of stay, time to anticoagulation, in-hospital bleeding, and use of advanced treatment. The pre-PERT cohort consisted of 315 patients, whereas the PERT cohort was comprised of 367; however, only 201 patients received a PERT consultation. Patients were excluded from data collection if they were diagnosed with low-risk PE or had been transferred from another hospital already diagnosed with a PE.[1]

The post-PERT cohort was more likely to undergo a comprehensive risk stratification assessment, including an echocardiogram and laboratory tests to evaluate RV enlargement or strain (75.5% in the PERT cohort versus 61.4% in the pre-PERT cohort; $p < 0.0001$).[1] Improved patient outcomes were demonstrated in the post-PERT cohort. A 20% reduction in 30-day mortality (p=0.0024), a decrease in total hospital length of stay (p=0.0001) and decreased time to anticoagulation administration (-0.25 hr, p=0.041).[1]

Study 5: Xenos et al. (2019)

Xenos et al. conducted a retrospective study comparing patient outcomes before the implementation of PERT, from October 2013 to 2016 and after the implementation of PERT from October 2015 to May 2017.[9] The patient outcomes evaluated in the study included ICU admission length of stay, 30-day readmission rates, mortality rate, and the observed-to-expected mortality ratio. The pre-PERT cohort consisted of 992 participants. The PERT cohort consisted of 77 participants, divided into intermediate-risk (n = 67, 87%) and high-risk (n = 10, 13%) groups. The emergency physician consulted PERT when a suspected or confirmed PE diagnosis was made.[9]

No statistically significant differences were found between the pre-PERT and PERT cohorts in terms of 30-day readmission rates or mortality rates.[9] The length of ICU admission and overall length of hospital stay demonstrated a numerical reduction, although the results did not reach statistical significance.[9]

Study 6: Chaudhury et al. (2019)

PERT was established in 2014 at the Cleveland Clinic to aid in risk stratification and management of intermediate and high-risk PE.[4] Chaudhury et al. conducted a retrospective cohort analysis of participants over 18 years of age diagnosed with PE on CT imaging to investigate how PERT affected patient outcomes. Data was collected from both the ED and inpatient units. Two groups were established: the pre-PERT cohort, for which data collection occurred from January 1, 2013, to June 30, 2014, and the PERT cohort, for which data collection occurred from January 1, 2015, to June 30, 2016. The primary outcome analyzed was all-cause mortality within 30 days of hospital admission. Other outcomes analyzed included time to initiation of anticoagulation.[4]

A reduction in all-cause 30-day mortality yielded statistically significant results in the PERT cohort (8.5% PERT vs 4.7% pre-PERT, p=0.034).[4] Decreased bleeding complications (8.5%

post-PERT vs 17% pre-PERT) and reduction in time to anticoagulation administration (12.6 hours PERT vs 16.3 hours pre-PERT; p=0.02) yielded statistically significant results in the PERT cohort.[4]

Discussion

Mortality Rate and Efficiency Metrics

The literature review reveals inconsistent findings regarding mortality rates following the implementation of PERT. For the studies that demonstrated a reduction in mortality rates, a correlation was noted with patient care efficiency metrics. A decrease in time to diagnosis and time to initiation of anticoagulation was associated with statistically significant reductions in mortality rates.[1,4,8,11] The 2019 study by Wright et al. highlighted the importance of teamwork, noting the pharmacist's crucial role in facilitating timely access to medication, which assisted in improving the timing of anticoagulation administration.[8] Building on the findings of the 2019 study, Wright et al. conducted a follow-up study in 2021, analyzing mortality rates after the implementation of PERT.[8,11] This was one of the first studies to show a reduction in six-month mortality (24% pre-PERT vs. 14% PERT; p = 0.025).[11] The time to diagnosis was an independent predictor of mortality, and improved outcomes with earlier initiation of anticoagulation.[11] A standardized 30-minute timeline for treatment decision-making was crucial in ensuring the earlier initiation of anticoagulation.[11] No other studies provided a timeline for initiating the treatment plan. Wright et al. suggested a shift of thinking regarding PE, focusing on time to diagnosis and anticoagulation as analogous to 'door-to-balloon time' associated with MI.[11] Protocols exist for MI and CVA, yet no established protocols exist currently for PE.

Patient care efficiency metrics, such as the timing of diagnosis, are important to consider. Wait times in the ED may pose several challenges. Wait times across the USA and other countries may vary, and the exact wait times were not provided in the studies analyzed. The

literature review yielded encouraging results regarding decreased time to diagnosis and lower mortality rates associated with PE.[11] Initiating a specific triage protocol to improve the timing of PE diagnosis could facilitate earlier PERT consultation, which may contribute to a reduction in mortality rates. Addressing long wait times within the ED is essential, as delays in diagnosis and initiation of anticoagulation can negatively impact patient outcomes.

Outpatient clinics following a PE diagnosis offer patients timely monitoring and management of complications. In a time when access to primary care is limited and there is a notable shortage of family physicians, these clinics should provide a bridge to accessing healthcare after discharge from the hospital. Physicians experienced in screening for PE long-term complications, with the ability to promptly order diagnostic imaging such as an echocardiogram, could significantly impact patient outcomes. Although this area was not explored in the literature review, examining the long-term effects of facilities with outpatient follow-up clinics versus those without could provide valuable insight into long-term mortality rates after a PE diagnosis.

Limitations

There are several limitations of note in this literature review. Study one is observational; therefore, there may be a risk of inherent bias. The authors note that the PERT group numbers may be skewed as staff had a greater clinical suspicion of PE.[11] There was a greater use of echocardiography and testing for PE, which could have affected the number of patients in the PERT group.[11] Another challenge with mortality is differentiating the cause of death related to PE versus comorbidities. Timing of the studies complete pose challenges, particularly those completed during the COVID-19 pandemic, often confounding cause of death.

Further Direction

Timely PERT consultation and evaluation facilitated rapid decision-making regarding treatment decisions. The factors specific to facilitating timely PERT consultation were not discussed in the studies and could be an area for future research exploration. Educational sessions provided enhanced awareness of PERT and guidance regarding high-risk features of PE.[11] Offering educational sessions should be considered by current facilities or those looking to implement PERT. A protocol specific to PE to aid in timely diagnosis is an area that warrants further exploration. Factors and barriers affecting the timely administration of anticoagulation warrant further exploration.

Replication of studies demonstrating improved patient outcomes after implementing PERT is essential. Research on long-term mortality rates is limited. However, facilities with outpatient follow-up clinics can play a valuable role in data collection regarding long-term mortality rates and complications of PE. PERT is a relatively new concept in Canada; however, established research from other countries can guide facilities looking to implement PERT within Canada. Conducting research in Canada is crucial for determining whether results can be replicated in different medical systems.

Conclusion

PERT has proven to be effective in delivering an individualized approach to risk stratification and treatment decisions since its inception in 2012. This literature review yielded mixed results regarding the impact of mortality rates after the implementation of PERT. While some studies didn't show a statistically significant reduction in mortality rates, they did, however, show a numerical reduction. This suggests a need for further research to establish the definitive effectiveness of PERT on patient mortality and patient efficiency metrics. Finally, the timing of

anticoagulation has been shown to improve mortality rates in PE and may represent the most critical focus for future research.

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Appendix A

"European Society of Cardiology Guidelines

- Low risk: characterized by the absence of both hemodynamic instability and signs of RV strain.
- Intermediate risk: evidence of new RV strain or dysfunction seen on echocardiography or CT imaging and/or elevated cardiac biomarkers indicative of RV strain without hemodynamic instability.
- High-risk: characterized by hemodynamic instability, defined as systolic blood pressure < 90mmHg or cardiac arrest, in addition to evidence of new RV strain, dysfunction found on echocardiography or CT imaging, and elevated cardiac biomarkers indicative of RV strain (troponin I, >0.034 ng/ml; troponin I, high sensitivity, > 59ng/L; BNP, 100pg/ml; and/or N-terminal prohormone BNP, < 125pg/ml)."[3 p.1140]