

Pulmonary Embolism Literature Highlights

Study Uses The PERT Consortium Registry Data to Examine Practice Patterns and Outcomes in High-Risk Pulmonary Embolism

In a retrospective analysis using data from The PERT Consortium registry, Kobayashi et al found high rates of in-hospital mortality and major bleeding in patients with high-risk pulmonary embolism (PE) as compared with intermediate-risk PE. Results were published in *Journal of the American College of Cardiology*.¹

Investigators used The PERT Consortium registry, which collects prospective data from PE response team (PERT) activations/consultations from 35 sites in the United States, to identify patients presenting with intermediate- and high-risk PE between October 16, 2015, and April 8, 2022. Patients were categorized as intermediate, high, and catastrophic based on the European Society of Cardiology guidelines.

The primary outcomes of interest were in-hospital mortality and in-hospital major bleeding, as defined by the International Society on Thrombosis and Haemostasis criteria.

Statistical analyses for patient characteristics were performed using the chi-square test for categorical variables and Student's t-test for continuous variables. Associations between clinical characteristics and in-hospital mortality and major bleeding were assessed using multivariable logistic regression models.

A total of 5,790 patients were included; 2,976 (51.4%) were categorized as intermediate risk and 1,442 (24.9%) were categorized as high risk. Of the high-risk patients, 197 (13.7%) and 1,245 (86.3%) presented with catastrophic and noncatastrophic PE, respectively.

High-risk patients were more likely to receive advanced therapies as compared with intermediate-risk patients (39.4% vs 30.1%; $P < .001$), including mechanical circulatory support with extracorporeal membrane oxygenation (ECMO; 6.3% vs 0.5%; $P < .001$), surgical embolectomy (2.8% vs 1.3%; $P < .001$), and systemic thrombolysis (13.1% vs 2.8%; $P < .001$). Catheter-based

KEY FINDINGS

- Overall in-hospital mortality was 20% in high-risk PE patients.
- Patients with high-risk PE were more likely to receive advanced therapies, such as systemic thrombolysis, surgical embolectomy, and mechanical circulatory support.
- Vasopressor use, ECMO, identified clot-in-transit, and malignancy were associated with in-hospital mortality.
- In-hospital mortality was 42.1% for high-risk patients with catastrophic PE.
- In-hospital major bleeding risk increased proportionally with the severity of PE presentation.

therapies were used with similar frequency in both groups (25% vs 26.4% in intermediate- and high-risk groups, respectively; $P = .32$).

The in-hospital mortality rate was 20.6% for high-risk patients as compared with 3.7% for intermediate-risk patients ($P < .001$). In-hospital major bleeding was also higher in high- versus intermediate-risk patients (10.5% vs 3.5%; $P < .001$), and median hospital length of stay was longer (7 days vs 3 days; $P < .001$). In high-risk patients, factors associated with in-hospital mortality as determined by multivariable logistic regression included vasopressor use (odds ratio [OR], 4.56; 95% CI, 3.27-6.38; $P < .01$), use of ECMO (OR, 2.86; 95% CI, 1.12-7.30; $P = .03$), identified clot-in-transit (OR, 2.26; 95% CI, 1.13-4.52; $P = .02$), malignancy (OR, 1.70; 95% CI, 1.13-2.56; $P = .01$), and hypoxia at presentation (OR, 1.50; 95% CI, 1.08-2.09; $P = .02$).

CARDIAC INTERVENTIONS TODAY ASKS...

Study investigator Jay Giri, MD, with Perelman School of Medicine at University of Pennsylvania in Philadelphia, Pennsylvania, provided some insight into the findings and their implications in real-world practices.

Can you briefly explain the nature of The PERT Consortium registry and its utility in exploring clinical questions in patient groups that may be excluded from conventional studies?

The PERT Consortium registry allows for the collection of real-world data from several dozen hospitals around the country with clinical expertise in the management of acute PE. The current analysis represents one of the strengths of clinical research performed in the registry, as patients not traditionally focused on in prospective research are captured in this registry and potentially at large scale.

In this study, the presence of clot-in-transit was associated with in-hospital mortality, and you noted that this was a relatively novel finding. How might this be factored into current risk stratification algorithms?

I feel that progress in acute PE risk stratification algorithms is predicated on moving beyond simple two-dimensional measurement of the right ventricle on CT and assessment of traditional cardiac biomarkers. It is important for us to account for functional characteristics that logically associate with the potential for acute decompensation. We all know that clot-in-transit is a relevant mechanism for this, but given the 2% to 4% incidence of clot-in-transit in the setting of acute PE, prior research has not been able to clearly define this association in a rigorous fashion. The current analysis provides objective evidence that allows future risk stratification algorithms to take this into account.

This study shows that mortality remains high in high-risk PE despite interventional and surgical advancements and implementation of PERTs. What additional strategies need to be considered to further reduce this rate?

A potentially optimistic finding in the study is that at these expert PERT programs, in-hospital mortality

was about 20%. This compares favorably with modern comparative observational literature, which has identified mortality rates around 30%.¹ This may reflect the benefits of having a PERT program that can efficiently marshal consultation and resources for this critically ill population. However, I would argue that acute PE remains a reversible cause of death, so 20% mortality is still unacceptably high. We are now in a position to consider true comparative prospective randomized studies of advanced therapies in this population, but they will be complex to organize and implement. In the meantime, I would argue that current guidelines recommending algorithmic utilization of systemic thrombolysis in high-risk PE are not evidence based and hold an inappropriate position of primacy in the management of this population. Hence, the best strategy currently is to build a multidisciplinary PERT program and then tailor advanced therapy use in these cases to the unique circumstances of the individual patient. In some cases, this will involve the use of systemic thrombolysis. However, a well-run PERT program may choose alternative initial strategies in many cases (as was seen in the current analysis).

What are some examples of PE questions that might be explored using a registry analysis such as this one versus a prospective study?

The PERT registry allows for analysis of a host of questions due to the real-world nature, nationally representative patient population, and overall size. These may include the development of novel risk stratification algorithms, the development and assessment of process metrics to improve PE care, descriptive analyses of the state of PE care at expert PERT programs, and carefully considered comparative effectiveness analyses of alternative management strategies for PE.

1. Silver MJ, Giri J, Duffy A, et al. Incidence of mortality and complications in high-risk pulmonary embolism: a systematic review and meta-analysis. *JSCAI*. 2023;2:100548. <https://doi.org/10.1016/j.jscai.2022.100548>

Advanced therapies were used at similar rates in high-risk patients presenting with and without catastrophic PE (45.9% vs 41.2%; $P = .22$). Use of ECMO (13.3% vs 4.8%; $P < .001$) and systemic thrombolysis

(25.5% vs 11.3%; $P < .001$) was more likely and catheter-based therapies (16.8% vs 26.2%; $P < .001$) and surgical embolectomy (0.5% vs 3.1%; $P = .04$) were less likely in catastrophic versus noncatastrophic PE patients.

Unadjusted in-hospital mortality was 42.1% in catastrophic and 17.2% in noncatastrophic PE patients ($P < .001$), and rates of in-hospital bleeding were higher in catastrophic PE patients (23.3% vs 8.4%; $P < .001$). Multivariable logistic regression analysis showed that no single factor was statistically significantly associated with in-hospital mortality or major bleeding in patients with catastrophic PE.

Investigators noted the following study limitations: Use of The PERT Consortium registry represents the experience of mostly tertiary care centers with active PERTs and may not capture patients admitted to hospitals without PERTs; potential for varying definitions

of catastrophic PE and hemodynamic instability by local PERT center; inability to derive results of a specific endovascular technique on mortality or bleeding in high-risk patients due to the relatively low utilization of advanced therapies; and the potential for confounding and lack of power to detect the reported associations identified as true independent correlates of mortality.

This analysis confirms that high-risk PE patients are the predominant driver of short-term mortality in hospitalized PE patients, concluded the investigators.

1. Kobayashi T, Pugliese S, Sethi S, et al. Contemporary management and outcomes of patients with high-risk pulmonary embolism. *J Am Coll Cardiol*. 2024;83:35-43. doi: 10.1016/j.jacc.2023.10.026

Study Evaluates Outcomes of Catheter-Based Therapy for Patients With Cancer and Intermediate- or High-Risk Pulmonary Embolism

A study published online in *Catheterization and Cardiovascular Interventions* by Leiva et al evaluating outcomes of patients with cancer hospitalized with intermediate- or high-risk pulmonary embolism (PE) found a lower risk of in-hospital death or cardiac arrest and a higher risk of major bleeding after treatment with catheter-based therapies (CBT) as compared with no CBT.¹

Investigators used the National Inpatient Sample to identify patients with ICD-10 codes for a primary or secondary diagnosis of PE and at least one code for cancer from October 1, 2015 to December 31, 2018.

The primary outcome measures included in-hospital death or cardiac arrest and major bleeding, defined as a composite of in-hospital gastrointestinal, intracranial, procedure-related, and other bleeding (retroperitoneal, hemoperitoneum, epistaxis, and hemoptysis).

Statistical analysis compared outcomes of CBT use versus no CBT use in patients with intermediate- or high-risk PE (both combined and separately) and looked at outcomes between patients who received CBT or systemic thrombolysis alone. Propensity scores were estimated using nonparsimonious multiple logistic regression, and then scores were used to perform inverse probability treatment weighting (IPTW) analysis. Variables that were unbalanced after IPTW were adjusted using IPTW multivariable logistic regression.

A total of 2,084 patients with cancer and intermediate- or high-risk PE were included (1,231 with intermediate-risk PE, 861 with high-risk PE; mean age, 66.4 years; 49.1% female; 31.7% non-White race). Of these, 136 (6.5%) were treated with CBT: 94 (69.1%) with CBT alone, 35 (25.7%)

KEY FINDINGS

- CBT was associated with a decreased risk of in-hospital death or cardiac arrest and an increased risk of major bleeding.
- As compared with systemic thrombolysis alone, treatment with CBT alone was associated with a lower risk of in-hospital death or cardiac arrest and no difference in major bleeding.

with mechanical thrombectomy alone, and 7 (5.1%) with both. Overall mortality was 27.3%.

After IPTW, CBT was associated with a lower rate of in-hospital death or cardiac arrest (16.9% vs 27.9%; $P < .001$) and a higher rate of major bleeding (22.6% vs 11.9%; $P = .006$), including postprocedural bleeding (16.8% vs 11.9%; $P < .001$) and other bleeding (7.4% vs 4.6%; $P < .001$), as compared with no CBT. After adjusting for unbalanced variables of hypertension and vasopressor use after IPTW, patients who received CBT still had lower odds of in-hospital death and cardiac arrest (adjusted odds ratio [aOR], 0.54; 95% CI, 0.46-0.64) and higher odds of major bleeding (aOR, 1.41; 95% CI, 1.21-1.65).

After analyzing by PE risk type, the risk of in-hospital death or cardiac arrest was lower with CBT in both intermediate (aOR, 0.52; 95% CI, 0.36-0.75) and high-risk PE groups (aOR, 0.48; 95% CI, 0.33-0.53), and major bleeding risk was increased only in the intermediate-risk

CARDIAC INTERVENTIONS TODAY ASKS...

Study authors Orly Leiva, MD, and Sripal Bangalore, MD, with New York University Grossman School of Medicine, in New York, New York, commented on the current approach to intermediate- and high-risk PE in special patient populations and how this study helps inform clinical practice.

PE trials have typically excluded special patient populations, such as pregnant patients and patients with cancer. What does the current decision-making for CBT versus no CBT look like for cancer patients with PE? Does this algorithm change in light of the study's results?

Typically, if a patient with cancer is thought to have a fair long-term prognosis (typically > 1 year, depending on the institution and operator), the same treatment decision algorithm is generally applied to those patients. I think this study highlights the possible efficacy of CBT in patients with cancer, but clinicians should take these results with a grain of salt given the retrospective nature and potential for unmeasured confounders. That being said, these results suggest that cancer should not be considered a contraindication for CBT in PE, and decisions for CBT should be made in a multidisciplinary fashion with incorporation of the patient's overall prognosis and goals of care into the decision-making process.

The CBT group was mainly composed of patients who received catheter-directed thrombolysis, while a minority received mechanical thrombectomy or both. Does this have any implications for the increased risk of major bleeding seen in this study? How might this be clarified in future studies?

Although CBT in theory delivers thrombolytics locally, it is known that systemic exposure is possible

and occurs with CBT. Patients with cancer have myriad reasons for increased bleeding, including thrombocytopenia, compromised mucosal integrity due to cancer therapies, and tumor invasion. Therefore, it is difficult to discern the exact mechanisms of bleeding in our study. Further prospective studies with more granular data on laboratory values, cancer staging, and cancer treatments are needed to characterize the risk of bleeding.

You note that this study highlights the importance of evaluating this high-risk patient population in future trials. What are the key outcomes and unanswered questions to evaluate going forward?

I think confirming our results in a prospective and randomized clinical trial is important going forward. Additionally, further risk stratification for bleeding is important, especially among patients with cancer.

Cancer patients often have significant comorbidities confounding treatment options and timing of interventions if deemed appropriate. How can cancer teams and PE response teams (PERTs) ensure timely care in this population?

Collaboration of cancer teams and PERTs is important, especially for prognostication of cancer and other risk factors for cardiovascular disease in cancer. Cardio-oncology is a growing field, and incorporation of cardio-oncology in patients with PE and cancer should also be considered and investigated in future studies.

group (aOR, 2.12; 95% CI, 1.67-2.69; high-risk PE group: aOR, 0.84; 95% CI, 0.66-1.07).

In an analysis of patients who underwent either CBT (N = 124) or systemic thrombolysis alone (N = 165), patients treated with CBT alone had a lower risk of in-hospital death or cardiac arrest as compared with those treated with systemic thrombolysis alone (aOR, 0.49; 95% CI, 0.33-0.74), but there was no difference in risk of major bleeding (aOR, 1.12; 95% CI, 0.74-1.68).

Investigators noted several study limitations, including its retrospective design and use of the National Inpatient

Sample database, potential residual unmeasured confounding despite statistical adjustments, and use of ICD-10 codes to classify PE types and cancer diagnoses.

Results of this study suggest that CBT may be useful in cancer patients with intermediate- or high-risk PE, an important finding considering that this patient population is typically excluded from clinical trials, noted the investigators. ■

1. Leiva O, Yuriditsky E, Postelnicu R, et al. Catheter-based therapy for intermediate or high-risk pulmonary embolism is associated with lower in-hospital mortality in patients with cancer: Insights from the National Inpatient Sample. *Catheter Cardiovasc Interv*. 2024;103:348-358. doi: 10.1002/ccd.30917