LITERATURE HIGHLIGHTS

Cohort Study Shows Association Between PERT Implementation and Mortality in Patients With High-Risk PE

In an observational cohort study, Cameron et al demonstrated an association between the implementation of a multidisciplinary pulmonary embolism response team (PERT) and a sustained reduction in mortality at 6 months for patients with submassive and massive pulmonary embolism (PE). The analysis was published in *The American Journal of Cardiology* (2021;161:102-107).

Investigators aimed to determine whether implementing a multidisciplinary PERT improves mortality in patients with high-risk PE through an identifiable management strategy or treatment.

Patients with submassive and massive PE who presented to the emergency department of the University of Rochester Medical Center/Strong Memorial Hospital were divided into two cohorts based on whether they arrived before (pre-PERT cohort, 2014-2015) or after (post-PERT cohort, 2016-2019) the center instituted PERTs. The pre- and post-PERT cohorts included 137 and 231 patients, respectively.

Those in the pre-PERT group received the standard of care, which was determined at the treating physicians' discretion. In the post-PERT group, care was determined by the multidisciplinary PERT team. Patient data, baseline characteristics, management decisions, type of anticoagulant, use of advanced therapies, and efficiency of care were recorded for both groups. A multivariate model was used to adjust hazard ratio (HR) estimates by differences in baseline patient characteristics.

The primary outcome was all-cause mortality at 6 months, which was evaluated by univariate and multivariate analyses and displayed using the Kaplan-Meier survival estimate.

Investigators found that mortality was significantly lower in the post-PERT cohort compared to the pre-PERT cohort through 6 months after diagnosis (14% vs 24%; HR, 0.583; relative risk reduction, 41.7%; absolute risk reduction, 10%; log-rank *P* = .025).

Although HRs estimated 1-month post-presentation showed no difference in mortality risk among the two groups (HR, 1.11; 95% CI, 0.55-2.26; *P* = .766), the post-PERT cohort had a sustained reduction in mortality compared with the pre-PERT group between 1 and 6 months post-presentation with acute PE (HR, 0.42; 95% CI, 0.19-0.95; *P* = .037).

Secondary outcomes were length of hospital stay, in-hospital or 30-day major bleeding, and hemodynamic decompensation. No significant differences were seen in hemodynamic collapse or major bleeding, but there was

KEY FINDINGS

- A sustained reduction in mortality was seen in the post-PERT group compared to pre-PERT at 6 months (14% vs 24%; unadjusted HR, 0.57; relative risk reduction, 43%; *P* = .025).
- Post-PERT patients received more efficient care, defined as reduced time from triage to PE diagnosis, from diagnosis to anticoagulation administration, and from triage to hospital admission.
- Time from triage to PE diagnosis was an independent predictor of mortality (HR, 1.05; 95% CI, 1.00-1.09; *P* = .034).
- Post-PERT patients had a reduced hospital length of stay (9.1 vs 6.5 days; *P* = .007).

an increase in the post-PERT group in the use of catecholamines. Patients in the post-PERT group also had a reduced hospital stay (6.5 ± 9.8 vs 9.1 ± 10.8 days; *P* = .007).

With the association of multidisciplinary management of patients with intermediate- and high-risk PE via PERT and mortality reduction established, the goal was to identify whether there was a specific management strategy responsible for the favorable patient outcomes associated with PERT.

In the univariate analysis, those in the post-PERT group received more efficient care, increased use of advanced therapies and of enoxaparin as the initial anticoagulant, and higher rates of admission to an intensive care unit (ICU) or step-down level of care. Except for time from triage to hospital admission, these metrics improved with PERT in the multivariate analysis.

The primary clinical intervention that was an independent predictor of patient mortality was the time from triage to PE diagnosis (HR, 1.05; 95% CI, 1.00-1.09; *P* = .034), indicating that more rapid diagnosis of PE may be a contributor to the mortality reduction post-PERT.

As noted by the investigators, other factors that may have played a part in the favorable outcomes with PERT include an emphasis on hemodynamic monitoring, institutional education on high-risk PE management, enhanced awareness, and treatment with enoxaparin.

Limitations to the study include the risk of inherent biases, a greater use of techniques that can better identify PE in the post-PERT group, the possibility of patients with PE for whom PERT wasn't activated, and the inability to adjudicate the cause of death.

The authors noted that future studies should confirm these observations about PERT and mortality and further clarify how PERTs can improve care for these patients with high-risk PE. ■

ENDOVASCULAR TODAY ASKS…

Scott J. Cameron, MD, PhD, with the Cleveland Clinic in Cleveland, Ohio, shared further insight into the study findings and their real-world application.

How different were the standard of care and hospital protocols pre-PERT compared with post-PERT?

Pre-PERT, there was no consensus whatsoever on a care pathway in the treatment of patients with massive and submassive PE. This was very clear to me when I was a cardiology fellow. Surgical embolectomy, for example, never occurred pre-PERT until a talented surgeon (Dr. Igor Gosev) who trained at Brigham and Women's Hospital arrived and initiated this technique, training other surgeons along the way. Acute PE patients who underwent surgical embolectomy had 0% mortality, even when conducted in the context of cardiogenic shock or full arrest. Post-PERT, the medical ICU and coronary care unit evaluated patients with PE together any time of day or night, an echocardiogram was typically conducted at the bedside (which never occurred pre-PERT), and imaging data were used to formulate a consensus-based care pathway. Post-PERT, there was increased use of percutaneous thrombectomy (FlowTriever [Inari Medical], EkoSonic endovascular system [Boston Scientific Corporation], and occasionally Arrow-Trerotola [Teleflex]). However, that is because the emergency department was finding almost double the number of patients with submassive PE post-PERT over a similar observational period.

Neither ICU level of care or advanced interventions were significant mortality predictors post-PERT. Why do you think this is?

It is probably a numbers issue because 79% of patients post-PERT were cared for in the ICU or step-down, which was double the number pre-PERT. Candidly, I think the human element (ie, a fundamental change in culture and collaboration) impacted so many facets of health care delivery, from education to disposition of patients with PE with right ventricular (RV) dysfunction. This made it impossible to assign the clear and sustained decrease in death (out to 6 months) to any one intervention. I also think that time from PE diagnosis to anticoagulation decreasing by almost 50% and more use of low-molecular-weight heparin post-PERT (the latter of which was also an independent predictor of survival) may have "crossed and canceled" other singular interventions for PE—especially given that the emergency department was far quicker to recognize a patient with PE post-PERT.

How would you describe the elements of a PERT that do contribute to the mortality reduction? What other developments during this period, aside from a PERT, may have positively affected mortality rates?

The pulmonary medicine service takes responsibility for all PERT patients after discharge, carefully monitoring RV function, exercise tolerance, anticoagulation, and residual thrombus burden. The mortality benefit that was noted was not observed until 1-month post-PERT, so it is possible that elements of outpatient care improved simultaneously with the inpatient team concept.

Are there plans to study mortality beyond 6 months? Do you have theories for what mortality might look like at that point?

Malignancy was observed in around one-third of the patients with acute PE in this study, both before and after PERT implementation. This is common in other clinical enterprises. I believe and have observed that longer-term mortality is not always secondary to residual RV dysfunction after PE; many patients unfortunately succumb to their underlying malignancies. Importantly, the mortality benefit was observed mostly for patients with submassive PE in our group, not massive PE. This is not unexpected because the 3-month mortality for massive PE is around 45%. It's hard to fight against that statistic in the long term.

This study highlighted the importance of expeditious diagnosis of PE on mortality, as it results in earlier treatment initiation and earlier admission to a setting with more intensive monitoring. Along with the establishment of a PERT program, what else can be done to enact wide-scale improvement in this area?

I credit my colleagues in the emergency department for this because their skillset in keeping a broad differential while instantly recognizing that the potential was a poor clinical outcome led to a large reduction in the presentation to diagnosis time which, as you pointed out, was an independent predictor of survival after acute PE in this study. We need to implement and show accountability to a metric in PE care that resembles the door-to-balloon time in cardiology and the door-to-needle time in vascular neurology.

Now that the association between PERT implementation and sustained mortality reduction has been shown, what are the real-world implications of this study?

This manuscript was previously reviewed favorably by a top-flight medical journal but ultimately not accepted because we did not show randomization to PERT. I personally think this is an excessive request when patients clearly do better with team-based decision-making, and we are not the first to show this. Every large clinical enterprise should have a PERT. As Dr. Jeffrey Kline points out with his "guess the weight of a cow" slide, the centroid of every guess (or team consensus) is better for patients. PE is a disease that should never be owned by any one specialty. Patients always do better with collaborative care. We also need to move to understanding the long-term consequences of residual thrombus burden in the lung and how the biology of the vascular wall changes with chronic thrombus. So, there is still room for basic scientists to do their best work!