The implementation of a pulmonary embolism response team in the management of intermediate- or high-risk pulmonary embolism

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ABSTRACT

Background: Massive and submassive pulmonary embolism (PE) can be life-threatening. Treatment options include anticoagulation, fibrinolysis, catheter-directed or open surgical thrombus removal, and extracorporeal membrane oxygenation. With increasing patient complexity and advanced therapeutic options, the approach to optimal care for patients with intermediate- to high-risk PE is not clearly established. Multidisciplinary, rapid response teams can optimize risk stratification and expedite management. A PE response team (PERT) composed of specialists from cardiology, vascular surgery, emergency medicine, pulmonary and critical care, interventional radiology, cardiac surgery, hospital medicine, and pharmacy was created at our institution. The team is tasked with evaluating and treating patients with massive and submassive PE by use of a risk stratification and treatment algorithm. We describe our initial experience with this approach.

Methods: The records of patients treated by the PERT since inception in October 2015 through May 2017 were reviewed (intervention group). The diagnoses codes of the PERT patients were retrieved from the Vizient database. A retrospective control cohort group was created using these specific diagnoses and a matching set of demographics (age, sex), Medicare Severity Diagnosis Related Group, admission severity of illness, and admission risk of mortality. Statistical analysis was performed using the Fisher exact test, the Pearson χ^2 statistic, Student *t*-test, and Cochran-Cox approximation. $P < .05$ was considered significant.

Results: During the time interval, 77 patients with massive or submassive PE were treated by PERT activation; 992 patients included in the control group were treated at the discretion of an attending physician without use of the algorithm from October 2013 to 2016. Both groups had similar demographics, similar distribution of risk of mortality and severity of illness, and similar average Medicare Severity Diagnosis Related Group weighting. There was no statistically significant difference in the mortality rate between the two groups. The PERT group had significantly lower intensive care unit stay and overall length of stay. No difference was seen in direct cost between the two groups despite higher use of interventional treatment modalities in the PERT group.

Conclusions: In our institution, assembly of a dedicated team to treat patients with massive or submassive PE according to a clinical algorithm resulted in expedited treatment and reduced variation of care. Intensive care unit stay and overall length of stay were reduced by this approach, with no impact on direct cost despite the use of advanced modalities of treatment. We believe that this paradigm can be of potential value in other disease entities, particularly when multiple disciplines are involved. (J Vasc Surg: Venous and Lym Dis 2019;7:493-500.)

Keywords: Pulmonary embolism; PERT

Acute pulmonary embolism (PE) is a relatively common condition that represents a severe manifestation along the spectrum of venous thromboembolic disease. Massive and submassive PE can be life-threatening,[1] with an estimated 100,000 deaths from acute PE in the United States annually.[2] For other acute life-threatening conditions, such as myocardial infarction, institutions have employed rapid response teams and directed approaches to coordinate the management, risk stratification, and intervention for these critical and complicated patients.[3] With increasing patient complexity and advanced therapeutic options, the approach to optimal care for patients with intermediate-risk (submassive) to high-risk (massive) PE is not clearly established, and

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during the last few years, PE response teams (PERTs) have emerged to rapidly triage PE patients.[4-6] A PERT team was created at our institution in 2015.

Whereas there are numerous retrospective and prospective studies examining a specific treatment of severe PE (eg, catheter-directed therapy, systemic thrombolysis, surgical embolectomy),[7,8] there are few reports on the experience of individual PERTs. To understand the impact of our approach, we performed a retrospective analysis of submassive and massive PE patients triaged by our PERT and leveraged our data submitted to the Vizient Clinical Data Base and Resource Manager (CDB/RM) analytic platform (Vizient, Irving, Tex) to create a stratified control group. We report on our process and in-hospital outcomes using this approach.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study of implementation of a pulmonary embolism response team (PERT) comparing controls with the PERT cohort
- **Key Findings:** Compared with the historical controls, implementation of PERT resulted in higher use of extracorporal membrane oxygenation (1.7% vs 7.8%; $P = .0043$) and catheter-directed thrombolysis (1.8% vs 46.3%; $P < .0001$), fewer intensive care unit days (6.9 ± 9.4 days vs 4.4 ± 5.1 days; $P < .005$), and shorter lengths of stay (9.2 ± 16.1 vs 6.3 ± 7.4 days; $P < .005$), with no change in mortality or cost of care.
- **Take Home Message:** The data suggest that PERT management of severe pulmonary embolism results in higher use of advanced treatment modalities and shorter intensive care unit and hospital lengths of stay.

METHODS

A PERT was created at our institution in 2015. The various diagnostic and treatment approaches to patients with massive and submassive PE were evaluated by a multidisciplinary team composed of specialists from cardiology, vascular surgery, pulmonary and critical care, hematology, emergency medicine, interventional radiology, hospital medicine, cardiac surgery, nursing, and pharmacy, and a clinical pathway was mutually agreed on. Information was widely disseminated across our health care enterprise to all providers regarding the availability of the team, and a single pager number is used to activate the team to evaluate and to treat patients with massive and submassive PE by use of a PE risk stratification and treatment algorithm (Fig). Providers were encouraged to activate PERT if there was suspected or confirmed PE diagnosis. The UK HealthCare enterprise supported this quality improvement initiative as part of efforts to reduce variation of care and to support evidence-based practice. Support was provided in the form of data collection and analytics, provider education, dissemination of information, and access protocols.

The records of patients who were treated by the PERT since its inception in October 2015 up to May 2017 were reviewed (intervention group). Demographics, risk stratification, treatment method, and outcomes were recorded. The study was approved by the University of Kentucky Institutional Review Board. Informed consent was not obtained; waiver of consent was approved by the Institutional Review Board. The *International Classification of Diseases* (ICD) diagnosis codes of these patients were retrieved from the Vizient CDB/RM. The Vizient CDB/RM is an analytic platform for performance improvement. "Admit risk of mortality" and "admit severity of illness" are two variables in the Vizient Case Profile Report based on the 3M All Patient Refined Diagnosis Related Group (DRG) Classification System (3M Health Information Systems, Salt Lake City, Utah). There are four categories for each variable: extreme, major, moderate, and minor.

A control cohort group was created using these ICD diagnosis codes and a matching set of demographics, admission severity of illness, and admission risk of mortality employing the following methodology. After the group of PERT cases was finalized, analysis of their ICD-10 diagnosis codes was performed to determine the correct codes to use to create a control group. We identified two ICD-10 diagnosis codes: I26.92, saddle embolus of pulmonary artery without acute cor pulmonale; and I26.99, other pulmonary embolism without acute cor pulmonale.

A set of "control" PE patients were identified retrospectively from CDB/RM by using these two ICD-10 codes corresponding to PERT intervention cases. To expand the control group to cover patients before the implementation of ICD-10 codes, we crosswalked the two ICD-10 codes to three additional ICD-9 codes; these were used to query the Vizient CDB/RM between October 2013 and September 2015. They are ICD-9 codes 415.13, saddle embolus of pulmonary artery; 415.11, iatrogenic pulmonary embolism and infarction; and 415.19, other pulmonary embolism and infarction. Crosswalk of ICD-10 codes to ICD-9 codes allowed us to expand the control group to cover patients before the implementation of ICD-10 codes in October 2015. The control group's patients were treated from October 2013 to 2016.

The criteria to determine the control cohort of patients were as follows:

similar demographics between the two groups (PERT intervention vs control): age and sex.
similar distribution of admit severity of illness and admit risk of mortality in the Vizient CDB/RM. There

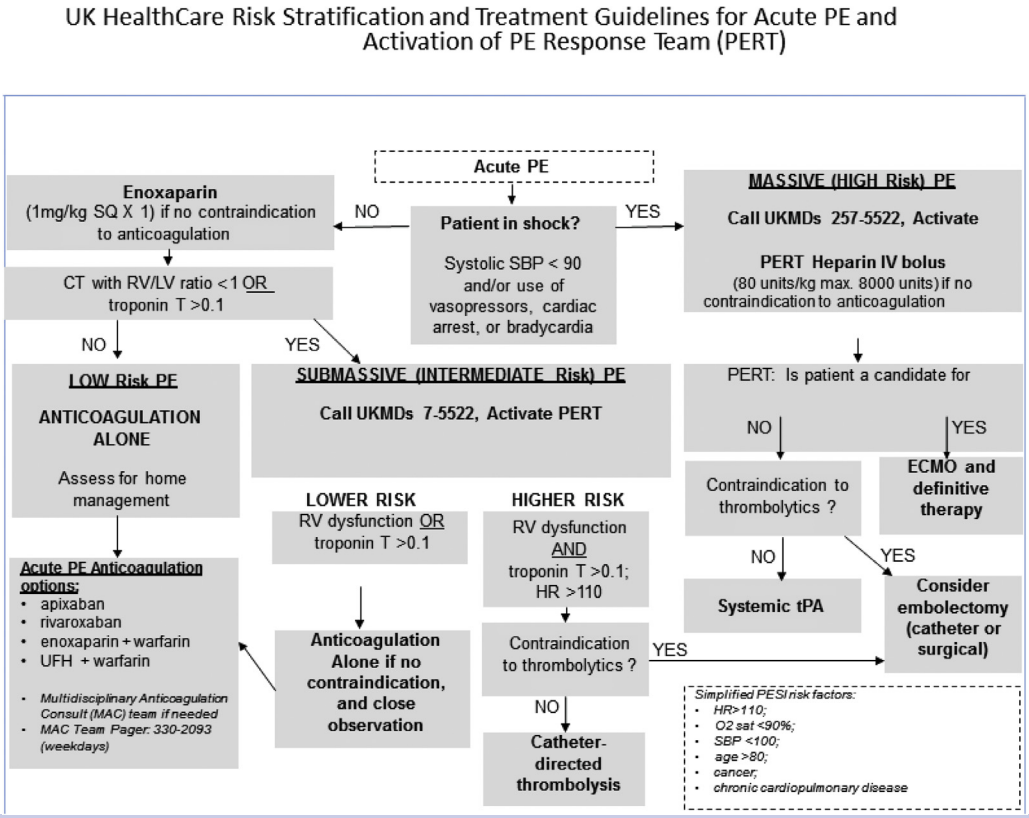

Fig. University of Kentucky pulmonary embolism (*PE*) risk stratification and treatment algorithm. *CT,* Computed tomography; *ECMO,* extracorporeal membrane oxygenation; *HR,* heart rate; *IV,* intravenous; *PERT,* pulmonary embolism response team; *PESI,* Pulmonary Embolism Severity Index; *RV,* right ventricle; *RV/LV,* right ventricular/left ventricular ratio; *SBP,* systolic blood pressure; *SQ,* subcutaneous; *tPA,* tissue plasminogen activator; *UFH,* unfractionated heparin.

are four levels on admit severity of illness and admit risk of mortality: minor, moderate, major, and extreme. similar average Medicare Severity DRG (MS-DRG) weight between the two groups. MS-DRG weight is the average amount of resources it takes to treat a patient in that DRG. Even though the MS-DRG weight is a monetary term, that weight reflects the severity of a patient's conditions.

Outcomes examined were length of stay (LOS), LOS observed/expected ratio, direct cost, intensive care unit (ICU) days, 30-day related readmission rates, mortality, and mortality observed/expected index. Statistical analysis was performed using Fisher exact test, Pearson χ^2 statistic, Student *t*-test, and Cochran-Cox approximation. *P* value $<.05$ was considered significant.

RESULTS

The PERT activation group included 88 patients from October 2015 to May 2017; hospice, pediatric, and obstetric patients were excluded. Of these, 11 were for low-risk PE and 77 were for high- or intermediate-risk PE. There were 992 patients included in the control group. Patients in the control group were treated at the discretion of an attending physician without involvement of the PERT from October 2013 to 2016.

The age and sex distribution for the high- and intermediate-risk PE and control groups is shown in Table I. There was no significant difference between the two groups in regard to severity of illness and risk of mortality on admission, age group, or sex ($P > .05$ for all variables; Table I).

Within the PERT intervention group, 10 patients (13%) were diagnosed with massive PE and 67 with submassive PE. A combination of catheter-directed thrombolysis (CDT), extracorporeal membrane oxygenation (ECMO), and systemic thrombolysis was used for all massive PE patients in addition to anticoagulation (Table II). Of the 67 patients diagnosed with submassive PE, 1 (1.5%) was placed on ECMO, 1 (1.5%) received systemic thrombolytics, and 26 (34%) underwent CDT (Table II). The remainder had unfavorable risk-benefit considerations for interventions or contraindications to lytic therapy. No surgical embolectomy was performed during this time on the basis of the individual patient's risk-benefit assessment by a cardiothoracic surgeon.

In the PERT intervention cohort, the mortality for massive PE patients was 80% and the mortality for patients with

Table I. Demographics, severity of illness, and risk of mortality of pulmonary embolism response team (*PERT*) intervention and control groups

Group	No. of patients	Male, %	Age, years, mean ± SD	
Control	992	48.59	56.57 ± 17	
PERT intervention	77	54.55	58.45 ± 15.3	
(N = 1069)	**Admission risk of mortality**	**Age group**	**Admission severity of illness**	**Sex**
Pearson χ^2 *P* value	.51	.53	.75	
Fisher exact test *P* value				.18

SD, Standard deviation.

submassive PE was 4.4%. Two high-risk submassive and one low-risk submassive PE patients did not survive.

Eight patients with massive PE did not survive. Of these, four were transferred from other facilities, three after presenting with cardiac arrest. One patient received systemic lytic therapy, three patients were treated with CDT, and four were placed on ECMO (one in conjunction with CDT).

In comparing the two groups, ICU stay and overall LOS were significantly lower in the PERT intervention group, whereas the direct cost was not increased (Table III) despite the higher utilization of interventional treatment (ECMO, CDT) in the PERT group (Table IV). No statistically significant differences were detected for mortality rate and 30-day related readmissions (Table III) between the two groups.

DISCUSSION

Acute PE is currently classified into three categories: low risk, submassive (ie, intermediate risk), and massive (ie, high risk). Low-risk PE is defined by the absence of right-sided heart strain and systemic arterial hypotension. The majority of patients diagnosed with PE present to the hospital without hypotension or heart strain, and these patients with low-risk PE (<1% short-term mortality rate) can be successfully managed with prompt initiation of therapeutic anticoagulation.[9] Submassive or intermediate-risk PE is defined by the presence of right-sided heart dysfunction in the setting of normal blood pressure, and this represents as many as 25% of all cases of acute PE. Massive PE (also called hemodynamically unstable PE) results in hypotension or need for vasopressor support. The treatment of massive or submassive PE is challenging, and there is a lack of consensus regarding optimal management.[10]

Table II. Treatment methods of the massive and submassive pulmonary embolism (*PE*) patients

Massive PE		(n = 10)
CDT		3
ECMO		3
Systemic lysis		2
CDT and ECMO		2
Submassive PE	**High risk (n = 34)**	**Low risk (n = 33)**
CDT	21	5
ECMO	1	
Systemic lysis	1	

CDT, Catheter-directed thrombolysis; *ECMO,* extracorporeal membrane oxygenation.

Management of patients with submassive and massive PE is logistically complex, given the heterogeneous nature of the disorder and patients. Overall short-term mortality ranges from 5% to 11% and can be as high as 32% in hemodynamically unstable patients, with approximately 50% of deaths occurring within the first 72 hours of presentation.[10,11]

There is evidence to support the use of thrombolysis primarily in hemodynamically unstable patients (class IIA), with a weaker recommendation (class IIB) in those with massive PE (right ventricular dysfunction or major myocardial necrosis).[9,12] The mortality benefit afforded by thrombolytic therapy in hemodynamically unstable patients is accompanied by an increased risk of major bleeding and intracranial hemorrhage.[8,13-15]

Other treatment options in addition to anticoagulation include catheter-directed or open surgical thrombus removal and ECMO.[16-18] Recent PE treatment options offer the potential for improved safety and have broadened the use of advanced therapies, including catheter-based fibrinolysis in a greater proportion of high-risk patients.[19,20] Advances in extracorporeal life support have made it a feasible option for salvage therapy in unstable patients.

Without a strong body of evidence demonstrating the superiority of any one treatment, therapeutic dilemmas are frequently encountered in severe PE cases. The concept of a team with membership from a broad range of specialties providing diagnostic and therapeutic expertise in PE management to improve rapid recognition and therapy has supported the creation of such rapid response teams in several institutions.[21] Rapid response teams were initially developed to evaluate patients with acute clinical deterioration while they were on an inpatient general medical or surgical floor. A rapid response team implementation can reduce cardiorespiratory arrest outside the ICU and may

Table III. Treatment by pulmonary embolism response team (*PERT*) resulted in lower length of stay (*LOS*), lower LOS observed/expected, and fewer intensive care unit (*ICU*) days but no difference in mortality, readmissions, or direct cost between intervention and control groups

	LOS, days		LOS observed/expected		ICU, days		Vizient direct cost, $		30-Day related readmissions, %		Mortality, %	
	Control	PERT	Control	PERT	Control	PERT	Control	PERT	Control	PERT	Control	PERT
No.	992	77	992	77	351	48	992	77	992	77	992	
Mean	9.22	6.31	1.22	0.94	6.86	4.4	12,219.7	16,843.2	0.91	0	13.38	15.07
SD	16.09	7.44	1.62	0.73	9.35	5.05	20,957.6	25,242.5		N/A		
P value	<.005		<.005		<.005		.12		1		.72	

N/A, Not applicable; *SD*, standard deviation.

decrease hospital mortality.[22] Assembly of a team of specialists with coordination of PE care through a system similar to the management of ST-segment elevation myocardial infarction has been described at several institutions.[5,6] Multidisciplinary PE response teams can coordinate and expedite risk assessment, management decisions, and implementation of treatment.[23]

There is no universal PERT model, and the concept is evolving; but in general, PERT teams are multidisciplinary. The disciplines most frequently represented are pulmonary critical care, cardiology, emergency medicine, cardiac surgery, vascular surgery, and interventional radiology. A notification system using a dedicated pager or telephone number is in place in most institutions. The patient is typically evaluated by a single discipline, and then discussions ensue in person and by telephone, text, or, in some cases, web conference.[24]

At the University of Kentucky, a PERT was established as part of quality improvement initiatives through an institutional approach based on local expertise and using a consensus approach. As a foundation, current published reports and society guidelines were reviewed, and an institutional protocol was established taking into account local expertise. The key to team management is activation of the PERT with a single phone call. PERT activation was encouraged for higher risk submassive and massive PE. We estimate that PERT is activated in approximately 30% of all PE patients in our institution. In the first 20 months, the PERT was activated for 67 submassive PEs and 10 massive PEs. The PERT's responsibility is to assess each case in a timely manner, to examine the patient, to review the available data, to perform any additional testing, and then (in conjunction with the patient, family members, and care team) to develop a consensus regarding the optimal treatment plan. In certain patients with massive PE and rapid deterioration, the decision to give fibrinolytic agents, to perform a percutaneous intervention, to proceed with ECMO, or to consider surgical thrombectomy should be made urgently.

The PERT model has been described previously, but data from PERTs have been relatively scarce. A series published by Kabrhel et al[6] included an analysis of 314 confirmed PEs, 72% of which were severe (submassive or massive); a total of 11% were treated with thrombolytics (CDT or systemic) compared with 41% in our series. The overall 30-day mortality rate in the series of Kabrhel was 12%. Our overall mortality rate was 15% but was heavily skewed by a high mortality of 80% for patients with massive PE. Of the eight patients with massive PE who died, four were transferred from outside hospitals. There was no difference between the overall mortality of the control group and the PERT group in our comparison. Sista et al[13] have reported their experience treating 87 patients with a PERT; in this series, the in-hospital mortality was 13.7%, similar to the mortality rate in our population.

Although during this initial period we were not able to demonstrate a reduction in mortality of patients with severe PE compared with a matched patient group, we found that ICU stay and overall LOS were reduced in the PERT group. The LOS after PE has been reported to range between 5 and 11 days.[25] It is conceivable that the reduction in LOS and ICU LOS is attributed to improved care coordination by the PERT. However, the PERT may also affect LOS on the basis of the management of severe PE. Our PERT employed CDT for a large

Table IV. Rates of utilization of extracorporeal membrane oxygenation (*ECMO*) and catheter-directed thrombolysis (*CDT*) were higher in the pulmonary embolism response team (*PERT*) group

	ECMO		CDT	
	Controls	PERT	Controls	PERT
No.	992	77	992	77
Rate, %	1.71	7.79	1.81	40.25
Fisher exact *P* value	.0043		<.0001	

percentage of cases, and there are studies indicating that use of CDT is associated with shorter LOS.[26]

In addition, the direct cost was not increased despite the use of advanced modalities of treatment as there was higher utilization of interventional treatment in the PERT group, as shown in Table IV. It is also possible that there is a cost benefit associated with the reduced LOS.

We used matching diagnoses, risk of mortality, and severity of illness to construct the control group, and the reliance on coded—not clinical—data is a limitation of our study. Nevertheless, we believe that matching severity of illness, mortality risks, and diagnoses builds a risk profile that allows valid comparisons. Our analysis of resource utilization and cost may have been affected by the comparison of two different time periods. As this is a retrospective examination of a single PERT, it cannot be used to recommend the routine implementation of a PERT for the management of PE. Moreover, our model of PERT may be different from other models; therefore, our outcomes cannot be generalized. The study also focused on submassive and massive PE, so outcomes for low-risk PE were not assessed. In addition, many of our patients are transferred from outside facilities, and our PERT has no impact on diagnosis or treatment before transfer; this may partially explain the observed mortality rate. Nevertheless, our report describes the early experience of the implementation of the PERT approach. In our institution, treatment of massive and submassive PE by the PERT resulted in decreased LOS and ICU LOS without increase in direct costs, notwithstanding higher rates of utilization of interventional treatment of PE. Further prospective reviews will be necessary to delineate impact on mortality and to better define the role of such a team in the management of PE. UK HealthCare is a member of the PERT Consortium. We enter our data in the national PERT Consortium database, which will allow us to compare our performance with local regional and national metrics and to identify opportunities for quality improvement initiatives. We are periodically evaluating our data to determine the role of each treatment modality in our care pathway. It is conceivable that our approach will be modified as more data accumulate.

CONCLUSIONS

Our results indicate that PERT management of severe PE results in higher utilization of advanced treatment modalities and lower hospital and ICU LOS. During this initial implementation period, there was no impact on direct cost and mortality.

AUTHOR CONTRIBUTIONS

Conception and design: EX, GD
Analysis and interpretation: EX, GD, QH, SS
Data collection: EX, QH, AG
Writing the article: EX
Critical revision of the article: GD, QH, AG, SS
Final approval of the article: EX, GD, QH, AG, SS
Statistical analysis: AG
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Overall responsibility: EX

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DISCUSSION

Dr Charles B. Ross (*Atlanta, Ga*). Pulmonary embolism (PE) is the third leading cause of cardiovascular mortality. During the past decade, therapeutic options for management of patients with large-burden PE have expanded dramatically. As Dr Xenos rightly points out, matching the best therapeutic option to achieve optimal outcome for a given patient is not always straightforward. This is precisely why modern care for PE has evolved toward the PE response team (PERT). This approach is characterized by the rapid response of a multidisciplinary team to develop and implement a management plan for an individual patient based on risk stratification and patient characteristics, such as comorbidity and age.

Through analysis of the outcomes of a recent cohort of patients who received PERT care at University of Kentucky Medical Center compared with a matched group of patients from the Vizient database, identified through diagnostic codes and matching demographics, severity of illness, and risk of mortality, Dr Xenos has shown no mortality benefit attributable to PERT care. However, lower intensive care unit length of stay, lower overall length of stay, and, even though invasive intervention was used more frequently in the PERT group, no cost difference compared with controls were observed.

I have a few observations and questions. The essence of PERT activation is to identify and to select best management for an individual patient to prevent clinical deterioration. Considering that most PERT activations occur for patients with intermediate-risk PE who have a low predicted mortality regardless of treatment selected and considering that 5% to 10% of PERT activations occur for massive PE patients, many of whom may die regardless of the approach used, was this study powered adequately to prove or to refute a mortality benefit attributable to the PERT approach? I sincerely hope that no one interprets this negative finding to mean that the PERT approach does not make a difference.

Although there are signals of improvement in recent reports, mortality from massive PE is generally reported in the range of 50%. In the experience that you have reported in this manuscript, mortality is 80%. What interventions has your PERT considered to reduce this mortality? Have you considered adding transfer algorithms, such as systemic lysis before initiating transport or even during transport in the case of in-transit deterioration?

Has your PERT ever experienced a major complication of PE intervention in a patient who might have done better if treated with a different option? Does your PERT have an active quality assurance program, and if so, how is this program refining PERT practices at your institution?

As your secondary data points showed, I believe that the PERT approach is advancing care for PE, and I think this is only the beginning. I think the PERT approach, from care of individual patients to sharing of best practices and research, offers the best hope for making a substantial, positive impact in reducing mortality and morbidity from PE. I enjoyed your paper, appreciated

early receipt of the manuscript, and I greatly appreciate the honor from the Society to open this discussion.

Dr Eleftherios S. Xenos. Dr Ross, thank you for your comments. They are very insightful. I do not believe our study was underpowered. Initially, when we did the review, we had about 435 patients in the control group, and we expanded that to about 992. We found a difference in the intensive care unit length of stay and the overall length of stay, so I think if there was a mortality difference, we would have detected it. The data I presented showed that the mortality of the PERT group and the mortality of the control group were similar between 14% and 15%, so I'm not sure this was a power problem. For your second question, indeed 80% mortality for the massive PE is a very high number, I agree. I think it kind of reflects our pattern of practice. Most of these people conceivably reached us without a chance of our having an impact on the outcome, and what you said about transfer algorithms is probably one solution to the problem. At this point, our PERT does not have reach outside of our institution, we do not even know sometimes that the patient has a PE until they get to us, so we don't intervene before they get to the University of Kentucky. To do so is a consideration, but it does have some medical-legal and logistic ramifications that we have not explored yet. Regarding your third question, the comparison I show you was with our own patients; these 992 patients were University of Kentucky patients. We just used the Vizient database. That is our database. We don't have a different database to extract data from for these patients, we don't have a separate database for that. So these were our own patients before the PERT implementation. Regarding the fourth question about the complications, if we had treated these patients otherwise—I would say that I would have to speculate about that. Once a complication happens, everything is in hindsight, and you can change your approach; but so far, we haven't made any changes, and we do have a quality program. We do review all of these cases, and we do have our data, and we hope that with our participation in the PERT Consortium we will be entering our data to the registry and will have a clearer understanding of our performance compared with others. Thank you.