

# The Current Evidence of Pulmonary Embolism Response Teams and Their Role in Future

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## Abstract

### Keywords

- pulmonary embolism
- PERT
- catheter-directed treatment
- ultrasound-accelerated thrombolysis
- percutaneous thrombectomy

Acute pulmonary embolism (PE) remains a critical medical condition requiring prompt and accurate management. The introduction and growing significance of pulmonary embolism response teams (PERT), also termed EXPERT-PE teams, signify a paradigm shift toward a collaborative, multidisciplinary approach in managing this complex entity. As the understanding of acute PE continues to evolve, PERTs stand as a linkage of optimized care, offering personalized and evidence-based management strategies for patients afflicted by this life-threatening condition. The evolving role of PERTs globally is evident in their increasing integration into the standard care pathways for acute PE. These teams have demonstrated benefits such as reducing time to diagnosis and treatment initiation, optimizing resource utilization, and improving patient outcomes.

## Introduction

Acute pulmonary embolism (PE) is a critical medical emergency with potentially life-threatening consequences. It arises from the sudden obstruction of pulmonary arteries by thrombi, typically originating in the deep veins of the lower extremities—a condition known as venous thromboembolism (VTE).<sup>1</sup> Acute PE can lead to acute right heart failure and in severe cases, hemodynamic instability due to obstructive shock—and death can occur within seconds to hours after onset.<sup>2</sup> Its prompt diagnosis and management are crucial for improving patient outcomes. Over the past few decades, understanding of acute PE has evolved significantly, leading to advancements in diagnostic techniques, risk

stratification, and therapeutic strategies.<sup>3–5</sup> Alongside these advances, a collaborative and multidisciplinary approach to the management of acute PE has developed, with the introduction and increasing role of pulmonary embolism response teams (PERTs) worldwide. PERTs represent a comprehensive and integrated strategy involving various medical specialists to provide timely and personalized care for patients with acute PE. The heterogeneity of patients, ranging from stable individuals with small emboli to those with massive and hemodynamically compromising emboli, necessitates a tailored approach.<sup>6</sup> PERTs typically comprise a team of experts including interventional cardiologists, pulmonologists, radiologists, vascular surgeons, anesthesiologists, and

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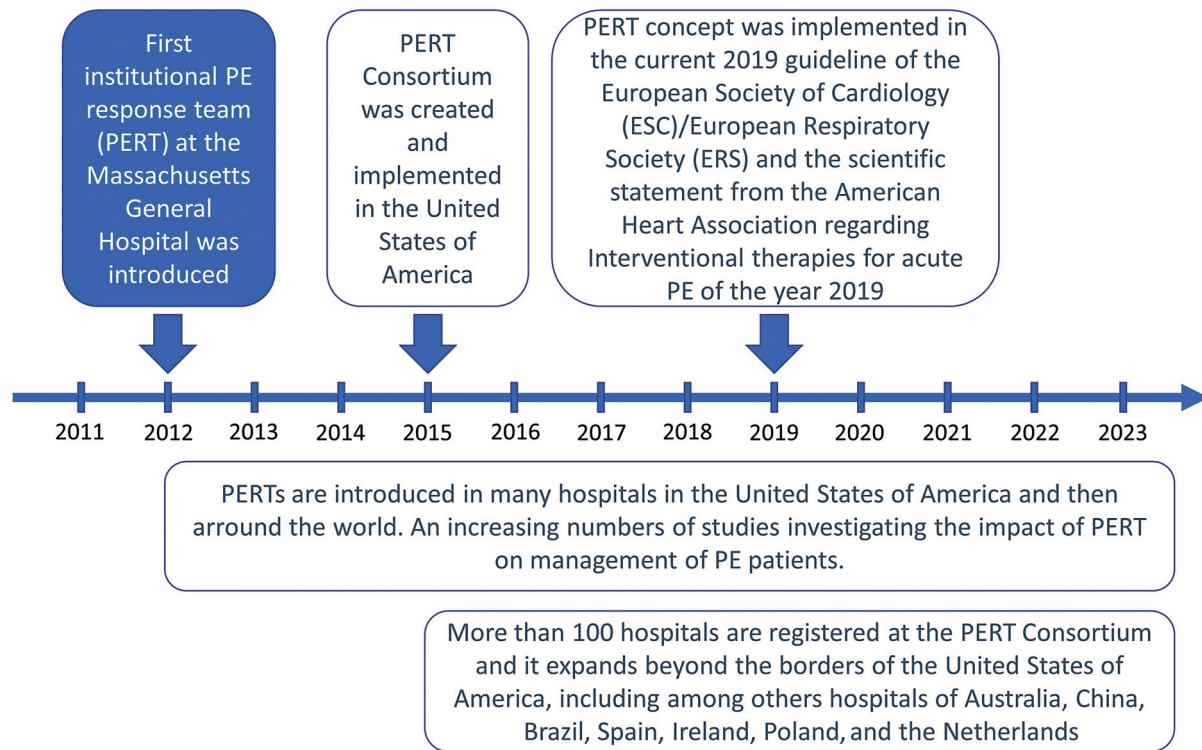
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critical care specialists.<sup>7</sup> This collaborative effort enables a holistic evaluation of each case, considering the clinical, imaging, and hemodynamic characteristics, to determine the optimal treatment strategy. The primary objectives of PERTs are divided into optimized approaches regarding diagnostic, risk stratification, and treatment. First, they aim to expedite the diagnosis of acute PE through the utilization of advanced imaging modalities such as computed tomography pulmonary angiography (CTPA), transthoracic echocardiography, and ventilation-perfusion (V/Q) scans.<sup>8</sup> Second, PERTs facilitate risk stratification, employing scoring systems like the Pulmonary Embolism Severity Index (PESI) or Hestia criteria and biomarker levels and information about right ventricle (RV) dysfunction, to guide appropriate patient management.<sup>9,10</sup> Finally, PERTs play a pivotal role in decision-making concerning the selection of anticoagulant therapy, thrombolytic administration, and, in select cases, invasive interventions like catheter-directed treatment (low-dose thrombolysis or thrombectomy), surgical embolectomy, or extracorporeal membrane oxygenation (ECMO).<sup>11,12</sup> Moreover, PERTs serve as platforms for education, fostering knowledge dissemination and skill enhancement among medical professionals regarding the complexities of acute PE management.<sup>13</sup>

## PERT Establishment Across Countries Worldwide

As aforementioned, PE is an important cause of mortality and morbidity worldwide.<sup>2,14–17</sup> In the light of increasing incidence of PE in many countries,<sup>2,13,14,17</sup> it is promising that annual short-term mortality decreased over the last decades.<sup>2,13,18</sup> However, PE is still accompanied with approximately 100,000 deaths in the United States<sup>17,19</sup> and close to 12,500 deaths in Germany,<sup>2</sup> and remarkably, the mortality rate of high-risk or intermediate-high-risk patients is still substantially higher.<sup>2,14,15,17</sup> In these PE patients with hemodynamical instability or pending hemodynamic compromise, reperfusion treatments are beneficial to avoid early death and are recommended from the disease-specific guidelines.<sup>14,15,20</sup> Nevertheless, studies indicate an underuse of these life-saving reperfusion treatments in high-risk and intermediate-high-risk patients notwithstanding absence of contraindications, potentially driven by the fear of treating physicians regarding the occurrence of major bleeding.<sup>2,15,21</sup> Despite enormous efforts to improve treatment of patients with acute PE with increasing numbers of catheter-directed treatments, especially high-risk or intermediate-high-risk patients, the mortality rate does not decrease satisfactorily over time, which might be in part attributed to the hesitation to use more aggressive reperfusion treatment strategies due to the fear of bleeding complications.<sup>15,17</sup> For many physicians, aggressive reperfusion treatments in the early treatment phase of high-risk or intermediate-high-risk patients are not uncontroversial standards given the physicians' pronounced fear regarding bleeding complications especially when the individual treating physician has to make a

unilateral decision on whether or not to use this treatment and not in collaboration with different physicians and specialists.<sup>13,19,22</sup> In this context, it is striking that management of acute PE does not belong to one specialty, but, instead, it can involve many different medical and surgical specialties and not everyone has the same expertise regarding risk stratification and the advanced reperfusion therapies.<sup>13,19,23</sup> To overcome these problems and inspired by the experiences of the established “heart team” and other rapid response teams (e.g., stroke teams, shock teams, trauma teams, and cardiac arrest teams), PERTs have been developed.<sup>13,15,22,23</sup> The “heart team” approach is an important tool in optimizing patient selection for different treatment options and selection of the most beneficial treatment for the individual patient with an urgent cardiovascular disease such as myocardial infarction, stroke, and acute aortic syndromes by a shared decision-making of experts (primarily cardiologist and cardiothoracic surgeons).<sup>13,22</sup> On the basis of this “heart team” concept, PERTs were developed and established for the first time in 2012 in the United States at the Massachusetts General Hospital (→Fig. 1).<sup>17,19,22,23</sup> Shortly after this, other community-based hospitals in the United States followed this promising example and built their own institutional PERTs.<sup>19,22</sup> With this establishing and expanding evidence and experience regarding PERTs, in May 2015 the PERT Consortium was created with the aim to promote research in the field of PE and establish PERT in hospitals, improve management of PE, and provide infrastructure for assessment of interventional approaches and devices.<sup>13,15,17,19,24</sup> Many centers are entering actively their PERT patient data in the centralized database of the PERT Consortium.<sup>13,15</sup> Since the introduction of the PERT Consortium, more than 100 hospitals have registered at the consortium and it expands beyond the borders of the United States, including among others hospitals in Australia, China, Brazil, Spain, Ireland, Poland, and the Netherlands (→Fig. 1).<sup>19</sup> The PERT concept has the advantages of gathering input of different clinicians and experts, coordination of patient care, improving timelines, and increasing access to advanced therapies by a multidisciplinary and multispecialty team of experts.<sup>13,15,19</sup> PERTs help address these problems by facilitating a consensus shared decision of experts of different specialties, tailoring the management of the PE to the individual demands of the patients.<sup>13,15</sup> Thus, with growing evidence, the PERT concept was endorsed in the current 2019 guideline of the European Society of Cardiology (ESC)/European Respiratory Society (ERS)<sup>14</sup> and the 2019 scientific statement from the American Heart Association regarding interventional therapies for acute PE (→Fig. 1).<sup>15</sup> PERT might serve as a future platform regarding research studies for better management of acute PE and might help in the investigation of novel devices for treatment of acute PE.<sup>15</sup> In addition, studies about PERT around the world provide further evidence of the establishment of PERTs in various countries (→Table 1). Besides the large number of reports from the United States,<sup>7,15,17,22,24–34</sup> study results are also published in Poland,<sup>35</sup> Mexico,<sup>36</sup> China,<sup>37</sup> Canada,<sup>38</sup> and Singapore.<sup>39</sup>



**Fig. 1** Pulmonary embolism response team (PERT) development across countries.

## PERT Composition

Established in the United States in 2015, the Pulmonary Embolism Response Team Consortium disseminated a consensus-based directive pertaining to the composition of PERTs. This paradigmatic recommendation underscored the imperative inclusion of specialists from the domains of cardiac surgery, cardiac imaging, both interventional and noninterventional cardiology, critical care, emergency medicine, hematology, clinical pharmacy, pulmonary medicine, diagnostic and interventional radiology, vascular medicine, and vascular surgery. A recent meta-analysis included eight studies and found that 31.5% of individuals with acute PE, irrespective of their stratified risk class, underwent comprehensive evaluation by a PERT. The results of a recent meta-analysis regarding PERT composition can be summarized as the following<sup>7</sup>: Across the spectrum of the encompassed studies, the median count of distinct medical specialties contributing to the constitution of PERTs was 6.5, demonstrating a range spanning from 2 to 10 specialties. Remarkably, within 13 distinct studies, the participation of up to 11 disparate specialties was documented within the framework of PERTs. Activation of PERTs was commonly encouraged by a constellation of indicators, as reported by two studies: severe clinical manifestations such as tachycardia, hypotension, and hypoxia; indicators of right ventricular compromise; prior VTE or thrombophilia; familial history of VTE; or the absence of recent malignancy or surgical interventions. Referrals of PERTs predominantly originated from emergency departments (59.4%), followed by medical or surgical wards (29.1%), and the intensive care unit (ICU) (9.9%). Those individuals who

underwent evaluation through engagement with a PERT exhibited an average age of 60 years, with a demographic composition reflecting 48.7% females and 23.5% of the cohort burdened by malignancies. Right ventricular dysfunction was discernible in 55% of the investigated patient cohort. The classification of the PE cases revealed that 74.5% were allocated to the intermediate-risk category, while 16% were stratified as high-risk PE patients. Evaluating the participation of specialties within a recent meta-analysis, cardiologists or cardiac/vascular surgeons were consistently encompassed in all PERT activations, followed by pulmonologists or critical care experts (92.9%) and radiologists (71.4%; ~Fig. 2).<sup>7</sup>

Given the heterogeneity of localized administrative frameworks, the composition of PERTs should be adapted to the available resources in each institution.

The composition of these interdisciplinary teams should not solely be about who should perform specific tasks, but should also take into consideration who possesses the most experience and what resources are available within the local health care setting. This determination significantly influences the efficiency and safety of managing clinical situations involving intermediate- to high-risk PE.<sup>40</sup> Galmer et al proposed three potential levels of response within PERTs: basic, advanced, and centers of excellence.<sup>41</sup> Mortality rates in patients with acute PE with signs of hemodynamic instability range from 16 to 46%. This rate rises to 52 to 84% once patients deteriorate and have a cardiac arrest.<sup>2,42</sup> This raises the question of medical resource allocation. The necessity of ICU treatment and especially the need of extracorporeal circulatory support should be considered a key factor regarding the treatment of patients with cardiac arrest.<sup>43</sup> The

**Table 1** Overview of studies on PERT modified according to the literature<sup>6,7</sup>

Study	Country	Population	Study design/control	No. of patients	Risk groups (%)
Annabathula et al <sup>32</sup>	United States	Acute PE (all-comers) <i>Exclusion criteria:</i> no CTPA, no evaluation of the RV	Cohort/historical cohort	530	NR
Araszkiewicz et al <sup>58</sup>	Poland	All PERT activations	Cohort/no	680	Low: 22.8; intermediate-low: 24.2; intermediate-high: 42.9; high: 10.1
Carroll et al <sup>30</sup>	United States	Acute PE (all-comers)	Cohort/historical cohort	2,042	I: Low: 46.4; intermediate: 49.8; high: 3.8 C: Low: 61.4; intermediate: 33.8; high: 4.8
Chaudhury et al <sup>31</sup>	United States	Acute PE (all-comers) <i>Exclusion criteria:</i> sub segmental PE, outpatient care	Cohort/historical cohort	769	I: Low: 11.3; intermediate and high: 88.7 C: Low: 15.7; intermediate and high: 84.3
Deadmon et al <sup>33,a</sup>	United States	All PERT activations	Cohort/no	561	Low: 15.7; intermediate: 50.2; high: 34.2
Finn et al <sup>59</sup>	United States	PERT consultations before and after COVID-19	Cohort/no	100	Intermediate and high: 65.7
Groth et al <sup>60,b</sup>	United States	Acute PE, massive or submassive	Cohort/historical cohort	573	I: Intermediate-high: 79; high: 21 C: Intermediate-high: 74; high: 26
Jen et al <sup>39</sup>	Singapore	Acute PE (all-comers)	Cohort/historical cohort	321	I: Low: 9; intermediate: 79; high: 9.1 C: Low: 9.1; intermediate: 82.5; high: 8.4
Kendall et al <sup>61</sup>	United States	PE patients with massive or submassive PE and evaluated by PERT	Cohort/no	40	Intermediate: 57; high: 43
Khaing et al <sup>62</sup>	United States	PE patients evaluated by PERT	Cohort/no	52	Low: 0; intermediate: 94.2; high: 5.8
Kwok et al <sup>63,c</sup>	United States	Acute PE (all-comers) before and after COVID-19	Cohort/no	60	Low: 18.3; intermediate: 76.6; high: 5
Melamed et al <sup>56</sup>	United States	Acute PE (all-comers)	Cohort/historical cohort	728	NR
Mortensen et al <sup>34,a</sup>	United States	Acute PE transferred to the ED	Cohort/no		Low: 56.9; intermediate and high: 43.1

**Table 1** (Continued)

Study	Country	Population	Study design/control	No. of patients	Risk groups (%)
Myc et al <sup>24</sup>	United States	Acute PE (all-comers)	Cohort/historical cohort	554	I: Low: 35; intermediate: 36.6; high: 28 C: Low: 30; intermediate: 36.7; high: 33
Parikh et al <sup>64</sup>	United States	PERT activations	Cohort/no	69	Low: 20.3, Intermediate: 65.2, High: 14.5
Romano et al <sup>38</sup>	Canada	PERT activations	Cohort/no	128	Low: 3.1; intermediate: 85.2; high: 11.7
Rosovsky et al <sup>57,a</sup>	United States	Acute PE, eligible only if the hospital's criteria for PERT activation are met	Cohort/historical cohort	440	I: Low: 19.3; intermediate: 49.1; high: 31.6 C: Low: 36.8; intermediate: 31.6; high: 31.6
Schultz et al <sup>25,f</sup>	United States	PERT activations	Cohort/no	416	Low: 18.8; intermediate: 69; high: 12.3
Sista et al <sup>26</sup>	United States	PERT activations, massive or submassive	Cohort/no	87	Low: 0; intermediate: 90.8; high: 9.2
Wiske et al <sup>27,c</sup>	United States	PERT activations	Cohort/no	179	Intermediate: 91.3; high: 8.7
Wright et al <sup>29,b</sup>	United States	PERT activations, massive or submassive	Cohort/historical cohort	368	I: Low: 0; intermediate-low: 36.8; intermediate-high: 46.8; high: 16.5 C: Low: 0; intermediate-low: 45.3; intermediate-high: 28.5; high: 26.3
Xenos et al <sup>28</sup>	United States	PERT activations	Yes	1,069	Intermediate-high: 87; high: 13

Abbreviations: C, control population (not evaluated by PERT); CTPA, computed tomography pulmonary angiogram; ED, emergency department; I, intervention population (evaluated by PERT); NR, not reported; PE, pulmonary embolism; PERT, pulmonary embolism response team; RV, right ventricle; VTE, venous thromboembolism.

<sup>a</sup>Studies from the Massachusetts General Hospital.

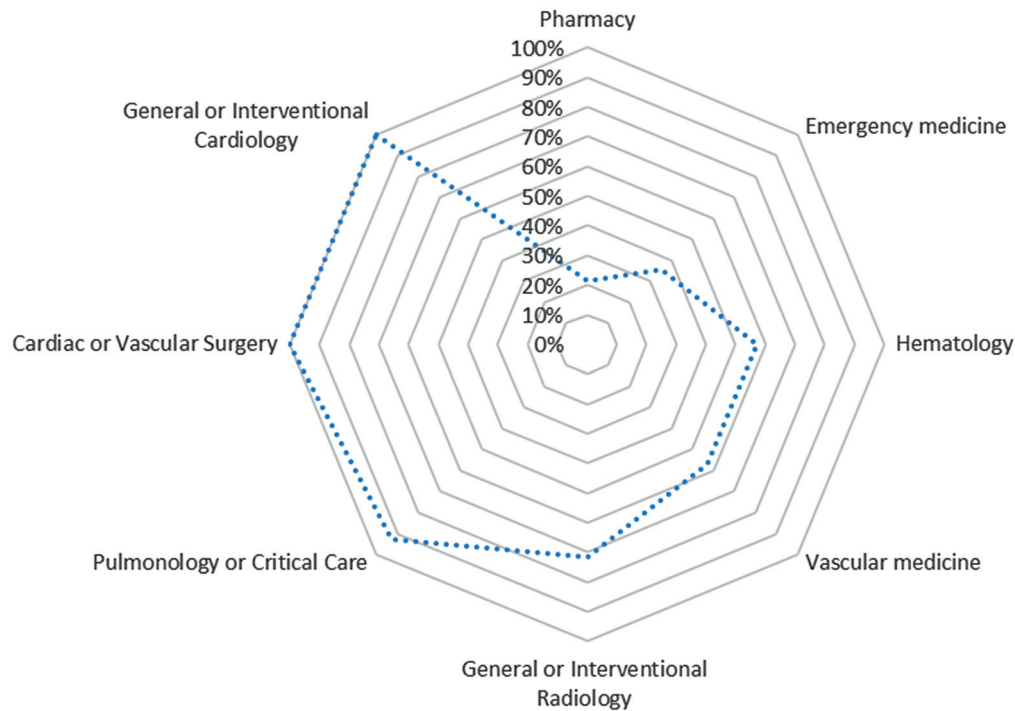
<sup>b</sup>Studies from the University of Rochester Medical Center/Strong Memorial.

<sup>c</sup>Studies for the University Langone New York. <sup>f</sup>Multicenter study comprising several centers included in this review. All studies with duplicated data were not pooled together to avoid unit-of-analysis error.

staffing of a critical resource in an ICU must be reserved for severe cases. For this reason, the composition of the PERT should be chosen based on the severity of PE. In the cases where significant complications are not expected, a PERT *basic* team (cardiologist, radiologist) may be adequate. In the cases in which more complex circumstances are present such as elevated bleeding risk, new catheter-directed treatment

options or surgical embolectomy can be employed and should be discussed in a PERT *plus* team (e.g., interventional cardiologists, pulmonologists, radiologists, anesthesiologists, and cardiac surgeons). In severe cases, in which complex intensive care interventions (e.g., ECMO, mechanical ventilation) are additionally required, a PERT *advanced* team is needed to act and decide rapidly (e.g., interventional





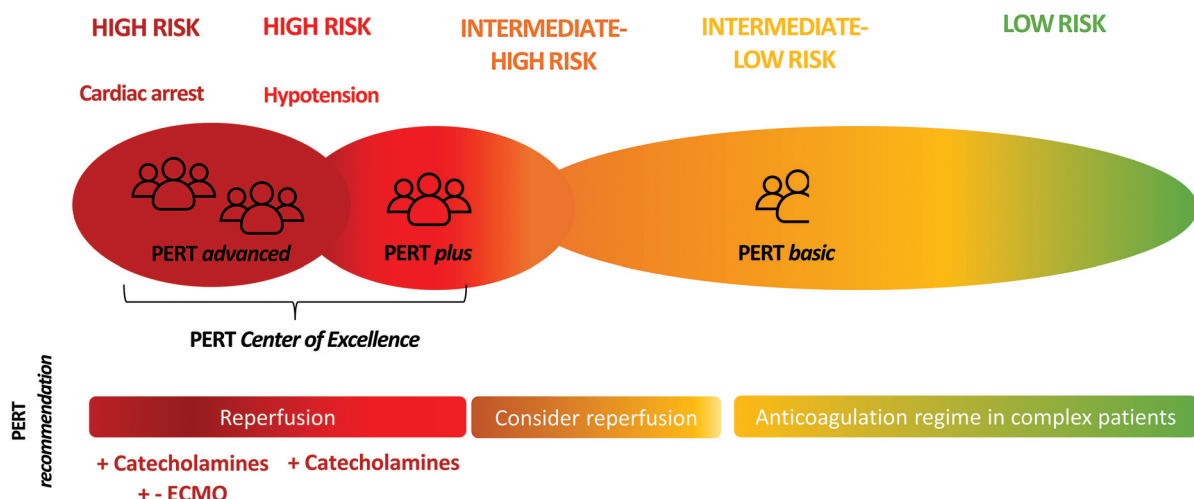
**Fig. 2** Pulmonary embolism response team (PERT) composition across countries modified according to the literature.<sup>7</sup>

cardiologists, pulmonologists, radiologists, anesthesiologists, cardiac surgeons, and critical care physicians). In this context, all patients with high- or intermediate-risk PE with high bleeding risk or signs of hemodynamic compromise should be reviewed (onsite or via telemedicine) by a PERT center of excellence, which is capable of multimodality management to decide the initial treatment after review of all relevant data. A PERT center of excellence should have standardized operation procedures and should gather together at least a *PERT plus* team, although a *PERT advanced*

team instantly available with interventional cardiologists, pulmonologists, radiologists, anesthesiologists, cardiac surgeons, and critical care physicians is preferable (→ **Fig. 3**).

### PERT and Use of Advanced Treatment Options

A paradigm shift can currently be observed in the management of intermediate-high-risk and high-risk PE. Catheter-directed therapies (CDT) have emerged as an alternative to



**Fig. 3** Perspective of pulmonary embolism response team (PERT) and its proposed future role based on risk stratification and necessity of advanced intensive care support. ECMO, extracorporeal membrane oxygenation.

the “classic” reperfusion therapies, which include systemic thrombolysis and surgical embolectomy.<sup>44</sup> Systemic thrombolysis is primarily reserved for reperfusion treatment in high-risk PE only. The Pulmonary Embolism Thrombolysis (PEITHO) randomized controlled trial demonstrated an excess risk of intracranial and major extracranial bleedings in patients with intermediate-high-risk PE.<sup>45</sup> Surgical embolectomy is a complex procedure, which is only reserved for critically ill patients with contraindications to thrombolysis and favorably low surgical risk.<sup>14,46</sup> CDT includes the use of catheter-directed thrombolysis (with or without ultrasound assistance) and catheter-based thrombectomy.<sup>44</sup> For both treatment options, there are several cohort studies that show the short- and long-term effectiveness regarding acute and chronic hemodynamic and functional amelioration, as well as safety regarding the endpoints of mortality and bleeding.<sup>3,47–50</sup> However, randomized controlled trials powered for clinical outcomes are currently being conducted,<sup>51</sup> and those systems have not yet been established as standard treatment in the acute phase of PE management, but are rather reserved for patients who failed thrombolysis or those with contraindications to systemic administration of thrombolytics.<sup>14</sup> Nonetheless, their use in the “real world” has been showing increasing trends.<sup>52</sup> In addition, ECMO therapy has been increasingly used in patients who are at the far end of the severity spectrum, while it is common hemodynamically unstable or cardiac arrest patients to require a multimodality management plan including ECMO and reperfusion.<sup>11,43,53</sup> The establishment of PERT is an excellent paradigm of multidisciplinary consultation to justify the optimal treatment approach in the management of complex patients with intermediate-high- and high-risk acute PE. The concept of PERT was developed particularly in response to the new emerging therapies in the field of acute PE, and also in view of the lack of high-quality data.<sup>31,54</sup> Thus, in most studies comparing treatment administration in the pre- and post-PERT era, an increase in the use of advanced therapy (defined as the use of reperfusion and/or ECMO) has been observed, up to a 2.5-fold difference in a meta-analysis of PERT studies.<sup>7</sup> This possibly depicts the overall increase in temporal usage of CDT among expert centers, such as those with PERT implementation, rather than an etiological association between PERT consultation and advanced therapy use. In fact, there have been reports that PERT may be associated with a decrease in advanced therapies administered to acute PE patients without an impact on clinical outcomes.<sup>55</sup> However, prospective and randomized clinical studies are still lacking to firmly establish the notion that PERT may lead to a more prudent and targeted use of advanced therapy and improve outcomes in patients with higher risk of PE.

### Comparison of the Pre- and Post-PERT Era

After aggregating the data from nine controlled studies,<sup>24,28–32,39,56,57</sup> a recent meta-analysis included a total of 6,821 patients.<sup>7</sup> Both Chaudhury et al<sup>31</sup> and Myc et al<sup>24</sup> identified an association between improved mortality and the establishment of PERT. In addition, Myc et al

reported a diminished rate of hospital readmissions among PERT group patients in comparison to a historical cohort (the control group), even though their cohort exhibited a higher level of acute illness.<sup>24</sup> Chaudhury et al also noted that the mortality benefit was more pronounced in cases of intermediate- and high-risk PE.<sup>31</sup> In a current meta-analysis<sup>7</sup>, when considering all risk classes, there was a slight difference in the mortality rate in pre- and post-PERT implementation (relative risk [RR]: 0.89; 95% confidence interval [CI]: 0.67–1.19). However, upon examining the intermediate- and high-risk classes exclusively, it became apparent that treatment during the PERT era tended, but not significantly, to reduce mortality rates compared to that in the pre-PERT era (RR: 0.71; 95% CI: 0.45–1.12). In this context, the authors noted that there was substantial heterogeneity among the investigated studies ( $I^2 = 70\%$ ,  $p < 0.01$ ), and the funnel plot indicated that larger studies were more likely to show a favorable effect of PERT establishment on mortality, while smaller studies were more inclined to report a RR less than 1. However, another meta-analysis revealed similar results.<sup>6</sup> In both, the overall population and the subgroup of patients with intermediate- and high-risk PE, no significant differences were found in the 30-day readmission, bleeding (major and overall), or ICU admission rates. However, the total length of hospital stay was shorter during the PERT era compared to the pre-PERT era (mean difference [MD]: –1.61 days; 95% CI: –3.21 to –0.02). This reduction in hospital stay also extended to ICU stays (MD: –1.79 days; 95% CI: –3.29 to –0.28 days). The utilization of advanced therapies, when aggregated, was more frequent in the PERT era compared to the pre-PERT era (RR: 1.89; 95% CI: 1.03–3.45). Specifically, higher rates were observed for systemic thrombolysis (181/3,242 [5.6%] in the PERT era vs. 79/2,510 [3.1%] in the pre-PERT era; RR: 1.70 [95% CI: 0.73–3.98]) and catheter-directed thrombolysis (214/3,319 [6.4%] in the PERT era vs. 104/3,502 [3.0%] in the pre-PERT era; RR: 3.30 [95% CI: 1.28–8.48]). However, there were no significant differences for surgical thrombectomy (22/2,527 [0.9%] in the PERT era vs. 15/1,967 [0.8%] in the pre-PERT era; RR: 0.87 [95% CI: 0.29–2.62]) and ECMO (29/2,513 [1.2%] in the PERT era vs. 36/2,819 [1.3%] in the pre-PERT era; RR: 1.39 [95% CI: 0.52–3.69]). Interestingly, the use of inferior vena cava (IVC) filters was lower during the PERT era compared to the pre-PERT era (191/1,901 [10%] vs. 224/1,464 [15.3%]; RR: 0.66 [95% CI: 0.55–0.79]).<sup>7</sup>

### Conclusion

Many studies examining PERTs have notable limitations, including their descriptive nature, nonrandomized design, or reliance on data from a single institution. Most of these studies were retrospective rather than prospective, limiting their possible impact on patient outcomes. Consequently, current guidelines recommend the establishment of PERTs to aid in acute PE decision-making. Diverse and complex treatment options have recently become available for personalized therapy for patients with acute intermediate- and high-risk PE, making guidance by a team of experts more and more

important. With growing recognition of the burden of PE and the expanding array of therapeutic options, PERTs are increasingly being incorporated into PE management worldwide. As more institutions adopt these teams, more data will be collected to inform treatment decisions and guidelines for best practices. PERT establishment should place equal emphasis on patient management, improvement of local institutions, and physician education. Regarding the complexity of different treatment options, levels of expertise within PERT should be evaluated.

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### Conflicts of interest

L.H. received lecture/consultant fees from MSD, INARI, Johnson & Johnson, and Boston Scientific, outside the submitted work. L.H. also reports personal fees from MSD, personal fees from Johnson & Johnson, personal fees from INARI, and personal fees from Boston Scientific, outside the submitted work. I.T.F. reports no conflict of interest. D.D. received speaker's honoraria from Boston Scientific, Bayer, Daiichi Sankyo, BMS, and Pfizer. D.D. also reports grants from DFG, grants from DZHK, during the conduct of the study; personal fees from Boston Scientific, personal fees from Bayer, personal fees from Daiichi Sankyo, personal fees from BMS, and personal fees from Pfizer, outside the submitted work. K.K. reports no conflict of interest.

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