The Modern PE Landscape: Three Key Ways Our Practice Has Changed

Advancements in diagnosis, technology, and treatment for pulmonary embolism that have changed the approach to its management.

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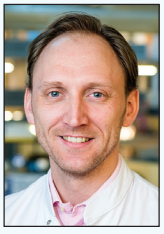

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Over the past decade, large prospective studies and technical developments have resulted in major changes to the management of patients with acute pulmonary embolism (PE) in daily practice throughout all stages of the patient pathway, starting with the diagnosis. First, in a post hoc analysis of the large diagnostic studies performed between 2000 and 2010, the diagnostic algorithm of suspected PE was improved, particularly in terms of efficiency. PE could be excluded in more patients without performing potentially harmful and expensive imaging tests by changing the D-dimer assay threshold. Although the introduction of the age-dependent D-dimer threshold improved the specificity of the D-dimer test considerably for elderly patients, the pretest-dependent threshold allowed the exclusion of PE in 50% of patients across all age categories. Indeed, the ADJUST-PE, YEARS, and Artemis studies confirmed the safety and efficacy of these approaches, reducing the length of stay in the emergency department, emergency department costs, and the number of potentially irrelevant subsegmental PE diagnoses.[1-3]

In addition to more efficacious diagnostic management, several advancements were made regarding initial risk stratification and treatment of acute PE. The PEITHO study revealed that the combination of right ventricular (RV) overload and abnormal troponin test indicated that patients are at "intermediate-high" risk of an adverse outcome and that reperfusion therapy reduces the risk of hemodynamic deterioration and PE-related death in these patients.[4] However, full-dose systemic thrombolysis, until recently the only available reperfusion technique other than surgical thrombectomy, caused an unacceptable increase in major bleeding and stroke. Therefore, although the guidelines underline the need for careful monitoring of such patients in the first days after diagnosis, they advise against primary reperfusion.[5] With the introduction of catheter-directed techniques and teams with PE expertise allowing for a fast multidisciplinary discussion on optimal therapeutic management, safer reperfusion options have become available and are being used in clinical practice. Notably, since the published literature lacks high-quality clinical outcome trials focusing on clinically relevant outcomes such as hemodynamic collapse and death, these techniques should not be used routinely in patients with hemodynamically stable PE, unless rescue reperfusion therapy is needed.

The currently enrolling HI-PEITHO study will establish the first-line treatment in intermediate-high–risk PE patients with imminent hemodynamic collapse. It is a multinational, multicenter, randomized, controlled, parallel-group comparison trial in which patients with hemodynamically stable intermediate-high–risk PE with additional clinical criteria indicating an elevated risk of early death are randomized 1:1 to treatment with a standardized protocol of ultrasound-facilitated catheter-directed thrombolysis (CDT) plus anticoagulation versus anticoagulation alone. HI-PEITHO is expected to inform international guidelines and set the standard for state-of-the-art evaluation of catheter-directed reperfusion options in the future.

On the other end of the spectrum, the randomized controlled VESTA, HOT-PE, and HOME-PE studies have firmly established that patients without any of the so-called Hestia criteria or at low risk of death based on the simplified Pulmonary Embolism Severity Index score can be safely treated at home, increasing patient satisfaction and lowering health care costs.[6-8]

Finally, much has been learned regarding long-term outcomes of patients with PE. Up to 50% may develop post-PE syndrome, with chronic thromboembolic pulmonary hypertension (CTEPH) as its most severe clinical presentation.[9] Strategies aimed at earlier identification of patients with post-PE syndrome, and especially with CTEPH, will lead to better survival and quality of life.[10] The recently published ICHOM-PE standard set of outcome measures[11] will help capture all relevant sequelae of acute PE, which is expected to improve the quality of care and empower PE patients. The introduction of these outcomes into clinical trials will further improve our knowledge on optimal individualized treatment decisions in the near future.

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Historically, PE has been treated with three strategies: (1) anticoagulation alone for those who are not critically ill; (2) systemic thrombolytics in patients with hemodynamic compromise; and (3) surgical embolectomy, which is reserved for patients with ongoing hemodynamic embarrassment but who have contraindications to thrombolytics and/or are refractory to other treatment modalities.[1-3] In the last decade, less invasive and more rapid methods for thrombus alteration have emerged, changing the landscape of practice. CDT with or without ultrasound-assisted delivery allows for localized infusion of fibrinolytics to decrease the total administered dose and minimize systemic absorption.[4-6] Compared to anticoagulation alone, this method has been shown to improve the RV/left ventricular ratio more efficiently; however, long-term clinical outcomes are lacking.

More recently, the advent of large-bore thrombectomy catheters has disrupted many treatment algorithms.[7] The ability to quickly debulk large-burden thrombus may be helpful in unloading the RV outflow obstruction, but we currently lack head-to-head evidence of large-bore thrombectomy versus either CDT or anticoagulation alone. Nonetheless, a potential advantage for large-bore thrombectomy exists with its ability to be combined with venoarterial extracorporeal membrane oxygenation[8] in those at the brink of or exhibiting signs of massive PE in an effort to halt the RV shock spiral.[9]

Despite these novel technologic advancements, perhaps the most influential change in PE treatment in the last decade has been the development of the PE response team (PERT).[10] PERTs allow for an immediate, multidisciplinary discussion with patient-focused analysis in an effort to formulate evidence-based treatment plans and optimize clinical outcomes.[11,12] Although PERT programs have been shown to convey advantages in reducing overall adverse outcomes,[11] we look forward to results from

currently enrolling randomized controlled trials that will help further elucidate the role of various endovascular treatment modalities in the management of patients with submassive and massive PE.

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1. In most intermediate-risk patients, we wait. As PEITHO demonstrated, only a small minority of patients (~5%) will deteriorate if anticoagulation is promptly initiated. Although the mechanism is unclear, many patients begin to feel immediately better after a few hours of heparin, and by the next morning, vitals have stabilized, and they are able to ambulate. However, in select patients with intermediate-risk PE, severe dyspnea persists with ambulation, and RV function on echocardiography does not improve. In these patients, we proceed with reperfusion therapy—most commonly, use of catheter-directed therapy.

2. In deteriorating patients, we partner with cardiac anesthesiologists. We convert our interventional suite into a sophisticated cardiac intensive care unit or operating room because deteriorating PE patients need the highest level of expertise to maximize their chance of survival. Having cardiac anesthesiologists with deep knowledge of right heart physiology and pharmacology allows interventionalists to focus on establishing flow into the left heart and restoring systemic blood pressure.

3. We speak as one team. We realized soon after the formation of our PERT that we needed consensus on the type of treatment, the rapidity of treatment, and periprocedural PE care (eg, intubation, anesthesia, pre- and postintervention monitoring). Our pulmonologists frequently come to the interventional radiology suite to speak with the interventionalist and anesthesiologist (if present) to ensure that everyone agrees on the approach, including the level of anesthesia, which agents to avoid, and what we would do in the event of deterioration. We have a single note in the electronic medical record that reflects the collective plan. ■