

Unmet needs in the management of pulmonary embolism: catheter-directed therapy looks set to fill the void

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The presentation of acute pulmonary embolism (PE) varies widely, and may range from absence of symptoms, to cardiogenic shock and sudden death. Consequently, risk stratification of patients with acute PE is mandatory for determining the most appropriate therapeutic management. Haemodynamic instability and the presence of right ventricular (RV) dysfunction are major determinants of short-term prognosis and define high-risk and intermediate-high risk PE, which have mortality rates of >25% and 10%, respectively at 30 days. This is much higher than the 1% mortality at 30 days observed in patients with low-risk PE, characterized by the absence of haemodynamic instability and RV dysfunction. Therefore, there is clearly a compelling need to adjust the therapeutic options according to the gravity of the clinical presentation. In this regard, new treatment options need to be envisaged on top of anticoagulation for patients with high-risk or intermediate-high risk PE.

Alternative therapies are all the more warranted in high-risk PE, where around two-thirds of patients do not receive systemic thrombolysis, even when they are eligible.¹ Surgical embolectomy, which is an alternative to systemic thrombolysis, is rarely considered an option because the poor preoperative state together with frequent comorbidities make the majority of patients poor candidates for surgery. As a result, a substantial proportion of high-risk PE patients remain under-treated. The situation is even more critical in patients with intermediate-high risk PE, since, as shown in the PEITHO trial, intravenous thrombolysis cannot be considered as first line therapy due to the unacceptably high risk of severe intracranial and extracranial bleeding, despite a significant reduction in haemodynamic decompensation.²

The use of alternative revascularization strategies with a more favourable safety profile than standard intravenous

thrombolysis, or even than surgical embolectomy, is therefore mandatory. Catheter-directed treatment (CDT) is emerging as a potentially promising approach, since it enables targeted therapy, via mechanical or pharmacomechanical thrombus removal, and it has the additional advantages of being quick, easy to implement and often more widely available than surgery. Modern CDT reperfusion techniques use low profile catheters to achieve mechanical fragmentation or aspiration of the thrombus, or to deliver *in situ* thrombolysis. The aim of this approach is to restore pulmonary artery permeability, and reverse life-threatening right heart strain. In view of the exponential relation between pulmonary vascular obstruction and total pulmonary resistance, even a minimal reduction in pulmonary vascular obstruction is associated with a substantial reduction in pulmonary resistance, making it possible to stabilize haemodynamics and reduce the risk of decompensation.

The pharmacomechanical approach combining local delivery of thrombolytic agents with ultrasound assistance is the most widely studied technique and has shown promising results. In *in vitro* models, the ultrasonic waves disrupt the fibrin strands of the thrombus, allowing more binding sites for the thrombolytic agent.³ Nonetheless, a number of prospective studies and registries have confirmed the findings of the randomized ULTIMA study, which showed that ultrasound-assisted catheter-directed thrombolysis was superior to anticoagulation alone in reversing RV dilatation in intermediate-risk PE patients.⁴

Beyond their established efficacy on RV dysfunction, catheter-based PE interventions present a number of potential advantages, notably the fact that they are easy and rapid to implement, use low doses of thrombolytics, and above all, enjoy a favourable safety profile, with a major bleeding rate around 6%, and extremely low rates of fatal or intracranial haemorrhage. Conversely, they also suffer from some limitations that need to be taken into account,

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including the need for appropriate expertise and resources, and the need for additional data regarding the efficacy of CDT in high-risk PE. Above all, there is gaping lack of long-term clinical data regarding the rate of recurrence, mortality and the rate of chronic thromboembolic pulmonary hypertension (CTEPH), and studies to investigate these parameters constitute a fundamental step towards the definitive validation of CDT in the treatment of acute PE. The most recent guidelines of the European Society of Cardiology for the management of PE stipulate that, in high-risk PE patients, percutaneous catheter-directed treatment should be considered for patients in whom thrombolysis is contra-indicated or has failed, if appropriate expertise and resources are available.⁵ In those with intermediate-high risk PE, CDT should be considered as an alternative to rescue thrombolytic therapy for patients with haemodynamic deterioration on anticoagulant therapy.⁵ In patients undergoing extracorporeal membrane oxygenation (ECMO) in the setting of refractory shock or cardiac arrest, additional therapies such as surgical or catheter embolectomy, may be considered.⁵

This issue of *European Heart Journal Supplement—the Heart of the Matter* is entirely dedicated to catheter-based therapies for the treatment of PE. To set the scene, Valerio *et al.*⁶ address the limitations of reperfusion strategies, namely systemic thrombolysis and surgical embolectomy, in patients with high-risk or intermediate-high risk PE. Next, de Winter *et al.*⁷ outline the importance of evaluating the risk-benefit ratio of each possible therapeutic approach, if possible with the support of a dedicated PE response team. A review of the currently available evidence regarding CDT by Chopard *et al.*⁸ summarizes the data coming from observational studies and clinical trials using the different devices. Finally, Sharp and Attallah⁹ call for hard outcome data, which will shape the future of percutaneous approaches to PE management and would mandate it as a first-line treatment in any spectrum of the disease. We hope that this issue, with its comprehensive review of catheter-based therapies, will be a useful one-stop shop for the most up-to-date information on these promising techniques.

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