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Editorial comment

Catheter-directed therapies in various risk categories of pulmonary embolism: standard of care or last resort?

Tratamientos por catéter en diversas categorías de riesgo de embolia pulmonar: ¿estándar de atención o último recurso?

Felix Mahfoud,* Felix Götzinger, and Lucas Lauder

Department of Internal Medicine III, Cardiology, Angiology, and Intensive Care Medicine, Homburg University Hospital, Saarland University, Homburg, Germany

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Pulmonary embolisms (PE) and venous thromboembolisms remain the third leading cause of death from cardiovascular diseases after myocardial infarction and stroke, affecting millions worldwide every year.[1,2] PE is a complex and variable disease that can be asymptomatic or lead to hemodynamic deterioration or sudden death:[3] In PE, thrombi that usually originate in the proximal deep veins occlude the pulmonary arteries, resulting in right ventricular stress, impaired systemic oxygenation, and, in the most severe cases, obstructive shock.[4] According to current guidelines from both Europe and the United States, management of PE should be guided by risk stratification for death.[5,6] While patients with low- and intermediate- to low-risk profiles often benefit from anticoagulation alone, those with intermediate- to high-risk and high-risk profiles may be suitable candidates for reperfusion therapies, including device-based approaches.[5,6] Reperfusion is typically performed by intravenous administration of systemic thrombolysis. Thrombolysis can reduce morbidity and mortality but is associated with major bleeding, which can sometimes be life-threatening, and is recommended for cases of high-risk PE without contraindications to lysis.[4]

Novel interventional reperfusion strategies have been developed and are currently under clinical and scientific investigation in these patients. Interventional therapies for PE include aspiration thrombectomy (with or without fragmentation), local catheter-directed thrombolysis, and ultrasound-assisted thrombolysis. These therapies have been shown to improve right ventricular dysfunction, right-to-left ventricle diameter ratio, and hemodynamic parameters such as pulmonary artery pressure, mainly in nonrandomized studies.[4]

In a recent article published in *Revista Española de Cardiología*, Salinas et al. report data from the Spanish registry of catheter-directed therapy (CDT) in PE, offering valuable insights into the use of these advanced technologies in clinical practice.[7] The study comprised 253 consecutive patients with high-risk or intermediate- to high-risk PE who were eligible for CDT. The authors report data on in-hospital all-cause mortality, in-hospital complications, and procedural success. Among the 253 patients, 93 (36.8%) had high-risk PE, and 160 (63.2%) had intermediate- to high-risk PE as per the current European guidelines.[5]

Most patients were treated with local thrombolysis (70.8%) or aspiration thrombectomy (51.8%), while almost one-fourth of the patients (23.3%) received both treatments. During the observation period spanning from 2014 to 2022, only one-fifth of the patients underwent CDT using dedicated devices designed for PE treatment. In 2022, however, the use of dedicated CDT devices increased significantly to include 73% of the patients.

Salinas et al. report a procedural success rate of 90.9%. Systolic pulmonary artery pressure decreased by 11.8 mmHg (n = 179), while systolic blood pressure increased by 10.5 mmHg. The overall in-hospital mortality rate was 15.5%, with substantial differences across risk categories. The mortality rate was only 2.5% in patients with intermediate- to high-risk PE, but was a staggering 37.6% in high-risk PE. This trend persisted in the 1-month mortality data, showing a rate of 29.3% in high-risk PE vs 1.3% in intermediate- to high-risk PE. Interestingly, the 24-month mortality rate was similar between the 2 groups (5.8% in intermediate- to high-risk individuals vs 5.3% in high-risk individuals).

When used by well-trained staff at experienced centers, procedural complication rates are low. In the current study, complications occurred in 7 of 253 patients (2.8%), with 4 complications occurring in high-risk patients and 3 in intermediate- to high-risk patients. Of these 7 complications, 2 were deemed device- and/or procedure-related, and 2 deaths were likely device-related (cardiac tamponade and a probable traumatic atrioventricular block). These rates are well within previously published complication rates documented in CDT registries and studies.[8,9]

Notably, 72% of high-risk patients required vasopressors, 42% mechanical ventilation, and 7.5% extracorporeal membrane oxygenators, underscoring the severity of the disease in these patients.

The authors conclude that, despite a high procedural success rate, the mortality rate remained high, especially in high-risk patients. They acknowledge that the mortality rate of 37.6% in high-risk patients undergoing CDT remained within the expected, historical mortality range of about 39% for patients undergoing

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* Corresponding author.
E-mail address: felix.mahfoud@uks.eu (F. Mahfoud).
@felixmahfoud (F. Mahfoud), @lucaslauder (L. Lauder)

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reperfusion therapies.[10] A plausible speculation is that these results could have been impacted by the time from admission to initiation of CDT therapy, which was between 2 and 24 hours after presentation in 77.3% of all patients and 71.2% of patients with high-risk PE. Moreover, 13% of patients did not receive anticoagulation before CDT (14% of patients with high-risk PE).

Another important point to mention is the diversity of treatment strategies used in the study, as some techniques and devices for CDT were used more frequently than others. Also important is the lack of procedural standardization across sites. The current registry was observational in design and although patient management was guided by PE response teams, no predefined criteria were used for individual selection of the respective CDT approaches (ie, catheter-directed lysis vs thrombectomy). Additionally, only 1 out of 5 patients underwent a procedure using a dedicated PE device.

In recent years, the use of dedicated devices for CDT has increased in intermediate- to high-risk and high-risk PE. In line with previous studies and registries, hemodynamic parameters were improved following the procedure. However, it remains unknown whether these improvements in hemodynamic parameters translate to improvements in short- and long-term morbidity and mortality. Moreover, whether certain patients benefit more from one catheter-based approach than another remains to be answered. Against this background, several large randomized, controlled trials are ongoing: the HI-PEITHO trial (NCT04790370) is investigating whether ultrasound-assisted CDT, in addition to anticoagulation, improves PE-related mortality and PE recurrence compared with anticoagulation alone. The randomized controlled PEERLESS trial (NCT05111613) is investigating the safety and efficacy of large-bore aspiration thrombectomy and CDT in patients with intermediate- to high-risk PE and signs of right heart dysfunction. The trial plans to include 550 patients, with 150 of them having an absolute contraindication to thrombolysis. The primary outcome of the trial is a hierarchical composite of all-cause mortality, intracranial hemorrhage, major bleeding, clinical deterioration (including hemodynamic and respiratory worsening, and the need for intensive care unit treatment). The prospective randomized PEERLESS II trial will compare the outcomes of intermediate- to high-risk PE treated with mechanical thrombectomy vs anticoagulation in up to 1200 patients.

As we await further evidence, CDT for PE represents an attractive alternative for certain patients at risk. Importantly, all patients undergoing CDT should be included in registries or studies to assess immediate and long-term outcomes, as well as cost-effectiveness. The benefits of CDT are real, but the stakes are high too. Let's stay excited but ever cautious.

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CONFLICTS OF INTEREST

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