

Mechanical thrombectomy for pulmonary embolism revisited: technological breakthrough or simple renovation?

Tobias Rheude*, MD; Sebastian Kufner, MD

Klinik für Herz- und Kreislauferkrankungen, Deutsches Herzzentrum München, Munich, Germany

Pulmonary embolism (PE) represents the third most frequent cardiovascular cause of death on a global scale, with a slight increase in incidence rates over time¹. Current guidelines recommend reperfusion therapy in haemodynamically unstable patients and for those suffering from haemodynamic deterioration despite adequate anticoagulation². In this regard, systemic thrombolysis has, until recently, been recommended as the first-line treatment of choice^{2,3}. However, despite being highly effective, its application entails a significantly elevated bleeding risk, with a 9.9% rate of severe bleedings and a 1.7% rate of intracranial haemorrhage⁴. Therefore, a considerable number of patients do not receive systemic thrombolysis because of an increased bleeding risk or contraindications to thrombolytics.

In recent years, catheter-directed therapies (CDT) have been increasingly used for primary mechanical reperfusion, which is paralleled by the growing scientific attention in these therapies². Several catheter-directed reperfusion techniques, including thrombus fragmentation, mechanical embolectomy and local (ultrasound-accelerated) catheter-directed thrombolysis have become available⁵. However, robust data regarding the clinical efficacy and potential harm of these technologies remain scarce, and results from adequately powered trials are warranted.

In this issue of EuroIntervention, Toma et al report acute outcomes from the FlowTrieve All-Comer Registry for Patient Safety and Hemodynamics (FLASH) study⁶. This prospective

single-arm study included 799 patients across 50 US sites with high-risk (7.9%) and intermediate-risk (92.1%) PE treated with mechanical thrombectomy using the FlowTrieve system (Inari Medical). Of note, one-third of patients had thrombolytic contraindications. The primary safety endpoint was major adverse events (MAE) within 48 hours of the procedure, defined as a composite of device-related death, major bleeding or intra-procedural adverse events. Secondary effectiveness endpoints included haemodynamic and functional parameters, such as the echocardiographic right ventricle (RV)/left ventricle (LV) ratio, systolic pulmonary artery pressure (sPAP), total pulmonary vascular resistance (TPVR) and dyspnoea improvement. All-cause mortality was 0.3% at 48 hours, with no device-related deaths, and MAE occurred in 1.8% of patients, mainly driven by major bleedings. Immediately after mechanical thrombectomy, the following parameters decreased significantly: the RV/LV ratio (from 1.23 to 0.98; $p < 0.0001$), sPAP (from 53.2 to 40.4 mmHg; $p < 0.0001$), TPVR (from 6.65 to 4.99 mmHg*min/L; $p < 0.0001$) and heart rate (from 102 to 90 bpm; $p < 0.0001$).

Article, see page 1201

As current evidence regarding CDT is limited, Toma and colleagues are to be commended on their effort to gather the largest cohort of PE patients undergoing interventional treatment to date with the following caveats. Firstly, despite being an all-comers registry, the applicability of the results to a general PE

*Corresponding author: Klinik für Herz- und Kreislauferkrankungen, Deutsches Herzzentrum München, Lazarettstraße 36, 80636 Munich, Germany. E-mail: rheude@dhm.mhn.de

population is limited by the fact that patients were deemed eligible for mechanical thrombectomy at the discretion of the treating physician without prespecified inclusion criteria. As routine use of CDT is not justified by current guideline recommendations as an alternative to systemic thrombolysis (class IIa recommendation, level of evidence C), appropriate patient selection for interventional treatment remains crucial; this central question remains unanswered in the current trial. Secondly, although the 30-day mortality rates of <1% are encouraging, especially as the majority of patients being categorised with more than intermediate risk with a simplified pulmonary embolism severity index (sPESI) ≥ 1 in 84% and positive cardiac biomarkers in 95% of patients⁷, comparisons across studies regarding mortality rates should be taken with caution. In this regard, the possibility of post-procedural consent might have introduced further selection bias. Thirdly, an immediate effect of mechanical thrombectomy was postulated because of a significant decrease in the mean RV/LV ratio, sPAP, TPVR and heart rate. These beneficial results with regard to surrogate parameters – especially the RV/LV ratio, which has become the standard to evaluate CDT effectiveness – confirm previous study results with other devices^{8,9}. Nevertheless, additional prospective trials are needed to confirm that surrogate parameters translate into improved clinical outcomes and that mechanical reperfusion changes the detrimental course of disease. An improvement of self-reported dyspnoea and a decrease of supplemental oxygen requirements following thrombectomy were reported by the authors and support the potency of CDT.

Overall, the FLASH study adds an important piece of puzzle to the growing body of evidence in the (interventional) treatment of this potentially fatal disease condition. Currently, there are several ongoing randomised trials that compare different CDT to either each other, anticoagulation alone or systemic thrombolysis⁵. In the meanwhile, the indications for CDT should be based on an individualised patient assessment taking comorbidities, bleeding risk and local expertise into consideration.

Conflict of interest statement

T. Rheude received speaker fees from AstraZeneca and SIS Medical, not related to the current work. S. Kufner received

speaker and consulting fees from AstraZeneca, Bristol-Myers Squibb, Translumina, and Bentley, not related to the current work.

References

- Keller K, Hobohm L, Ebner M, Kresoja KP, Münzel T, Konstantinides SV, Lankeit M. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany. *Eur Heart J*. 2020;41:522-9.
- Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, Huisman MV, Humbert M, Jennings CS, Jiménez D, Kucher N, Lang IM, Lankeit M, Lorusso R, Mazzolai L, Meneveau N, Ni Áinle F, Prandoni P, Pruszczyk P, Righini M, Torbicki A, Belle V, Zamorano JL; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J*. 2020;41:543-603.
- Meyer G, Vicaut E, Danays T, Agnelli G, Becattini C, Beyer-Westendorf J, Bluhmki E, Bouvaist H, Brenner B, Couturaud F, Dellas C, Empen K, Franca A, Galiè N, Geibel A, Goldhaber SZ, Jimenez D, Kozak M, Kupatt C, Kucher N, Lang IM, Lankeit M, Meneveau N, Pacouret G, Palazzini M, Petris A, Pruszczyk P, Rugolotto M, Salvi A, Schellong S, Sebbane M, Sobkowicz B, Stefanovic BS, Thiele H, Torbicki A, Verschuren F, Konstantinides SV; PEITHO Investigators. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med*. 2014;370:1402-11.
- Marti C, John G, Konstantinides S, Combes C, Sanchez O, Lankeit M, Meyer G, Perrier A. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. *Eur Heart J*. 2015;36:605-14.
- Pruszczyk P, Klok FA, Kucher N, Roik M, Meneveau N, Sharp ASP, Nielsen-Kudsk JE, Obradović S, Barco S, Giannini F, Stefanini G, Tarantini G, Konstantinides S, Dudek D. Percutaneous treatment options for acute pulmonary embolism: a clinical consensus statement by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function and the European Association of Percutaneous Cardiovascular Interventions. *EuroIntervention*. 2022;18:e623-38.
- Toma C, Jaber WA, Weinberg MD, Bunte MC, Khandhar S, Stegman B, Gondí S, Chambers J, Amin R, Leung DA, Kado H, Brown MA, Sarosi MG, Bhat AP, Castle J, Savin M, Siskin G, Rosenberg M, Fanola C, Horowitz JM, Pollak JS. Acute outcomes for the full US cohort of the FLASH mechanical thrombectomy registry in pulmonary embolism. *EuroIntervention*. 2023;18:1201-12.
- Lankeit M, Jiménez D, Kostrubiec M, Dellas C, Hasenfuss G, Pruszczyk P, Konstantinides S. Predictive value of the high-sensitivity troponin T assay and the simplified Pulmonary Embolism Severity Index in hemodynamically stable patients with acute pulmonary embolism: a prospective validation study. *Circulation*. 2011;124:2716-24.
- Piazza G, Hohlfelder B, Jaff MR, Ouriel K, Engelhardt TC, Sterling KM, Jones NJ, Gurley JC, Bhatheja R, Kennedy RJ, Goswami N, Natarajan K, Rundback J, Sadiq IR, Liu SK, Bhalla N, Raja ML, Weinstock BS, Cynamon J, Elmasri FF, Garcia MJ, Kumar M, Ayerdi J, Soukas P, Kuo W, Liu PY, Goldhaber SZ; SEATTLE II Investigators. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: The SEATTLE II Study. *JACC Cardiovasc Interv*. 2015;8:1382-92.
- Tapson VF, Sterling K, Jones N, Elder M, Tripathy U, Brower J, Maholic RL, Ross CB, Natarajan K, Fong P, Greenspon L, Tamaddon H, Piracha AR, Engelhardt T, Katopodis J, Marques V, Sharp ASP, Piazza G, Goldhaber SZ. A Randomized Trial of the Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism: The OPTALYSE PE Trial. *JACC Cardiovasc Interv*. 2018;11:1401-10.