The Importance of the PE-TRACT Trial

A discussion of why PE-TRACT is so badly needed at the present time.

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Intermediate-risk (submassive) pulmonary embolism (PE) has seen a flurry of interventional clinical trial activity in the last 7 years. In 2014, the first and only randomized controlled trial of catheter-directed thrombolysis (CDT) was published (ULTIMA).[1] In 2015, the Ekos catheter (Boston Scientific Corporation) was cleared by the FDA after publication of the SEATTLE II study.[2] In 2018, results of the OPTALYSE study were published, which investigated whether shorter durations and lower doses of thrombolytics were effective.[3] In 2019 and 2021, two studies that described the safety and efficacy of two novel aspiration thrombectomy devices (FLARE[4] with the FlowTriever device [Inari Medical] and EXTRACT-PE[5] with the Indigo aspiration system [Penumbra, Inc.]) facilitated FDA clearance for each.

WHY PE-TRACT IS IMPORTANT

Despite the previously mentioned studies, we remain woefully short of answering the fundamental question of whether catheter therapy should be routinely used to treat intermediate-risk PE. There are two reasons.

1. Lack of randomization: More than 1,500 patients have been randomized to systemic thrombolysis versus anticoagulation (AC) alone, whereas only 59 have been randomized to CDT versus AC alone. Therefore, it is unknown whether early CDT is better than prompt initiation of AC, close monitoring, and advanced supportive care.
2. Insufficient outcomes data: Since SEATTLE II, the standard outcome measure has been the right ventricular/left ventricular ratio 48 hours postprocedure. Although this outcome served as a useful surrogate in preliminary and pilot studies, it has outlived its use and has taken on outsized importance because the FDA has accepted it as the primary efficacy measure. Data are needed on short-term clinical deterioration and longer-term exercise tolerance, functional capacity, and quality of life in the year after a PE—outcomes that matter to patients and physicians—to truly assess catheter therapy.

The PE-TRACT study is designed to overcome these shortcomings. It is in submission to the National Heart, Lung, and Blood Institute within the National Institutes of Health (the same institute that funded the ATTRACT trial and funds the C-TRACT trial). If funded, PE-TRACT would be the largest study to date (approximately 500 patients) of CDT for PE, and its rigorous, randomized comparison of CDT to AC alone is exactly what is needed in the interventional PE space.

However, PE-TRACT would accomplish so much more than addressing this single question. Just as the ATTRACT trial provided major insights into the biology of deep vein thrombosis (DVT) and which patients with proximal DVT should be considered for catheter therapy, PE-TRACT would (1) clarify the long-term natural history of PE, as we are just now starting to understand the scope of the long-term toll PE takes on patients, with nearly 50% having a below-normal peak oxygen consumption during exercise 1 year after PE per the ELOPE study[6]; (2) identify novel risk factors (eg, blood biomarkers, baseline comorbidities, hemodynamic parameters) for the development of long-term disability and short-term deterioration; and (3) offer biological insights that would drive research toward novel device and pharmacologic therapies. Consequently, PE risk stratification will become more refined and precise, delineating which patients with submassive PE are at highest risk for short-term deterioration and death, those at highest risk for long-term disability, and those who will truly benefit in the short and long term from targeted reperfusion therapy. PE-TRACT will also begin to offer insight into some of the technical aspects of catheter therapy, including correlating the amount of thrombus removed with clinical out-

comes. In addition, PE-TRACT will increase precision around major bleeding estimates.

SUMMARY

Ultimately, the PE community must demand more rigorous studies of catheter-based devices used to treat intermediate-risk PE. The rapid increase in CDT procedures may be putting patients at risk without evidence-based benefit. The true opportunity lies in gaining a deeper knowledge about the disease and (if PE-TRACT is positive) improving the short- and long-term cardiopulmonary health of thousands of patients. ■

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