

# Implementation of the OPTALYSE Study for Submassive Pulmonary Embolism: Patient Selection Criteria and Protocols

BY NOAH J. JONES, MD, FACC, FSCAI



Our hospital was one of the highest-enrolling sites in the OPTALYSE PE trial, which demonstrated that patients with submassive pulmonary embolism (PE) who received Acoustic Pulse Thrombolysis™ (APT or EKOS® therapy, BTG International) using the EKOS® catheter (BTG International) experienced rapid and significant reduction in the right ventricular/left ventricular (RV/LV) ratio and reversal of RV dysfunction, even with doses of the thrombolytic agent as low as 4 mg per catheter.<sup>1</sup> The results of OPTALYSE PE have allowed us to refine our institutional protocols for the treatment of submassive PE in a way that improves outcomes, safety, and patient satisfaction.

## OUR EXPERIENCE

We began offering Acoustic Pulse Thrombolysis™ therapy with the EKOS® device in 2011 and have treated more than 350 patients presenting with submassive PE with EKOS®. Before OPTALYSE PE, there was no reported experience on the safety and efficacy of very low-dose and short-duration treatment strategies. Since the early days of the SEATTLE II trial,<sup>2</sup> our institutional protocol was to adhere to a regimen of 1 mg of tissue plasminogen activator (tPA) administered bilaterally for 12 hours (total of 24 mg), and we were very comfortable with that protocol.

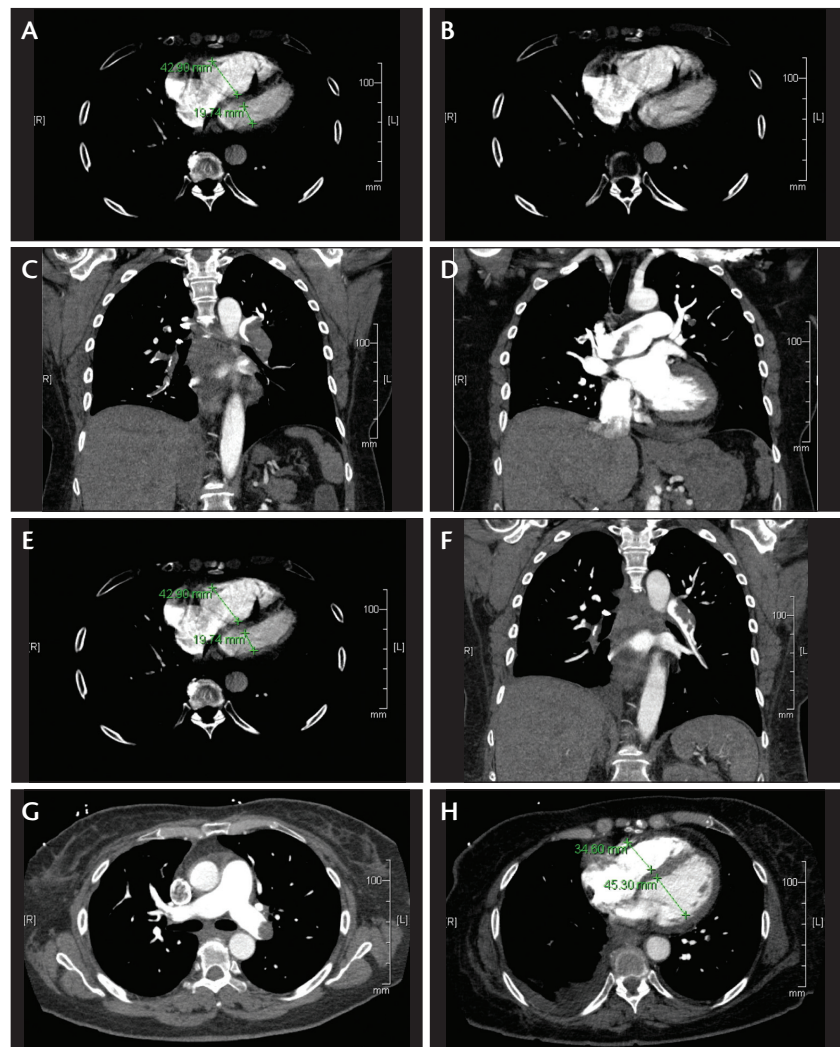


Figure 1. CTA imaging from OPTALYSE PE patient number two, a 59-year-old woman with a history of metastatic breast cancer (currently in remission), deep vein thrombosis, and prior inferior vena cava filter placement. She was experiencing shortness of breath over 3 days. We evaluated her troponin (0.33 ng/mL) and her vitals stabilized. We conducted CTA of the ST and right axis deviation. Before treatment, the RV/LV ratio was 2.17 (E). After OPTALYSE PE protocol of 1 mg per hour per lung over 6 hours for a total of 12 mg of tPA (F–H), RV/LV was 0.76 (H).

However, the results of OPTALYSE PE have given us a variety of new options for treating patients with submassive PE, providing significantly greater flexibility when choosing doses and duration of treatment (Figure 1). At our institution, we have already adopted the 6-hour, 12-mg protocol as an initial strategy, with a plan to extend treatment to a 12-hour duration if we feel it is clinically necessary for the patient. For example, for patients with a higher bleeding risk because of advanced age or recent surgery, we typically choose lower doses and shorter durations of therapy, sometimes < 6 hours. At the other end of the scale, we very rarely exceed a total of 24 mg in a 12-hour dosing.

Risk stratification remains essential when initially evaluating acute PE patients. Many realize that, even within the category of submassive PE, there is a spectrum of risk. At the high end of the submassive risk spectrum are patients with abnormal biomarkers, such as a positive troponin and brain natriuretic peptide and evidence of RV dysfunction on CT or echocardiography. We would typically offer these patients Acoustic Pulse Thrombolysis™ therapy. In some institutions, patients with submassive PE are treated with anticoagulation, and for those patients who are at the lower-risk end of the spectrum, that may be reasonable. However, submassive PE is not a benign disease process, and it carries a 3-month mortality risk that can range as high as 25%.<sup>3</sup> We have compelling data from the ULTIMA,<sup>4</sup> SEATTLE II, and now OPTALYSE PE trials indicating that Acoustic Pulse Thrombolysis™ therapy, administered with the EKOS® device, rapidly and safely reverses RV dysfunction, which, in effect, moves an intermediate-to-high-risk patient for cardiovascular complications into the low-risk end of the spectrum. This cannot be done rapidly with anticoagulation alone, as the ULTIMA study showed.

Most of the referrals our team receives for PE management come from a mix of hospitalists, emergency

room physicians, and pulmonary/critical care physicians. Having options for lower tPA dosing and shorter duration has opened the door for new treatment alternatives in a subset of patients that we probably would not have considered before we had the OPTALYSE PE data. When we talk to patients, their response has been uniform, both within the trial and in practice. They are excited to hear that there is an option for lower-dose, shorter-duration therapy than what we had to offer in the past. At our institution, we are pleased to be able to offer an effective treatment that improves patient safety and comfort.

## SUMMARY

OPTALYSE PE demonstrated that EKOS® therapy can rapidly reverse RV dysfunction with safe, low doses of a thrombolytic agent during a short duration of infusion time. Offering more advanced treatments, such as EKOS® therapy, has become the standard for how we treat our submassive PE patients after appropriate risk stratification. ■

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## Noah J. Jones, MD, FACC, FSCAI

Interventional Cardiologist

Mount Carmel Health System

Columbus, Ohio

*Disclosures: Consultant and speaker for Ekos*

*Corporation, a BTG International group company.*