Endovascular Management of Acute Pulmonary Embolism Using the Ultrasound-Enhanced EkoSonic System

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Abstract

Acute, symptomatic pulmonary embolism (PE) in the massive and submassive categories continues to be a healthcare concern with significant risk for increased morbidity and mortality. Despite increased awareness and venous thromboembolism prophylaxis, endovascular treatment is still an important option for many of these patients. There are a variety of techniques and devices used for treating PE, but none have been evaluated as extensively as the EkoSonic endovascular system that is also currently the only FDA-approved device for the treatment of pulmonary embolism. This article describes the use of the EkoSonic device for this patient population.

Keywords

- pulmonary embolism
- ultrasound-enhanced thrombolysis
- EKOS
- endovascular treatment
- interventional radiology

Objectives: Upon completion of this article, the reader will be able to discuss the role of ultrasound-facilitated delivery of thrombolytic drug in the pulmonary embolism patient population.

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Acute pulmonary embolism (PE) affects up to 600,000 patients and accounts for nearly 300,000 deaths per year in the United States alone.[1] The overall incidence of PE is rising, with approximately 112 cases per 100,000.[2] The incidence of PE increases with age,[3] and remains the number one cause of preventable in-hospital deaths in the United States.[4] Acute PE is classified as massive (high risk), submassive (intermediate risk), and nonmassive (low risk), a categorization that helps determine treatment. If left untreated, acute PE has an overall mortality of up to 30%; this can be significantly reduced with anticoagulation.[5] However, for those patients who survive the acute PE episode, they are at risk not only for recurrent PE but also for developing chronic thromboembolic pulmonary hypertension (CTEPH) that may carry its own significant morbidities.

Data suggest that a more aggressive treatment of submassive PE with a thrombolytic agent may result in lower short-term morbidity and the likelihood of clinical deterioration during the hospital stay.[6] The rationale for PE thrombolysis is to reduce the thrombus burden that is not achieved with anticoagulation alone, which would result in a reduced right ventricular (RV) strain, reversal of the RV afterload, improved pulmonary perfusion and gas exchange, and decrease risk of developing CTEPH.[7]

A retrospective study by Kennedy et al,[8] as well as the ULTIMA trial,[9] has shown that pharmacomechanical thrombolysis for acute PE using the EkoSonic ultrasound-

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enhanced infusion system (EKOS-BTG, Bothell, WA) is both safe and effective at reversing RV dysfunction at 24 hours and 90 days, without the reported risks of full-dose systemic thrombolysis. The SEATTLE II trial[10] demonstrated that both the RV function and pulmonary artery (PA) pressures were safely and effectively improved at 48 hours post–EKOS-assisted thrombolysis.

With the current increased awareness in the diagnosis and treatment of venous thromboembolism (VTE) and PE, as well as its rising incidence combined with the Center for Medicare and Medicaid Services' institutional quality measures and growing interest in developing pulmonary embolism response teams, endovascular treatment of massive and submassive PE will likely increase.

Currently, there are a variety of techniques and devices that can be used in the treatment of acute, symptomatic PE; however, the focus of this article will be on ultrasound-accelerated thrombolysis (USAT) using the EkoSonic system (►**Fig. 1**).

EkoSonic Endovascular System

The EKOS Mach 4E is the latest version of the ultrasound-enhanced infusion system, with in vitro studies showing a 40% improved time to lysis compared with the previous Mach version.[11] The EkoSonic Endovascular System consists of three components: an intelligent drug delivery catheter, a removable MicroSonic Device containing multiple small ultrasound transducers distributed over the treatment zone, and the EkoSonic control unit.[9]

A thrombolytic agent is delivered via the infusion catheter, which contains an ultrasonic core wire that delivers high frequency, low-power ultrasound waves into the surrounding thrombus. This technology has the added benefit of causing the fibrin strands to thin and loosen, allowing for greater exposure of intrathrombus plasminogen receptor sites as well as increasing thrombus permeability, which can result in greater penetration of the drug. The EKOS catheter delivers the lytic drug, while the noncavitational ultrasound energy gently drives the drug deeper into the clot; this in turn limits the amount of drug that escapes into the systemic circulation. In vitro studies have demonstrated that thrombus exposed to ultrasound absorbed 48% more t-PA in 1 hour and 84% more in 2 hours than thrombus not exposed to ultrasound.[12,13] USAT benefits have been described to include less time to complete dissolution over standard catheter thrombolysis; a decreased total lytic dose; and a lack of clot fragmentation, downstream embolization, and hemolysis.[14,15]

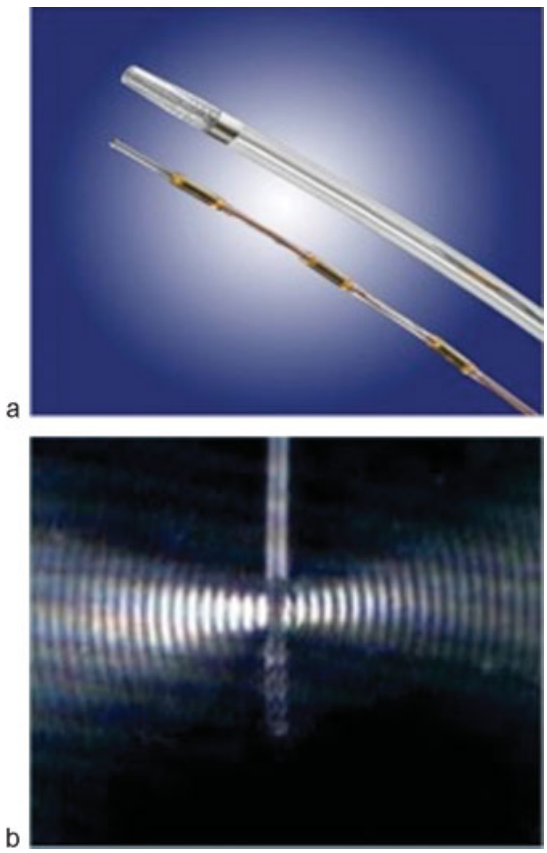

Fig. 1 (**a**) The EkoSonic Mach 4E Endovascular System with larger infusion catheter (arrow) and removable inner core wire with ultrasound transducers (arrowhead). (**b**) Schlieren photograph of acoustic streaming from the EkoSonic catheter emitting ultrasound energy (image courtesy of EKOS-BTG).

Technique

Standard interventional techniques are used to gain access to the venous system. Ultrasound-guided micropuncture of the femoral or jugular vein can be safely used in any patient presenting for potential thrombolytic therapy. Preplanning with review of the pulmonary CTA is instrumental in deciding the access route. If bilateral PA thrombolysis is to be performed, then either a dual lumen or triple lumen sheath (St. Jude Medical, St. Paul, MN) is placed. Alternatively, two femoral accesses should be obtained, but the author prefers the former approach. The benefit of using the triple lumen sheath during bilateral PA lysis is that a follow-up pulmonary arteriogram and pressure measurements can be obtained using a catheter placed via the third lumen without disturbing the bilateral infusion catheters (which is particularly useful if thrombolysis is to be continued). There are a variety of pulmonary catheters available for selecting the main and subsequently the right and left PAs for pressure measurements and performing angiography. Once arteriography is completed, the pulmonary catheter can be exchanged for a selective catheter to select the pulmonary branch with the greatest clot burden. Over a stiff exchange length guide wire, the selective catheter is replaced with the appropriate treatment zone length EKOS catheter. The EKOS catheter comes in working lengths of 106 and 135 cm with 0.035″ compatibility, and treatment zones of 6, 12, 18, 24, 30, 40, and 50 cm. The shorter treatment zone catheters are likely the ones that will be used for isolated pulmonary thrombi, and the catheter used is determined by treatment zone length needed to cover

the burden of clot. USAT is initiated per physician-preferred doses, but one can reference the ULTIMA or SEATTLE II trials for published volumes and rates. The ULTIMA trial used a recombinant tissue plasminogen activator (r-tPA) dose of 1 mg/hour × 5 hours, which was subsequently decreased to 0.5 mg/hour × 10 hours. The coolant infusion in this trial was saline at 35 mL/hour. The SEATTLE II protocol used an r-tPA dose of 1 mg/hour per device × 24 hours. The typical r-tPA infusion that the author used can vary between 0.5 and 1.0 mg/hour depending on the total volume of PE, and the medical state, size, and age of the patient. The coolant volume typically varies between 35 and 50 mL saline. Infusion will often proceed for minimum of 12 hours before a follow-up PA angiogram is performed. The patients are monitored in the intensive care unit for close observation per institutional pulmonary embolism thrombolytic protocol. Some institutions will cease infusion at a predetermined r-tPA dose or lytic time without bringing the patient back to the interventional suite. At the author's institution, the patient returns to the interventional suite for follow-up evaluation, including pressure measurements and pulmonary angiography. The procedure is either continued or terminated per the interventionist's discretion.

Case Example

The patient is a 24-year-old woman with a prior history of repair of a fractured patella 2.5 weeks prior to presentation. She presented with chest pain and shortness of breath, and evaluation included pulmonary computed tomographic angiogram (CTA) (►**Fig. 2**). The right ventricular/left ventricular (RV/LV) ratio from the CTA was determined to be 1.4, and an echocardiogram confirmed right heart strain. She presented for thrombolytic therapy the same day and was enrolled in the SEATTLE II Trial. Her initial PA pressure measurements elevated RV (50/4 [26] mm Hg) and main PA (50/1 [27] mm Hg) pressures. Her initial selected right pulmonary angiogram (►**Fig. 3**) demonstrates a large burden PE with pruning of the peripheral pulmonary branches and overall poor parenchymal perfusion. The right PA had a greater thrombus burden than the left. Bilateral EKOS catheters were placed, per protocol, and she received r-tPA at 1 mg/hour through each catheter for 12 hours, for a total dose of 24 mg Alteplase (Genentech South San Francisco, CA). Her posttreatment, 12-hour repeat arteriogram (►**Fig. 4a, b**) reveals significant interval lysis of thrombus bilaterally with concomitant decreased pressures in both the RV (38/0 [7] mm Hg) and main PA (36/9 [11] mm Hg). Her postlysis RV/LV ratio was decreased to 0.78. She was discharged from the hospital 3 days after admission, and remained completely asymptomatic during her recovery.

Summary

As PE becomes more recognized as a significant contributor to severe morbidity and mortality in the hospitalized patient population, the role of catheter-directed thrombolysis will likely continue to become important. By facilitating catheter-directed delivery of thrombolytic drug into the clot, ultrasound catheters such as the EKOS system will likely plan an increasing important role in this population.

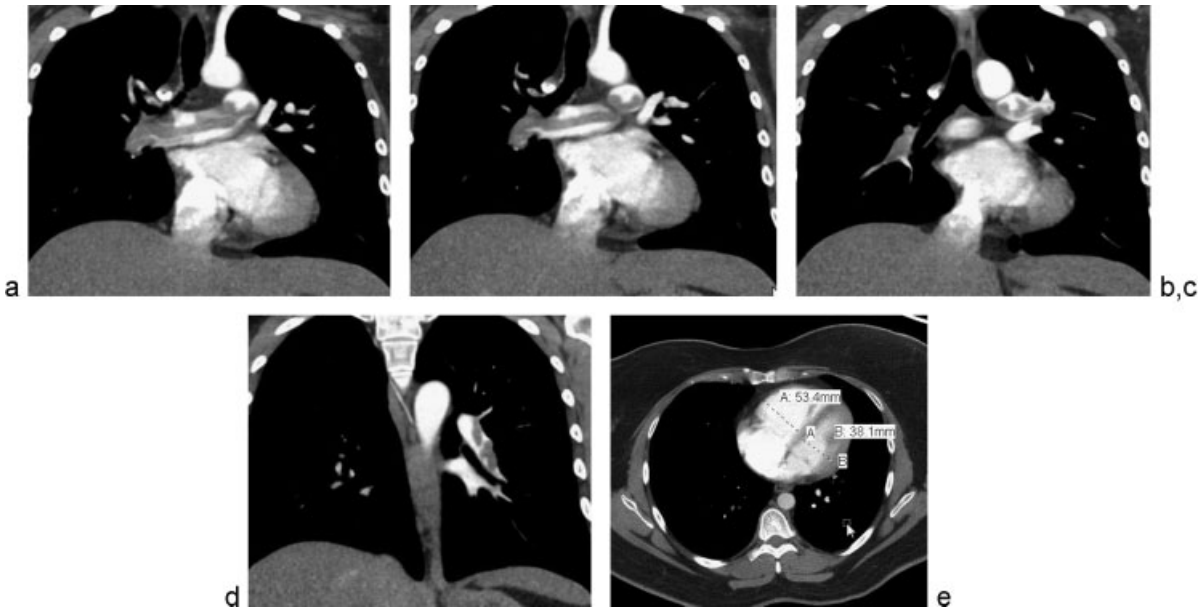

Fig. 2 (**a**–**d**) Contrast-enhanced coronal images from a pulmonary CTA demonstrating an extensive saddle pulmonary embolism extending from right to left pulmonary arteries (arrowheads) and extending into the right and left central and subsegmental braches. (**e**) Axial image from the CTA demonstrates right heart strain with bowing out of the interventricular septum toward the left, with the right ventricular/left ventricular ratio of 1.4.

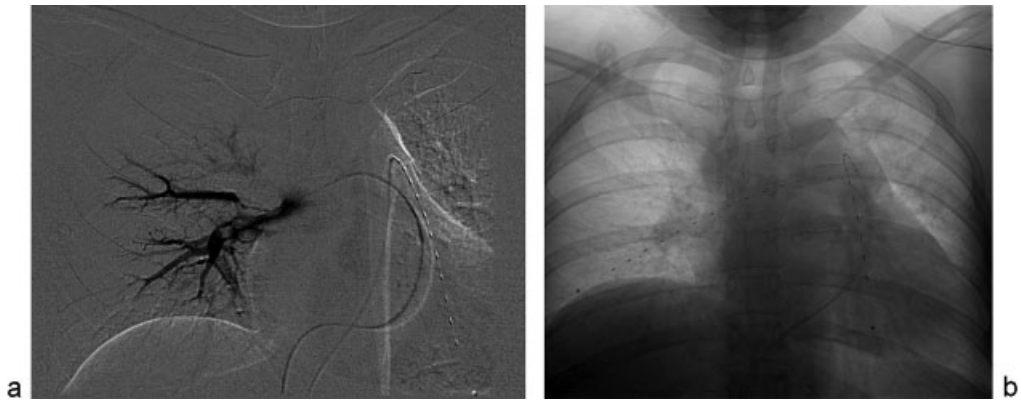

Fig. 3 (**a**) Selected right pulmonary angiogram demonstrates extensive thrombus in all branches of the right pulmonary artery (arrows), with pruning of the distal branches and poor parenchymal perfusion. (**b**) Radiograph demonstrating appropriate placement of the bilateral pulmonary EKOS catheters (arrows).

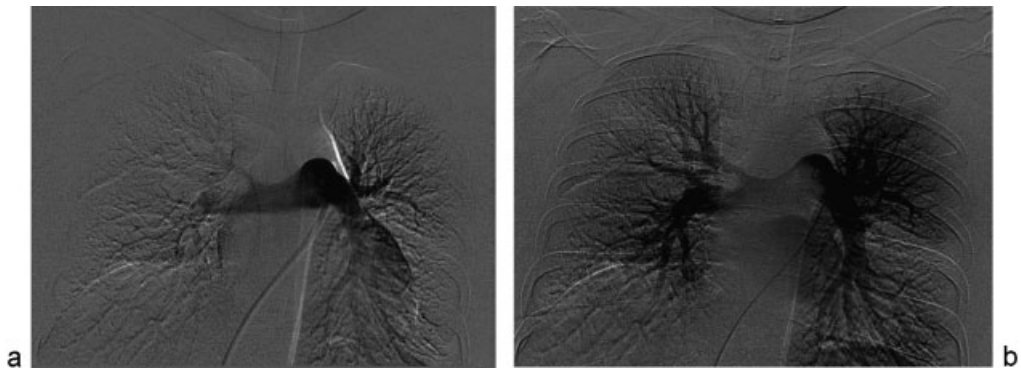

Fig. 4 12-hour follow-up pulmonary angiograms post–EKOS infusion in early (**a**) and delayed (**b**) phases demonstrate interval thrombolysis bilaterally with significantly improved pulmonary perfusion and associated decreases in right ventricular and pulmonary pressures as well as the right ventricular/left ventricular ratio.

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