Bilateral Catheter-Directed Thrombolysis for an Acute Bilateral Pulmonary Embolism Patient with Severe Right Ventricular Strain: from Intensive Care Unit to Home on Postoperative Day 1.

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Background	A healthy, 52-year-old male presented with acute bilateral submassive pulmonary embolisms and severe right heart strain and underwent bilateral catheter-directed thrombolysis.
Summary	Morbidity and mortality after massive and submassive pulmonary embolism (PE) is related to the magnitude of right heart dysfunction. Currently, for massive PE, systemic thrombolytic therapy effectively prevents mortality; however there is an increased risk of major bleeding complications. Catheter-directed thrombolysis (CDT) with ultrasound-assistance is noted as a possible alternative compared to systemic thrombolytics for massive and submassive PE. We present a case of a male that presented with acute bilateral PE with severe right ventricular (RV) strain that underwent bilateral EndoWave Infusion Catheter System (EKOS) placement. Postoperatively, the patient's symptoms resolved, normal RV function was restored, and the patient was discharged from the intensive care unit (ICU) to home on postoperative day (POD) 1.
Conclusion	We present a patient that underwent bilateral EKOS placement for acute bilateral submassive PE with resolution of symptoms and RV strain on POD 1. This is the first documented case report of ICU to home on POD 1 for bilateral EKOS catheter placement in a patient that suffered a submassive PE with severe right heart strain.
Keywords	Pulmonary embolism, catheter-directed thrombolysis; EndoWave Infusion Catheter System (EKOS); right ventricular strain

DISCLOSURE:
The authors have no conflicts of interest to disclose.

ABBREVIATIONS:
PE - Pulmonary embolism
CDT - Catheter-directed thrombolysis
EKOS - EndoWave Infusion Catheter System
POD – Post operative day
ICU – Intensive Care Unit
SOB – Shortness of breath
CTA – Computed tomography angiogram
RV – Right ventricular
LV – Left ventricular

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Case Description

We present a case of a 52-year-old male with a past medical history of diabetes and no smoking history or previous venous thromboembolisms presented to the emergency department with right leg pain and shortness of breath (SOB) for 1–2 days. A computed tomography (CTA) pulmonary angiogram and 3D reconstruction demonstrated occlusive and nonocclusive pulmonary embolisms within the right and left main pulmonary arteries (Figure 1). The CTA confirmed severe right heart strain with right ventricular (RV) to left ventricular (LV) ratio of 1.8 (Figure 2).

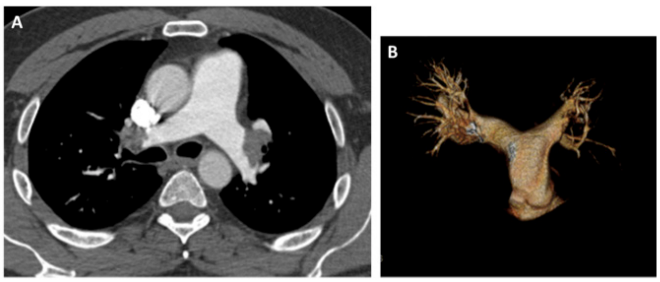

Figure 1. Occlusive and non-occlusive pulmonary embolisms with the right and left main pulmonary arteries. A) CTA and B) 3D reconstruction of main pulmonary arteries

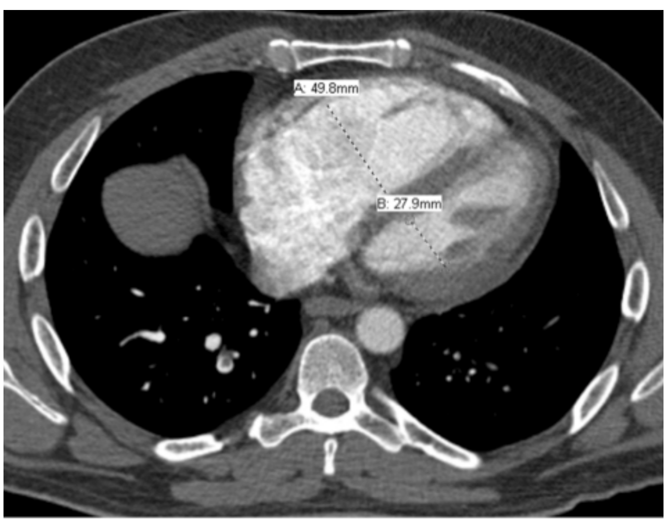

Figure 2. CTA confirming right heart strain with a RV/LV ratio of 1.8

The patient was started on a high intensity heparin drip and immediately went to the operating room for thrombolysis catheter placement. One-hour period was noted from patient presentation to starting a heparin 18 unit/kg/hr drip with a goal PTT of 60 to 100. Another two hours passed between starting a heparin drip and the patient arriving in the operating room.

Intraoperatively, two 6Fr sheaths were accessed via left common femoral vein under ultrasound guidance. Two guidewires and catheters were advanced with an angiogram demonstrating primarily lower lobe occlusions of the left and right pulmonary arteries (Figure 3). After cannulation, the EKOS catheters over wire were placed into the left and right pulmonary arteries. Within the EKOS catheter are treatment zones for focal segmental activation of the acoustic pulse and thrombolytic infusion. Figure 4 illustrates the treatment zones by the radiopaque marker bands with the arrows depicting the zones for the individual catheters.

Figure 3. Angiogram showing filling defect of the left and right pulmonary arteries before treatment of the EKOS catheter

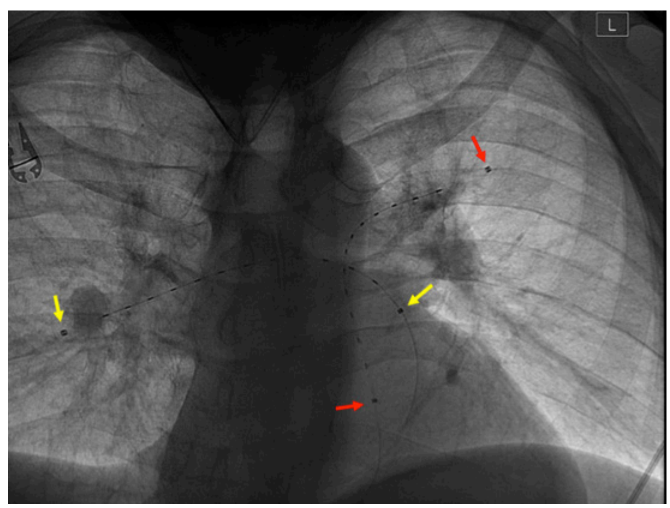

Figure 4. EKOS treatment zones marked by radiopaque bands with the yellow and red arrows depicting the segments for the catheters in the right and left pulmonary arteries

Once the EKOS catheters were adequately placed, the catheter and sheaths were secured and connected to tissue plasminogen activator infusion ports and insertion of the ultrasound intraluminal core. The intraluminal core is activated intraoperatively by a control unit to emit high frequency (2.2 MHz) and low-power (3.5 W) ultrasonic energy. A continuous tPA rate of 0.5mg/hr/catheter and normal saline coolant rate of 35ml/hr/catheter was started and continued postoperatively.

The patient tolerated the procedure well and was transported to the ICU in stable condition. In the surgical ICU, the heparin drip was transitioned to 250units/hr and goal PTT <40. Fibrinogen levels every six hours were followed with the target fibrinogen >200 and if <150 the tPA rate would be decreased by half. The patient's fibrinogen levels throughout the postoperative period range from 170-183 and did not require any adjustment of the tPA rate.

On POD 1, approximately 30 hours after EKOS catheters placement, the patient underwent a transthoracic echocardiogram that showed resolution of right heart strain, with RV/LV of 0.88 from 1.8. The EKOS catheters were removed one hour after the echocardiogram. Pressure was held for 30 minutes at the puncture sites and did not require additional medical management. Approximately 39 hours since the time of procedure, the patient was hemodynamically normal, afebrile, SOB resolved, no oxygen requirement, ambulating without leg pain, and deemed appropriate for discharge. The patient was started on Rivaroxaban (Xarelto) and received initial follow-up with anticoagulation clinic and primary care provider. The patient was seen in vascular surgery clinic one month later—an echocardiogram continued to show normal RV function with return to baseline health.

Discussion

Acute pulmonary embolism (PE) is a common event resulting in 100,000–180,000 deaths per year in the United States.[1] The majority of PE patients present minimally symptomatic and can be treated medically with anticoagulation alone with excellent short-term prognosis.[2-3] However, a subset of patients may present with right ventricular (RV) compromise or hemodynamic instability requiring acute intervention to decrease clot burden.

Systemic thrombolysis is the standard of treatment for massive PE, leading to improvement of RV function and hemodynamic status; however, it is associated with a high risk of major bleeding complications (20 percent) and intracranial hemorrhage (three percent).[4] Therefore, alternative modalities have aimed to be effective in reversing RV dilation and dysfunction and reducing adverse clinical events. The FDA approved procedural intervention for PE, including surgical embolectomy, aspiration thrombectomy, and CDT. Surgical embolectomy has fallen out of favor due to lack of collective surgical expertise and medical comorbidities precluding surgery. Aspiration thrombectomy using a Greenfield suction embolectomy removes the centrally located embolus by applying negative pressure to the tip by manual suction; however, the major disadvantage is the large lumen catheter is difficult to manipulate because of its size, rigidity, and the lack of guidewire assistance.[2-4]

Catheter-directed thrombolysis with ultrasound has demonstrated excellent clinical results.[5-6] The general aim of catheter-directed therapy in the setting of compromised hemodynamics or cardiac function with acute PE is to debulk or redistribute the obstructive clot.[7] In recent years, the EkoSonic Endovascular System (EKOS) has risen in practice as a catheter-based system that uses high frequency and lower-energy ultrasound waves to aid in the delivery and uptake of thrombolytic agent within the clot.[8] The EkoSonic ultrasound-assisted catheter directed thrombolysis has been utilized to treat acute massive and submassive PE at multiple institutions.[5, 8-10]

The SEATTLE II and the ULTIMA studies looked at the clinical applications of CDT for PE patients that either suffered from RV dysfunction or were hemodynamically unstable. The studies demonstrated improved RV function, decreased intracranial hemorrhage, and similar mortality and morbidity compared to systemic thrombolysis.[3, 6-7] Yet, additional evidence and studies are needed in the short- and long-term on CDT before the intervention can be deemed the standard of care compared to systemic thrombolysis. That said, it is important to note that, for patients with massive and submassive PE, CDT does play a role in clinical application.[7, 11] Currently, multiple institutions have used CDT for patients with submassive and massive PE or contraindications for systemic thrombolysis.[6, 8-10] For the past two years, our institution's vascular surgery department has used CDT for massive and submassive PE (Figure 5) based on the protocols of other institutions that have long-established track records of CDT use in their clinic practices.[3,4,8-10]

Evaluating right heart strain secondary from a PE helps determine morbidity and mortality for PE patients, and this step plays a major role in CDT application (Figure 5). The degree of right heart dysfunction is quantified using the right ventricle to left ventricle (RV/LV) ratio; a RV/LV ratio <0.9 is normal, 0.9–1.2 = mild dysfunction, 1.2–1.5 = moderate dysfunction, and >1.5 severe right = heart dysfunction. The RV/LV is measured by CTA chest or echocardiogram. For patients with RV/LV >1.5 or hemodynamic unstable secondary from an acute PE, emergent catheter-directed thrombolysis should be considered as a possible intervention. Postoperatively all patients at our institution underwent an echocardiogram to evaluate RV function and improvement prior to removal of EKOS catheters.

The patient presented in this case report was noted to have acute submassive pulmonary embolism leading to severe RV strain with a RV/LV ratio of 1.8. Our patient postoperatively on day 1 was noted to have resolution of symptoms and underwent an echocardiogram that demonstrated an RV/LV of 0.88 with no signs of RV dysfunction. The patient was noted to be a very healthy individual and was discharged from the ICU to home with anticoagulation therapy on postoperative day 1.

According to the literature, the average hospital length of stay for massive and submassive PE patients who underwent CDT is 3.3–8.4 days.[5,6,8,10] It should be noted that the treatment for massive PE skewed the average length of stay compared to submassive PE. The average length of stay for patients undergoing EKOS placement at our institution is 3.7 days. The patient presented was classified as a submassive PE with hemodynamically normal vitals, which has a significantly better morbidity and mortality compared to a massive PE. Based upon our patient having minimal comorbidities, postoperative normal RV/LV ratio, and resolution of symptoms made him an ideal candidate to be discharged on POD 1. It is important to be cautious and selective of patients to be discharged in an expedite manner postprocedural—particularly with patients with massive PE, hemodynamically unstable on presentation, and symptomatic postprocedural.

CDT in a meta-analysis has a major bleeding complication rate of 2.4 percent compared to 20 percent for systemic TPA.[10] That said, CDT does carry a mild risk of intraoperative and postprocedural bleeding—this risk is significantly lower than systemic thrombolysis. Potential pitfalls and concerns for rapid patient discharge are the serious and minor complications associated with CDT. Notable severe complications include death, cardiac ischemia, stroke, and bleeding complication requiring surgical intervention. Notable minor complications include puncture site hematomas, arteriovenous fistula formation, and bleeding that interrupts or stops CDT without requiring transfusion or resuscitative support. Our patient progressed without any serious or minimal adverse events, and therefore was a candidate to be discharged swiftly.

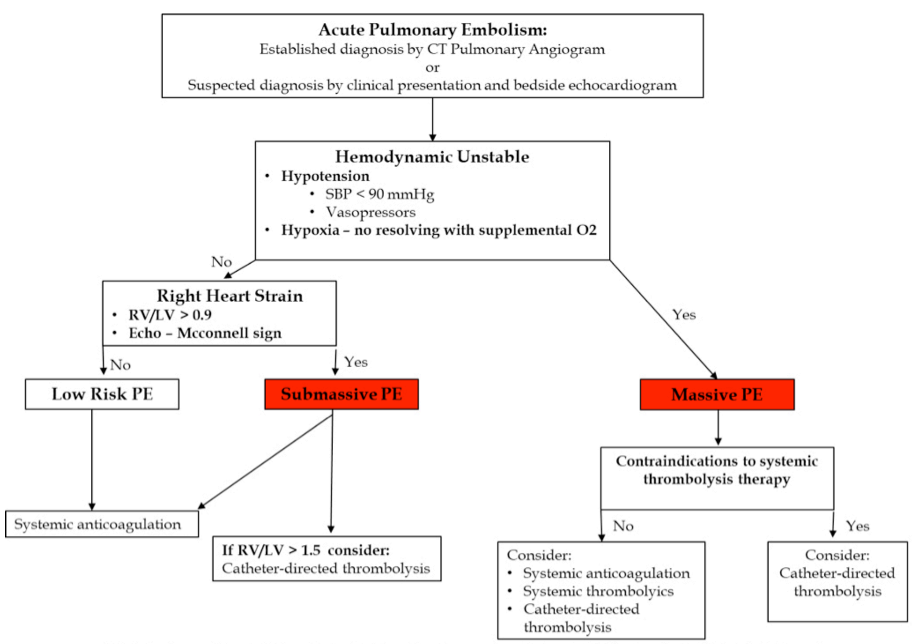

Figure 5. Acute pulmonary embolism algorithm to determine catheter-direct thrombolysis application

Conclusion

We present a patient that underwent bilateral EKOS placement for acute bilateral submassive PE with resolution of symptoms and RV strain on POD 1. This is the first documented case report of ICU to home on POD 1 for bilateral EKOS catheter placement in a patient that suffered a submassive PE with severe right heart strain.

Lessons Learned

CDT, which has been implemented at multiple institutions for select patients with massive and submassive, highlights EKOS therapy for selected patients with submassive PE to reverse heart strain. Additionally, it resolves symptoms within a short hospital stay, with minimal risk of major bleeding and a low rate of adverse effects.

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