

**Journal Club Synopsis**  
**Block 3, September 17, 2014**  
**Discussion Leader: Sundeep Punia**  
**Mentors: Dr. Leslie Vojta and Dr. James Olson**

**Scenario**

You're working alone on your first attending night shift and you are presented with an elderly female brought in by EMS with significant shortness of breath. Her BP is 91/70. She has sinus tachycardia at 140 bpm. She is tachypneic. Her SpO<sub>2</sub> is 85% and improves to 95% on NRB. She has RLE swelling with calf tenderness and mild warmth to the touch. Lungs are clear b/l. On questioning, you learn that she recently had a hemorrhagic stroke two months ago and has consequently been relatively immobile in rehab. She has a history of DVTs and PEs, and has active malignancy. She takes exogenous estrogen. Otherwise, she has no hemoptysis and pleuritic chest pain. You throw an US probe on her chest and note right ventricular heart strain. Stat CXR is normal. You remember hearing about intra-arterial tPA and think this might be your best bet in this case. How good are patient outcomes with this treatment compared to other treatments for PE?

**Introduction**

Pulmonary embolism can present in multiple ways and, accordingly, has various treatment modalities, including heparin, tPA, catheter-directed therapy (CDT), and surgical embolectomy. Sorting out the indications for each of these therapies can be a challenge, especially when the sickest of these patients present rarely to the ED and are managed differently on a case-by-case basis. Some authorities have recommended treating high risk submassive PEs and massive PEs with CDT, even those with higher bleeding risks. In theory it provides local thrombolytic therapy at smaller doses without as much risk, particularly of hemorrhage, to the patient. Although this made sense to me physiologically, I wanted to explore the evidence behind these recommendations. I searched Pub Med for articles pertaining to catheter-directed therapy. I also looked at critical care blogs to determine which articles were most frequently referenced. Because this therapy is relatively new, there is a scarcity of high-quality literature on this topic. Nonetheless, the three articles below were chosen.

**Article 1**

Kuo WT, Gould MK, Louie JD, Rosenberg JK, Sze DY, Hofmann LV. Catheter-Directed Therapy for the Treatment of Massive Pulmonary Embolism: Systematic Review and Meta-analysis of Modern Techniques. *J Vasc Interv Radiol*. 2009 Nov 20(11):1431-40.

This was a systemic review and meta-analysis of studies published from January 1990 through September 2008 that evaluated the safety of CDT in those with shock from massive PE. It looked at clinical success, particularly at stabilization of hemodynamics, resolution of hypoxia, and survival to hospital discharge in 594 patients from 35 studies. It found CDT to be highly effective (86.5% clinical success rate) with few major complications (2.4%). Although thorough, this study unfortunately only possessed level 2 data and did not compare CDT to other treatments.

## **Article 2**

Kucher N, Boekstegers P, Müller OJ, Kupatt C, Beyer-Westendorf J, Heitzer T, Tebbe U, Horstkotte J, Müller R, Blessing E, Greif M, Lange P, Hoffmann RT, Werth S, Barmeyer A, Härtel D, Grünwald H, Empen K, Baumgartner I. Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism. *Circulation*. 2014 Jan 28;129(4):479-86.

The ULTIMA trial was a multicenter European RCT that showed US-assisted CDT with heparin was superior in treating submassive PE than heparin alone, as measured by the difference in RV/LV ratio via echocardiography from baseline to 24 hours (0.30 vs 0.03, respectively) without an increase in bleeding complications. Unfortunately, this study had a small sample size of 59 pts, was funded by EKOS, excluded most pts of interest (particularly age > 80 yo, prior head bleeds, and bleeding diatheses), and assumed RV dilation reduction correlated with better pt outcomes.

## **Article 3**

Kennedy RJ, Kenney HH, Dunfee BL. Thrombus Resolution and Hemodynamic Recovery Using Ultrasound-Accelerated Thrombolysis in Acute Pulmonary Embolism. *J Vasc Interv Radiol*. 2013 Jun;24(6):841-8.

This was a retrospective single-center study evaluating the efficacy of US-accelerated CDT with heparin in the treatment of submassive and massive PEs as measured by pulmonary artery pressure (PAP) reduction, Miller score (measurement of anatomic embolus obstruction and lung perfusion) reduction, and increased percentage of thrombus clearance without significant bleeding complications. Again, this study had a small sample size of 60 pts, excluded pts of interest, and assumed PAP and Miller score reduction correlated with better pt outcomes. Additionally this study had weak inclusion criteria. Some of these parameters weren't measured in some patients without explanation and thrombolytic doses were adjusted without any criteria to reduce bleeding complications.

## **Bottom Line**

These studies show that CDT, particularly EKOS, is a safe and effective treatment modality for submassive and massive PEs and improves physiologic parameters. Without comparisons to other standards of care, using a patient-centered outcome, or including an encompassing patient population of interest to emergency care, the conclusions of these articles were not readily useful, especially when some of the study designs were questionable (funding, missing data). However, these articles shed light on the importance of further studies on this evolving therapy, as I feel that there may be promise in expanding the indications of CDT, if proven to be successful, even to those high-risk surgical embolectomy candidates where systemic tPA is contraindicated. Until then, the patient in this case would benefit most from surgical embolectomy and IVC filter placement after multidisciplinary consultation with Pulm/ICU, CT Surgery, and IR.