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CLINICAL VIGNETTE

Catheter-Directed Thrombolysis in a Case of Submassive Pulmonary Embolism Refractory to Systemic Thrombolysis

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Introduction

While the treatment algorithm for massive pulmonary embolism (PE) is well established, there is still controversy regarding the optimal clinical management for submassive PE. This case illustrates gaps in treatment standards and clinical evidence for submassive PE.

Case Presentation

A 25-year-old man with recent ankle fracture, presented with calf pain, dyspnea, and pleuritic chest pain. His initial vital signs were: T36.7, P 123, RR 30, BP 101/83, and SpO2 99% 10L/min on face mask. CT angiogram of his chest showed saddle embolus involving the distal main pulmonary artery as well as extensive segmental and subsegmental pulmonary emboli. (Figure 1) Initial troponin-I was 0.162 ng/mL and BNP was 1591 pg/mL.

Intravenous heparin was initiated and cardiology was consulted. Echocardiogram showed a severely dilated right ventricle, diastolic septal wall flattening, positive McConnell's sign, and estimated pulmonary systolic pressure of 49 mmHg. (Figure 2)

Half dose alteplase 50mg was administered with improvement in pulse to low 100s.

Duplex ultrasound confirmed presence of a deep vein thrombosis in his right popliteal vein.

On hospital day 3, the patient was still tachycardic, tachypneic, and hypoxic requiring 3L/min of supplemental oxygen with dyspnea and chest pain. Repeat CT angiogram showed persistent saddle embolus. Echocardiogram demonstrated dilated right ventricle (greater than left ventricle) and pulmonary artery systolic pressure of 52 mmHg.

He underwent ultrasound-assisted catheter-directed thrombolysis (UA-CDT) with an EKOS™ catheter. He received alteplase 1mg/hr for 8 hours via the catheter. (Figure 3)

His vitals subsequently normalized, echocardiographic features of right heart strain substantially improved, and his symptoms resolved. He was transitioned to rivaroxaban for therapeutic anticoagulation and did well on follow up clinic visits.

Discussion

Acute pulmonary embolism is a common condition that can result in significant mortality and morbidity.[1] There are over 100,000 deaths attributable to pulmonary embolism in the US annually with as many as 25% presenting with sudden death.[2]

Pulmonary embolisms are divided into three categories: high risk or massive (hemodynamically unstable, systolic blood pressure <90), intermediate risk or submassive (hemodynamically stable but with signs of RV dysfunction), and low risk (hemodynamically stable without signs of RV dysfunction). The treatment strategy varies depending of the risk category.

The use of systemic thrombolytics in massive pulmonary embolisms is standard of care.

Low risk pulmonary embolisms are treated with anticoagulation alone. However, with submassive PE the optimal treatment is less clear and is often different for each clinical scenario.

For submassive PE, the PEITHO trial, a randomized control trial, showed thrombolytics improved mortality but at the increased risk of bleeding. Patients with submassive PE receiving systemic thrombolytics, had an incidence of 2.6% of the primary outcome (death or hemodynamic decompensation), lower than the control group receiving standard anticoagulation, with a 5.6% incidence of the primary outcome.[1]

However, patients who received thrombolytics experienced hemorrhagic stroke (2%) and major extracranial bleeding (6.3%).[1] One meta-analysis of thrombolytics confirmed these findings. It showed thrombolytics significantly improved mortality (OR 0.48, 95%CI 0.25-0.92) at a cost of increased major bleeding (OR 3.19, 95%CI 2.07-4.92).[2]

The landmark MOPETT trial, demonstrated that half dose

thrombolytics with anticoagulation when compared to anticoagulation alone was effective at lowering pulmonary hypertension (16% vs 57%, P<0.001) as well as a composite end point of pulmonary hypertension and recurrent PE (16% vs 63%, P<0.0001).[3] The thrombolytics group also had shorter hospital length of stay (2.2 vs 4.9 days, P <0.001). There was also a trend towards reduced incidence of recurrent PE and decreased mortality. No patients in either arm experienced major bleeding.[3] The MOPETT trial suggests half dose thrombolytics may be a viable alternative to full dose thrombolytics to reduce mortality while lower the risk of major bleeding.

A retrospective cohort study compared half dose thrombolytics and found similar mortality (propensity matched cohort OR 0.83 P = 0.37) and no difference in adverse events related to thrombolytic administration including cerebral and GI hemorrhage. Patients who received half dose thrombolytics had a higher incidence of treatment escalation (54% vs 41%, P<0.01), as defined by initiation of vasopressors, need for secondary thrombolysis, assisted ventilation, embolectomy, catheter thrombus fragmentation, inferior vena cava filter placement, or cardiopulmonary resuscitation occurring after the first dose of thrombolytics.[4] This difference was driven primarily by the need for secondary thrombolytics (25.9% vs 7.3%, P < 0.01) and the need for thrombosis fragmentation by catheter (14.2% vs 3.8% P<0.01).[4]

Surgical embolectomy and catheter-based treatments including aspiration thrombectomy, thrombus fragmentation, and rheolytic fragmentation are also available for patients with submassive PE.[5] However, further research is needed before considering these options as first line treatment.

Our patient received half dose thrombolytics and was refractory to systemic thrombolytics and subsequently did require treatment escalation with UA-CDT. Currently, there is little data on the appropriate management of PE refractory to thrombolysis and risk of bleeding in this situation.[5]

UA-CDT may minimize bleeding risk of systemic thrombolysis while localizing its benefits to the treatment target.[6,7]

One prospective randomized trial showed UA-CDT to be superior to heparin alone.[7] In the UA-CDT arm, RV/LV ratio decreased on average 0.30 vs 0.03 compared to the heparin only arm (P < 0.001). Following UA-CDT, pulmonary artery systolic pressure dropped an average of 12.3 mmHg compared with baseline (P < 0.001).[7]

Our case further demonstrates that UA-CDT may be efficacious in the management of submassive PE refractory to systemic thrombolytics without major bleeding complications. It also poses the question whether UA-CDT would have been more effective as first line therapy instead of systemic thrombolytics, as suggested by a recent meta-analysis.[8]

Disclosures
None

Figures

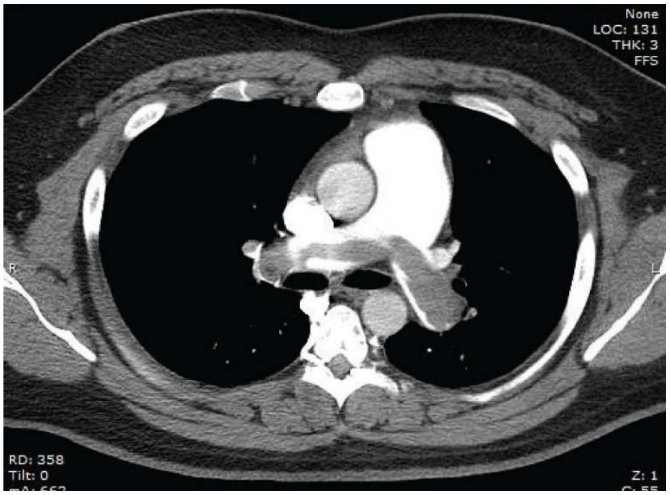

Figure 1: CT Angiogram demonstrating saddle pulmonary embolus

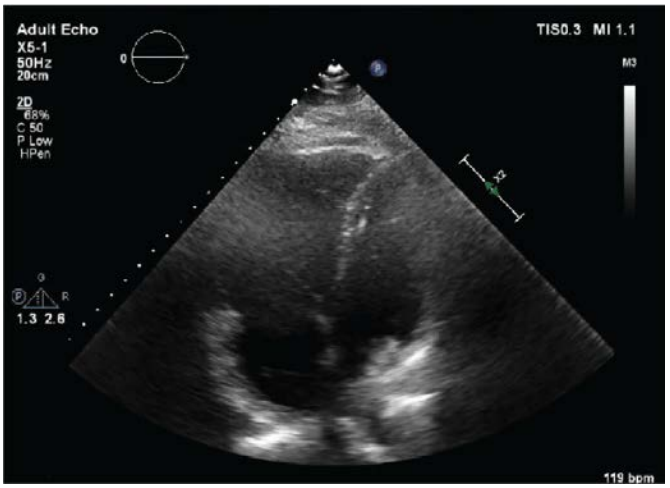

Figure 2: Transthoracic echocardiogram demonstrating RV dilation

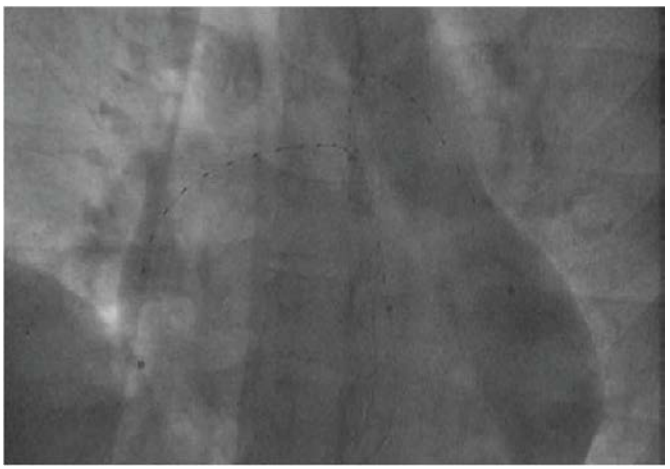
Figure 3: Fluoroscopy image of EKOS catheter during UA-CDT

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