Ultrasound-Accelerated Catheter-Directed Thrombolysis for Acute Submassive Pulmonary Embolism

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ABSTRACT

Purpose: To evaluate the safety and efficacy of ultrasound-accelerated catheter-directed thrombolysis (USAT) in patients with submassive pulmonary embolism (PE).

Materials and Methods: This retrospective study comprised 45 consecutive patients (15 prospective, 30 retrospective) who underwent USAT for submassive PE from June 2012–May 2014. Inclusion criteria were right ventricular dysfunction (RVD) as indicated by right ventricle-to-left ventricle (RV:LV) ratio > 0.9, symptoms of < 2 weeks' duration, and absence of absolute contraindication to thrombolysis. All patients underwent pulmonary artery catheterization with a standardized protocol (24 mg recombinant tissue plasminogen activator). Hemodynamic evaluation immediately after USAT, RV:LV ratio evaluation at 48–72 hours after USAT by computed tomography angiography and echocardiography, and adverse event reporting for a minimum of 30 days were performed. Outcomes and complications are reported as per the Society of Interventional Radiology Reporting Standards for Endovascular Treatment of Pulmonary Embolism.

Results: USAT was technically successful in 100% (n = 45) of patients. Main pulmonary artery pressure significantly decreased from 49.8 mm Hg to 31.1 mm Hg ($P < .0001$). RVD significantly improved with mean RV:LV ratios decreasing from 1.59 to 0.93 ($P < .0001$). There were 6 complications: 4 minor bleeding episodes at access sites and 2 major bleeding complications (flank and arm hematoma). All-cause mortality at 30 days was 0%. There were no readmissions for PE at 30 days after discharge.

Conclusions: Ultrasound-accelerated catheter-directed thrombolysis using a standardized low-dose protocol is a safe and efficacious method of treatment of submassive PE to reduce acute pulmonary hypertension and RVD.

ABBREVIATIONS

CDT = catheter-directed thrombolysis, PE = pulmonary embolism, RVD = right ventricular dysfunction, RV:LV = right ventricle-to-left ventricle, USAT = ultrasound-accelerated catheter-directed thrombolysis

Pulmonary embolism (PE) is the third most common cause of cardiovascular-related death in the United States, following myocardial infarction and stroke (1). Submassive PE, which exhibits right ventricular dysfunction (RVD) without hemodynamic instability, is associated with escalation of therapy (cardiopulmonary resuscitation, intubation, vasopressor support), short- and intermediate-term mortality and chronic thromboembolic pulmonary hypertension (2–6). RVD as defined by a right ventricle-to-left ventricle (RV:LV) end-diastolic diameter ratio of greater than 0.9 is an independent predictor of mortality secondary to PE (7–9).

Currently, there are no uniformly accepted recommendations for systemic thrombolysis in the treatment of submassive PE (10–12). There is growing evidence that systemic thrombolysis in submassive PE reduces hemodynamic collapse, improves RVD and decreases late onset pulmonary hypertension, however, this is at the expense of increased bleeding complications (13–16).

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Studies involving catheter-directed thrombolysis (CDT) with and without ultrasound have demonstrated a significant comparative improvement with RVD and pulmonary artery pressures without increased risk of major bleeding complication (17–22). Some authors have suggested that catheter directed therapy be utilized in patients with contraindications to systemic thrombolysis as this population is at intermediate to high risk of death (23,24), however a variety of treatment algorithms were reported. We present our retrospective experience of ultrasound-accelerated catheter-directed thrombolysis (USAT) in the treatment of submassive PE using a standardized low-dose treatment protocol.

MATERIALS AND METHODS

This study included 45 consecutive patients (25 men and 20 women; mean age, 56.5 y) with submassive PE treated at a single institution from June 2012–May 2014. Demographics are presented in **Table 1**, and risk factors for venous thromboembolism are listed in **Table 2** (25). The first 15 patients were enrolled in a prospective multicenter trial (SEATTLE II [A Prospective, Single-arm, Multi-center Trial of EkoSonic Endovascular System and Activase for Treatment of Acute Pulmonary Embolism], ClinicalTrials.gov Identifier: NCT01513759), and the subsequent 30 patients were retrospectively evaluated. The treatment protocol was identical for all patients. All patients signed informed consent form, and the study was performed in compliance with the Health Insurance Portability and Accountability Act with institutional review board approval of prospective and retrospective cohorts.

Inclusion criteria were acute PE documented by computed tomography (CT) with symptom onset < 2 weeks, RVD indicated by an RV:LV ratio of > 0.9 on CT angiography (26), and systemic systolic blood pressure >90 mm Hg without the need for vasopressor support. Patients were excluded if they had a contraindication to receiving thrombolytic medication (27). All patients underwent right heart and pulmonary artery catheterization with hemodynamic evaluation followed by USAT (12 h, n = 3; 24 h, n = 42) with a total dose of 24 mg of recombinant tissue plasminogen activator (tPA). Concomitant anticoagulation with heparin was administered with a target partial thromboplastin time of 40–60 seconds.

When a single unilateral catheter (n = 3) was placed, a 24-hour of infusion of 24 mg of tPA alteplase (Activase; Genentech, Inc, South San Francisco, California) was performed at a rate of 1 mg/h (24 mg in 250 mL normal saline); when bilateral catheters (n = 42) were placed, a 12-hour infusion was performed via two catheters at a rate of 1 mg/h each (12 mg tPA in 250 mL normal saline for two bags). Venous access was via a transfemoral route in 3 patients and transjugular route in 42. EkoSonic Endovascular System thrombolytic infusion catheters (EKOS Corp, Bothell, Washington) were placed in all patients with the operator-dependent decision for placement of unilateral versus bilateral

Table 1. Demographics

Baseline demographics		
Age, y, mean ± SD	56.5 ± 13.6	
Body mass index, mean ± SD	32.5 ± 8.2	
Men, n (%)	25/45	(55.6%)
Women, n (%)	20/45	(44.4%)
Comorbidities and risk factors		
Systemic hypertension, n (%)	23/45	(51.1%)
Hyperlipidemia, n (%)	17/45	(37.8%)
Tobacco use, n (%)	7/45	(15.6%)
Diabetes mellitus, n (%)	6/45	(13.3%)
Obesity, n (%)	18/45	(40.0%)
Renal insufficiency (GFR < 60 mL/min), n (%)	17/45	(37.8%)
Chronic obstructive pulmonary disease, n (%)	3/45	(6.7%)
Cancer, n (%)	8/45	(17.8%)
Congestive heart failure, n (%)	0/45	(0.0%)
Coronary artery disease, n (%)	4/45	(8.9%)
Prior stroke, n (%)	1/45	(2.2%)
Prior deep vein thrombosis, n (%)	6/45	(13.3%)
Prior PE, n (%)	6/45	(13.3%)
PE severity		
Tachycardia > 100 beats/min, n (%)	18/43	(41.9%)
Systolic arterial pressure, mm Hg, mean ± SD	135.8 ± 16.3	
Diastolic arterial pressure, mm Hg, mean ± SD	76.8 ± 10.1	
Heart rate, beats/min, mean ± SD	90.8 ± 17.0	
Respiratory rate, breaths/min, mean ± SD	21.3 ± 4.9	
Oxygen supplementation, n (%)	20/38	(52.6%)
Oxygen saturation during oxygen supplement, mean ± SD	97% ± 2.7	
Troponin test positive, n (%)	29/43	(67.4%)
RV:LV ratio by CT, before procedure, mean ± SD	1.59 ± 0.54	
RV:LV ratio by CT, after procedure, mean ± SD	0.93 ± 0.17	
Bilateral main pulmonary artery embolism, n (%)	43/45	(93.3%)
Unilateral main pulmonary artery embolism, n (%)	3/45	(6.7%)
Pulmonary pressure, before procedure, mm Hg, mean ± SD	49.8 ± 13.76	
Pulmonary pressure, after procedure, mm Hg, mean ± SD	31.1 ± 9.9	
Hospital stay, days (range)	5.64	(2–6)
30-day follow-up	No readmissions	

CT = computed tomography, GFR = glomerular filtration rate, PE = pulmonary embolism, RV:LV = right ventricle-to-left ventricle.