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# Improved early right ventricular function recovery but increased complications with catheter-directed interventions compared with anticoagulation alone for submassive pulmonary embolism

**Efthymios D. Avgerinos, MD**, **Nathan L. Liang, MD**, **Omar M. El-Shazly, MD**, **Catalyn Toma, MD**, **Michael J. Singh, MD**, **Michel S. Makaroun, MD**, **Rabih A. Chaer, MD**

Division of Vascular Surgery, University of Pittsburgh Medical Center.

## Abstract

**Objective:** The purpose of this study was to determine the short-term and midterm outcomes of catheter-directed intervention (CDI) compared with anticoagulation (AC) alone in patients with submassive pulmonary embolism (sPE).

**Methods:** This was a retrospective review of all patients treated for sPE between January 2009 and October 2014. Two groups were identified on the basis of the therapy: AC and CDI. End points included complications, mortality, and change in echocardiographic parameters. Standard statistical techniques were used.

**Results:** There were 64 patients who received AC and 64 patients who received CDI (five were initially treated with AC but did not improve or worsened; six received ≤8 mg of tissue plasminogen activator). Most baseline characteristics, including the Pulmonary Embolism Severity Index, were similar among the AC and CDI groups. There was no difference in PE-related death (one in each group) or major bleeding events (three in the AC group, four in the CDI group), but CDIs had two additional procedural complications that required open heart surgery. CDIs showed significantly more minor bleeding events (6 vs 0; $P = .028$) and significantly shorter intensive care unit stay (2.7 ± 2.1 vs 5.6 ± 7.5 days; $P = .04$). The mean difference in right ventricular/left ventricular ratio from baseline to the first subsequent echocardiogram (within 30 days) showed a trend for higher reduction in favor of CDI (AC, 0.17 ± 0.12; CDI, 0.27 ± 0.15; $P = .076$). Between

Correspondence: Rabih A. Chaer, MD, Professor of Surgery, Division of Vascular Surgery, University of Pittsburgh Medical Center, 200 Lothrop St, Ste A1011, Pittsburgh, PA 15213 (chaerra@upmc.edu).

AUTHOR CONTRIBUTIONS

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Analysis and interpretation: EA, NL, OE, CT, MS, MM, RC

Data collection: EA, NL, OE

Writing the article: EA, NL, RC

Critical revision of the article: CT, MS, MM, RC

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3 and 8 months, significant improvement was evident within groups in all assessed right-sided heart echocardiographic parameters, but there was no difference between groups. Pulmonary hypertension (pulmonary artery pressure >40 mm Hg) was present in 7 of 15 of the AC group vs 6 of 19 of the CDI group ($P = .484$). During the follow-up, dyspnea or oxygen dependence, not existing before the index PE event, was recorded in 5 of 49 (10.2%) of the AC patients and 8 of 52 (15.4%) of the CDI patients ($P = .556$).

**Conclusions:** CDI for sPE can result in faster restoration of right ventricular function and shorter intensive care unit stay, but at the cost of a higher complication rate, with similar midterm outcomes compared with AC alone. A potential effect of CDI on mortality and pulmonary hypertension needs further investigation through larger studies.

Acute pulmonary embolism (PE) is a major cause of mortality, morbidity, and hospitalization.[1] Recent studies suggest that the 90-day mortality rate may be as high as 10% for patients presenting with acute PE.[2,3] Management is mainly guided by the acuity and severity of clinical presentation. Initial systemic anticoagulation (AC) is the standard of care, and treatment is escalated on the basis of the clinical presentation and characteristics of the patients that may stratify them to a higher mortality risk. The goals of therapy are primarily to prevent mortality and secondarily to prevent late-onset chronic thromboembolic pulmonary hypertension and to improve quality of life.

Massive PE is characterized by sustained hemodynamic instability, whereas patients with submassive PE (sPE) are hemodynamically stable but demonstrate signs of abnormal right ventricular (RV) function or evidence of myocardial necrosis.[4] Systemic intravenous thrombolysis is universally recommended by all guideline bodies for massive PE but remains controversial for sPE.[4–7] In a recent meta-analysis, subgroup analysis of eight sPE trials (1993–2014; n = 1775) showed that thrombolytic therapy was associated with a mortality reduction (1.39% vs 2.92%; odds ratio, 0.48; 95% confidence interval, 0.25–0.92) but with an increase in major bleeding (7.74% vs 2.25%; odds ratio, 3.19; 95% confidence interval, 2.07–4.92).[8] These results were limited by heterogeneity of the patients and short follow-up times in individual studies and were mainly driven by the largest randomized trial (Pulmonary Embolism Thrombolysis [PEITHO] trial, 1006 patients).[9] The limitations and complications of systemic thrombolysis have shifted contemporary practice toward catheter-directed interventions (CDIs) as a first-line treatment in the appropriate clinical setting as a way to provide the potential benefits of thrombolytic therapy with minimizing adverse events.[10–14] The purpose of our study was to determine the short-term and midterm outcomes of CDI compared with AC alone in patients with sPE.

## METHODS

The study protocol was approved and exempted from informed consent by the Quality Review Board of the University of Pittsburgh Medical Center.

### Study design.

Consecutive patients who received in-hospital treatment for acute PE between January 2009 and October 2014 were identified from our institution’s electronic medical records. Patients

with low risk (no imaging or biomarker signs of RV dysfunction) or massive PE (systolic blood pressure <90 mm Hg for at least 15 minutes or requiring inotropic support) on presentation and those who received systemic thrombolysis were excluded. The remaining were the sPE (systolic blood pressure ≥90 mm Hg with either RV dysfunction or myocardial necrosis) patients, who were then separated into two groups on the basis of treatment; one group received CDI in combination with AC, whereas the other received AC alone.

Records were reviewed for demographics, baseline risk factors, lower extremity venous studies, indications, biomarkers at baseline (troponin or natriuretic peptide plasma level), echocardiographic parameters, intraprocedural data, periprocedural complications, and midterm outcomes. The simplified Pulmonary Embolism Severity Index (sPESI) was calculated for risk stratification (low vs high risk). The sPESI combines six demographic parameters (age >80 years), clinical signs (heart rate ≥80, systolic blood pressure <100 mm Hg, oxygen saturation <90%), and comorbidities (chronic pulmonary disease, history of cancer). Each one of them is assigned 1 point. Patients with sPESI of 0 are classified as low risk (30-day mortality risk, 0.0%−2.1%), and those with sPESI of 1 are classified as high risk (30-day mortality risk, 8.5%−13.2%).[15]

Outcomes were assessed at 30 days and within 1 year and included death, minor and major bleeding events, and other related complications and changes in echocardiographic parameters. A composite end point for major adverse events was used to better portray the complication profiles of AC and CDI. A major adverse event was defined as any treatment-related event that required surgical intervention or transfusion, stroke, or need for dialysis as a result of the provided PE treatment. Clinical success was defined using a composite end point of prevention of PE-related hemodynamic decompensation (systolic blood pressure <90 mm Hg) and absence of major adverse events or in-hospital death.

### Echocardiography.

Available echocardiograms were reviewed by two blinded independent physicians. The studies that were reviewed and recorded, when available, were the first echocardiogram that confirmed the diagnosis of PE associated with RV strain, the echocardiogram that was done within 30 days of initiation of treatment, and the follow-up 1-year echocardiogram.

The echocardiographic parameters that were extracted from the reports were the subannular end-diastolic RV/left ventricular (LV) ratio, RV systolic dysfunction (none, mild, moderate, or severe), tricuspid regurgitant jet velocity, and pulmonary artery pressure.

Calculation of the RV/LV ratio was performed as described in the Ultrasound Accelerated Thrombolysis of Pulmonary Embolism (ULTIMA) trial.[11]

### Treatment protocol.

Patients not receiving unfractionated heparin at the time of PE diagnosis were given an intravenous bolus of 80 IU/kg (omitted if they were already receiving AC), followed by an infusion of 18 IU/kg/h. The heparin infusion was adjusted to achieve and to maintain an activated partial thromboplastin time of 68 to 106 per institutional protocol.

The choice of treatment, AC vs CDI, was based on the physician's preference for more than half of the patients. Since 2014, a multidisciplinary PE response team (PERT) has been established in the major facility of our institution responsible for all urgent and routine consultations for patients with sPE and massive PE. The PERT involves pulmonary, critical care, cardiology, vascular surgery, and cardiothoracic surgery specialists, ensuring 24/7 availability of catheter-directed thrombolysis, systemic thrombolysis, surgical embolectomy, and hemodynamic support. For patients treated since 2014, the choice of treatment was by PERT consensus, based on an evolving protocol that currently considers only high-risk sPE patients (sPESI = 1 or echocardiographic RV dysfunction plus myocardial necrosis) as candidates for CDIs.

The heparinization protocol during catheter lysis varied during our early experience, and in general we have shifted from conservative subtherapeutic dosing to full therapeutic protocols. All patients were continued on systemic AC after the lysis intervention. Both groups (AC and CDI) were eventually transitioned to long-term oral AC.

The duration of AC was determined on the basis of the underlying cause and the presence of a hypercoagulable state as recommended in the American College of Chest Physicians guidelines.[1] Although these were the goals and recommendations relayed to patients on discharge and future follow-up, this was limited by compliance of the patient and socioeconomic factors.

### Catheter intervention technique.

Ultrasound-guided femoral or internal jugular vein access was used in the majority of patients. Dual-lumen jugular or femoral sheaths or two single-lumen femoral vein sheaths were used for bilateral PEs. If an inferior vena cava filter was considered necessary, it was placed before pulmonary artery catheterization. A pigtail catheter was then navigated within the main pulmonary artery, and a pulmonary arteriogram was obtained to assess the exact location of the clot. The standard protocol included placement of unilateral or bilateral 5-cm multi-side hole catheters (5F Cragg-McNamara [Boston Scientific, Marlborough, Mass] or UniFuse [AngioDynamics, Latham, NY]) across the heaviest clot burden (unilateral or bilateral), on-table infusion of 2 to 4 mg of tissue plasminogen activator (tPA), and initiation of lytic infusion at a rate of 0.5 to 1 mg/h. Variation of this protocol included use of ultrasound-assisted thrombolysis (USAT) with the EkoSonic catheter (EKOS Corp, Bothell, Wash). Rarely, aspiration thrombectomy, rheolysis using the AngioJet device (Boston Scientific), catheter-based mechanical fragmentation, and on-table-only catheter-directed infusion of thrombolytic (without initiation of continuous infusion) were used per the physician's preference. Patients undergoing any CDI were monitored in the intensive care unit (ICU). No adjunct medication (eg, prostanoids) was used for pulmonary hypertension. During our initial experience, patients returned to the angiography suite every 8 to 12 hours for a repeated angiogram to evaluate thrombus burden reduction. This was later abandoned as a routine practice; termination of catheter-directed thrombolytic infusion with bedside catheter removal is currently based on improvement of clinical, hemodynamic, and echocardiographic parameters or on any complications that necessitate discontinuation of therapy. Filter retrieval was usually performed on a later date.

### Follow-up.

Patients were followed up by pulmonary medicine within 2 weeks after discharge to assess the appropriateness of AC and to schedule inferior vena cava filter retrieval if needed. A repeated echocardiogram was done at 1 to 2 months after discharge to assess pulmonary artery pressures, and subsequent echocardiograms were obtained as needed. Pulmonary hypertension tests (eg, 6-minute walk test) were done selectively. A hypercoagulable workup, if not done, was obtained during the follow-up period in consultation with a hematologist.

### Statistical analysis.

Descriptive characteristics are reported as mean ± standard deviation or as number of cases and percentages. Comparison of binary data between and within groups was performed with the $\chi^2$ and Fisher exact tests. Between-group and within-group comparisons of continuous data were performed with the two-sided paired *t*-test. Survival functions were estimated by the Kaplan-Meier method. Results were considered statistically significant when *P* value was < .05. Interobserver agreement for the echocardiographic baseline RV/LV ratio between the two investigators' measurements was assessed by Bland-Altman analysis. Data analysis was performed using Statistical Package for the Social Sciences, version 17 (SPSS Inc, Chicago, Ill).

## RESULTS

During the study period, 28 patients with massive PE and 141 patients with sPE were identified. Of the sPE cohort, 13 patients who received systemic thrombolysis were excluded, leaving 128 patients for analysis; 64 received AC only, and 64 received AC plus a CDI. The mean age of the cohort was 59.3 ± 16.7 years, and 63 (49.2%) were women. Baseline characteristics, including sPESI stratification and echocardiographic parameters, were similar between groups, except for recent travel and prior thromboembolism being more frequent and the troponin level being higher in the CDI group (Tables I and II).

CDIs were used as "rescue therapy" in five patients who had no improvement or worsening of hemodynamic and respiratory profiles after initial treatment with AC.

CDIs were used in four patients with absolute and seven patients with relative contraindications for systemic lysis as defined by the American Heart Association.[2]

In 94% of analyzed echocardiograms, there was inter-observer agreement of the RV/LV ratio measurements (within two standard deviations of the RV/LV ratio mean difference that was 0.27).

### Procedural data for CDI group.

The majority of CDI patients received USAT (37 [57.8%]); 24 (37.5%) received standard catheter-directed lysis. Early in our experience, one patient received pharmacomechanical thrombolysis with the AngioJet device. He was initially considered to have a massive PE because of a syncopal event and had major abdominal surgery 2 months earlier. He received 7 mg of tPA and had temporary intraprocedural bradycardia but no other major adverse

events. Another patient, with high-risk sPE, underwent aspiration thrombectomy with the AngioVAC device (AngioDynamics). No tPA was used because of recent craniotomy for brain abscess. Although it successfully removed the clot, the procedure was complicated by tricuspid valve injury that required open valve repair with a good final outcome. Finally, one patient received on-table-only tPA catheter infusion, in combination with pharmacomechanical thrombolysis for deep venous thrombosis.

Interventions were bilateral in 57 cases (89.1%), with an average total tPA infusion of 27.0 ± 13.5 mg (median, 23.8 mg; range, 0–62 mg). An inferior vena cava filter was inserted or pre-existed in 57 cases (89.1%). The majority of patients (30 [46.9%]) required a single trip to the angiography suite, with the catheters removed at bedside and termination of the infusion based on improvement of hemodynamic, respiratory, and echocardiographic parameters. The mean infusion time was 17.6 ± 9.6 hours (median, 15 hours; range, 0–51 hours).

### In-hospital outcomes.

Clinical success was similar between groups (AC, 58 [90.6%]; CDI, 56 [87.5%]; $P = .571$). The CDI group had higher rates of major adverse events than the AC group, although this was not statistically significant (AC, 3 [4.7%]; CDI, 5 [7.8%]; $P = .718$). Major adverse events in the AC group included two retroperitoneal hematomas and one rectus sheath hematoma. Major adverse events in the CDI group consisted of a coronary sinus perforation that required open heart surgery, one tricuspid valve injury (discussed previously), a large groin hematoma at a recent access site for cardiac catheterization, a rectus sheath hematoma, and postoperative intra-abdominal bleeding after a ventral hernia repair that did not require reintervention. There were no ischemic strokes or intracranial bleeds in either group.

Minor bleeding events were significantly more common in the CDI group (AC, 0; CDI, 7 [10.9%]; $P = .013$) and included two patients with hematochezia, one with intra-abdominal bleed of unknown origin, two with groin hematomas, one with breast hematoma, and one with hemoptysis. All resolved conservatively with no need for intervention or transfusion.

Among the 11 patients who underwent a CDI with a systemic lysis-defined absolute or relative contraindication, only 1 had a major bleeding event (ventral hernia repair bleeding postoperative day 3) and 3 had a minor bleeding event.

Three patients in the CDI group and none in the AC group had hemodynamic decompensation related to their PE; one subsequently improved with a good outcome and no further intervention, one received extracorporeal membrane oxygenation and surgical thrombectomy with a good outcome, and the other one died. The patient who died was one of five patients who had been escalated to a catheter intervention as a rescue treatment because of lack of response to AC alone.

Overall death (AC, 3; CDI, 1) and PE-related death (AC, 1; CD, 1) rates were similar between the two groups. A bowel leak after sigmoid resection and a visceral perforation, both leading to multiple organ failure and eventually death, were considered non-PE-related deaths.

The average ICU length of stay was significantly higher for the AC group (AC, 5.6 ± 7.5 days; CDI, 2.7 ± 2.1 days; $P = .004$).

Following the baseline echocardiogram, the first echocardiogram after initiation of treatment was done on average 11.1 ± 10.3 days later for AC but significantly earlier at 3.3 ± 3.6 days for CDI ($P = .015$). In the AC group, the mean RV/LV ratio had a nonsignificant reduction from 1.1 ± 0.23 at baseline to 0.97 ± 0.19 ($P = .070$). In the CDI group, the mean RV/LV ratio was significantly reduced from 1.04 ± 0.19 at baseline to 0.88 ± 0.14 ($P = .001$). The mean difference in RV/LV ratio from baseline to the first subsequent echocardiogram (within 30 days) showed a trend for higher reduction in favor of CDI (AC, 0.17 ± 0.12; CDI, 0.27 ± 0.15; $P = .076$). All other assessed echocardiographic right-sided heart parameter comparisons between and within groups were not significant (Table II).

### Midterm outcomes.

Twenty-four patients (13 AC, 11 CDI) had no relevant clinical follow-up after 30 days because they either were lost to follow-up (21 patients) or died (three patients). Excluding these, the average clinical follow-up was 14.2 ± 12.8 months (median, 8.9 months; range, 1.0–48.1 months) for the AC group and 13.8 ± 12.0 months (median, 10.5 months; range, 1.8–68.1 months) for the CDI group.

At 90 days, there were no new episodes of decompensation or death in either group.

During the follow-up, dyspnea or oxygen dependence, not existing before the index PE event, was recorded in 5 of 49 (10.2%) of the AC patients and 8 of 52 (15.4%) of the CDI patients ($P = .556$). Survival at 1 year was 94.6% and 91.4% for the AC and CDI groups, respectively (log-rank, .980).

A follow-up echocardiogram, beyond 30 days, was available for comparative analysis in 17 patients from the AC group and 21 patients from the CDI group. The available follow-up echocardiogram was done at a mean follow-up of 5.1 ± 2.8 months for the AC group and 3.5 ± 3.0 months for the CDI group ($P = .098$). Significant improvement (baseline to follow-up) was evident within groups in all assessed right-sided heart echocardiographic parameters, but there was no difference between groups (Table II).

Pulmonary hypertension (pulmonary artery pressure ≥40 mm Hg) was evident in 7 of 15 of the AC group vs 6 of 19 of the CDI group ($P = .484$).

## DISCUSSION

Our study demonstrated that CDIs for sPE, compared with AC alone, can achieve faster RV function recovery and reduce the ICU length of stay. This, however, came at the cost of significantly higher minor and potentially major complication rates, with no evident reduction in mortality or decompensation rates. It was otherwise difficult to demonstrate a survival benefit of either treatment modality, given that mortality is infrequent in patients with sPE. Echocardiographic parameters, including pulmonary hypertension, seem to even out within 3 to 8 months, irrespective of treatment modality.

The role of catheter-directed therapy for acute sPE is rapidly evolving, following the results of PEITHO[9] and a large meta-analysis[8] that indicated systemic thrombolysis as superior in preventing hemodynamic decompensation and mortality but with a high bleeding complication rate compared with AC alone. There is also some recent evidence from three small randomized studies and a prospective uncontrolled trial that pulmonary artery pressures rise in the majority of patients with sPE but decline in those who are treated with thrombolysis, potentially altering exercise tolerance and quality of life.[16–19] CDIs have emerged as an alternative that can potentially provide the benefits of systemic thrombolysis but without its associated complications, given the lower dose of lytics that need to be delivered. Both the American Heart Association and more recently the European Society of Cardiology have acknowledged CDT as a viable treatment alternative for high-risk acute sPE (echocardiographic RV dysfunction and elevated troponin), if appropriate expertise is available and particularly when the bleeding risk precludes systemic thrombolysis.[4,6]

The ULTIMA trial was the first randomized controlled trial to include CDIs for sPE comparing standardized fixed-dose USAT (10 mg of tPA per lung during 15 hours) and AC with AC alone.[11] In the USAT group but not in the AC group, the mean RV/LV ratio was significantly reduced at 24 hours but became comparable between the two groups at 90 days. The RV systolic function was significantly improved in the USAT group vs the heparin group at both 24 hours and 90 days. In both study groups, minor bleeding complications were rare, and there were no major bleeding complications.[11] Whereas our results are in agreement with regard to faster RV function recovery, we noticed a much higher minor complication rate, a nonsignificantly higher major complication rate, but no stroke. This was mainly driven from the catheter intervention itself (tricuspid rupture and coronary sinus perforation) rather than from the lytic-related bleeding events that were essentially similar to the AC group. Whereas all involved operators were experienced enough, the role of the learning curve cannot be underestimated; it cannot, however, be assessed because of the small number of events. Notably, the ULTIMA trial was limited by selection bias and enrollment of an idealized trial population.[20] The Prospective, Single-arm, Multi-center Trial of EkoSonic Endovascular System and Activase for Treatment of Acute Pulmonary Embolism (SEATTLE II) trial, a single-arm study evaluating the effectiveness of USAT, showed also an RV/LV ratio improvement at 48 hours. There were no hemorrhagic strokes, but the major bleeding complication rate was 11.4%.[21] An older meta-analysis and four recent studies on catheter interventions for PE reported major complications ranging between 0% and 4%.[12,22–25]

Another interesting finding of our study is the reduced ICU length of stay for CDIs compared with AC alone. This can be an expected finding, given that RV function recovers faster, which translates to a faster improvement of hemodynamic and respiratory parameters. This finding has not been elaborated in the current literature and may have significant implications in the cost-effectiveness of CDIs. A recent study indicated conflicting results on ICU length of stay; however, this may have been driven by the investigators' institutional protocol and the fact that their sample included several cases of massive PE.[22] It is our routine practice currently to pull the catheters in the ICU at the bedside and to transfer the patient to a regular ward the next day if not the same day. Omitting the repeated angiogram

to terminate lysis reduces the ICU length of stay and all associated operating room and ICU costs.

At midterm follow-up, our study failed to show any echocardiographic or clinical benefit of CDIs. Within 3 to 8 months, RV function, echocardiographic and clinical pulmonary hypertension, and PE recurrence did not differ compared with AC alone. Regarding RV function recovery, our results are in agreement with ULTIMA, which also showed that RV parameters normalize in a delayed fashion with AC alone, with no clinical sequelae.[11] Whereas there is some preliminary evidence for midterm benefits of systemic thrombolysis in respect to exercise tolerance and quality of life, there is no study to date focusing on the midterm to long-term clinical outcomes of CDIs.[16–18] Our follow-up sample was otherwise too small to show any meaningful differences between the two groups in the incidence of shortness of breath or oxygen dependence.

Apart from the small sample and the likelihood of a type II error in our comparisons, the study has several other limitations, and the results should be interpreted with caution. This is a retrospective study, and despite the two groups compared being similar at baseline, selection bias cannot be ruled out, with higher risk patients potentially having been allocated to the CDI group. For example, CDIs were used as rescue therapy in a few patients who were initially receiving AC, but their hemodynamic and respiratory profile did not improve or worsened. There was also no standardized protocol for CDIs, as is the case for the rest of the relevant literature. The optimal technique, dose of lytics, and timing of termination remain unclear. Notably, there is currently no clear proven superiority of USAT for PE and non-ultrasound-assisted lysis techniques.[22,26] Finally, the number of patients who received an echocardiogram during the follow-up was relatively low. Despite its limitations, this study represents one of the first real-world experience comparative studies with midterm follow-up.

## CONCLUSIONS

CDIs do have a role in contemporary practice, provided they are applied through a multidisciplinary team, in the appropriate setting, and in carefully selected high-risk sPE patients. A faster RV function recovery may extrapolate to reduced events of hemodynamic decompensation that we failed to show because of our small sample. Despite the absence of neurologic ischemic and intracranial bleeding complications, minor and occasionally major complications should be anticipated. A potential effect of CDIs on quality of life outcomes therefore needs further investigation, and as the techniques and expertise continue to evolve, relevant clinical and patient-centered end points will need to be identified to better define clinical success and to guide selection of patients.

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## DISCUSSION

**Dr Martin Veller** (*Johannesburg, South Africa*). How do you explain the reduction in terms of intensive care unit (ICU) stay? Selecting patients with intermediate symptoms would suggest that both groups would have equal lengths of stay.

**Dr Efthymios D. Avgerinos**. I believe that this is the effect of the thrombolytics. Faster clot lysis (when compared to anticoagulation alone) allows the right ventricular (RV) function to recover faster and the patient show earlier signs of clinical improvement, thus getting out of the ICU. It is a trade-off that we have to do. We gain faster RV function recovery, but it seems this comes at the cost of complications.

**Dr Veller**. The question then really arises whether you, in fact, are not preselecting the patients, so are they really equal groups?

**Dr Avgerinos**. Well, in our analysis, unfortunately the sample is small but still the baseline characteristics were similar in univariate analysis.

**Dr Vikram Rao** (*Cleveland, Ohio*). I know you have pretty small numbers, but did you notice any difference in the length of stay when you used standard vs ultrasound-assisted catheter-directed thrombolysis (CDT)?

**Dr Avgerinos**. This is a very good question. We have actually already presented this data (American Venous Forum 2015). We compared catheter-directed with the standard catheter vs ultrasound-assisted. There was no difference in the clinical outcomes. The ultrasound-assisted, though, seemed to decrease the ICU length of stay, but again the numbers are small to make definite decisions.

**Dr Rao**. The follow-up question is: how did you assess clearance of clot burden, comparing standard vs ultrasound-assisted CDT.

**Dr Avgerinos**. That's a very good question actually. As you know, there is no standard protocol in catheter-directed interventions. Early in our experience, we were chasing the clot, we were trying to see an actual clot reduction in our imaging, and we were getting the patient back and forth in the operating room. But, for the past few years, we have changed policy and we go with physiologic parameters. We will not bring the patient back to the interventional suite; we will just watch his vitals and do a repeat echocardiogram to see that the RV function is improving, and that will be enough to pull the catheters on the bedside. So, this is an evolving strategy and protocol that we haven't still finalized.

**Dr Rao**. Would you recommend just doing standard CDT for the sake of saving money now?

**Dr Avgerinos**. It's probably early to make conclusions, but this may be the case.

**Dr Allan Conway** (*New York, NY*). Very nice presentation. We're doing kind of a similar study where we are in New York regarding patients with submassive pulmonary embolisms (PEs). Some we're treating with anticoagulation; the sicker ones we're taking to the cath lab to intervene on. What are your criteria for taking a patient to intervene on with the catheter-directed therapy?

**Dr Avgerinos**. Well, the strategy has evolved and now we have a multidisciplinary pulmonary embolism team making these decisions, and we carefully select patients choosing the high-risk submassive PEs. “High risk” is defined as positive troponins and ECHO RV dysfunction. They need to have both of these criteria to get lysis.

**Dr Randall DeMartino** (*Rochester, Minn*). I enjoyed your presentation. Thank you.

As you notice, for submassive PEs, they’re hard to select who you should intervene on. Do you have a PERT team and is that evolving at your institution and where do you think vascular surgery should play a role in the PERT response?

**Dr Avgerinos**. Thank you for this question. Again, we only select high-risk submassive PEs, defined as positive troponins and ECHO RV strain. Yes, we do have a PERT team. This actually came together approximately 2 years ago, and it has been functioning very well over the past year. This PERT team includes a pulmonologist, a cardiologist, a vascular surgeon, and a thoracic surgeon. So, each one of us brings something different: we have the experience with thrombolysis; cardiologists have the experience with the cardiac cath; pulmonologists are the ones admitting the patients and assume the overall care; and coordination and cardiac surgeons are responsible for the ECMO when needed and the surgical thrombectomies. We share decisions in a multidisciplinary fashion. And, we’ve seen that since the PERT protocol has been on board, patients are captured better and our success rates are improving.

**Table I.**

Characteristics of study population by treatment type

| | Overall | AC (n = 64) | CDI (n = 64) | *P* value |
|---|---|---|---|---|
| Age, years | 59.3 ± 16.7 | 60.1 ± 17.3 | 58.5 ± 16.1 | .571 |
| Male gender | 63 (49.2) | 33 (51.6) | 30 (46.9) | .596 |
| Acute DVT | 70 (54.7) | 35 (54.7) | 35 (54.7) | 1.000 |
| Hypercoagulable state | 13 (10.2) | 9 (14.1) | 4 (6.3) | .143 |
| Recent surgery (within 1 month) | 26 (20.3) | 13 (20.3) | 13 (20.3) | — |
| Recent trauma (within 1 month) | 7 (5.5) | 5 (7.8) | 2 (3.1) | .244 |
| Malignant disease | 22 (17.2) | 14 (21.9) | 8 (12.5) | .160 |
| Contraceptives | 7 (5.5) | 1 (1.6) | 6 (9.4) | .115 |
| Recent travel | 16 (12.5) | 4 (6.3) | 12 (18.8) | .033 |
| Recurrent VTE | 17 (13.3) | 3 (4.7) | 14 (21.9) | .004 |
| Hypertension | 65 (50.8) | 32 (50.0) | 33 (51.6) | .860 |
| Coronary disease | 17 (13.3) | 10 (15.6) | 7 (10.9) | .604 |
| Cardiac failure | 9 (7.0) | 7 (10.9) | 2 (3.1) | .164 |
| Pulmonary disease | 19 (14.8) | 7 (10.9) | 12 (18.8) | .214 |
| Current smoking | 20 (15.6) | 9 (14.1) | 11 (17.2) | .626 |
| GFR | 84.5 ± 39.6 | 82.6 ± 30.8 | 86.5 ± 47.0 | .580 |
| No lysis contraindications | 98 (76.6) | 45 (70.3) | 53 (82.8) | .095 |
| Absolute contraindications | 7 (5.5) | 3 (4.7) | 4 (6.3) | |
| Relative contraindications | 23 (18.0) | 16 (25.0) | 7 (10.9) | |
| Inferior vena cava filter | 55 (43) | 25 (39.1) | 30 (46.9) | .372 |
| Troponin | 0.5 ± 0.9 | 0.23 ± 0.32 | 0.81 ± 1.22 | .001 |
| BNP | 371 ± 335 | 333 ± 246 | 404 ± 398 | .357 |
| PESI high risk | 105 (82.0) | 51 (79.7) | 54 (84.4) | .490 |

*AC*, Anticoagulation; *BNP*, brain natriuretic peptide; *CDI*, catheter-directed intervention; *DVT*, deep venous thrombosis; *GFR*, glomerular filtration rate; *PESI*, Pulmonary Embolism Severity Index; *VTE*, venous thromboembolism.

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as number (%).



*J Vasc Surg Venous Lymphat Disord*. Author manuscript; available in PMC 2020 April 12.

**Table II.**

Echocardiographic parameters

| | Baseline | | Within 30 days | |
|---|---|---|---|---|
| | **AC** | **CDI** | **AC** | **CDI** |
| RV/LV ratio | 1.1 ± 0.23 | 1.04 ± 0.19 | 0.97 ± 0.19 | 0.88 ± 0.14 |
| Number of patients | 47 | 53 | 12 | 21 |
| Between-group comparison, AC vs CDI | *P* = .099 | | *P* = .101 | |
| Within-group comparison | — | — | — | — |
| RV systolic dysfunction, none/mild/moderate/severe | 19/15/18/10 | 14/11/26/10 | 7/2/4/0 | 11/6/4/1 |
| Number of patients | 62 | 61 | 13 | 22 |
| Between-group comparison, AC vs CDI | *P* = .253 | | *P* = .991 | |
| Within-group comparison | — | — | — | — |
| Tricuspid regurgitant jet velocity | 3.10 ± 0.61 | 3.10 ± 0.64 | 2.84 ± 0.70 | 2.86 ± 0.63 |
| Number of patients | 51 | 51 | 9 | 18 |
| Between-group comparison, AC vs CDI | *P* = .941 | | *P* = .924 | |
| Within-group comparison | — | — | — | — |
| Pulmonary artery pressure | 50.4 ± 17.4 | 50.7 ± 17.0 | 44.6 ± 13.0 | 43.0 ± 17.3 |
| Number of patients | 52 | 49 | 9 | 18 |
| Between-group comparison, AC vs CDI | *P* = .936 | | *P* = .813 | |
| Within-group comparison | — | — | — | — |

| Within 12 months | | Difference: Baseline vs 30 days | | Difference: Baseline vs 1 year | |
|---|---|---|---|---|---|
| **AC** | **CDI** | **AC** | **CDI** | **AC** | **CDI** |
| 0.84 ± 0.11 | 0.79 ± 0.17 | 0.17 ± 0.12 | 0.27 ± 0.15 | 0.22 ± 0.15 | 0.31 ± 0.16 |
| 17 | 20 | 11 | 17 | 17 | 19 |
| *P* = .311 | | *P* = .076 | | *P* = .087 | |
| — | — | *P* = .07 | *P* = .001 | *P* < .001 | *P* < .001 |
| 15/0/0/0 | 18/2/2/0/0 | 60.0%[a] | 61.1%[a] | 100%[a] | 95.2%[a] |
| 15 | 22 | 10 | 18 | 11 | 21 |
| *P* = .056 | | *P* = 1.000 | | *P* = .462 | |
| — | — | — | — | — | — |
| 2.67 ± 0.36 | 2.33 ± 0.83 | 0.50 ± 0.41 | 0.45 ± 0.37 | 0.57 ± 0.45 | 0.86 ± 0.96 |

| Within 12 months | | Difference: Baseline vs 30 days | | Difference: Baseline vs 1 year | |
|---|---|---|---|---|---|
| **AC** | **CDI** | **AC** | **CDI** | **AC** | **CDI** |
| 15 | 20 | 7 | 13 | 14 | 16 |
| *P* = .156 | | *P* = .761 | | *P* = .285 | |
| — | — | *P* = .234 | *P* = .181 | *P* = .010 | *P* < .001 |
| 38.2 ± 8.6 | 35.0 ± 15.3 | 9.0 ± 8.2 | 11.4 ± 8.6 | 14.9 ± 12.3 | 20.4 ± 19.6 |
| 15 | 19 | 9 | 14 | 15 | 14 |
| *P* = .479 | | *P* = .505 | | *P* = .370 | |
| — | — | *P* = .341 | *P* = .107 | *P* = .001 | *P* = .001 |

*AC*, Anticoagulation; *CDI*, catheter-directed intervention; RV/LV, right ventricular/left ventricular. Continuous variables are presented as mean ± standard deviation.

[a]Percentage of patients with available studies for comparison who showed improvement by at least one category.