From the Society for Clinical Vascular Surgery

# Catheter-directed thrombolysis versus suction thrombectomy in the management of acute pulmonary embolism

Efthymios D. Avgerinos, MD, Adham Abou Ali, MD, Catalin Toma, MD, Bryan Wu, MD, Zein Saadeddin, MD, Barry McDaniel, BS, George Al-Khoury, MD, *and* Rabih A. Chaer, MD, MSc, *Pittsburgh, Pa*

## ABSTRACT

**Background:** Catheter-directed thrombolysis (CDT) is increasingly performed for acute pulmonary embolism (PE) because it is presumed to provide similar therapeutic benefits to systemic thrombolysis, while decreasing the dose of thrombolytic required and the associated risks. Contemporary suction thrombectomy (ST) devices have entered the market as minimal or no-lytic alternatives, but there is no evidence on their comparative effectiveness. This study aims to compare clinical outcomes of these two interventional alternatives.

**Methods:** Consecutive patients who underwent a ST catheter intervention for massive or submassive PE between 2011 and 2017 were identified. For each of these patients, a nearest-neighbor matching was implemented to identify at least three CDT patients who matched as closely as possible on the following six variables: PE type, age, gender, acute deep venous thrombosis, pulmonary disease, and year of procedure. The end point was clinical success defined as meeting all the following criteria: survival to hospital discharge without major bleeding (Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries moderate or severe), perioperative stroke or other major adverse procedure-related event, and decompensation for submassive or persistent shock for massive PE.

**Results:** Of 277 patients who received an intervention for acute PE, 54 CDT (63.5 ± 14.2 years of age; 18 massive PE) were matched with 18 ST (64.1 ± 14.1 years of age; 6 massive PE) patients. In the CDT group, 38 (70.4%) received ultrasound-assisted thrombolysis. The ST group had significantly more patients who had a major contraindication for lytics (1 [1.9%] for CDT vs 9 [50%] for ST; $P < .001$). There was no difference in major bleeding (8 [14.8%] for CDT vs 3 [16.7%] for ST; $P > .999$; Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries severe 1 [1.8%] for CDT vs 1 [5.6%] for ST; $P > .999$), stroke (3.7% for CDT vs 0 for ST; $P = .408$), or death (3.7% for CDT vs 16.7% for ST; $P = .096$). One patient in the ST group suffered tricuspid valve rupture and two patients in CDT group required surgical thrombectomy. Clinical success was not statistically different between groups (75.9% for CDT vs 61.1% for ST; $P = .224$). The association was similar when assessing the right/left ventricular ratio improvement (0.30 ± 0.19 for CDT vs 0.17 ± 0.16 for ST; $P = .097$), or the subgroup of patients with submassive PE (86.1% for CDT vs 66.7% for ST; $P = .135$).

**Conclusions:** CDT seems to have similar outcomes with ST in the management of acute PE, although larger, more homogenous data are needed. In our experience, ST should be viewed as a complementary alternative for patients with contraindication for thrombolytics or severely compromised hemodynamic profile and can yield good outcomes in an otherwise highly morbid population. (J Vasc Surg: Venous and Lym Dis 2019;7:623-8.)

**Keywords:** Acute pulmonary embolism; Catheter thrombolysis; Suction thrombectomy; Aspiration thrombectomy

Acute pulmonary embolism (PE) is a leading cause of in-hospital morbidity and mortality that can vary in severity.[1] Over the past two decades, the increase in the incidence of PE, partly owing to the higher diagnosis rates and the aging population, has driven practice toward more advanced treatment modalities.[2] The aim of treatment is mainly focused on preventing mortality and, secondarily, PE recurrence and any potential late-onset PE complications.

The current standard of care guidelines recommend anticoagulation for low-risk PE and systemic thrombolysis for high-risk (massive) PE associated with hypotension.[3-5] In selected patients without hypotension but with evidence of cardiopulmonary deterioration manifested by elevated cardiac biomarkers and findings of right ventricular (RV) strain (intermediate risk or submassive PE), the risk-benefit ratio may also be in favor of thrombolytic therapy to help to prevent decompensation.[3-5]

The inherent limitations with systemic thrombolytics have driven contemporary practice toward catheter-directed interventions that are presumed to provide

From the Heart and Vascular Institute, University of Pittsburgh Medical Center.

Author conflict of interest: none.

Presented during the plenary session at the Forty-sixth Annual Symposium of the Society for Clinical Vascular Surgery, Las Vegas, Nev, March 17-21, 2018.

Correspondence: Efthymios D. Avgerinos, MD, Heart and Vascular Institute, South Tower, Bldg 3, Office 351.1, Presbyterian University Hospital, 200 Lothrop St, Pittsburgh, PA 15213 (e-mail: avgerinose@upmc.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X



https://doi.org/10.1016/j.jvsv.2018.10.025

similar therapeutic benefits while decreasing complication rates owing to the lower doses or even the absence of lytics.[6-9] The Ultrasound-Assisted Catheter Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism (ULTIMA) randomized trial, the prospective SEATTLE II trial, the Pulmonary Embolism Response to Fragmentation, Embolectomy, and Catheter Thrombolysis (PERFECT) registry, and multiple other studies, including our institutional experience, have demonstrated the efficacy and relative safety of catheter-directed thrombolysis (CDT) triggering more interest in catheter interventions as first-line treatment for acute massive and high-risk submassive PE.[7-13] Alongside, novel suction thrombectomy (ST) devices have been introduced primarily for high-risk PE cases, but they are also under investigation for use in intermediate-risk PE.[14] These devices carry unique advantages based on their ability to rapidly physically remove thrombus, avoiding use of thrombolytics (and their associated complications) or the need for major open surgery. However, no evidence currently exists on their effectiveness compared with the smaller profile "standard" catheter thrombolysis. The aim of the study is to compare clinical outcomes of these two interventional options.

## ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective cohort study
- **Key Findings:** Suction thrombectomy in 18 patients and catheter-directed thrombolysis in 54 matched patients resulted in similar clinical success with no difference in major bleeding, stroke, or death rates.
- **Take Home Message:** This study suggests that suction thrombectomy is a potential alternative or complementary option to catheter-directed thrombolysis for patients with pulmonary embolism with contraindication to thrombolytics or severely compromised hemodynamic profile.

## METHODS

This study 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 CDT or ST for acute high-risk (massive) and intermediate-risk (submassive) PE between 2011 and 2017 were identified from a prospectively maintained database. PE types were classified according to published guidelines.[3-5] High-risk PE is defined as hypotension sustained for at least 15 minutes or requiring vasopressors. Intermediate-risk PE is defined as RV dysfunction on echocardiography or computed tomography scans and/or positive cardiac biomarkers in a hemodynamically stable patient.

Chart review included demographics, risk factors and cardiac biomarkers (troponin and brain natriuretic peptide), lower extremity venous duplex studies, intraprocedural records, and periprocedural outcomes and complications. Baseline and postintervention echocardiographic parameters were also collected.

The end point was clinical success, which was defined as survival to hospital discharge without major bleeding, perioperative stroke, or other major procedure-related adverse event (eg, heart or valve injury) and without decompensation or persistent shock for the submassive and massive PE groups, respectively.

Major bleeding events were defined according to the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) classification where both GUSTO moderate and GUSTO severe constitute major bleeding.[15] GUSTO moderate includes bleeding requiring transfusions without causing hemodynamic instability, whereas GUSTO severe includes bleeding that causes hemodynamic compromise and requires an intervention or bleeding that is intracranial. Absolute and relative contraindications for thrombolysis were defined as per the American Heart Association guidelines.[16,17]

Echocardiographic parameters for assessing pretreatment and post-treatment RV function were blindly and independently reviewed by two raters (E.A. and A.A.). Mean values were used for study analysis. Echocardiographic measurements were in accordance with the ULTIMA protocol.[7]

**Treatment protocol.** Patients not on heparin at the time of admission were given a bolus of 80 IU/kg, followed by an infusion of 18 IU/kg/h intravenously. If on heparin at admission, an infusion was continued to maintain an activated partial thromboplastin time of 68 to 106 seconds per institutional protocol. The decision to undergo any intervention was determined by the institution's multidisciplinary PE response team (PERT) consisting of pulmonary, critical care, cardiology, vascular surgery, and cardiothoracic services.

The PERT decision for any intervention is based on an evolving protocol that considers patients with intermediate to high risk (RV dysfunction on imaging and positive cardiac biomarkers [troponin >0.1 ng/mL and brain natriuretic peptide >100 pg/mL]) and high-risk PE as potential candidates. RV dysfunction is defined as an RV/LV ratio of greater than 0.9 on echocardiography or computed tomography scanning.

An inferior vena cava (IVC) filter is generally used in patients with contraindication to anticoagulation, selectively in patients with submassive PE with low cardiopulmonary reserve, and in most patients with massive PE. An institutional protocol for IVC filter retrieval is carried out by dedicated staff where patients are followed and contacted to return for filter retrieval.

**Catheter intervention technique.** Techniques and device selection have evolved over the years and are guided by multiple variables including the PERT, device availability, learning curve, physician preference, and level of comfort with each technique. Other than the contraindication for lytics recently being in favor of ST, there is no strict procedure type. Our institution has been otherwise participating in past and ongoing trials for CDT and ST, so we have tried to accommodate all alternatives. The reported procedures have been performed by eight physicians (vascular surgeons and cardiologists).

Ultrasound-guided femoral or internal jugular vein access is attained in all patients. For bilateral PE, two single-lumen femoral sheaths or dual-lumen jugular or femoral sheaths are used. An IVC filter is inserted before pulmonary artery catheterization, if necessary. A wire is then directed toward the pulmonary arteries. The wire may go through the chordae tendineae of the tricuspid valve as it crosses the right atrium into the right ventricle. As long as a small bore (≤6F) catheter/device is used, this procedure will be uneventful. With larger catheters, the chordae can rupture, resulting in tricuspid valve insufficiency. To prevent such complication, a pigtail or an inflated balloon catheter (eg, Swan Ganz) should be used to cross the tricuspid valve when large devices are considered. A pulmonary arteriogram is obtained to locate the clot. Standard CDT protocol involves the use of unilateral or bilateral 5-cm multiside 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 is given when needed, followed by lysis initiation at a rate of 0.5 to 1.0 mg/h. Ultrasound-assisted thrombolysis with the Eko-Sonic catheter (EKOS Corp, Bothell, Wash) is another frequently used CDT alternative.

When ST is considered (per physician preference), the intended for use device is introduced over a stiff wire. Devices used in this series were: AngioVac (Angiodynamics), Arrow-Trerotola (PTD; Arrow, Reading, Pa), Indigo (Penumbra, Alameda, Calif), and FlowTriever (INARI Medical, Irvine, Calif).

Patients are typically monitored in the intensive care unit. The heparinization dosing protocol during catheter directed lysis has changed from being subtherapeutic early in our experience to low therapeutic (activated partial thromboplastin time of 40–60 seconds). After the intervention, all patients are maintained on full systemic anticoagulation and are eventually transitioned to long-term oral anticoagulation. No additional medications, such as prostanoids, were used for pulmonary hypertension. CDT termination gradually evolved from operating room lysis check to bedside catheter removal depending on the improvement of different parameters: clinical (oxygen requirement/oxygen saturation, shortness of breath, chest pain), hemodynamic (blood pressure, heart rate), and echocardiographic (eg, RV strain), or any adverse event that necessitates cessation of treatment. IVC filters were retrieved at a later date, if applicable.

**Statistical analysis.** Patients were divided in two groups, the CDT group and the ST group. Because the number of ST cases was significantly lower and to minimize selection bias, a nearest-neighbor matching was applied to identify at least three patients that matched as closely as possible on the following six variables: age, gender, type of PE, acute deep venous thrombosis, pulmonary disease, and year of procedure.

Descriptive characteristics are reported as number of cases and percentages or as mean ± standard deviation. The $\chi^2$ and Fisher exact tests were used to compare dichotomous covariates between the two groups (CDT and ST), and independent and paired *t*-tests were used to assess continuous covariates. Interobserver agreement for the echocardiographic parameters between the two investigators' measurements was previously assessed by Lin's concordance correlation coefficient, (rho-c) 0.552, 95% confidence interval, 0.462–0.642, and by Bland-Altman analysis (mean RV/LV difference between the two raters: −0.075 (95% confidence interval, −0.452 to 0.302).[14,18] Results were considered statistically significant if $P < .05$. Analysis was performed using Statistical Package for the Social Sciences, version 22 (SPSS Inc, Chicago, Ill) and Stata 14 (Stata Corp LP, College Station, Tex).

## RESULTS

During the study period, 277 patients diagnosed with acute PE received an intervention. Fifty-four CDT patients (63.5 ± 14.2 years of age; 18 massive, 36 submassive PE) were matched to 18 ST (64.1 ± 14.1 years of age; 6 massive, 12 submassive PE) patients. Baseline characteristics of the two groups are summarized in Table I. Significantly more patients in the ST group had a major contraindication for lytics (1.9% for CDT vs 50% for ST; $P < .001$).

**Procedural data.** In the CDT group, 38 (70.4%) were treated with ultrasound-assisted thrombolysis and the rest were dripped using a standard multisidehole catheter. The mean alteplase dose was 24 ± 12 mg. An IVC filter was inserted in 14 patients (25.9%).

In the ST group, 1 Arrow-Trerotola PTD (Teleflex, Wayne, Pa), 1 AngioVac (Angiodynamics), 8 Indigo (Penumbra), and 8 FlowTriever (INARI Medical) devices were used. Three patients received on-table alteplase (4, 10, and 30 mg) and an IVC filter was placed in eight patients (44.4%).

**In-hospital clinical outcomes.** Table II summarizes the clinical outcomes by treatment modality. There was no significant difference in major bleeding (8 [14.8%] for CDT vs 3 [16.7%] for ST; $P > .999$; GUSTO severe 1 [1.8%] for CDT vs 1 [5.6%] for ST; $P > .999$), transfusions (7 [13.0%] for CDT vs 2 [11.11%] for ST; $P > .999$), and stroke (2 [3.7%]

**Table I.** Characteristics of study population by treatment type

| | CDT (n = 54) | ST (n = 18) | *P* value |
|---|---|---|---|
| PE type (massive) | 18 (33.3) | 6 (33.3) | >.999 |
| Arrest/CPR | 4 (7.4) | 2 (11.1) | .636 |
| Age | 63.5 ± 14.2 | 64.1 ± 14.1 | .871 |
| Male sex | 22 (40.7) | 9 (50) | .492 |
| Acute DVT | 43 (79.6) | 12 (66.7) | .262 |
| Malignancy | 11 (20.4) | 7 (38.9) | .116 |
| Hypercoagulable state | 2 (3.7) | 17 (5.6) | >.999 |
| Pulmonary disease | 10 (18.5) | 3 (16.7) | >.999 |
| Troponin, ng/mL | 0.79 ± 1.77 | 0.97 ± 1.40 | .702 |
| BNP, pg/mL | 493.3 ± 383.0 | 266.7 ± 237.5 | .056 |
| RV/LV ratio preoperatively | 1.12 ± 0.24 | 1.11 ± 0.13 | .839 |
| Contraindication for lysis | | | <.0001 |
| Major | 1 (1.9) | 9 (50.0) | |
| Minor | 19 (35.2) | 3 (16.7) | |

*BNP,* Brain natriuretic peptide; *CDT,* catheter-directed thrombolysis; *CPR,* cardiopulmonary resuscitation; *DVT,* deep venous thrombosis; *LV,* left ventricular; *PE,* pulmonary embolism; *RV,* right ventricular; *ST,* suction thrombectomy.
Values are presented as mean ± standard deviation or number (%).

for CDT vs none for ST; $P = .408$). None of the three patients who received on-table alteplase in the ST group suffered any major bleeding event. Death rates appear higher for ST but the difference did not reach significance (2 [3.7%] for CDT vs 3 [16.7%] for ST; $P = .096$).

One patient (AngioVac) from the ST group suffered tricuspid valve rupture and two patients in CDT group required surgical thrombectomy. Clinical success was not significantly different between groups (75.9% for CDT vs 61.1% for ST; $P = .224$). The association was similar when assessing the RV/LV ratio improvement (0.30 ± 0.19 for CDT vs 0.17 ± 0.16 for ST; $P = .097$).

In the subgroup of patients with submassive PE, clinical success was not statistically different between groups (86.1% for CDT vs 66.7% for ST; $P = .135$).

## DISCUSSION

Our results suggest that CDT seems to have similar outcomes with ST in the management of acute PE. Based on our experience and practice, ST should be primarily viewed as a complementary option for patients with contraindication for thrombolytics or severely compromised hemodynamic profile and can yield good results in an otherwise highly morbid population. Our data can serve as a pilot for future analyses of larger and more homogenous cohorts.

The increased use of catheter interventions has been attributed to both an increased incidence of PE and to a presumably improved efficacy and safety profile as compared with systemic thombolysis.[6,7,18-20] This current appeal for catheter interventions comes as an

**Table II.** Clinical outcomes by treatment modality

| | CDT (n = 54) | ST (n = 18) | *P* value |
|---|---|---|---|
| Clinical success | 41 (75.9) | 11 (61.1) | .224 |
| Intensive care length of stay | 3.96 ± 6.83 | 3.65 ± 3.26 | .855 |
| Hospital length of stay | 7.51 ± 6.78 | 8.88 ± 4.69 | .441 |
| Transfusions | 7 (13.0) | 2 (11.1) | >.999 |
| Major bleeding | 8 (14.8) | 3 (16.7) | |
| GUSTO severe | 1 (1.8) | 1 (5.6) | >.999 |
| Surgical thrombectomy | 2 (3.7) | 0 | >.999 |
| Heart/valve injury | 0 | 1 (5.6) | .250 |
| Stroke | 2 (3.7) | 0 | >.999 |
| Death | 2[a] (3.7) | 3[a] (16.7) | .096 |
| RV/LV improvement | 0.30 ± 0.19 | 0.17 ± 0.16 | .097 |

*CDT,* Catheter-directed thrombolysis; *GUSTO,* Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries; *LV,* left ventricular; *RV,* right ventricular; *ST,* suction thrombectomy.
Values are presented as mean ± standard deviation or number (%).
[a]One on-table death.

extrapolation from the Pulmonary Embolism Thrombolysis trial and a consequent meta-analyses, which demonstrated superior mortality and decompensation prevention for systemic thrombolysis when compared with anticoagulation alone but at the expense of high stroke and bleeding rates.[8,9] The prospective ULTIMA trial and PERFECT registry, along with multiple other single-center studies, exemplified the relative safety profile of these procedures, which have been shown to result in improved early RV function recovery as compared with anticoagulation.[7,13,20] Technically, catheter thrombolytics are administered through small mutisidehole catheters that have been navigated inside the clot. These catheters can be enhanced with ultrasound wires, providing the so-called ultrasound-assisted thrombolysis (Ekos Corp.).

Because catheter interventions have been increasingly used for PE, new endovascular devices have entered the field offering treatment alternatives without the need for lytics, which even in smaller doses are not always risk free. ST is not a new concept and has already been introduced in the past by Greenfield and others, but was never widely adapted. The need to remove large amounts of clot from the large pulmonary arteries and avoid lytics has led to the introduction of new flexible large bore systems. The most popular and widely used devices in U.S. practice are the Flowtriever (Inari Medical) and the Indigo CAT 8 (Penumbra) devices. The Flowtriever is a 20F catheter and uses self-expanding disks that are unsheathed to engage the thrombus. The thrombus is removed by simultaneous manual aspiration and withdrawal of the disks. The FLARE registry was recently completed with favorable results and U.S. Food and Drug Administration approval is awaited.[21] The Indigo system works on the principle of thrombus aspiration and consists of an 8F angled or straight catheter connected to a suction pump. The EXTRACT PE registry is actively recruiting patients and the results will be available in 2019. Of note, both devices lack a means to return blood to the patient and can lead to significant blood loss, if not embedded in clot. Finally, the AngioVac system (Angiodynamics), although very powerful and successful in retrieving thrombus from the IVC, it is too rigid to navigate in the pulmonary arteries and it is no longer marketed for this indication.

Our study is the first to our knowledge to attempt a comparison between catheter thrombolysis and ST. The sample was small to prompt significant differences between groups, but outcomes were largely similar, while acknowledging that ST was used primarily in patients with contraindications for CDT. In our practice, as of now, we favor CDT because it is a technically easier procedure requiring small catheters; the ST devices are larger and cumbersome to use requiring a longer learning curve. Interestingly, a recent study analyzed the computed tomographic pulmonary angiograms of 60 patients with submassive and massive PE treated with ultrasound-assisted thrombolysis and correlated the change in blood volume of the pulmonary arteries from baseline to 48 hours with change in RV volume measured by computed tomographic scans. The investigators found that increased blood volume through the distal, but not central, pulmonary artery vasculature correlates with reduction in RV volume.[22] It is self-explanatory that thrombolytics can reach the distal lung perfusing branches, whereas the ST devices can mainly remove more centrally located thrombus. This finding, coupled with the study described elsewhere in this article, may point to an at least technical advantage for CDT.

It needs to be stressed that ST devices can be an excellent tool for those patients who are contraindicated for lytics and for those patients who are about to decompensate or indicate signs of worsening instability that may lead to an arrest because there is no need to wait as with catheter-directed lytics to achieve a clinically meaningful effect. It is also of note that our ST group experienced no strokes, whereas the thrombolysis group had two strokes. ST, in experienced hands, can yield optimal results and selectively replace the need for open surgical thrombectomy, known to be related to high complication rates.[23,24]

In our era of cost-effective medicine, it would be worth taking into consideration a cost comparison between the different techniques; however, our data are not sufficient for a thorough analysis of overall costs, particularly because multiple ST devices were used. Device costs are roughly estimated as follows: standard multisidehole catheter approximately $120 (time two for bilateral infusion), EKOS catheter approximately $2600 (times two for bilateral infusion), Flowtriever approximately $5040, Indigo CAT8 approximately $5580, and AngioVac approximately $11,500.

The results of our study need to be interpreted with caution. This is a retrospective small study with inherent biases. Despite matching the two groups, still patients who received ST may have been sicker within the intermediate- or high-risk PE spectrum. It is unlikely that a randomized comparative trial will ever be performed, but similar series from high-volume centers will allow more reliable conclusions.

We acknowledge the contribution of our biostatistician Dr Larry Fish in the statistical analysis of the data and the interpretation of our results.

## AUTHOR CONTRIBUTIONS

Conception and design: EA, CT, GK, RC
Analysis and interpretation: EA, AAA, CT, GK, RC
Data collection: EA, AAA, BW, ZS, BM
Writing the article: EA, AAA, CT, BW, ZS, BM, RC
Critical revision of the article: EA, GK, RC
Final approval of the article: EA, AAA, CT, BW, ZS, BM, GK, RC

Statistical analysis: EA, AAA
Obtained funding: Not applicable
Overall responsibility: EA

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Submitted May 18, 2018; accepted Oct 1, 2018.