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Catheter-directed interventions compared with systemic thrombolysis achieve improved ventricular function recovery at a potentially lower complication rate for acute pulmonary embolism

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Abstract

Objective: Catheter-directed interventions (CDIs) are increasingly performed for acute pulmonary embolism (PE) as they are presumed to provide similar therapeutic benefits to systemic thrombolysis (ST) while decreasing the associated complications. The purpose of this study was to compare outcomes between CDI and ST.

Methods: Consecutive patients who underwent CDIs or ST for massive or submassive PE between 2006 and 2016 were identified. Clinical and echocardiographic parameters at baseline and after treatment were recorded. Clinical success was defined as decompensation resolution (or prevention) without major bleeding, stroke, other major treatment-related event, or in-hospital death. The χ^2 test and t-test were used for between-groups comparisons.

Results: There were 213 patients who received CDIs (standard catheter thrombolysis in 56, ultrasound-assisted thrombolysis in 146, suction thrombectomies in 10, and pharmacomechanical thrombolysis in 1) and 104 patients who received ST (94 high dose [100 mg], 10 low dose [50 mg]). At baseline, CDI and ST groups had comparable echocardiographic parameters, demographics, and comorbidities, except for PE type (massive PE, 8.5% for CDIs vs 69.2% for ST; $P < .001$), age (60.2 ± 14.9 years for CDIs vs 55.9 ± 17.3 years for ST; $P = .023$), and renal

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function (glomerular filtration rate, 78.1 ± 33.7 mL/min/1.73 m^2 for CDIs vs 64.1 ± 35.2 mL/min/1.73 m^2 for ST; P =.001). Without stratifying per PE type, CDIs had a higher clinical success rate (87.8% vs 66.3%; P < .001) and a lower rate of major bleed (8.0% vs 19.2%; P =.003), stroke (1.4% vs 4.8%; P = .120), and death (1.4% vs 13.5%; P < .001). On stratifying by PE type, there was no difference in clinical success between groups. The mean reduction in right ventricular/left ventricular diameter ratio between baseline and the first post-treatment echocardiographic examination (within 30 days) was significantly higher for CDI (0.27 ± 0.20 vs 0.18 ± 0.15; P =.037). Beyond 30 days, there was no echocardiographic difference between groups. There was no significant difference in clinical outcomes and echocardiographic parameters between standard and ultrasound-assisted CDIs.

Conclusions: CDIs provide improved recovery of right ventricular function compared with ST. Major bleeding and stroke complications may be lower, but larger studies are needed to validate this. CDIs are complementary to ST, and their use should be individualized on the basis of the patients' clinical presentation, risk profile, and local resources.

Acute pulmonary embolism (PE) is a leading cause of in-hospital morbidity and mortality with a broad spectrum of severity.[1] Its increased incidence during the past two decades, in part due to the higher diagnosis rate and the aging population, has driven practice toward newer treatment modalities.[2] The goal of treatment is focused primarily on preventing mortality and secondarily on preventing PE recurrence and late-onset chronic thromboembolic pulmonary hypertension. PE risk classification has evolved to reflect the severity and subsequent mortality of an acute episode. Standard of care guidelines recommend anticoagulation for low-risk PE; systemic thrombolysis (ST) is reserved for high-risk (massive) PE associated with hypotension.[3–5] In selected patients without hypotension but with evidence of cardiopulmonary deterioration, such as right ventricular (RV) strain and elevated cardiac biomarkers (intermediate-risk or submassive PE), the risk-benefit ratio may also favor thrombolytic therapy to prevent decompensation.[3–5] Because of the high associated risks, mainly those of major bleed and stroke, and because of a wide spectrum of contraindications, only 30% of patients who need it are actually receiving ST.[6] The inherent limitations with ST use have driven contemporary practice toward catheter-directed interventions (CDIs) that are presumed to provide similar therapeutic benefits while decreasing complication rates as a result of the lower doses or even the absence of lytics.[7–10] The Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism (ULTIMA) randomized trial, A Prospective, Single-arm, Multicenter Trial of EkoSonic Endovascular System and Activase for Treatment of Acute Pulmonary Embolism (SEATTLE II), the Pulmonary Embolism Response to Fragmentation, Embolectomy, and Catheter Thrombolysis (PERFECT) registry, and multiple case series, including our institutional experience, have demonstrated a relative safety and efficacy of CDI, triggering more interest in CDI as first-line treatment of acute massive and high-risk submassive PE.[8,11–16]

Whereas both CDI and ST have been shown to improve and to reverse RV dysfunction, comparative studies investigating the degree of RV function improvement for each modality are lacking.[8,17] The significance of RV function was assessed in a recent meta-analysis showing an increase in short-term mortality in hemodynamically significant PE patients with

RV dysfunction.[18] Studies directly comparing clinical outcomes of CDI vs ST are few and controversial. The U.S. National Inpatient Sample (NIS) analysis has led to conflicting results regarding mortality differences yet matching results regarding the consistently lower stroke rates for CDI.[7,19]

The objective of this study was to compare the clinical and echocardiographic outcomes between CDI and ST for acute massive and submassive PE.

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 treatment for acute PE between January 2006 and September 2016 were identified from our institution's electronic medical records. Patients with low-risk PE on presentation were excluded from the analysis, leaving patients with acute high-risk (massive) and intermediate-risk (sub-massive) PE treated with CDI and ST. This classification of PE types is in accordance with published guidelines.[3,5] High-risk PE is defined as sustained hypotension for at least 15 minutes or requiring vasopressors. Intermediate-risk PE is defined as RV dysfunction on echocardiography or computed tomography scans or presence of cardiac biomarkers but without hypotension.

Records were reviewed for demographics, risk factors, laboratory markers such as glomerular filtration rate (which was calculated using the Modification of Diet in Renal Disease method) and cardiac biomarkers (troponin and brain natriuretic peptide), lower extremity venous duplex ultrasound studies, intraprocedural data, and periprocedural complications as well as longer term data when available. Echocardiographic parameters were collected for each group at baseline, after CDI or ST, and at follow-up. The post-CDI or post-ST echocardiography was performed within 30 days of procedure or treatment, respectively. Follow-up echocardiographic parameters were obtained from the most recent report beyond the initial 30-day period after treatment. Patients were stratified into intermediate-risk vs high-risk PE groups per our definition.

Our primary outcome was 30-day clinical success, a composite outcome defined as decompensation resolution for massive PE (or prevention of decompensation for submassive PE) without major bleeding, stroke, other major treatment-related adverse event (eg, heart or valve injury), need for surgical embolectomy, or in-hospital death. Decompensation was defined as persistent hypotension (and need for pressor support) for patients with massive PE and as development of hypotension for patients with submassive PE despite treatment.

Major bleeding events were defined according to the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) classification, whereby both GUSTO moderate and GUSTO severe constituted major bleeding.[20] GUSTO moderate includes bleeding requiring transfusions without hemodynamic compromise,

whereas GUSTO severe includes bleeding that causes hemodynamic instability and requires an intervention and bleeding that is intracranial.

Absolute and relative contraindications to thrombolysis were defined per the American Heart Association guidelines.[21]

Echocardiographic parameters for assessing RV function before and after treatment were blindly and independently reviewed by two raters (A.N.A.A. and N.L.L.), and mean values were used for analysis. Echocardiographic measurements were made in accordance with the ULTIMA protocol.[8]

Treatment protocol.

Patients not receiving heparin at the time of admission were given an intravenous bolus of 80 IU/kg, followed by an infusion of 18 IU/kg/h. If the patient was receiving heparin at admission, infusion was continued to maintain an activated partial thromboplastin time of 68 to 106 seconds per institutional protocol. Between 2006 and 2009, ST was the only treatment modality. Since 2009, CDI procedures gradually entered our practice on a physician-based preference; and since 2014, the decision to undergo CDI vs ST vs surgical thrombectomy vs anticoagulation alone for PE treatment was determined by the institution's multidisciplinary PE response team consisting of pulmonary, critical care, cardiology, vascular surgery, and cardiothoracic services.

The PE response team's decision is based on an evolving protocol that considers intermediate- to high-risk (echocardiographic RV dysfunction and presence of cardiac biomarkers [troponin >0.1 ng/mL and brain natriuretic peptide >100 pg/mL]) and high-risk (systolic blood pressure <90 mm Hg for at least 15 minutes or requiring inotropic support) PE patients potential candidates for CDI. RV dysfunction is defined as echocardiographic or computed tomographic RV/left ventricular (RV/LV) diameter ratio >0.9. The majority of the patients (>90%) receive baseline echocardiography. In our current practice, CDIs are favored in submassive PE cases eligible for thrombolysis, whereas massive PE treatment is individualized on the basis of the patient's risk profile.

An inferior vena cava filter was generally used in patients with a contraindication to anticoagulation and selectively in high-risk patients with low cardiopulmonary reserve. An institutional protocol for inferior vena cava filter retrieval is in place; patients are followed up and contacted by dedicated staff and asked to return for filter retrieval.

Systemic lysis protocol.

All PE patients receiving ST are monitored and treated in an intensive care unit setting. Barring any contraindication, PE patients received an ST dose of 50 mg or 100 mg of recombinant tissue plasminogen activator infused during 2 hours. Unfractionated heparin infusion is typically held within this time interval.

Catheter intervention technique.

Ultrasound-guided femoral or internal jugular vein access is used in all patients. Dual-lumen jugular or femoral sheaths or two single-lumen femoral sheaths are used for bilateral PEs. If

necessary, an inferior vena cava filter is inserted before pulmonary artery catheterization. A wire is then navigated toward the pulmonary arteries. As the wire crosses from the right atrium into the right ventricle, it may go through the chordae tendineae of the tricuspid valve. As long as the catheter or device used is small bore (#8F), this will be uneventful. When larger catheters are used, the chordae can rupture, leading to tricuspid valve insufficiency. To prevent this, when large devices are considered, crossing of the tricuspid valve should be done either with a pigtail or with an inflated balloon catheter (eg, Swan-Ganz). A pulmonary arteriogram is obtained to assess the clot's location. Standard CDI protocol includes 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 is given if it is deemed necessary, followed by the initiation of lysis at a rate of 0.5 to 1 mg/h. Another frequent CDI alternative involves the use of ultrasound-assisted thrombolysis with the EkoSonic catheter (EKOS Corp, Bothell, Wash). In a few cases, aspiration thrombectomy using the AngioVac device (AngioDynamics) or the Arrow-Trerotola thrombolytic device (PTD; Arrow, Reading, Pa), rheolysis using the AngioJet device (Boston Scientific), catheter-based mechanical fragmentation, and on-table only catheter-directed infusion (without initiation of continuous infusion) were used per the physician's preference. Patients are monitored in the intensive care unit.

Our heparinization protocol during catheter-directed lysis shifted from subtherapeutic dosing early in our experience to low therapeutic dosing (activated partial thromboplastin time of 40–60 seconds). After intervention, all patients remained on full systemic anticoagulation, after which they were transitioned to long-term oral anticoagulation. No adjunct medications (eg, prostanoids) are used for pulmonary hypertension. Termination of catheter-directed thrombolysis gradually evolved through operating room lysis check to bedside catheter removal based on improvement of clinical (oxygen requirements, oxygen saturation, shortness of breath, chest pain), hemodynamic (blood pressure, heart rate), and echocardiographic (RV strain) parameters or any complication that necessitates discontinuation of treatment. Pulmonary artery pressures are transduced before catheter removal at bedside and compared with the intraoperative ones. Filter retrieval is performed at a later date, if applicable.

Statistical analysis.

Descriptive characteristics are reported as mean ± standard deviation or as number of cases and percentages. Dichotomous covariates between the two groups (CDI and ST) were compared using the χ^2 and Fisher exact tests; continuous covariates were assessed using independent and paired *t*-tests. A univariate χ^2 analysis was performed between the clinical outcomes and mode of treatment (CDI vs ST) stratified according to PE type.[22] This model was repeated using inverse propensity score weighting, with propensity scores computed using the variable "age," "PE type," and "contraindication for lytics." Interobserver agreement for the echocardiographic parameters between the two investigators' measurements was assessed by Lin's concordance correlation and by Bland-Altman analysis. Results were considered statistically significant if $P<.05$. Data analysis was

performed using Statistical Package for the Social Sciences, version 22 (IBM Corp, Armonk, NY) and Stata 14 (including Pscore by S.O. Becker and A. Ichino; StataCorp LP, College Station, Tex).

RESULTS

During the study period, 213 patients received CDI and 104 patients received ST for the treatment of acute PE. The mean age of the cohort was 58.8 ± 15.8 years, and 152 (47.9%) were male. Baseline characteristics are listed in Table I. The CDI group was older (60.2 ± 14.9 vs 55.9 ± 17.3 years; $P = .023$), with better renal function (glomerular filtration rate, 78.1 ± 33.7 vs 64.1 ± 35.2 mL/min; $P = .001$) and with a preponderance of submassive PEs (91.5% vs 30.8%) compared with ST, which was mainly used in massive PEs (8.5% vs 69.2%; $P < .001$). Although not statistically significant, catheter interventions were used more frequently in cases with absolute contraindications to thrombolytics (5.2% vs 2.9%; $P = .239$).

Procedural data.

Data are summarized in Table II. The majority of CDI patients received ultrasound-assisted thrombolysis (146 [68.5%]); 56 (26.3%) received standard catheter-directed thrombolysis, 10 (4.7%) patients received aspiration thrombectomy, and 1 (0.5%) patient underwent rheolytic thrombectomy. The mean alteplase dose was 23.2 ± 10.7 mg (median, 23 mg; range, 0–63 mg), and the mean infusion time was 17.0 ± 9.1 hours (range, 0–51 hours). Interventions were bilateral in most CDI cases (196 [92.0%]). An inferior vena cava filter was inserted in 56 (26.3%) patients; 171 (80.3%) patients required a single trip to the angiography suite, with catheters removed at bedside and termination of infusion based on clinical and echocardiographic parameters. In the ST group, mean alteplase dose was 95.8 ± 16.3 mg (range, 40–142 mg); 94 (90.4%) patients received the high thrombolytic dose (≥100 mg), whereas 10 (9.6%) patients received the low thrombolytic dose (range, 40–50 mg).

In-hospital outcomes.

Clinical success was observed in 187 (87.8%) patients in the CDI group and in 69 (66.3%) patients in the ST group ($P < .001$). In-hospital mortality rates (CDI, 1.4%; ST, 13.5%; $P < .001$), major bleeding rates (CDI, 8.0%; ST, 19.2%; $P = .003$), and stroke rates (CDI, 1.4%; ST, 4.8%; $P = .120$) were lower in the CDI group. Two major CDI procedural events included a coronary sinus perforation leading to cardiac tamponade and tricuspid valve injury when the AngioVac was used (both included in the major bleed rate). Both patients underwent open heart surgery with good outcomes.

Multivariate analysis and propensity matching for clinical success confirmed PE type as the most powerful predictor, abolishing the effect of all other confounders including the type of treatment.

On stratifying per PE type (massive and submassive), there were no significant differences between the CDI and ST groups in all outcomes, despite that ST was associated with a seemingly higher death rate in the massive PE subgroup (19.4% vs 5.6%; $P = .287$) and a higher stroke rate in the submassive PE subgroup (3.1% vs 1.0%; $P .367$; Table III). Of

patients with massive PE, 5.6% did not improve on CDI compared with 19.4% of patients in the ST group (P=.287). For submassive PEs, decompensation rates were equal between the groups (3.1%). Of note, during the last 3 years of our CDI practice (168 cases), we had no procedure-related adverse events along with a reduction in CDI failure rates from 15.6% to 11.3% (P= .440), indicating our shift toward more careful selection of patients.

There was no significant difference in clinical outcomes and echocardiographic parameters between standard and ultrasound-assisted CDIs.

Echocardiographic parameters.

Baseline echocardiographic parameters (RV/LV, pulmonary artery pressures, and tricuspid regurgitant jet velocity) were comparable between the two groups (P > .05). Within 30 days, CDI lysis achieved a significantly greater improvement of RV function compared with ST (0.27 ± 0.20 vs 0.18 ± 0.15; P .037).

The echocardiographic follow up (>30 days) based on 77 CDI and 13 ST patients was 99.9 ± 82.3 days and 141.9 ± 103.4 days, respectively. There was a higher proportion of patients missing their >30-day follow-up echocardiogram in the ST group compared with the CDI group (87.5% vs 63.8%; P<.001). The mean differences between baseline and follow-up echocardiograms (beyond 30 days) were comparable. All echocardiographic parameters are summarized in Table IV.

Regarding the interobserver agreement of the RV/LV ratio measurements, Lin's concordance correlation coefficient (ρc) was 0.552 (95% confidence interval, 0.462–0.642). The Bland-Altman model gave a mean RV/LV difference between the two raters of 0.075 (95% confidence interval, 0.452 to 0.302; Fig).

DISCUSSION

Our results suggest that CDIs might have an at least comparable if not superior effect in reversing RV dysfunction compared with ST; however, the lower lytic dose with CDI may not necessarily translate to higher clinical success rates. A potentially lower stroke or bleeding rate may be offset by procedural complications or more liberal use of CDIs against traditional contraindications.

The increased use of CDI has been attributed both to the increased incidence of PE and to a presumed better efficacy and safety profile over ST.[7,16] This current appeal for CDI comes as an extrapolation from the Pulmonary Embolism Thrombolysis (PEITHO) trial and a subsequent meta-analysis showing superior mortality and decompensation prevention for ST compared with anticoagulation alone, at the cost of high bleeding and stroke rates.[9,10] Given the concern for these risks and the standard contraindications to thrombolytics, ST is eventually used in approximately 30% of eligible patients.[10] The prospective ULTIMA trial and PERFECT registry exemplified the CDI safety profile with no major bleeding or stroke events.[8,15] However, the SEATTLE II trial along with retrospective series demonstrated that CDIs are not bleeding risk-free procedures, even if stroke rates appear to be very low.[14,16,23] The SEATTLE II trial had a CDI success rate of 85.3% with an in-hospital mortality of

2.7%, adverse events related to device rate of 2.0%, and major bleeding rate of 10.0% with only one (0.7%) GUSTO severe bleeding.[14] Nonetheless, CDI has been shown to improve early RV function recovery compared with anticoagulation, with higher reductions in the RV/LV ratio.[16]

Our results are consistent with the literature in showing comparable clinical success rates, in-hospital mortality, and major bleeding rates for CDI and ST. Apart from one randomized study, real-world studies have revealed a CDI success rate ranging between 86% and 94%, comparable to our 87.8%.[7,13–15] The NIS study revealed a CDI success rate of 83.4% with an in-hospital mortality rate between 9.2% and 13.4% and a major bleeding rate between 3.2% and 8.5%; the ST group had a success rate of 72.0% with an in-hospital mortality of 10.3% to 21.8% and a major bleeding rate of 4.6% to 8.8%.[7,19]

Comparative analyses between CDI and ST, however, have yielded controversial results.[7,19] The NIS sample was queried twice; one study showed lower mortality rates (13.4% vs 21.8%; $P = .007$) and intracranial hemorrhage rates (0% vs 1.4%; $P = .08$) with CDI with comparable major bleeding rates (3.2% vs 4.6%; $P = .380$),[7] whereas the other analysis revealed comparable mortality rates (9.2% vs 10.3%; P =.300) and major bleeding rates (8.5% vs 8.8%; $P = .700$) with consistently lower intracranial hemorrhage rates (1.3% vs 2.8%; $P = .010$).[19] The mortality discrepancy, apart from potential methodologic flaws, highlights the difficulty in eliminating the inherent patient selection bias favoring better outcomes for CDI over ST. The favorable unadjusted mortality benefit for CDI over ST, both in the NIS data analysis and in our study, appears to reflect patient selection rather than treatment efficacy; propensity matching and PE type stratification eliminate the presumed CDI mortality benefit.[19] The absence of mortality benefit is not surprising, given the rapid improvement in RV function seen with both modalities in multiple studies and in ours.[8,24] Still, head-to-head comparison of the effect of treatment modality on RV function was lacking, and our study is the first one to demonstrate a potentially faster recovery in favor of CDI. This should be interpreted with caution as ST can be administered immediately at the bedside, whereas a CDI requires time-consuming operating room preparation, and if it involves catheter thrombolysis, it will still need time for the lytics to take effect (typically 6–12 hours). This may be of importance for the higher risk unstable patients.

Consistent with the NIS analysis, our data showed lower major bleeding (8.0% vs 19.2%; P .003) and intracranial hemorrhagic stroke rates (1.4% vs 4.8%; $P = .120$) with CDI, even though stroke differences were not significant. Significance was lost for major bleeding events in stratifying for PE type, so no definite conclusions can be made. The ST stroke rate appears higher than the one reported in recent literature, potentially related to our aggressive treatment strategies in all comers or the small sample. The comparative trends in favor of CDI are otherwise consistent with a recent meta-analysis showing that the major bleed and stroke rate with CDI is 4.7% and 0.4% compared with 9.2% and 1.5% with ST, repectively.[7,10,19,25] We should not overlook the procedure-related complications that may offset these potential bleeding reduction benefits. Yet as experience improves and the decisions on selection of patients mature, procedural complications and overall failures are anticipated to decrease. Our institutional clinical failure (decompensation or major bleeding/stroke or other

major treatment-related adverse event) rates have decreased during the last 3 years from 15.6% to 11.3% (P= .440).

This study is among the first analyses to compare linical and echocardiographic outcomes between CDI and ST for the management of acute PE; however, the results should be interpreted with caution, given the retrospective nature of the study. The study was limited by the number of outcome events. Selection bias favoring a cohort of higher risk patients in the ST group cannot be ruled out despite stratifying the clinical outcomes by PE type. The echocardiographic parameters had several missing data. The unsatisfactory correlation between the echocardiographic raters prevents a comprehensive assessment of the differential impact of CDI and ST on RV function at this stage. In addition, there was a between-group differential loss to echocardiographic follow-up beyond 30 days, which precludes solid conclusions regarding the long-term impact of either treatment on RV function. This, however, was not our primary end point, whereas prior studies have demonstrated that RV function normalizes after 30 days irrespective of treatment modality, and this is in agreement with our results. Finally, as there is no standardized CDI protocol within our institution, the ideal CDI technique, thrombolytic dose, and duration remain heterogeneous and unclear.

CONCLUSIONS

Whereas current guidelines recommend ST for high-risk PE, ineligibility of the patient due to thrombolytic contraindications and the increased bleed and stroke rate make CDI a favorable alternative with efficacy (RV function improvement) comparable to if not better than that of ST. The differences lie within the complication profile of each treatment modality, with the lower thrombolytic dose with CDI being counterbalanced by its invasive procedural nature. Under this prism, both treatment modalities should be complementary as they both have a role in the appropriate setting. Careful selection of patients in high-volume centers with appropriate CDI expertise is essential. PE response teams can help in this direction.

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ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective comparative cohort study
- **Take Home Message:** Comparison of results of catheter-directed intervention (CDI) in 213 patients with systemic thrombolysis (ST) in 104 patients for treatment of pulmonary embolism (PE) was performed. On stratifying by PE type, there was no difference in clinical success among groups, but CDIs improved recovery of right ventricular function compared with ST.
- **Recommendation:** The authors suggest that CDIs are complementary to ST for treatment of PE, and their use should be individualized on the basis of the patients' clinical presentation, risk profile, and local resources.

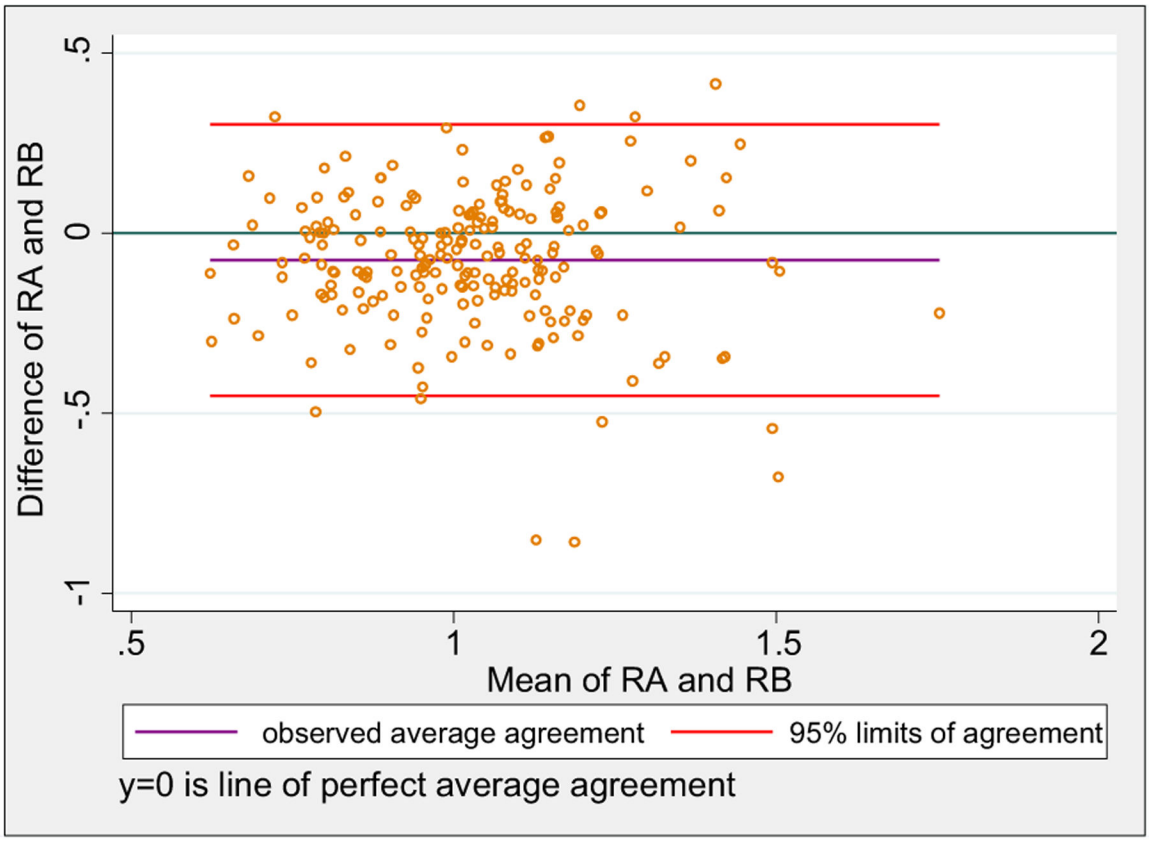

Fig.

Bland-Altman interobserver agreement plot of baseline right ventricular to left ventricular (*RV/LV*) ratio measured independently by two raters. The x-axis depicts RV/LV ratio by rater A (*RA*) plus RV/LV ratio by rater B (*RB*) divided by 2; the y-axis depicts RV/LV ratio by RA minus RV/LV ratio by RB.

Table I.

Characteristics of study population by treatment type

	Overall (N = 317)	CDI (n = 213)	ST (n = 104)	*P* value
Age, years	58.8 ± 15.8	60.2 ± 14.9	55.9 ± 17.3	.023
Male sex	152 (47.9)	106 (49.8)	46 (44.2)	.354
PE type, massive	90 (28.4)	18 (8.5)	72 (69.2)	<.001
sPESI score (=1)	294 (92.7)	191 (89.7)	103 (99.0)	.003
Acute DVT	192 (65.8)	132 (64.4)	60 (69.0)	.451
Hypercoagulable state	21 (6.7)	11 (5.2)	10 (9.6)	.141
Recent surgery	71 (22.4)	41 (19.2)	30 (28.8)	.054
Recent trauma	13 (4.1)	7 (3.3)	6 (5.8)	.304
Malignant disease	54 (17.0)	35 (16.4)	19 (18.3)	.683
Contraceptives	18 (5.7)	10 (4.7)	8 (7.7)	.288
Recent travel	22 (7.0)	19 (9.0)	3 (2.9)	.045
Previous DVT	51 (16.2)	38 (18.0)	13 (12.6)	.224
Previous PE	43 (13.7)	32 (15.2)	11 (10.6)	.265
Previous PE or DVT	43 (13.7)	34 (16.1)	9 (8.7)	.070
Previous stroke	4 (1.3)	3 (1.4)	1 (1.0)	.732
No contraindications	261 (82.3)	178 (83.6)	83 (79.8)	.239
Major contraindications	14 (4.4)	11 (5.2)	3 (2.9)	–
Minor contraindications	42 (13.2)	24 (11.3)	18 (17.3)	–
Hypertension	157 (49.7)	116 (54.7)	41 (39.4)	.011
Coronary disease	40 (12.7)	29 (13.5)	11 (11.0)	.664
Heart failure	18 (5.7)	11 (5.2)	7 (6.7)	.585
Pulmonary disease	61 (19.4)	47 (22.3)	14 (13.5)	.063
Oxygen on admission	19 (6.0)	13 (16.2)	6 (5.8)	.891
Pulmonary hypertension	11 (3.5)	5 (2.4)	6 (5.8)	.122
Current smoker	65 (20.6)	40 (18.9)	25 (24.3)	.266
Vena cava filter	85 (26.8)	56 (26.3)	29 (27.9)	.746
CFR >60 mL/min	207 (65.5)	153 (71.8)	54 (52.4)	<.001
GFR 30–59 mL/min	87 (27.5)	56 (26.3)	31 (30.1)	–

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	Overall (N = 317)	CDI (n = 213)	ST (n = 104)	*P* value
CFR <30 mL/min	22 (7.0)	4 (1.9)	18 (17.5)	–
CFR, mL/min	73.5 ± 34.8	78.1 ± 33.7	64.1 ± 35.2	.001
Troponin	1.1 ± 3.8	0.6 ± 1.0	2.2 ± 6.5	.020
BNP	440.1 ± 478.4	423.0 ± 484.1	492.4 ± 461.3	.361
Lysis dose	47.0 ± 36.5	23.2 ± 10.7	95.9 ± 16.6	<.001

BNP, Brain natriuretic peptide; *CDI*, catheter-directed intervention; *DVT*, deep venous thrombosis; *GFR*, glomerular filtration rate; *PE*, pulmonary embolism; s*PESI*, simplified Pulmonary Embolism Severity Index; ST, systemic thrombolysis.

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

Table II.

Procedural and treatment characteristics of catheter-directed intervention (CDI) and systemic thrombolysis (ST)

	CDI
Femoral access	167 (78.4)
Bilateral lysis	196 (92.0)
Type of intervention	
Standard catheter lysis	56 (26.3)
Ultrasound-assisted thrombolysis	146 (68.5)
Suction thrombectomy	10 (4.7)
Pharmacomechanical	1 (0.5)
Lysis fragmentation	5 (2.3)
On-table only infusion	
Mean tissue plasminogen activator, mg	23.2 ± 10.7
Operating room trips	
1	171 (80.3)
2	32 (15.0)
3	9 (4.2)
4	1 (0.5)
	ST
High alteplase dose (100 mg)	94 (90.4)
Low alteplase dose (50 mg)	10 (9.6)

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

Table III.

Clinical outcomes by treatment modality and pulmonary embolism (*PE*) type

	CDI No. (%)	ST No. (%)	*P* value
Overall (N = 317)	(n = 213)	(n = 104)	
Clinical success	187 (87.8)	69 (66.3)	<.001
In-hospital death	3 (1.4)	14 (13.5)	<.001
Major bleeding	17 (8.0)	20 (19.2)	.003
Stroke	3 (1.4)	5 (4.8)	.120
Massive PE (n = 90)	(n = 18)	(n = 72)	
Clinical success	11 (61.1)	39 (54.2)	.596
In-hospital death	1 (5.6)	14 (19.4)	.287
Major bleeding	5 (27.8)	19 (26.4)	.905
Stroke	1 (5.6)	4 (5.6)	1
Submassive PE (n = 227)	(n = 195)	(n = 32)	
Clinical success	176 (90.3)	30 (93.8)	.747
In-hospital death	2 (1.0)	0(0)	1
Major bleeding	12 (6.2)	1 (3.1)	.699
Stroke	2 (1.0)	1 (3.1)	.367

CDI, Catheter-directed intervention; *ST*, systemic thrombolysis.

Table IV.

Echocardiographic parameters at baseline, after treatment, and at follow-up

	Baseline		Within 30 days		Within 12 months		Difference: baseline vs 30 days		Difference: baseline vs 12 months	
	CDI	ST	CDI	ST	CDI	ST	CDI	ST	CDI	ST
RV/LV ratio	1.01 ± 0.22	1.06 ± 0.19	0.83 ± 0.18	0.93 ± 0.18	0.75 ± 0.17	0.83 ± 0.11	O.27± 0.20	0.18 ± 0.15	0.28 ± 0.18	0.35 ± 0.21
No.	150	70	103	45	72	13	61	31	48	9
Between-group comparison, CDI vs ST	*P*= .161		*P* = .002		*P*= .105		*P* = .037		*P* = .306	
Within-group comparison	–	–	–	–	–	–	*P* < .001	*P* = .001	*P* < .001	*P* < .001
Tricuspid regurgitant jet velocity	3.04 ± 0.66	2.98 ± 0.58	2.77 ± 0.59	2.80 ± 0.62	2.54 ± 0.66	2.33 ± 0.49	0.42 ± 0.57	0.35 ± 0.49	0.53 ± 0.78	0.83 ± 0.82
No.	152	69	88	32	67	12	50	23	45	9
Between-group comparison, CDI vs ST	*P* = .546		*P* = .798		*P* = .280		*P*= .614		*P* = .305	
Within-group comparison	–	–	–	–	–	–	*P* = .002	*P* = .157	*P* < .001	*P* < .001
Pulmonary artery pressure	48.3 ± 16.6	47.4 ± 13.8	39.1 ± 14.6	40.5 ± 13.3	34.9 ± 15.8	29.4 ± 10.9	11.8 ± 15.6	9.9 ± 11.9	16.7 ± 18.6	24.6 ± 21.6
No.	149	73	89	37	67	12	52	28	43	9
Between-group comparison, CDI vs ST	*P* = .689		*P*= .619		*P*=255		*P* = .569		*P* = .267	
Within-group comparison	–	–	–	–	–	–	*P* < .001	*P* = .014	*P* < .001	*P* < .001

CDI, Catheter-directed intervention; *RV/LV*, right ventricular to left ventricular diameter ratio; *ST*, systemic thrombolysis.

Values are reported as mean ± standard deviation.