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ORIGINAL RESEARCH ARTICLE

Randomized Controlled Trial of Mechanical Thrombectomy With Anticoagulation Versus Anticoagulation Alone for Acute Intermediate-High Risk Pulmonary Embolism: Primary Outcomes From the STORM-PE Trial

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BACKGROUND: Patients with intermediate-high risk pulmonary embolism (PE) have an elevated right ventricular (RV) to left ventricular (LV) diameter ratio and are at risk of early clinical decompensation and mortality. Reperfusion therapy aims to rapidly relieve acute RV pressure overload and to normalize hemodynamics. STORM-PE (A Prospective, Multicenter, Randomized Controlled Trial Evaluating Anticoagulation Alone Versus Anticoagulation Plus Mechanical Aspiration With the Indigo Aspiration System for the Treatment of Intermediate-High Risk Acute Pulmonary Embolism) is the first reported randomized controlled trial to test the efficacy and to evaluate the safety of mechanical thrombectomy, specifically computer-assisted vacuum thrombectomy (CAVT) with anticoagulation compared to anticoagulation alone.

METHODS: STORM-PE is an international randomized controlled trial with 1:1 randomization to CAVT with anticoagulation or anticoagulation alone. Eligible adults had acute-onset (symptoms ≤14 days), intermediate-high risk PE and were normotensive, with an RV/LV ratio ≥1.0 on computed tomographic pulmonary angiography and elevated cardiac biomarkers. The primary end-point analysis tested for a difference between groups for the change in RV/LV ratio at 48 hours, assessed by a blinded independent imaging core laboratory. Secondary end points included major adverse events within 7 days (a composite of clinical deterioration necessitating rescue therapy, PE-related mortality, symptomatic recurrent PE, and major bleeding), adjudicated by an external clinical events committee. Additional outcomes included change in vital signs and core laboratory–assessed pulmonary artery obstruction at 48 hours.

RESULTS: A total of 100 patients enrolled across 22 sites were randomized to CAVT (n=47) or anticoagulation alone (n=53). Baseline characteristics were comparable between arms. At 48 hours, mean reduction in RV/LV ratio was greater for CAVT (0.52±0.37) than anticoagulation (0.24±0.40), a difference of 0.27 (95% CI, 0.12–0.43; $P<0.001$). Refined modified and modified Miller scores exhibited greater changes for CAVT than anticoagulation alone at 48 hours ($P<0.001$). Early normalization of vital signs within 48 hours was more frequent after CAVT. The major adverse event rate within 7 days was not different between groups (CAVT, 4.3% versus anticoagulation, 7.5%; $P=0.681$). Two PE-related deaths occurred in the CAVT arm.

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*The STORM-PE Investigators are listed in the Supplemental Appendix.

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CONCLUSIONS: CAVT was superior to anticoagulation alone in reducing RV/LV ratio within 48 hours in patients with intermediate-high risk PE, accompanied by earlier normalization of vital signs and major adverse event rates comparable to those for anticoagulation.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT05684796.

Key Words: anticoagulants ■ pulmonary embolism ■ randomized controlled trial ■ thrombectomy

Clinical Perspective

What Is New?

- STORM-PE (A Prospective, Multicenter, Randomized Controlled Trial Evaluating Anticoagulation Alone Versus Anticoagulation Plus Mechanical Aspiration With the Indigo® Aspiration System for the Treatment of Intermediate High Risk Acute Pulmonary Embolism) represents the first randomized controlled trial to test the efficacy and to evaluate the safety of mechanical thrombectomy with anticoagulation compared to anticoagulation alone for the treatment of intermediate-high risk pulmonary embolism.
- Treatment with mechanical thrombectomy resulted in a significantly greater reduction in right ventricular/left ventricular ratio at 48 hours compared with anticoagulation alone, with comparably low rates of major adverse events in both treatment arms.

What Are the Clinical Implications?

- In this novel international multicenter trial, the use of mechanical thrombectomy produced superior efficacy without an increased relative rate of major adverse events compared with anticoagulation alone, and the procedure was characterized by a high rate of technical success and short device time.
- Mechanical thrombectomy resulted in a superior reduction in right ventricular dysfunction and greater reduction in pulmonary artery obstruction relative to anticoagulation alone.
- Rapidly improved computed tomographic pulmonary angiography parameters achieved with mechanical thrombectomy occurred in conjunction with normalization of patient vital signs and hemodynamics.

Nonstandard Abbreviations and Acronyms

BARC	Bleeding Academic Research Consortium
BNP	brain-type natriuretic peptide
CAVT	computer-assisted vacuum thrombectomy
CEC	Clinical Events Committee
CTPA	computed tomographic pulmonary angiography
LV	left ventricular
NT-proBNP	N-terminal pro-B-type natriuretic peptide
NEWS2	National Early Warning Score 2
PA	pulmonary artery
PE	pulmonary embolism
RV	right ventricular
STORM-PE	A Prospective, Multicenter, Randomized Controlled Trial Evaluating Anticoagulation Alone Versus Anticoagulation Plus Mechanical Aspiration With the Indigo® Aspiration System for the Treatment of Intermediate High Risk Acute Pulmonary Embolism
UFH	unfractionated heparin

Pulmonary embolism (PE) affects 1 in 1000 adults globally per year, reflecting a considerable socioeconomic burden because of health care costs, as well as reduced functionality and quality of life among those surviving the acute phase.[1] Patients classified as having intermediate-high risk PE exhibit severe clinical manifestations, including imaging evidence of right ventricular (RV) strain and elevated biomarkers.[2] Although they appear hemodynamically stable at presentation, these patients have an elevated RV to left ventricular (RV/LV) diameter ratio associated with at least a 2-fold increased risk of short-term mortality, as well as a substantial risk of hemodynamic decompensation and other in-hospital adverse events.[2–8] A goal of effective reperfusion strategies in these patients is to rapidly improve RV dysfunction, which may prevent clinical decompensation and hemodynamic collapse.[9]

Although anticoagulation alone is still considered the mainstay of treatment for intermediate-high risk PE, growing evidence supports that endovascular therapy combined with anticoagulation is safe and leads to a reduction in RV/LV ratio for patients in this risk category.[10–14] The 2019 European Society for Cardiology guidelines recommend the use of endovascular therapy for acute PE in the event of hemodynamic deterioration while emphasizing the need for randomized controlled trials to assess the benefits versus risks of catheter-directed procedures combined with anticoagulation as first-line treatment among patients with intermediate-high risk PE.[2]

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Mechanical thrombectomy with computer-assisted vacuum thrombectomy (CAVT) is an endovascular therapy that uses a dynamic microprocessor-driven algorithm designed to aspirate thrombus while minimizing blood loss. Single-arm studies have reported improvements in RV function within 48 hours among patients with acute PE treated with CAVT, with a low rate of major adverse events.[15]

STORM-PE (A Prospective, Multicenter, Randomized Controlled Trial Evaluating Anticoagulation Alone versus Anticoagulation plus Mechanical Aspiration with the Indigo Aspiration System for the Treatment of Intermediate-High Risk Acute Pulmonary Embolism) is the first reported international randomized controlled trial to test the efficacy and to evaluate the safety of CAVT with anticoagulation compared with anticoagulation alone for the treatment of patients with intermediate-high risk PE.[16] Here we report the results of STORM-PE, focusing on the primary end point, reduction in RV/LV ratio, as well as thrombus burden, clinical stabilization with normalization of vital signs at 48 hours, and secondary safety outcomes at 7 days after randomization.

METHODS

Trial Design

STORM-PE is a registered study and can be accessed at https://clinicaltrials.gov/study/NCT05684796. All authors had access to the data at any time during the manuscript preparation. The data that support the findings of this trial are available from the corresponding author on reasonable request. The corresponding author prepared this article with input and approval from all authors. The study was jointly designed by the Steering Committee and Penumbra, the trial sponsor, and conducted in partnership with The PERT Consortium. A list of committee members and investigators is available in the Supplemental Material.

STORM-PE is a postmarket, international randomized controlled trial conducted to test the efficacy and to evaluate the safety of CAVT using the Lightning Flash 16F catheter system (Penumbra, Inc, Alameda, CA) with anticoagulation compared with anticoagulation alone in 100 patients with acute intermediate-high risk PE.[16] The trial primary end point was designed to demonstrate superiority of CAVT with anticoagulation over anticoagulation alone in reducing the RV/LV ratio, as measured by repeated computed tomographic pulmonary angiography (CTPA) at 48±6 hours after randomization. STORM-PE includes additional ongoing follow-up assessments up to 90 days after randomization, as previously outlined; randomization was considered day 0 for all follow-up visits.[16]

The STORM-PE trial was conducted according to the Declaration of Helsinki. Institutional review board or ethics committee approval was obtained at each site. Written informed consent was obtained per institutional review board or ethics committee policy consistent with Good Clinical Practice (ICH E6), ISO 14155, and 21 CFR 50 Protection of Human Subjects regulations. The overall safety of the trial was independently monitored by a data safety monitoring board (North American Science Associates, Northwood, OH). A Clinical Events Committee (CEC; North American Science Associates) comprising independent experienced physicians reviewed and adjudicated clinical events related to safety. An independent imaging core laboratory (VasCore, Boston, MA) blinded to treatment assignment adjudicated the primary end point and severity of pulmonary artery (PA) obstruction.

Patients and Randomization

Between July 2023 and June 2025, patients presenting to a trial site hospital were screened and enrolled at 22 sites in the United States, Canada, New Zealand, and Poland by multispecialty investigators (Figure 1; Supplemental Material). Eligibility criteria were previously described.[16] Briefly, adult patients (18 to

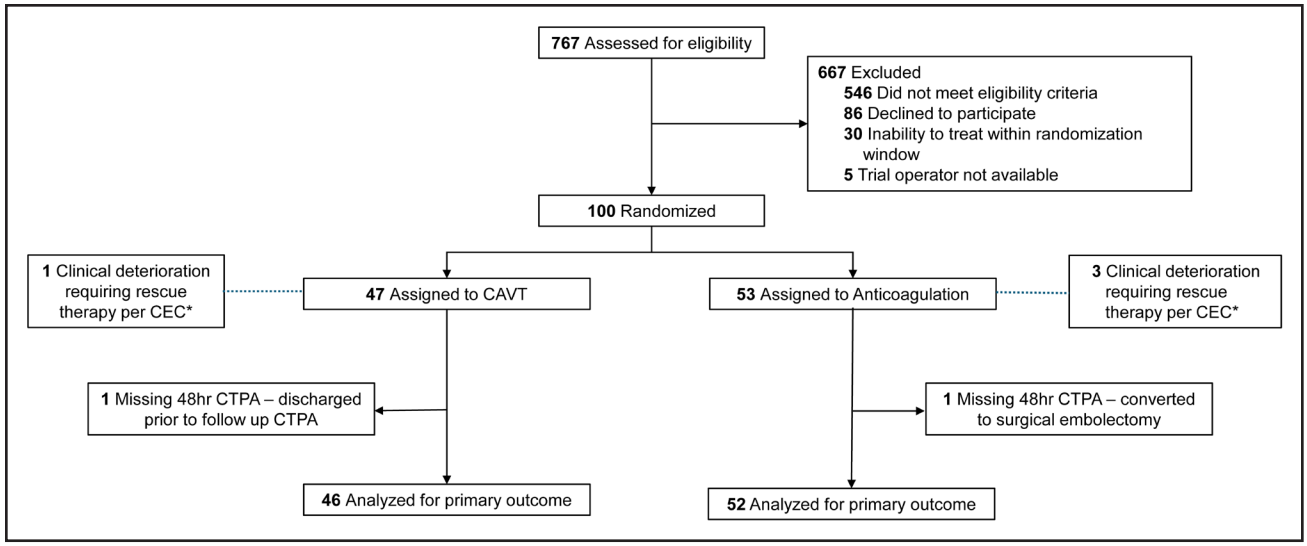

Figure 1. CONSORT diagram of patient flow through the STORM-PE trial.
CAVT indicates computer-assisted vacuum thrombectomy; CEC, Clinical Events Committee; CONSORT, Consolidated Standards of Reporting Trials; CTPA, computed tomographic pulmonary angiography; and STORM-PE, Comparison of Two Pulmonary Embolism Treatments. *Patients who have rescue therapy per CEC without right to left ventricular (RV/LV) ratio assessment before treatment are assigned a 0 change for the RV/LV ratio primary outcome.

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80 years of age) who were normotensive with confirmed acute intermediate-high risk PE (symptom onset within the past 14 days), presented with RV dysfunction indicated by an RV/LV ratio ≥1.0 on CTPA, and had elevated troponin or BPN (brain-type natriuretic peptide) or NT-proBNP (N-terminal pro-B-type natriuretic peptide) were randomized 1:1 to receive either CAVT with the 16F catheter system with anticoagulation or anticoagulation alone (Figure 1). Key exclusion criteria were hemodynamic instability, high risk of clinical deterioration using a National Early Warning Score 2 (NEWS2) score ≥9, or known contraindication to anticoagulation.[17,18] The treatment allocation was stratified by trial center. An online tool with a fixed, permuted block randomization scheme was used to randomize patients.

Intervention and Treatment Regimen

All patients received anticoagulation with either unfractionated heparin (UFH) or low-molecular-weight heparin as determined by the physician in accordance with current guidelines.[2,19] UFH or low-molecular-weight heparin was allowed to be administered before randomization. Patients who received low-molecular-weight heparin had it administered at a weight-/renal-adjusted therapeutic dose. The UFH bolus and infusion were adjusted to achieve and maintain activated partial thromboplastin time, partial thromboplastin time, or anti–factor Xa levels corresponding to therapeutic heparin levels. Postindex treatment anticoagulation therapy was left to the discretion of the investigators, with a minimum expected anticoagulation therapy duration of 3 months.

In addition to receiving anticoagulation, patients in the CAVT arm were treated with Lightning Flash (Indigo Aspiration System, Penumbra, Inc; Supplemental Material) per the instructions for use. CAVT is a recently developed endovascular therapy that uses an algorithm from a microprocessor designed to quickly detect and remove thrombus. A comprehensive review of CAVT with a 16F catheter system, which is used in conjunction with a vacuum pump, canister for thrombus removal, and an optional separator for catheter clearance, has been published.[20] The CAVT procedure was initiated within 24 hours from baseline CTPA and ≤12 hours from randomization.

Thrombectomy was performed with either common femoral or internal jugular vein access. The 16F catheter was advanced through a 16F minimum sheath placed to either the inferior vena cava or the main PA, at operator discretion, and advanced over a 0.035-in stiff exchange wire to navigate the catheter through the right-sided heart cavities and into the selected main PA (left and right). Safe crossing of the heart occurred with a pigtail or balloon tip or as preferred by the treating physician. Once at the treatment location, the exchange wire and the accompanying directional catheter were removed, and the aspiration catheter tip was placed proximal to the thrombus. The microprocessor was then activated, and the aspiration catheter was advanced into the thrombus. The thrombectomy procedure was completed at the investigator's discretion based on hemodynamic and clinical improvement or by completion of thrombus extraction.

Trial End Points

The primary end point was the change in RV/LV ratio assessed by CTPA at baseline (defined as at index PE presentation) and at 48±6 hours, as adjudicated by an independent, blinded imaging core laboratory. Secondary safety end points included the rate of major adverse events within 7 days after randomization, a composite of CEC-adjudicated clinical deterioration requiring rescue therapy, PE-related mortality, symptomatic recurrent PE, or major bleeding categorized by the Bleeding Academic Research Consortium (BARC) scale.[21] Major bleeding was defined as meeting BARC type 3a, 3b, 3c, or 5. Type 3a was not considered major bleeding if it was related to an expected decrease in hemoglobin level attributable to fluid administration and if transfusion was <2 U.

Additional secondary end points through 90 days will be reported in a future publication and include functional outcomes as assessed by the 6-minute walk test, New York Heart Association classification, post–venous thromboembolism functional status scale, modified Medical Research Council Dyspnea Scale, and Borg Scale; quality of life as assessed by the Pulmonary Embolism Quality of Life Questionnaire and EQ-5D-5L; all-cause mortality; PE-related mortality; and symptomatic PE recurrence.

Data Collection

The full schedule of assessments and the data collected were described previously.[16] Data were collected for the prespecified end points of efficacy and safety, as well as for demographics, medical history, and the additional analyses relating to clinical stability measured with vital signs, risk of clinical deterioration assessed by NEWS2, inferior vena caval reflux, and PA obstruction assessed by the refined modified Miller score and modified Miller score on CTPA.[16] The modified Miller score is a cumulative score ranging from 0 to 40 calculated by assigning a score of 0 for no obstruction, one for partial obstruction, and 2 for complete obstruction to each of the segmental arteries. The refined modified Miller score also ranges from 0 to 40 and allows finer distinction of partial obstruction into 3 categories.[22] The lowest hemoglobin level between 48 hours and discharge was reported as the hemoglobin nadir. For the CAVT arm, additional data relating to procedural details, including technical success (defined as the ability of the catheter to access the target thrombus and to perform aspiration), thrombectomy and procedure time, estimated blood loss, and intraprocedural hemodynamics, were also recorded. Starting at randomization, major adverse events within 7 days were collected.

Statistical Analysis

The primary analysis was performed on the intention-to-treat population, defined as all participants who were randomized. To determine statistical power, the assumed RV/LV ratio change for the anticoagulation arm was 0.10 based on a weighted average of RV/LV ratio changes across previous studies.[11,23–26] The assumed RV/LV ratio change for the CAVT arm was 0.35 based on the EXTRACT-PE study (Evaluating the Safety and Efficacy of the Indigo Aspiration System in Acute Pulmonary Embolism) results.[27] This yielded an assumed difference in RV/LV ratio change between CAVT and anticoagulation of 0.25. The common SD for the power calculation was 0.36 from the SEATTLE II study (Submassive and Massive Pulmonary Embolism Treatment With Ultrasound Accelerated Thrombolysis Therapy) results.[28] It was calculated that a sample size of 100 randomized patients, providing a minimum of 90 trial participants with evaluable imaging under the assumption of a 5% attrition rate, had 90% power for detecting superiority

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of CAVT compared with anticoagulation for a difference in RV/LV ratio change of 0.25 at 1-sided α of 0.025. The change in RV/LV ratio at 48 hours through CTPA for CAVT versus anticoagulation was tested with a 2-sample *t* test at 2-sided α of 0.025. For participants who received rescue therapy without RV/LV reassessment, a prespecified zero change in RV/LV ratio was assigned for analysis of the primary end point. The proportion of trial participants with a major adverse event within 7 days was analyzed with a 95% binomial CI and the Fisher exact test for the difference between the treatment groups.

Descriptive statistics were computed for all variables. For continuous variables, mean±SD values were calculated. Differences between groups were evaluated with the 2-sample *t* test for mean values or the Wilcoxon rank-sum test for median values. For within-group differences, the paired *t* test for means or Wilcoxon signed-rank test for medians was used. For categorical variables, frequencies and percentages are reported. Differences between groups were evaluated with the Fisher exact test, and for within-group differences, the McNemar test for 2×2 comparisons was used.

The groups were further compared in a nonprespecified analysis for the dichotomized change in the RV/LV ratio at 48 hours (>0.2 or ≤0.2). Previously, study success in Investigational Device Exemption trials for PE was based on a benchmark of >0.2 change in RV/LV ratio to indicate that the device achieved clinically meaningful improvement in RV strain.[14,27,29,30] An additional analysis compared the percentage of patients with a normalized RV/LV ratio (≤1.0) at 48 hours.

All statistical tests aside from the primary end point were 2 sided with a significance level of 0.05. Statistical analyses were carried out with SAS software (version 9.4, SAS Institute, Cary, NC).

RESULTS

Baseline and Clinical Characteristics

A total of 767 patients were assessed for initial eligibility, 100 of whom were enrolled in the trial and randomized 1:1 to the CAVT (n=47) or anticoagulation (n=53) arm. The Consolidated Standards of Reporting Trials diagram is shown in Figure 1. The most common reason for screen failure in 546 patients was not meeting trial eligibility criteria. The absence of both elevated RV/LV ratio and cardiac biomarkers (n=194, 25.3%) and active cancer (n=107, 14.0%) were the most common eligibility criteria not met. A total of 86 patients met eligibility criteria but declined to participate in the trial.

Baseline characteristics, medical history, and comorbidities were similar between arms (Table 1). Among the 100 patients, mean age was 59.5±13.22 years in the CAVT arm and 61.2±14.19 years in the anticoagulation arm. The percentage of females was 38.3% in the CAVT arm and 52.8% in the anticoagulation arm (*P*=0.164). The median time from PE symptom onset to hospital admission was similar, with 3.0 days (interquartile range, 0.0–6.0 days) in the CAVT arm and 2.0 days (0.0–6.0 days) in the anticoagulation arm (*P*=0.889). The percentage of patients transferred from another facility was also similar (CAVT versus anticoagulation, 48.9% versus 39.6%; *P*=0.421). All patients had elevated cardiac biomarkers, and 59.1% of patients in the CAVT arm and 74.5% in the anticoagulation arm had both elevated troponin and elevated BNP or NT-proBNP (*P*=0.128).

Procedural Characteristics and Hospital Resource Use

CAVT Procedure

CAVT procedural characteristics are presented in Table 2. For all patients, access was obtained through the femoral vein (4.3% [2/47] left and 95.7% [45/47] right). In the CAVT arm, the thrombectomy procedure was technically successful in all 47 patients (100%). The median thrombectomy time was 25.0 minutes (interquartile range, 15.0–41.0 minutes), and the median procedure time was 56.0 minutes (interquartile range, 42.0–69.0 minutes; Table 2). The optional separator was not needed in any of the CAVT cases. During the procedure, no adjunctive treatments for thrombus removal were necessary, specifically no thrombolytic therapy.

Intraprocedural Hemodynamics

In the CAVT arm, the systolic PA pressure was 50.0±14.38 mm Hg before the procedure and 39.4±15.14 mm Hg after the procedure, a reduction of 10.8±8.46 mm Hg (reduced by 21.7±16.66%; *P*<0.001; Table 2). The mean PA pressure was 30.9±9.90 mm Hg before the procedure and 23.0±9.75 mm Hg after the procedure, a reduction of 8.2±5.71 mm Hg (reduced by 27.3±19.70%; *P*<0.001).

Anticoagulation

During hospitalization, the type of heparin used (UFH or low-molecular-weight heparin) was balanced between patients treated with CAVT and those treated with anticoagulation (Supplemental Material). The median time from initiation of UFH to therapeutic level was similar between arms (CAVT versus anticoagulation, 6.8 hours [quartile 1–3, 4.8–12.2] versus 6.4 hours [quartile 1–3, 4.9–8.6]; *P*=0.701). Within the 48-hour visit, the percentage of all patients who were in therapeutic range did not differ between arms (Supplemental Material).

Hospital Resource Utilization

There were no differences in length of hospital stay, percentage of patients requiring the intensive care unit, or length of intensive care unit stay between the CAVT and anticoagulation arms (Table 3).

Primary End-Point Analysis

The primary end-point analysis was completed in 98% of patients (46/47) in the CAVT arm and 98% of patients (52/53) in the anticoagulation arm. One patient in each arm was missing the 48-hour CTPA scan. One patient

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Table 1. Baseline Characteristics and Presentation

Characteristic	CAVT (n=47)	AC (n=53)
Demographics		
Age, y	59.5±13.22	61.2±14.19
Female, n (%)	18 (38.3)	28 (52.8)
Race, n (%)*		
Black	18 (40.9)	13 (26.0)
White	22 (50.0)	35 (70.0)
Unknown	1 (2.3)	1 (2.0)
Not reported	3 (6.8)	0
Ethnicity, n (%)*		
Hispanic or Latino	3 (7.5)	0
Not Hispanic or Latino	37 (92.5)	49 (100)
BMI, kg/m^2	33.8±6.54	34.3±8.60
Comorbidities, n (%)		
DVT	30 (63.8)	32 (60.4)
Previous PE	12 (25.5)	10 (18.9)
History of cancer	4 (8.5)	6 (11.3)
Active cancer	1 (2.1)	3 (5.7)
Chronic kidney disease	4 (8.5)	5 (9.4)
Congestive heart failure	0	2 (3.8)
Chronic obstructive pulmonary disease	2 (4.3)	4 (7.5)
Asthma	7 (14.9)	11 (20.8)
Cor pulmonale (eg, ARDS, interstitial lung disease, sarcoidosis, cystic fibrosis)	1 (2.1)	1 (1.9)
Coronary artery disease	2 (4.3)	7 (13.2)
Diabetes	9 (19.1)	9 (17.0)
Arterial hypertension†	21 (44.7)	35 (66.0)
Additional parameters		
Syncope	9 (19.1)	8 (15.1)
Hemoglobin, g/dL	14.1±1.88	13.9±1.74
Normal levels	41 (87.2)	47 (88.7)
Abnormal levels‡	4 (8.5)	4 (7.5)
Hematocrit, %	42.7±5.13	41.9±4.64
Normal levels	36 (76.6)	41 (77.4)
Abnormal levels‡	4 (8.5)	6 (11.3)
Time from symptom onset to admission, d	3.0 (0.0, 6.0)	2.0 (0.0, 6.0)
Elevated biomarkers§	47 (100.0)	53 (100.0)
Elevated troponin and BNP/NT-proBNP	26 (59.1; n=44)	38 (74.5; n=51)

Data reported are mean±SD, number (percentage), or median (quartile 1, 3) unless otherwise noted.

AC indicates anticoagulation; ARDS, acute respiratory distress syndrome; BMI, body mass index; BNP, B-type natriuretic peptide; CAVT, computer-assisted vacuum thrombectomy; DVT, deep vein thrombosis; NT-proBNP, N-terminal pro-B-type natriuretic peptide; and PE, pulmonary embolism.

*Race and ethnicity information collected only for patients in the United States. "Unknown" and "Not reported" were prespecified options at the time of selection.

†Statistically significant difference between CAVT and AC ($P<0.05$).

‡Abnormal was defined as levels below the normal range.

§Above site laboratory reference ranges for BNP, NT-proBNP, troponin I/T, and/or high-sensitivity troponin I/T or elevated laboratory values of 90 pg/mL (BNP), 500 pg/mL (NT-proBNP), 0.04 ng/mL (troponin I), 0.015 ng/mL (high-sensitivity troponin I), 0.01 ng/mL (troponin T), or 0.014 ng/mL (high-sensitivity troponin T).

in each arm was imputed as a 0 change in RV/LV ratio because of clinical deterioration requiring rescue therapy. The RV/LV ratio at baseline was 1.63±0.36 in the CAVT arm and 1.56±0.35 in the anticoagulation arm.

The mean reduction in RV/LV ratio at 48 hours was 0.52±0.37 in the CAVT arm and 0.24±0.40 in the anticoagulation arm, a difference of 0.27 (95% CI, 0.12–0.43; $P<0.001$; Figure 2; Table 4). Additional analysis of

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Table 2. CAVT Arm Periprocedural Parameters

Periprocedural characteristics	CAVT (n=47)
On-table sPAP, mm Hg	
Before CAVT (n=46)	50.0±14.38
After CAVT (n=42)	39.4±15.14
Reduction*	10.8±8.46
P value	<0.001
On-table mPAP, mm Hg	
Before CAVT (n=47)	30.9±9.90
After CAVT (n=42)	23.0±9.75
Reduction*	8.2±5.71
P value	<0.001
Diagnostic CTPA to venous puncture time, h	19.3 (13.6, 22.1)
Thrombectomy time,† min	25.0 [15.0, 41.0]
Procedure time,‡ min	56.0 [42.0, 69.0]
Estimated blood loss, mL	296.5±179.4
Technical success, n (%)§	47 (100.0)

Data reported as mean±SD, number (percentage), or median (quartile 1, 3).

CAVT indicates computer-assisted vacuum thrombectomy; CTPA, computed tomographic pulmonary angiography; mPAP, mean pulmonary arterial pressure; and sPAP, systolic pulmonary arterial pressure.

*Paired data=42.

†Defined as first device insertion to last device removal.

‡Defined as time from venous puncture to access site closure or last device removal if access site was maintained for adjunctive treatment.

§The ability of the catheter to access the target thrombus and perform aspiration.

the primary end point did not identify differences in treatment effect by site, with a value of $P_{interaction}$>0.05 indicating the homogeneity of treatment effect across enrolling institutions.

Secondary End Point and Safety Outcomes

The secondary end-point analysis was completed in 100% of patients (47/47) in the CAVT arm and 100% of patients (53/53) in the anticoagulation arm. There were no differences in major adverse events within 7 days between the CAVT arm (4.3%, 2/47) and anticoagulation arm (7.5%, 4/53) as independently adjudicated by the CEC (*P*=0.681; Table 3). Clinical deterioration requiring rescue therapy occurred in one patient in the CAVT arm and 3 patients in the anticoagulation arm. The patient in the CAVT arm received cardiopulmonary resuscitation as a response to a major adverse event (no endovascular rescue therapy); in the anticoagulation arm, rescue therapy included one patient receiving systemic tPA (tissue-type plasminogen activator) followed by mechanical thrombectomy with CAVT using the 16F catheter, one patient receiving catheter-directed low-dose thrombolysis, and one patient receiving mechanical thrombectomy with CAVT using the 16F catheter. Two PE-related deaths occurred in the CAVT arm. The 2 deaths (occurring on postrandomization days 0 and 5) were independently adjudicated by the CEC as neither procedure nor device related (Supplemental Material). There was no recurrent PE in either group. Major bleeding occurred in one patient in each arm (BARC 5b in the CAVT arm and BARC 3a in the anticoagulation arm), each requiring a transfusion. There were no other blood transfusions before discharge (Supplemental Material). The clinical deterioration, day 0 death, and BARC 5b bleeding all occurred in the same patient from the CAVT arm.

Minor bleeding after discharge from an arterial line removal site occurred in 1 patient in the CAVT arm (BARC 1). No differences were observed in serious adverse events within 7 days between arms, with 8.5% (4/47) in the CAVT arm and 15.1% (8/53) in the anticoagulation arm (*P*=0.368). The composite major adverse event rate at 48 hours was similar, with 2.1% (1/47) and 3.8% (2/53) in the CAVT and anticoagulation arm, respectively. There were no access site complications in the CAVT arm. Safety event descriptions and additional details are included in Table 3 and the Supplemental Material.

Core Laboratory Imaging Outcomes, Clinical Parameters, and Laboratory Parameters

Core Laboratory CTPA Imaging Parameters

Outcomes for core laboratory–adjudicated imaging parameters are presented in Table 5 and the Supplemental Material. A higher proportion of patients in the CAVT arm had an RV/LV ratio reduction of >0.2 on CTPA at 48 hours compared with the anticoagulation arm (78.3% versus 51.9%, respectively; *P*=0.011; Supplemental Material). Within the same time frame, the absolute reduction in the percentage of patients with inferior vena caval reflux was 46.7% in the CAVT versus 25.0% in the anticoagulation arm (*P*=0.026; Table 5). The CAVT arm had no difference in baseline refined modified Miller score (*P*=0.241) and a higher baseline modified Miller score than the anticoagulation arm (15.9 versus 15.2, respectively; *P*=0.021; Table 5). Reduction in PA obstruction index at 48 hours, as measured with refined modified Miller score, was greater in the CAVT arm than in the anticoagulation arm (Δ=11.6 [42.1%] versus 3.8 [15.6%]; *P*<0.001); this was also the case for modified Miller score (Δ=3.2 [20.0%] versus 0.7 [5.1%], respectively; *P*<0.001; (Figure 3A; Table 5). A greater percentage of patients had an RV/LV ratio ≤1.0 at 48 hours in the CAVT arm compared with the anticoagulation arm (39.1% versus 13.5%, respectively; *P*=0.005; Supplemental Material).

Clinical Parameters

There were no differences between arms in vital parameters, including blood pressure, heart rate, and oxygen saturation, at baseline (Figure 3; Table 5). At 48 hours, the heart rate in the CAVT arm was lower than in the anticoagulation arm (*P*=0.014; Table 5), and baseline

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Table 3. Safety Outcomes and Hospital Resource Use

	CAVT (n=47)	AC (n=53)	Difference (95% CI), %	*P* value
Secondary safety end points, n (%)				
MAEs (composite) at 7 d	2 (4.3)*	4 (7.5)	−3.3 (−14.6 to 7.9)	0.681
Clinical deterioration requiring rescue therapy	1 (2.1)	3 (5.7)	−3.5 (−13.8 to 6.3)	0.620
PE-related mortality	2 (4.3)	0	4.3 (−3.1 to 14.6)	0.218
Symptomatic recurrent PE	0	0	0	>0.999
Major bleeding†	1 (2.1)	1 (1.9)	0.2 (−8.3 to 9.6)	>0.999
Safety events at 48 h, n (%)				
MAEs (composite) at 48 h	1 (2.1)	2 (3.8)	−1.6 (−11.4 to 8.0)	>0.999
Additional safety outcomes, n (%)				
Access-related complications	0	NA	NA	NA
BARC bleeding category, n (%)†				
Minor bleeding				
1	1 (2.1)	0	2.1 (−5.3 to 11.4)	0.470
2	0	0	0	>0.999
Major bleeding (part of MAE composite)				
3a	0	1 (1.9)	−1.9 (−10.1 to 5.9)	>0.999
3b	0	0	0	>0.999
3c	0	0	0	>0.999
5a	0	0	0	>0.999
5b	1 (2.1)	0	2.1 (−5.3 to 11.4)	0.470
Hospital resource use				
Length of hospital stay, d	5.0 (4.0, 6.0)	5.0 (4.0, 8.0)	−0.5 (−1.0 to 0.0)	0.470
Patients requiring ICU stay, n (%)	21 (44.7)	31 (58.5)	−13.8 (−32.9 to 6.1)	0.229
ICU stay,‡ n nights	3.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.5 (0.0 to 1.0)	0.179

Data reported as mean±SD, number (percentage), or median (quartile 1, 3).

AC indicates anticoagulation; BARC, Bleeding Academic Research Consortium; CAVT, computer-assisted vacuum thrombectomy; ICU, intensive care unit; MAE, major adverse event; NA, not applicable; PE, pulmonary embolism; and RV, right ventricular.

*Two patients experienced 4 MAEs: one patient experienced PE-related mortality, and the second patient experienced 3 MAEs: major bleeding, deterioration requiring rescue therapy, and PE-related mortality.

†Major bleeding was defined as meeting BARC type 3a, 3b, 3c, or 5.[21] Type 3a was not considered major bleeding if it was related to an expected decrease in hemoglobin level attributable to fluid administration and if transfusion was <2 U.

‡Includes only patients who were admitted to the ICU.

tachycardia (heart rate >100 bpm) was resolved in 100.0% versus 56.5% of cases, respectively (*P*=0.006; Figure 3B). Supplemental oxygen (liters per minute) reduction from baseline to 48 hours was greater in the CAVT arm (*P*=0.003), and more patients in the CAVT arm transitioned to room air by 48 hours (*P*<0.001; Figure 3C and 3D, respectively). Overall, the NEWS2 score was similar between arms at baseline (3.5±1.95 for CAVT versus 4.1±2.07 for anticoagulation; *P*=0.150) but significantly lower in the CAVT arm at 48 hours (1.8±1.73 versus 2.7±2.07; *P*=0.034; Table 5). Although the difference was significant at 48 hours, the relative reduction in NEWS2 score was not significantly different between treatment arms.

Laboratory Parameters

There were no differences between arms in baseline hemoglobin or hematocrit (Table 1). Baseline hemoglobin was normal in 87.2% of the CAVT arm and 88.7% of the anticoagulation arm, and hematocrit was normal in 76.6% and 77.4%, respectively. Both the CAVT and anticoagulation arms had a significant reduction in hemoglobin nadir through either 48 hours or discharge, with a greater reduction in the CAVT arm (CAVT versus anticoagulation, 2.5±1.44 versus 1.6±1.22; *P*=0.001). The hemoglobin nadir through either 48 hours or discharge for the CAVT and anticoagulation arms was 11.5±1.73 and 12.5±1.76 g/dL, respectively (*P*=0.014; Table 5).

DISCUSSION

STORM-PE is a randomized controlled trial directly comparing mechanical thrombectomy with anticoagulation and anticoagulation alone and the first to demonstrate the superiority of CAVT in reducing RV/LV ratio at 48 hours among patients with acute intermediate- to

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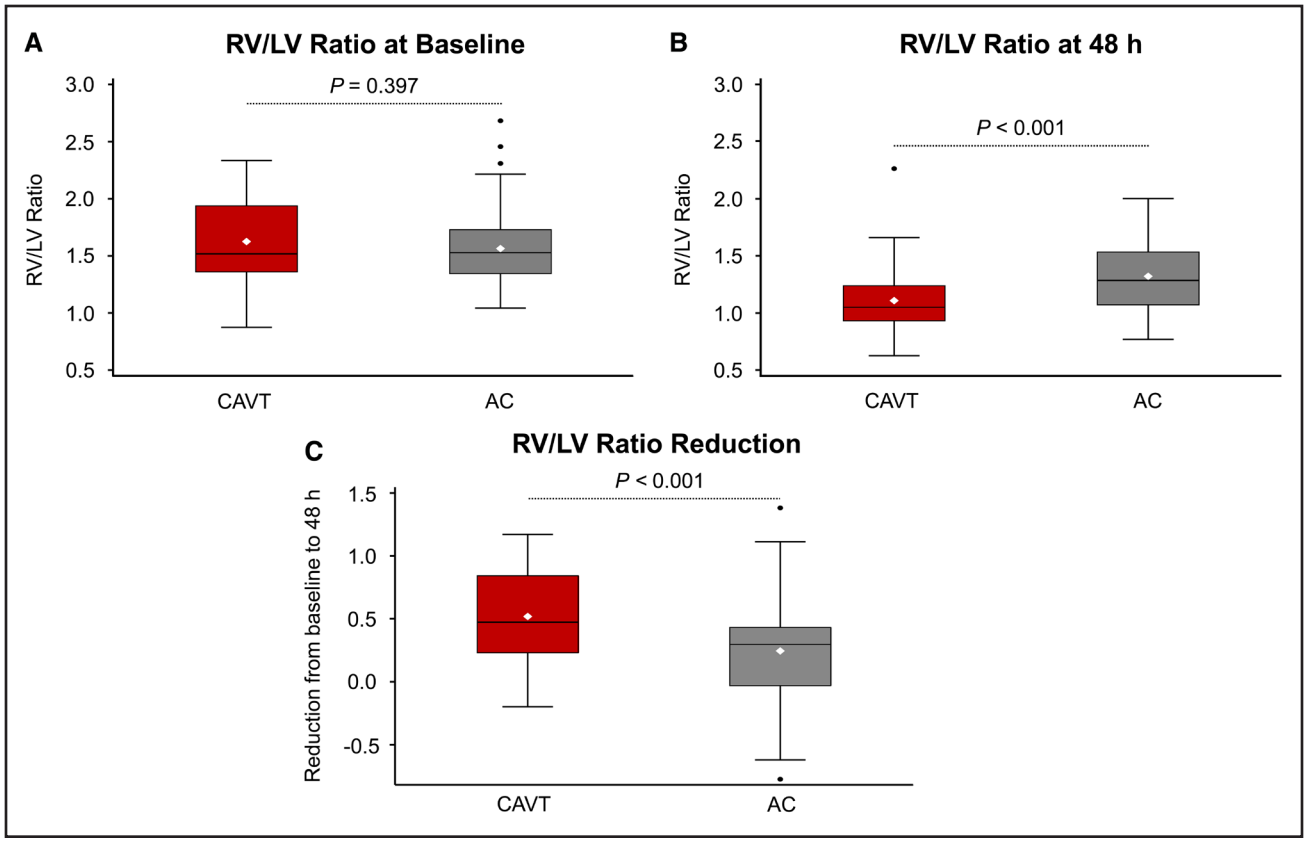

Figure 2. Primary effectiveness: RV/LV ratio change from baseline to 48 hours.
Right to left ventricular (RV/LV) ratio at baseline (**A**) and at 48 hours (**B**) for the computer-assisted vacuum thrombectomy (CAVT) and anticoagulation (AC) arm. **C**, Absolute reduction in RV/LV ratio from baseline at 48 hours per arm. Paired data for CAVT=46 and for AC=52. *P* values are calculated from the 2-sample *t* test.

high-risk PE. This trial shows that CAVT treatment may also be associated with clinical improvement of vital signs and of core laboratory–assessed PA obstruction reduction, without an increase in the rate of major adverse events.

Anticoagulation is an essential therapy in acute PE treatment. Although it inhibits the formation and propagation of new thrombus, it does not directly reduce existing thrombus burden, and there are no known effects on RV/LV ratio and angiographic PA obstruction during the first critical hours.[25,31] Several trials show no statistical effect of anticoagulation on RV/LV ratio as far out as 24 hours.[11,25,26] In this trial, the proportion of patients in both groups rapidly achieving therapeutic levels of anticoagulation was high.

In this analysis, the reduction in RV/LV ratio was greater with CAVT, and the proportion of patients in the CAVT arm with a normalized RV/LV ratio on CTPA at 48 hours was 3-fold higher compared with anticoagulation alone, a markedly greater proportion than previously reported.[32] The RV/LV ratio change at 48 hours with CAVT is the largest reported drop among mechanical thrombectomy trials in which the ratio was measured with CTPA.[14,27,29,30] Significant improvement in the RV/LV ratio with CAVT has been previously reported[15] and is now confirmed in the setting of a randomized controlled

Table 4. Primary End Point: RV/LV Ratio Changes at 48 Hours

RV/LV ratio	CAVT arm	AC arm	Difference between groups (95% CI)	*P* value
Baseline	1.63±0.36	1.56±0.35	0.06 (−0.08 to 0.20)	0.397
48 h	1.11±0.28	1.32±0.31	−0.21 (−0.33 to −0.09)	<0.001
Reduction: baseline−48 h	0.52±0.37*	0.24±0.40*	0.27 (0.12 to 0.43)	<0.001†
Relative reduction: baseline−48 h, %	29.7±18.2*	13.1±23.4*	16.7 (8.2 to 25.2)	<0.001

Data reported as mean±SD.
AC indicates anticoagulation; CAVT, computer-assisted vacuum thrombectomy; LV, left ventricular; and RV, right ventricular.
*Paired data for CAVT=46; paired data for AC=52.
†*P* value for a 1-sided 2-sample *t* test; *P*<0.001 for a 2-sided paired *t* test within each arm.

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Table 5. Changes in Vital Signs, Laboratory Values, and Core Laboratory Imaging Parameters From Baseline to 48 Hours After Randomization

Variable	Baseline		48 h		Reduction: baseline–48 h	
	CAVT	AC	CAVT	AC	CAVT	AC
Reflux of contrast into IVC, % (CAVT, n=45; AC n=52)	66.7	69.2	20.0	44.2	46.7	25.0
P, between-group comparison	0.830		0.017		0.026	
P, within-group comparison	NA		NA		<0.001	0.005
MMS (CAVT, n=45; AC, n=52)	15.9±0.61	15.2±2.01	12.7±3.34	14.5±2.99	3.2±3.38	0.7±1.84
P, between-group comparison	0.021		0.005		<0.001	
P, within-group comparison	NA		NA		<0.001	0.013
Relative reduction, %	NA		NA		20.0±21.1	5.1±15.0
RMMS (CAVT, n=45; AC, n=52)	27.3±3.89	26.1±5.51	15.6±4.75	22.3±6.35	11.6±5.24	3.8±3.76
P, between-group comparison	0.241		<0.001		<0.001	
P, within-group comparison	NA		NA		<0.001	<0.001
Relative reduction, %	NA		NA		42.1±17.83	15.6±16.32
Hemoglobin, g/dL* (CAVT, n=43; AC, n=51)	14.0±1.86	14.0±1.75	11.5±1.73	12.5±1.76	2.5±1.44	1.6±1.22
P, between-group comparison	0.992		0.014		0.001	
P, within-group comparison	NA		NA		<0.001	<0.001
Heart rate, bpm (CAVT, n=46; AC, n=53)	93.2±17.36	98.2±15.87	80.0±12.59	87.1±15.14	13.1±14.03	11.1±16.34
P, between-group comparison	0.134		0.014		0.511	
P, within-group comparison	NA		NA		<0.001	<0.001
NEWS2 (CAVT, n=46; AC, n=53)	3.5±1.95	4.1±2.07	1.8±1.73	2.7±2.07	1.7±2.29	1.5±2.19
P, between-group comparison	0.150		0.034		0.591	
P, within-group comparison	NA		NA		<0.001	<0.001
Oxygen saturation (pulse oximeter reading), % (CAVT, n=46; AC, n=53)	96.0±2.59	95.4±2.44	96.1±2.30	95.4±2.03	0.0±3.12	0.0±3.04
P, between-group comparison	0.204		0.097		0.896	
P, within-group comparison	NA		NA		0.925	0.928
Supplemental oxygen for all participants, L/min (CAVT, n=44; AC, n=52)	2.0 (0.0–4.0)	2.0 (0.0–3.0)	0.0 (0.0–0.0)	0.0 (0.0–2.0)	2.0 (0.0–4.0)	0.0 (0.0–2.0)
P, between-group comparison	0.129		0.025		0.003	
P, within-group comparison	NA		NA		<0.001	0.019

Data reported as mean±SD, number (percentage), or median (quartile 1, 3).

AC indicates anticoagulation; CAVT, computer-assisted vacuum thrombectomy; CTPA, computed tomographic pulmonary angiography; IVC, Inferior vena cava; MMS, modified Miller Score; NA, not applicable; NEWS2, National Early Warning Score 2; and RMMS, refined modified Miller score.

*Lowest value presented through either 48 hours or discharge.

trial. These findings indicate the potential for a more consistent and clinically meaningful treatment effect with CAVT relative to anticoagulation alone.

The significant reduction in RV/LV ratio was not the only improvement observed with CAVT relative to anticoagulation alone in this trial. The reductions observed at 48 hours on core laboratory–assessed CTPA in PA obstruction with CAVT point to more rapid recovery compared with anticoagulation alone and are supported by the decreased contrast reflux into the inferior vena cava. Within the same time frame, the CAVT arm had improved heart rate and oxygenation, indicating the potential added benefits of CAVT in early physiological recovery. The improved NEWS2 score further suggests a lower risk of clinical deterioration in patients receiving CAVT compared with anticoagulation therapy alone, but there was no significant difference between groups in relative reduction in NEWS2 score, warranting further investigation in a larger cohort. The ease of use was clearly demonstrated by the short procedure time and successful mechanical thrombectomy performed in all patients. The STORM-PE results highlight the developing role of mechanical thrombectomy in the PE treatment algorithm and enhance the existing evidence base. The rapid clinical improvement seen for patients treated with CAVT in this trial may create opportunities for treatment protocols

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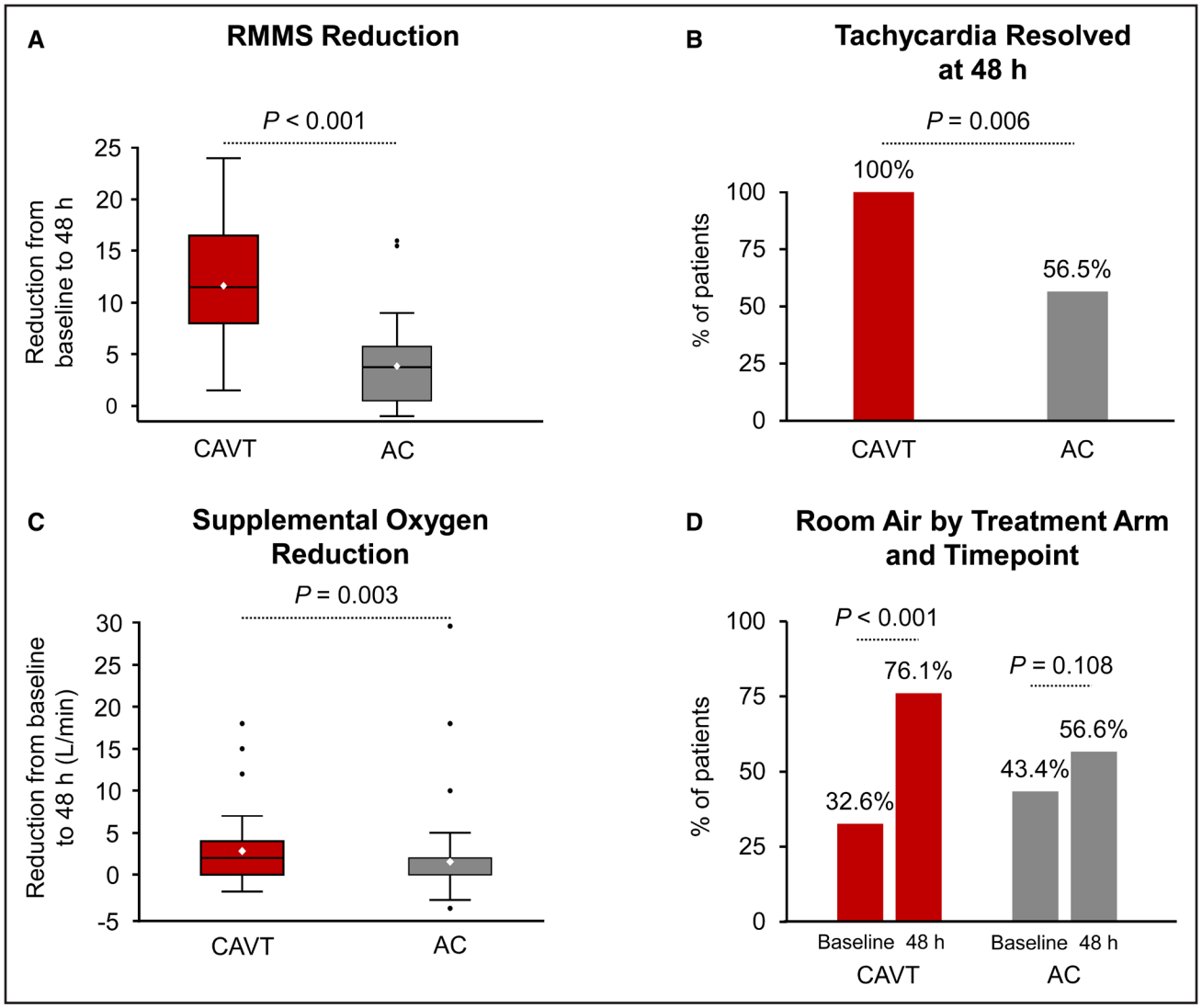

Figure 3. Additional outcomes between treatment arms.
A, Refined modified Miller score (RMMS) absolute reduction from baseline to 48 hours for each arm. Difference between computer-assisted vacuum thrombectomy (CAVT) and anticoagulation (AC; paired *t* test, *P*<0.001). Paired data for CAVT=45 and for AC=52. **B**, Percentage of patients with resolved baseline tachycardia (defined as heart rate >100 bpm). Difference between CAVT and AC (Fisher exact test, *P*=0.006). **C**, Reduced supplemental oxygen level from baseline to 48 hours for all patients. Patients who were on room air were assigned a value of 0 L/min. Difference between CAVT and AC (Wilcoxon median test, *P*=0.003). Paired data for CAVT=44 and for AC=52. **D**, Percentage of patients on room air at baseline and 48 hours for CAVT (McNemar test, *P*<0.001) and AC (McNemar test, *P*=0.108). Paired data for CAVT=46 and for AC=53.

to improve patient throughput in those presenting with symptomatic acute PE in the hospital setting.

In STORM-PE, several major adverse events were observed in both treatment groups, reinforcing the critical nature of this diagnosis. The number of major adverse events within 7 days was similar between the CAVT and anticoagulation arms. Specifically, 3 patients in the anticoagulation arm had objective clinical deterioration leading to escalation of therapy requiring endovascular intervention. Two patients in the CAVT arm had PE-related mortality unrelated to the endovascular procedure. Further research, including ongoing randomized controlled trials, may identify the long-term risks and benefits of these novel therapeutic options in patients with intermediate-high risk PE.[33–36]

The results of STORM-PE reinforce the findings of the ongoing prospective, international, single-arm STRIKE-PE study (A Prospective, Multicenter Study of the Indigo Aspiration System Seeking to Evaluate the Long-Term Safety and Outcomes of Treating Pulmonary Embolism), in which the majority of patients (87.3%) presented with intermediate-high risk PE.[15] Recently published interim results using CAVT demonstrated a 25.7% reduction in the RV/LV ratio (*P*<0.001), along with low rates of major adverse events (2.7% [4/150]) and device-related serious adverse events (1.3% [2/150]) within 48 hours of treatment.[15] PEERLESS assessed large-bore mechanical thrombectomy compared with catheter-directed thrombolysis for treatment of intermediate-risk PE,

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but given the major trial design differences between PEERLESS and STORM-PE, including the different primary end point and the lack of anticoagulation comparator arm in PEERLESS, a direct comparison of the safety and effectiveness of these technologies between the trials is not feasible.[37] Although not the primary end point for the study, the RV/LV ratio was reported in PEERLESS, with reductions in RV/LV ratio of 0.32 for large-bore mechanical thrombectomy and 0.30 for catheter-directed thrombolysis compared with 0.52 with CAVT and 0.24 with anticoagulation alone in STORM-PE. Future trials that compare mechanical thrombectomy and anticoagulation alone are underway (eg, PE-TRACT [Pulmonary Embolism–Thrombus Removal With Catheter-Directed Therapy][33] and PEERLESS II[38]) and will add to the growing clinical evidence on the safety and effectiveness of mechanical thrombectomy for PE.

This trial has several limitations. First, it was designed to include only patients with intermediate-high risk PE as defined by current guidelines[2]; therefore, the results cannot be extrapolated to patients with PE presenting with hemodynamic instability or without RV dysfunction and elevated cardiac biomarkers. Second, all participating sites had collaborative PE workflows such as PERT teams, and the results from this trial may not be generalizable to institutions without established PE programs. Third, randomization into the treatment arm was open label, although the end points were adjudicated by a CEC and a blinded independent core laboratory. Fourth, although there were no significant differences in baseline characteristics between the treatment arms, imbalances in randomization for sex, race, and elevated biomarkers driven by the sample size of 100 patients could affect study outcomes. Fifth, the primary end point, RV/LV ratio, is a surrogate end point. Last, STORM-PE was not powered to show significant differences beyond RV/LV ratio. However, the early favorable changes in patient vital signs and PA obstruction paralleled the changes observed in the RV/LV ratio, and the trial is testing multiple secondary end points focused on patient symptoms, functional status, and quality of life through 90 days of follow-up.

Conclusions

STORM-PE is the first reported randomized controlled trial to compare mechanical thrombectomy with CAVT to anticoagulation and anticoagulation alone in the treatment of intermediate-high risk PE. CAVT with anticoagulation was superior to anticoagulation alone in reducing RV/LV ratio at 48 hours without an increase in the rate of major adverse events. Patients treated with CAVT also exhibited greater improvement than those treated with anticoagulation alone in a range of physiological and CTPA parameters.

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Supplemental Material

Expanded Methods
Tables S1–S7
Figures S1–S4
Supplemental Appendix

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