Meta-Analysis Comparing Catheter-Directed Thrombolysis Versus Systemic Anticoagulation Alone for Submassive Pulmonary Embolism

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The optimal therapy for submassive pulmonary embolism (sPE), defined by right ventricular dysfunction without hemodynamic instability, is uncertain. We conducted a systematic review and meta-analysis to compare the outcomes of catheter-directed thrombolysis (CDT) versus systemic anticoagulation (SA) alone in patients with sPE. We searched PubMed, EMBASE, Cochrane, *ClinicalTrials.gov*, and Google Scholar (from inception through May 2022) for studies comparing outcomes of CDT versus SA in sPE. Studies were identified, and data were extracted by 2 independent reviewers. We used a random-effects model to calculate risk ratios (RRs) with 95% confidence intervals (CIs). Outcomes included in-hospital, 30-day, 90-day, and 1-year mortality, major and minor bleeding, and need for blood transfusion. A total of 12 studies (1 randomized, 11 observational) with 9,789 patients were included. Compared with SA, CDT was associated with significantly lower in-hospital mortality (RR 0.41, 95% CI 0.30 to 0.56, p <0.00001), 30-day mortality (RR 0.37, 95% CI 0.18 to 0.73, p = 0.004), 90-day mortality (RR 0.36, 95% CI 0.17 to 0.72, p = 0.004), and a tendency toward lower 1-year mortality (RR 0.56, 95% CI 0.29 to 1.05, p = 0.07). The risks of major bleeding (RR 1.31, 95% CI 0.57 to 3.01, p = 0.53), minor bleeding (RR 1.67, 95% CI 0.77 to 3.63, p = 0.20), and the rates of blood transfusion (RR 0.34, 95% CI 0.10 to 1.15, p = 0.08) were similar between the 2 strategies. In conclusion, in patients with sPE, CDT is associated with significantly lower in-hospital, 30-day, and 90-day mortality and a tendency toward lower 1-year mortality with similar bleeding rates compared with SA. This study expands the evidence supporting CDT as first-line therapy for sPE, and randomized controlled trials are indicated to confirm our findings. **(Am J Cardiol 2022;00:1−9)**

Introduction

Acute pulmonary embolism (PE) is the third most common cause of cardiovascular death in the United States.[1] Almost one-quarter of hemodynamically stable PE patients have submassive PE (sPE), defined by hemodynamic stability but evidence of right ventricular (RV) dysfunction on imaging or abnormal cardiac biomarkers.[2,3] The optimal strategy for managing acute sPE remains debated.[4,5] The 2019 European Society of Cardiology and the 2021 American College of Chest Physicians guidelines recommend against systemic thrombolysis (ST) in patients with sPE who are hemodynamically stable and instead recommend systemic anticoagulation (SA).[6,7] Catheter-directed thrombolysis (CDT) was developed to achieve a thrombolytic benefit similar to ST while minimizing bleeding complications using localized delivery with lower thrombolytic agent dosages.[8−10] Single-arm studies have demonstrated the safety and efficacy of CDT in treating sPE.[8] However, data comparing CDT with SA alone have shown conflicting results, particularly regarding mortality.[10−12] Therefore, we conducted a meta-analysis to compare CDT versus SA in terms of mortality, bleeding, and length of stay (LOS) in patients with acute sPE.

Methods

The systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2015

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and Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guidelines[13] and were registered with PROSPERO-CRD42022316232 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022316232). A comprehensive literature search was performed using the PubMed, EMBASE, Cochrane, *ClinicalTrials.gov*, and Google Scholar databases by 2 independent authors (MI and AMB) for randomized controlled trials (RCTs) and observational studies comparing CDT with SA alone in patients with sPE from the inception of each database to May 26, 2022. The following search terms and keywords were used: "Submassive," Pulmonary embolism," "Catheter," "Thrombolysis," "Thrombolytics," "Systemic," "Anticoagulation," "Heparin," "Systemic anticoagulation," "Mortality," "Survival," and "Bleeding." No language, sample size, publication date, or publication status restrictions were placed on the search. References of the retrieved studies were also manually checked for relevant studies.

After removing duplicate publications, all citations were downloaded and screened by 2 authors (MI and AMB) independently based on titles and abstracts. Potentially relevant studies were subjected to full-text review to assess further for eligibility. Discrepancies in study selection were discussed and resolved with another author (AMG). Eligible studies had to satisfy the following inclusion criteria: (1) studies comparing CDT versus SA for sPE; (2) availability of clinical outcomes data at one or more timepoints. We excluded studies that lacked clinical outcomes data and abstracts, case reports, review articles, editorials, and letters.

After relevant articles were identified, 2 authors (MI and AMB) independently extracted data (baseline characteristics, definitions of outcomes, and numbers of events) into a spreadsheet for analysis. From studies including both propensity-matched and unmatched analyses, we preferentially included data from the propensity-matched analyses. Any discrepancies were resolved by a third author (AMG). The same investigators (MI and AMB) independently and systematically assessed the methodological quality of the studies using the Risk of Bias Assessment Tool from the Cochrane Handbook for RCTs and the Newcastle-Ottawa Scale for observational studies. Publication bias for each outcome was assessed by visual inspection of funnel plots when data were available from at least 3 studies.

The definition of sPE was similar in all studies, described as evidence of PE with signs of concomitant RV strain (i.e., echocardiographic evidence of increased RV pressure, RV-to-left ventricular [RV/LV] ratio $\geq$1.0, or systolic dysfunction; biomarker elevation such as elevated troponin I or N-terminal pro−b-type natriuretic peptide levels) without hemodynamic instability (systolic blood pressure <90 mm Hg). Primary outcomes of interest were all-cause in-hospital, 30-day, 90-day, and 1-year mortality. Secondary outcomes included major and minor bleeding, blood transfusion, RV recovery, and hospital LOS. Definitions of major bleeding and minor bleeding were similar in all studies. Major bleeding was defined as intracranial bleeding, any other cause of bleeding that caused hemodynamic instability requiring treatment and/or blood transfusion, or according to the International Society of Thrombosis and Hemostasis criteria.[14] Minor bleeding was defined as any documented bleeding event that did not meet the criteria for major bleeding. RV recovery was established by normal RV size and function on follow-up echocardiogram.

For dichotomous outcomes, risk ratios (RRs) with 95% confidence intervals (CIs) were calculated from the available data in the included studies, and study-specific RRs were combined using the DerSimonian and Laird random-effects model with the estimate of heterogeneity taken from the Mantel−Haenszel model. For continuous outcomes, mean differences with 95% CIs were calculated from the available data in the included studies. A 2-tailed α value of p <0.05 was considered statistically significant. The "test for overall effect" was reported as a z value corroborating the inference from the 95% CI. The Higgins I-squared (I^2) statistic was used to quantify heterogeneity in the included studies; a value of 0% indicated no observed heterogeneity, and larger values indicated increasing heterogeneity. I^2 values of 25%, 50%, and 75% have been assigned adjectives of low, moderate, and high heterogeneity, respectively. All analyses were performed using the Cochrane Review Manager (RevMan) version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). Results were reported according to the PRISMA Protocol 2015 statement.

Results

The initial database search revealed 3,892 studies, from which 738 duplicates and 2,943 irrelevant titles and abstracts were excluded. The remaining 211 studies were subject to full-text review, which led to the further exclusion of 199 studies. Finally, 12 studies were selected for quantitative analysis.[9−12,15−22] Figure 1 displays the PRISMA flow diagram for study search and selection.

The studies' methodological quality was assessed using the Risk of Bias Assessment Tool from the Cochrane Handbook for RCTs and the Newcastle-Ottawa Scale for observational studies (Supplementary Table 1). Concerning clinical outcomes, there was no heterogeneity for in-hospital mortality (I^2 = 0%, p = 0.87), 30-day mortality (I^2 = 0%, p = 0.77), and 90-day mortality (I^2 = 0%, p = 0.99). Low heterogeneity was present for 1-year mortality (I^2 = 36%, p = 0.19), major bleeding (I^2 = 14%, p = 0.32), minor bleeding (I^2 = 8%, p = 0.37), and blood transfusion (I^2 = 17%, p = 0.31). Moderate heterogeneity was present for RV recovery (I^2 = 40%, p = 0.20), and high heterogeneity was present for hospital LOS (I^2 = 79%, p = 0.008). Overall, heterogeneity was low, and there was no evidence of publication bias on visual inspection of the funnel plots (Supplementary Figure 1).

A total of 11 observational studies and 1 RCT, ULTIMA (Ultrasound Accelerated Thrombolysis of Pulmonary Embolism), were included in the primary analysis.[9−12,15−22] These studies were comprised of 9,789 sPE patients, of whom 1,871 underwent CDT, and 7,918 received SA alone. The mean age of patients was >50 years in most studies, approximately half of the patients were male, and the median follow-up duration was 10 months. All patients included from 11 studies had sPE,[9−12,15−21] however, patients included from the Sista et al[22] study had either submassive (n = 79) or massive PE (n = 8). The 8 patients with massive PE represented a small percentage (0.08%) of our

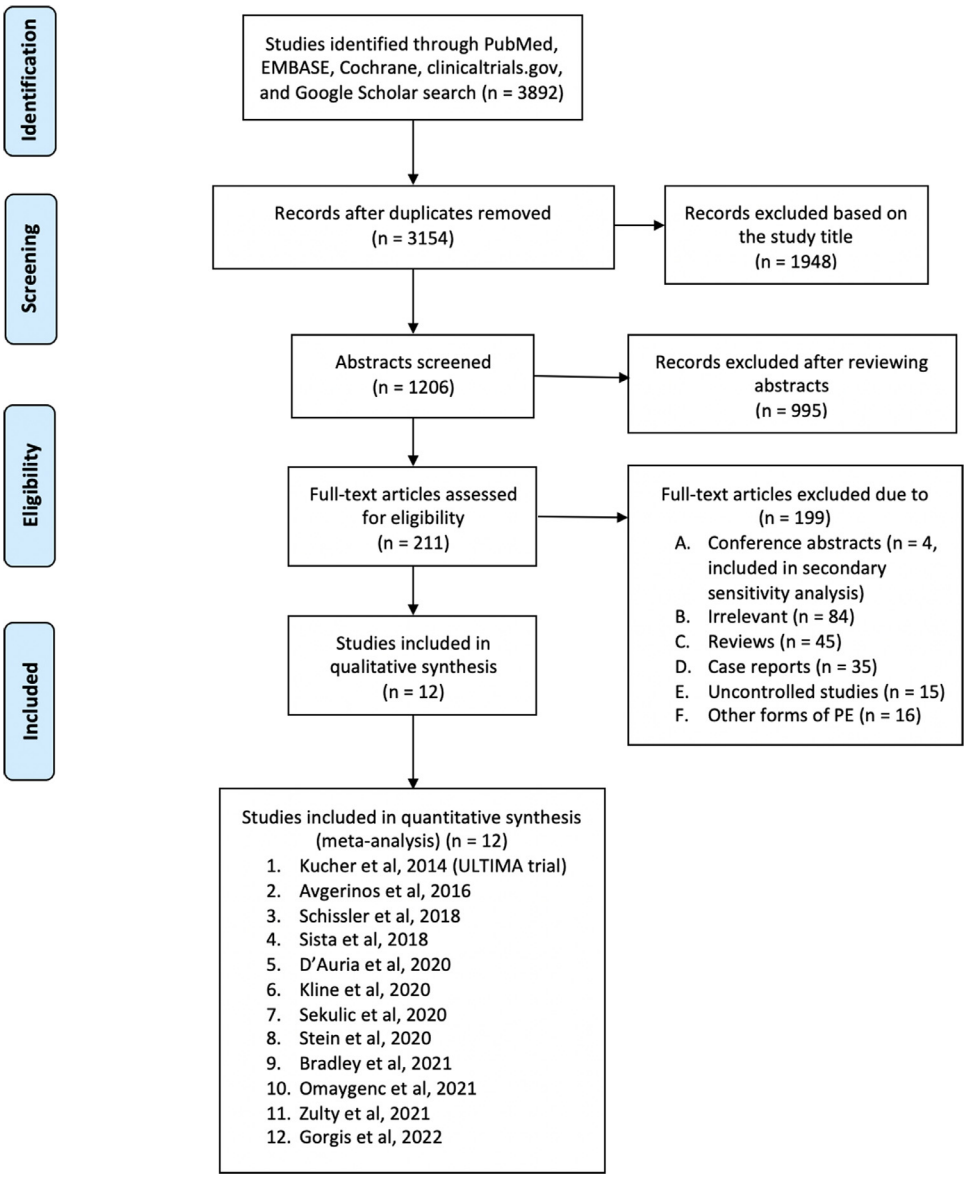

Figure 1. PRISMA flow diagram showing the selection process of the included studies.

9,789-patient meta-analysis. Although the SA group received only SA (most commonly unfractionated heparin), the CDT group received both CDT for focused delivery of thrombolytics and SA. Given the retrospective nature of most included studies, many authors performed propensity matching based upon demographic and clinical characteristics to reduce selection bias and potential confounding.[10–12,18,20] Most baseline characteristics were similar between the CDT and SA groups (diabetes mellitus [20% vs 24%], hypertension [50% vs 46%], smoking [27% vs 25%], coronary artery disease [8% vs 11%], congestive heart failure [4% vs 7%], chronic lung disease [13% vs 16%], previous stroke [6% vs 6%], previous deep vein thrombosis/PE [21% vs 24%], hypercoagulable state [4% vs 7%], hormonal contraceptive use [11% vs 10%], and recent surgery [19% vs 15%], respectively). However, the CDT group had more patients with obesity (43% vs 36%); the SA group had more patients with renal failure (11% vs 17%) and cancer (13% vs 21%). The characteristics of the included studies are listed in Table 1, and the baseline clinical characteristics of patients are listed in Table 2.

In patients with sPE, CDT was associated with significantly lower in-hospital mortality (RR 0.41, 95% CI 0.30 to 0.56, p <0.00001, I^2 = 0%; Figure 2), 30-day mortality (RR 0.37, 95% CI 0.18 to 0.73, p = 0.004, I^2 = 0%; Figure 2), 90-day mortality (RR 0.36, 95% CI 0.17 to 0.72, p = 0.004, I^2 = 0%; Figure 2), and a tendency toward lower 1-year mortality (RR 0.56, 95% CI 0.29 to 1.05, p = 0.07, I^2 = 36%; Figure 2) and improved RV recovery (RR 1.34, 95% CI 0.98 to 1.84, p = 0.07, I^2 = 40%; Figure 3) compared with SA. There were no statistically significant differences between the 2 strategies in major bleeding (RR 1.31, 95% CI 0.57 to 3.01, p = 0.53, I^2 = 14%; Figure 4), minor bleeding (RR 1.67, 95% CI 0.77 to 3.63, p = 0.20, I^2 = 8%; Figure 4), blood transfusion (RR 0.34, 95% CI 0.10 to 1.15, p = 0.08, I^2 = 17%; Figure 4), and hospital LOS (mean difference −0.35, 95% CI −2.73 to 2.04, p = 0.78, I^2 = 79%; Figure 3).

Table 1
Study characteristics of included investigations comparing CDT vs. SA in patients with submasssive PE

Study, year	Country	Study Period	Number of patients (n)			CDT device	Thrombolytic dose protocol	Contribution	Follow-up (months)	
			Total	CDT	SA				CDT	SA
Kucher et al, 2014[9]	Germany, Switzerland	2010-2013	59	30	29	USCDT (EkoSonic Endovascular System)	tPA 1 mg/h for 5 hours then 0.5 mg/h for 10 hours	90-day mortality, major and minor bleeding	3	3
Avgerinos et al, 2016[10]	USA	2009-2014	128	64	64	USCDT (EkoSonic Endovascular System) or conventional CDT (Cragg-McNamara or UniFuse)	tPA 2-4 mg bolus then 0.5-1 mg/h infusion	In-hospital, 90-day, and 1-year mortality, major and minor bleeding	12	12
Schissler et al, 2018[15]	USA	2011-2016	104	65	39	USCDT (EkoSonic Endovascular System)	Alteplase 0-5 mg bolus then 0.5-1 mg/h infusion	1-year mortality, major and minor bleeding, RV recovery, hospital LOS	12	12
Sista et al, 2018[22]	USA	2013-2014	79	25	54	USCDT (Ekowave) or conventional CDT (Cragg-McNamara or UniFuse)	tPA 1 mg/h for a total dose of 18-24 mg	In-hospital mortality, major bleeding, blood transfusion	-	-
D'Auria et al, 2020[20]	USA	2014-2016	198	99	99	USCDT or conventional CDT	tPA 1 mg/h for up to 12 hours	30-day and 1-year mortality, blood transfusion	24	24
Kline et al, 2020[16]	USA	2014-2019	130	40	90	USCDT (EkoSonic Endovascular System)	Alteplase 2 mg bolus then 0.75 mg/h infusion	In-hospital mortality, major and minor bleeding, blood transfusion	-	-
Sekulic et al, 2020[17]	Serbia, Bosnia, Herzegovina	2012-2018	251	24	227	USCDT (EkoSonic Endovascular System)	Alteplase 1-2 mg/h with a dose range of 12-50 mg	30-day mortality, major bleeding	1	1
Stein et al, 2020[11]	USA	2016	8,170	1,260	6,910	USCDT or conventional CDT	-	In-hospital mortality	-	-
Bradley et al, 2021[18]	USA	2011-2018	42	21	21	Conventional CDT	tPA 0.5 or 1 mg/h infusion	In-hospital mortality, minor bleeding, blood transfusion, hospital LOS	-	-
Omaygenc et al, 2021[21]	Turkey	2015-2019	30	14	16	USCDT (EkoSonic Endovascular System) or conventional CDT	Alteplase 5 mg bolus then 1 mg/h infusion for 24 hours	Major and minor bleeding, blood transfusion	-	-
Zulty et al, 2021[19]	USA	2017-2019	214	37	177	Conventional CDT	-	In-hospital and 90-day mortality, major and minor bleeding	3	3
Gorgis et al, 2022[12]	USA	2013-2019	384	192	192	USCDT (EkoSonic Endovascular System)	tPA 2 mg bolus then 0.5-1 mg/h infusion for total 24 mg	In-hospital, 30-day, 90-day, and 1-year mortality, major bleeding, RV recovery, hospital LOS	12	12

CDT = catheter-directed thrombolysis; LOS = length of stay; PE = pulmonary embolism; RV = right ventricle; SA = systemic anticoagulation; tPA = tissue plasminogen activator; USCDT = ultrasound-assisted catheter-directed thrombolysis. - = no information available.

Table 2
Baseline clinical characteristics in CDT vs. SA group

	Kucher et al, 2014		Avgerinos et al, 2016		Schissler et al, 2018		Sista et al, 2018		D'Auria et al, 2020		Kline et al, 2020		Sekulic et al, 2020		Stein et al, 2020		Bradley et al, 2021		Omaygenc et al, 2021		Zulty et al, 2021		Gorgis et al, 2022	
	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA	CDT	SA
Age (years)	64	62	58.5	60.1	53.9	58.4	62	64	58	59	58	66	59.2	66.3	60	60	55.3	58.3	57.1	67.1	-	-	58.9	59.8
Male	37%	59%	47%	52%	48%	39%	60%	46%	47%	58%	50%	41%	67%	52%	52%	48%	67%	52%	57%	38%	-	-	48%	50%
DM	20%	14%	-	-	20%	10%	-	-	-	-	18%	19%	8%	23%	17%	17%	19%	24%	29%	56%	-	-	25%	30%
HTN	67%	52%	52%	50	46%	56%	-	-	-	-	-	-	-	-	-	-	62%	48%	14%	13%	-	-	59%	58%
Smoking	13%	24%	17%	14%	32%	28%	-	-	-	-	15%	11%	27%	22%	-	-	43%	24%	-	-	-	-	41%	50%
CAD	7%	3%	11%	16%	-	-	-	-	10%	13%	5%	9%	8%	15%	-	-	-	-	-	-	-	-	7%	9%
CHF	7%	3%	3%	11%	2%	3%	4%	4%	4%	2%	-	-	8%	22%	1%	0%	-	-	-	-	-	-	5%	7%
Chronic lung disease	-	-	19%	11%	28%	28%	4%	7%	12%	22%	-	-	4%	15%	12%	13%	-	-	-	-	-	-	13%	14%
Renal failure	13%	17%	-	-	8%	5%	-	-	-	-	-	-	12%	40%	8%	9%	10%	19%	-	-	-	-	12%	12%
Prior stroke	0%	3%	-	-	-	-	-	-	-	-	-	-	12%	8%	-	-	-	-	-	-	-	-	-	-
Prior DVT/PE	-	-	22%	5%	23%	28%	-	-	19%	27%	15%	24%	-	-	-	-	-	-	-	-	-	-	27%	34%
Hyper-coagulable state	-	-	6%	14%	-	-	-	-	8%	2%	-	-	-	-	-	-	0%	5%	-	-	-	-	3%	5%
Cancer	17%	7%	13%	22%	-	-	32%	35%	12%	15%	8%	29%	8%	15%	16%	15%	5%	29%	0%	19%	-	-	18%	21%
Contraceptives	-	-	9%	2%	12%	18%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Recent surgery	-	-	20%	20%	-	-	-	-	-	-	-	-	29%	16%	-	-	-	-	-	-	-	-	9%	8%
Obesity (BMI $\geq$ 30 kg/m^2)	-	-	-	-	60%	59%	-	-	-	-	63%	51%	27%	21%	-	-	-	-	21%	13%	-	-	-	-

BMI = body mass index; CAD = coronary artery disease; CDT = catheter-directed thrombolysis; CHF = congestive heart failure; DM = diabetes mellitus; DVT = deep vein thrombosis; HTN = hypertension; PE = pulmonary embolism; SA = systemic anticoagulation; - = no information available.

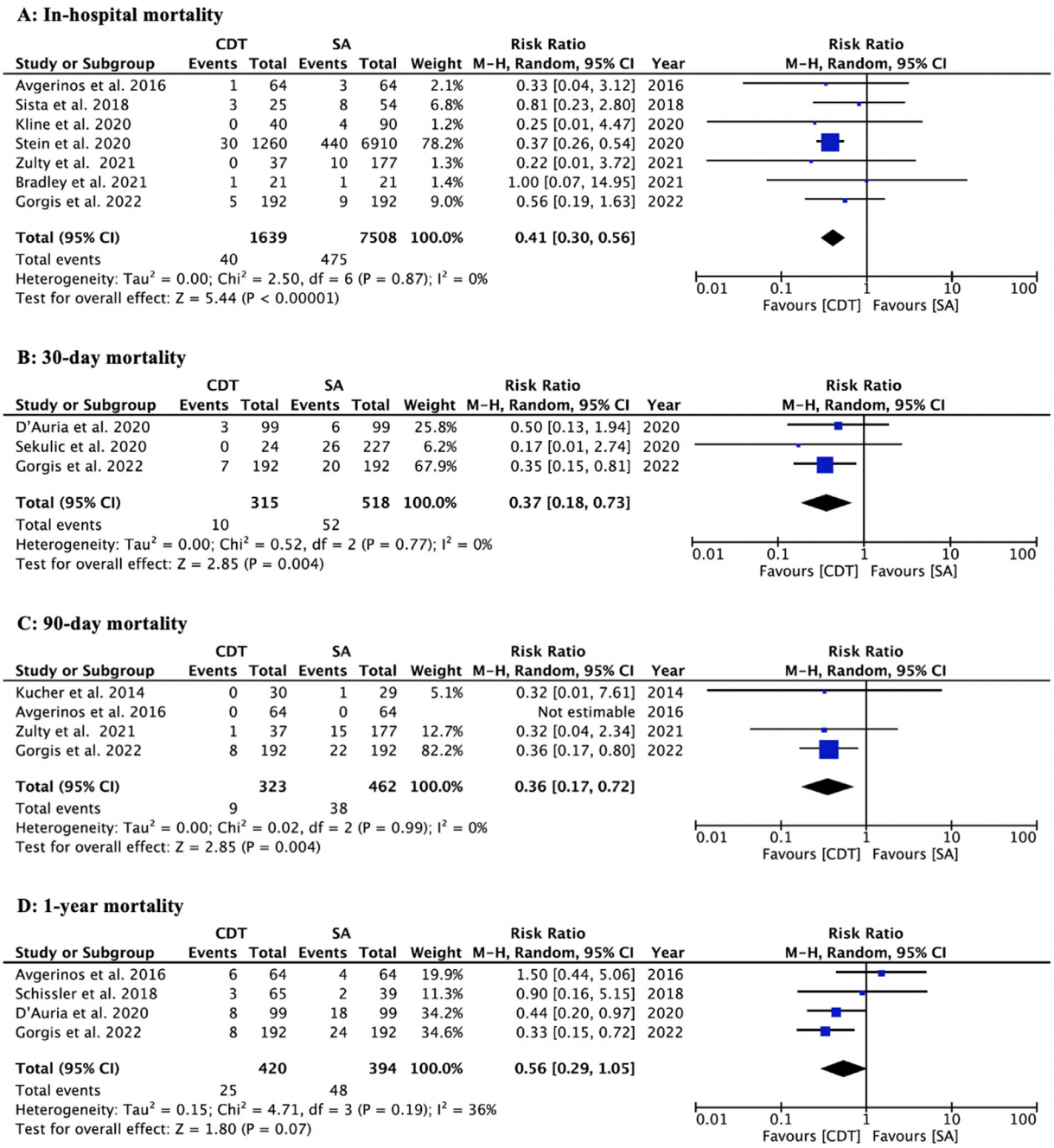

Figure 2. Forest plot for the comparison of CDT and SA alone for submassive PE. (*A*) In-hospital mortality; (*B*) 30-day mortality; (*C*) 90-day mortality; (*D*) 1-year mortality. Relative risks for individual studies are indicated by squares and 95% CIs by horizontal lines. Overall totals and their 95% CIs are represented by diamonds, in which the diamond's center denotes the point estimate, and the width denotes the 95% CI. The size of the squares and the diamonds are proportional to the statistical information conveyed. M-H = Mantel-Haenszel.

Discussion

The main findings of our meta-analysis include (1) CDT was associated with significantly lower in-hospital, 30-day, and 90-day mortality with a tendency toward lower 1-year mortality and improved RV recovery compared with SA alone in patients with sPE; (2) major and minor bleeding, blood transfusions, and hospital LOS were similar between the 2 strategies.

Our meta-analysis revealed lower rates of in-hospital mortality with CDT compared with SA alone for sPE. Many previous single studies found differences in in-hospital mortality to be statistically insignificant.[10,12,16,18,19,22] Perhaps because of the small magnitude of the difference, only the largest included study, involving 8,170 propensity-matched patients (1,260 [15%] CDT, 6,910 [85%] SA) with sPE identified from the Nationwide Inpatient Sample,

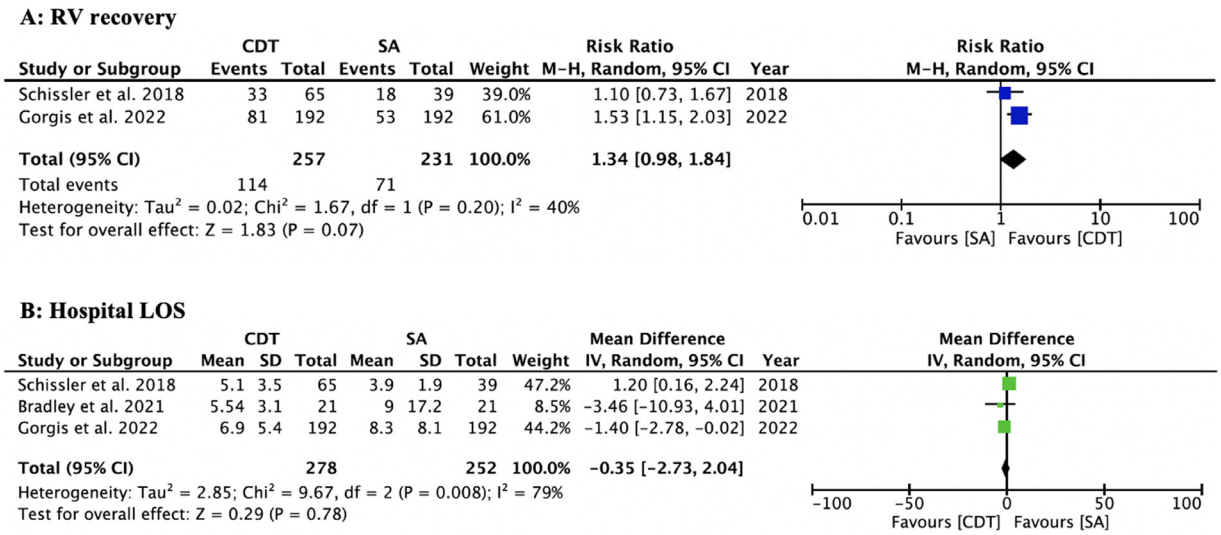

Figure 3. Forest plot for the comparison of CDT and SA alone for submassive PE. (*A*) RV recovery; (*B*) hospital LOS. Relative risks for individual studies are indicated by squares and 95% CIs by horizontal lines. Overall totals and their 95% CIs are represented by diamonds, in which the diamond's center denotes the point estimate, and the width denotes the 95% CI. The size of the squares and the diamonds are proportional to the statistical information conveyed. M-H = Mantel-Haenszel.

individually revealed significantly lower in-hospital mortality with CDT when administered within the first 3 days compared with SA (2.4% vs 6.4%, p <0.0001).[11] CDT was also associated with lower 30-day and 90-day mortality with a tendency toward lower 1-year mortality and improved RV recovery compared with SA. In contrast, the previous small meta-analysis by Siordia et al[23] reported similar 90-day mortality. However, our study included twice the number of studies (12 vs 6) and a sample size 12 times larger (9,789 vs 851), which increased the power of the present analysis. More importantly, our meta-analysis excluded abstracts from the primary analysis, which were included in the previous meta-analysis.[23]

The reduced mortality and improved RV recovery with CDT could be explained by enhanced lysis of the embolism, reducing the RV/LV ratio and thus preventing hemodynamic decompensation.[8,9,24] There is also a possibility of selection bias and residual confounding and that fewer sick patients with lower baseline risk profiles were selected for CDT. To date, the ULTIMA trial is the only RCT comparing CDT versus SA alone in treating sPE.[9] In this trial, 59 patients with sPE were randomized to receive either ultrasound-assisted CDT (USCDT) and unfractionated heparin (n = 30; CDT group) or unfractionated heparin alone (n = 29; SA group). At 24 hours from baseline, the primary end point of the RV/LV ratio was significantly lower in the CDT group versus the SA group (p <0.001).[9] These results support the findings presented in the SEATTLE II (Prospective, Single-arm, Multi-center Trial of EkoSonic Endovascular System and Activase for Treatment of Acute Pulmonary Embolism) and OPTALYSE PE (Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism) trials.[8,24] SEATTLE II demonstrated the effectiveness of CDT in reducing the mean RV/LV ratio and mean pulmonary artery systolic pressure at 48 hours from baseline (both p <0.0001). Although this trial compiled both massive (n = 31) and submassive (n = 119) PEs, a comparison between the 2 showed similar decreases in the RV/LV ratio (p = 0.31) and pulmonary artery systolic pressure (p = 0.81).[8] OPTALYSE PE recruited 100 patients with sPE and showed that even lower doses of tissue plasminogen activator and shorter delivery durations through USCDT were associated with improved RV/LV ratio (p = 0.0001) and reduced clot burden.[24]

Our meta-analysis found similar major and minor bleeding and blood transfusion rates between CDT and SA. LOS was also similar between the 2 strategies. CDT delivers thrombolytic therapy locally at the site of PE and at lower doses than ST, which could explain the difference between the similar bleeding rates with CDT and SA in our meta-analysis versus the higher bleeding rates with ST compared with SA in analyses comparing those 2 therapies.[25–27] The ULTIMA trial, which recruited 59 patients with sPE, reported no major bleeding episodes and 4 minor bleeding episodes (3 of 30 [10%] in the CDT group and 1 of 29 [4%] in the SA group, p = 0.61).[9] In contrast, 15 of 150 patients (10%) who underwent CDT in the SEATTLE II trial had major bleeding, with massive PEs causing more major bleeding events (p = 0.02). However, no intracranial hemorrhage was reported.[8] The OPTALYSE PE trial reported 4 major bleeding episodes after USCDT in 100 patients (4%), including 1 intracranial hemorrhage.[24]

Multiple larger RCTs comparing CDT plus SA versus SA alone in patients with sPE are ongoing, including the HI-PEITHO (Ultrasound-facilitated, Catheter-directed, Thrombolysis in Intermediate-high Risk Pulmonary Embolism, NCT04790370) trial. In the meantime, the present meta-analysis encompasses contemporary outcome data for CDT, which may help guide clinical decision-making for managing patients with sPE. Future trials in patients with sPE will inform an update to the current guidelines.[6,7]

Our meta-analysis has several limitations. First, most of the included studies were observational, which leads to

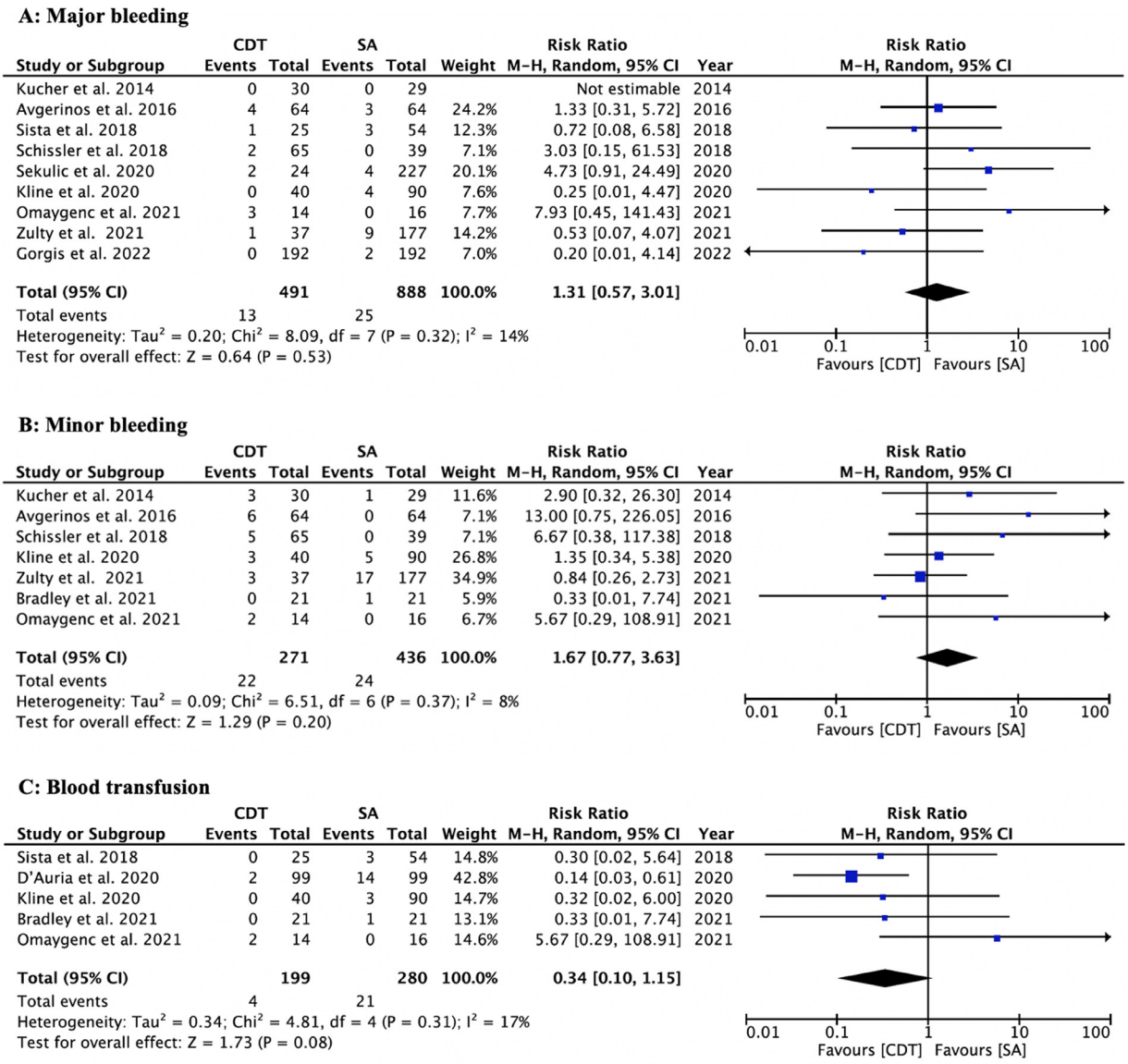

Figure 4. Forest plot for the comparison of CDT and SA alone for submassive PE. (*A*) Major bleeding; (*B*) minor bleeding; (*C*) blood transfusion. Relative risks for individual studies are indicated by squares and 95% CIs by horizontal lines. Overall totals and their 95% CIs are represented by diamonds, in which the diamond's center denotes the point estimate, and the width denotes the 95% CI. The size of the squares and the diamonds are proportional to the statistical information conveyed. M-H = Mantel-Haenszel.

inherent selection bias and unmeasured confounding. Only 1 RCT has addressed this topic to date.[9] More RCTs, such as the highly anticipated HI-PEITHO trial, are needed with larger sample sizes to mitigate biases and support more definitive conclusions. Second, patients in the CDT group received either USCDT or conventional CDT, and we were not able to perform a subgroup analysis based on the type of CDT received. However, USCDT and conventional CDT have previously been shown to achieve similar benefits in hemodynamics, RV recovery, and clinical outcomes.[28] Third, like all meta-analyses, the quality of our study depends upon the quality of the included studies. Despite these limitations, our study is strengthened by a large number of included studies and minimal heterogeneity in the selected studies.

In conclusion, in patients with sPE, CDT was associated with significantly lower in-hospital, 30-day, and 90-day mortality and a tendency toward lower 1-year mortality and improved RV recovery compared with SA alone. There were no significant differences in major and minor bleeding, blood transfusion, and hospital LOS between the 2 strategies. This study expands the evidence supporting CDT as first-line therapy for sPE, and more RCTs are indicated to confirm our findings.

Disclosures

Dr. Aronow is a Consultant for Philips and Silk Road Medical, neither of which are relevant to the study. The remaining authors have no conflicts of interest to declare.

Data availability

The data underlying this article are included in the article and its Supplementary Material.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.06.004.

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