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ORIGINAL ARTICLE

Transradial versus transfemoral approach for percutaneous coronary intervention in patients with ST-elevation myocardial infarction complicated by cardiogenic shock: a systematic review and meta-analysis

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Background In ST-elevation myocardial infarction (STEMI), transradial access (TRA) for percutaneous coronary intervention (PCI) is associated with less bleeding and mortality than transfemoral access (TFA). However, patients in cardiogenic shock (CS) are more often treated via TFA. The aim of this meta-analysis is to compare the safety and efficacy of TRA vs. TFA in CS.

Methods Systematic review was performed querying PubMed, Google Scholar, Cochrane, and clinicaltrials.gov for studies comparing TRA to TFA in PCI for CS. Outcomes included in-hospital, 30-day and ≥1-year mortality, major and access site bleeding, TIMI3 (thrombolytics in myocardial infarction) flow, procedural success, fluoroscopy time, and contrast volume. Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated using random effects models.

Results Six prospective and eight retrospective studies (TRA, $n = 8032$; TFA, $n = 23\,031$) were identified. TRA was associated with lower in-hospital (RR 0.59, 95% CI 0.52–0.66, $P < 0.0001$), 30-day and ≥1-year mortality, as well as less in-hospital major (RR 0.41, 0.31–0.56, $P < 0.001$) and access site bleeding (RR 0.42, 0.23–0.77, $P = 0.005$). There were no statistically significant differences in post-PCI coronary flow grade, procedural success, fluoroscopy time, and contrast volume between TRA vs. TFA.

Conclusions In PCI for STEMI with CS, TRA is associated with significantly lower mortality and bleeding complications than TFA while achieving similar TIMI3 flow and procedural success rates.

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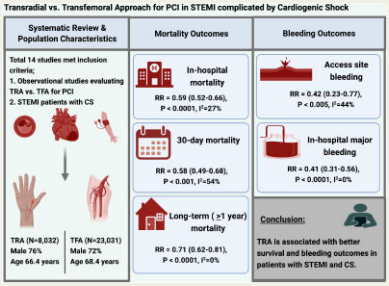
Graphical Abstract Transradial vs. transfemoral approach for PCI in STEMI complicated by cardiogenic shock.



Keywords

Introduction

Cardiogenic shock (CS) affects 4–12% of patients with acute ST-elevation myocardial infarction (STEMI) and is associated with increased mortality and morbidity.[1,2] Urgent percutaneous coronary intervention (PCI) remains the gold standard treatment for STEMI patients with CS. The concomitant use of antiplatelet and antithrombotic agents during the management of STEMI increases the risks of bleeding and PCI access site complications.[3]

Transradial access (TRA) for PCI has been shown to have lower rates of bleeding and mortality than transfemoral access (TFA) in emergent PCI in the setting of STEMI.[4,5] However, TFA has historically been preferred over TRA for patients with STEMI complicated by CS. This may be partially due to perceptions of achieving faster revascularization with TFA, using TFA access for mechanical circulatory support (MCS) device placement, and concerns about arterial vasoconstriction limiting TRA.[6] Whether TRA or TFA results in lower access-site complications has been minimally studied. The aim of this systematic review and meta-analysis is to compare outcomes in STEMI patients with CS undergoing PCI via TRA vs. TFA.

Methods

Data sources and search strategy

Systematic review and meta-analysis were performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) methodology.[7] A systematic search, without language restriction was performed in PubMed, EMBASE, Cochrane Library database, Google Scholar, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and ClinicalTrials.gov from inception to 9 October 2021 for studies comparing TRA vs. TFA in STEMI and CS. Conference proceedings of American College of Cardiology, American Heart Association, European Society of Cardiology (ESC) and Transcatheter Therapeutics (TCT) were also searched. The reference lists of original studies, conference abstracts, and relevant review articles were reviewed. We used combinations of the following keywords in our search strategy: radial access, TRA, femoral access, TFA, STEMI, acute myocardial infarction, acute coronary syndrome (ACS), PCI, coronary intervention, CS, randomized trial, and clinical trial. The search strategy was verified and independently validated by an experienced medical librarian.

Study selection, data extraction, and quality assessment

Studies that met the following criteria were included: (i) randomized trials or observational studies that included adults aged ≥18 years, (ii) studies evaluating the efficacy and safety of TRA vs. TFA, (iii) PCI (primary or rescue) in STEMI patients with CS. Case reports and editorials were excluded. Two investigators (SA and AL) independently performed the literature search, screened studies for eligibility, and extracted data using a standardized data collection form. Any differences in the included studies and collected data were resolved through consensus among the authors. The data for CS patients from the RIFLE-STEACS trial were abstracted from the meta-analysis by Pancholy et al., who reported that they had acquired the data from the authors of the paper by contacting them directly. The Newcastle and Ottawa Scale was used to assess the quality of observational studies (See supplementary material online, Table S3). The protocol for this meta-analysis was registered at PROSPERO, the international prospective register of systematic reviews.

Outcomes

The following clinical and procedural outcomes were extracted from individual studies: (i) all-cause mortality (cardiovascular and non-cardiovascular causes), (ii) study-defined major bleeding, (iii) access site bleeding, (iv) 30-day stroke, (v) 30-day major adverse cardiac and cerebrovascular events (MACCE), (vi) MCS utilization, (vii) post-PCI TIMI (Thrombolytics in Myocardial Infarction) flow grade, (viii) procedural success, (ix) procedure duration, (x) fluoroscopy time, (xi) contrast volume, and (xii) length of stay. Additionally, the definitions of MACCE and major bleeding were consistent across included studies. MACCE included mortality, myocardial reinfarction, target vessel revascularization, and cerebrovascular accident. Major bleeding used the TIMI definition of major bleeding.

Statistical analysis

The meta-analysis was performed using Review Manager (RevMan), Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Due to heterogeneity in the methodologies of the included studies, risk ratios (RRs) and 95% confidence intervals (CI) were calculated using the random effects Mantel–Haenszel method for dichotomous variables. Heterogeneity was assessed using Higgins' and Thompson's I^2 statistic, with I^2 values of <25%, 25–75%, and >75% corresponding to low, moderate, and high levels of heterogeneity,

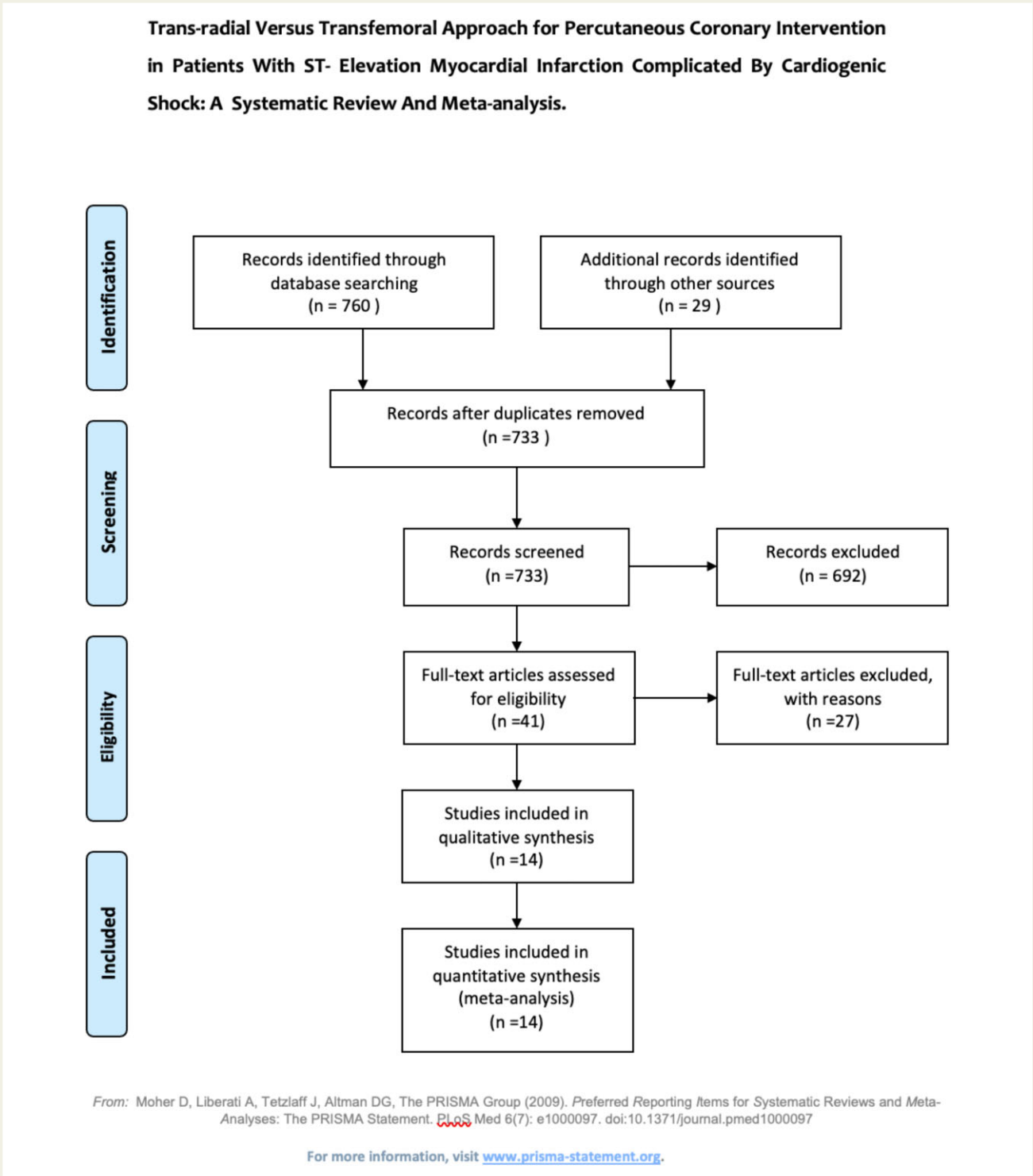


Figure 1 Flow diagram of systematic review and meta-analysis using the PRISMA methodology.

respectively. Since the duration of follow-up was variable among the included studies, we performed a sub-group analysis for mortality based on the duration of follow-up (in-hospital vs. 30 day or longer). We performed meta-regression analyses using STATA 17.0 (STATA CORP, College Station, TX, USA) to measure the influence of cardiac arrest (CA) prior to PCI, intra-aortic balloon pump (IABP) use, and access site bleeding on 30-day all-cause mortality. Sensitivity analysis was performed by the study exclusion method. Publication bias was estimated using Egger's test and using funnel plots for meta-analyses involving 10 or more studies.[8] The trim-and-fill method of Duval and Tweedie was employed to detect and adjust for any additional small study effects using JASP Version 0.15 (Amsterdam, The Netherlands).[9] A 2-tailed $P < 0.05$ was considered statistically significant for all analyses. The graphical abstract was created with BioRender.com (2022).

Table 1 Characteristics of included studies

First author	Year	Nation	Design	Total cohort	TRA	TFA	Study quality
RIFLE-STEACS (Romagnoli)[4]	2012	Italy	Post-hoc analysis of RCT	61	26	35	7
Rodriguez-Leor[16]	2013	Spain	Retrospective cohort	122	80	42	5
Radial Pump UP (Romagnoli)[10]	2013	Italy	Retrospective cohort	221	71	150	7
Bernat[11]	2013	Czech Republic	Prospective cohort	197	108	89	7
Mamas[15]	2014	United Kingdom	Retrospective cohort	7231	1877	5354	7
Fuji[12]	2014	Japan	Retrospective cohort	81	38	43	5
Iga[13]	2014	Japan	Retrospective cohort	85	60	25	5
Kedev[14]	2014	Macedonia	Prospective cohort	33	20	13	6
Roule[17]	2015	France	Prospective cohort	101	74	27	6
Kubo[20]	2019	Japan	Prospective cohort	16 740	4367	12 373	6
CULPRIT-SHOCK TRIAL (Guedeney)[18]	2020	Germany	Post-hoc analysis	673	118	555	7
Tehrani[19]	2020	USA	Retrospective cohort	153	82	71	7
Zahn[21]	2020	Germany	Retrospective cohort	1700	111	1589	5
Tokarek[22]	2021	Poland	Prospective cohort	3565	959	2606	7

RCT, randomized controlled trial; TRA, transradial access; TFA, transfemoral access

Results

Systematic review and study population

A total of 789 articles were identified through database search. After excluding duplicates and studies that did not meet inclusion criteria, a total of 14 studies (6 prospective and 8 retrospective) comparing TRA and TFA in STEMI PCI for CS were selected for this meta-analysis (Figure 1). Characteristics of included studies are listed in Table 1. The aggregate study population included 8032 TRA patients and 2303 TFA patients.[4,10–22] The TRA group had a mean age of 66.4 years comprised of 76% males; the TFA group had a mean age of 68.4 comprised of 72% males. The mean follow-up duration was 1.3 years. Baseline population characteristics are listed in Table 2. Utilization of MCS and procedural duration are summarized in Supplementary material online, Table S1. Target vessel and type of stent used are summarized in Supplementary material online, Table S2.

Mortality

In-hospital all-cause mortality was reported by 5/14 studies and was significantly lower in the TRA group as compared to the TFA group [RR 0.59 (95% CI 0.52–0.66), $P < 0.0001$, $I^2 = 27\%$, Figure 2A]. Similarly, 30-day mortality was reported by 11/14 studies and was lower in the TRA group as compared to the TFA group [RR 0.58 (0.49–0.68), $P < 0.001$, $I^2 = 54\%$, Figure 3A]. Mortality at the longest follow-up (>1 year) was reported by 4/14 studies and was similarly lower in the TRA group as compared to the TFA group [RR 0.71 (0.62–0.81), $P < 0.0001$, $I^2 = 0\%$, Figure 3B].

Bleeding, stroke, and MACCE

In-hospital major bleeding was reported by 7/14 studies and was lower in the TRA group compared to TFA group [RR 0.41 (0.31–0.56), $P < 0.0001$, $I^2 = 0$, Figure 2B]. Similarly, access site bleeding was reported by 7/14 studies and was lower in the TRA group as compared to the TFA group [RR 0.42 (0.23–0.77), $P = 0.005$, $I^2 = 44\%$, Figure 4A]. Thirty-day stroke was reported by 3/14 studies and was not statistically different between the two groups [RR 1.29 (0.37–4.47), $P = 0.69$, $I^2 = 53\%$, Supplementary material online, Figure S2B]. Thirty-day MACCE was reported by 7/14 studies and was lower in the TRA group as compared to the TFA group [RR 0.61 (0.50–0.75), $P < 0.001$, $I^2 = 52\%$, Figure 5B).

Procedural outcomes

Post-PCI TIMI-3 flow was reported by 8/14 studies and was not significantly different between the two groups [RR 1.02 (0.93–1.11), $P = 0.69$, $I^2 = 74\%$, Figure 4B]. Procedure success was reported by 5/14 studies and was not statistically different between the two groups [RR 1.15 (0.89–1.50), $P = 0.29$, $I^2 = 90\%$, Figure 5A]. IABP use was reported by 10/14 studies and was significantly higher in the TFA group as compared to the TRA group [RR 0.81 (0.73–0.91), $P = 0.0003$, $I^2 = 29\%$, Figure 6A]. Procedure duration was reported by 4/14 studies and was significantly lower in the TRA as compared to TFA group [mean difference (MD) −0.18 [−0.26–0.09], $P < 0.0001$, $I^2 = 0$, Figure 6B]. Fluoroscopy time was reported by 6/14 studies and was similar between the two groups [MD 0.30 (−0.25–0.85), $P = 0.28$, $I^2 = 0$, Supplementary material online, Figure S1A]. Contrast volume was reported by 9/14 studies and was similar between the two groups [MD 14.14 (−2.02–30.30), $P = 0.09$, $I^2 = 0$, Supplementary material online, Figure S1B]. Hospital length of stay was reported by 4/14 studies and was not statistically different between the two groups [MD −0.95 (−1.19 to −0.70), $P < 0.0001$, $I^2 = 0$, Supplementary material online, Figure S2A].

Sensitivity analyses

Sensitivity analysis of matched/randomized studies showed that use of TRA in CS patients was associated with lower in-hospital

Table 2 Baseline characteristics of study participants

First author	Year	Access	Age (y)	Male (%)	DM (%)	HTN (%)	HLD (%)	eGFR	Smoking (%)	CAD	Prior MI (%)	CA
RIFLE-STEACS (Romagnoli)[4]	2012	TRA	64	69	NR	NR	44	NR	35	NR	14	NR
		TFA	70	74	NR	NR	40	NR	34	NR	14	NR
Rodriguez-Leor[16]	2013	TRA	65	89	30	58	51	66	36	28	28	33
		TFA	68	74	19	57	62	53	26	45	45	38
Radial Pump UP (Romagnoli)[10]	2013	TRA	66	72	23	62	50	75	25	20	24	NR
		TFA	69	70	25	71	44	63	23	19	22	NR
Bernat[11]	2013	TRA	69	71	13	47	38	73	38	14	14	16
		TFA	64	71	26	54	46	72	44	18	18	15
Mamas[15]	2014	TRA	67	74	17	44	42	NR	30	21	21	NR
		TFA	67	69	21	47	42	NR	31	25	25	NR
Fuji[12]	2014	TRA	71	82	63	84	53	54	66	8	8	NR
		TFA	73	70	49	91	56	49	51	19	19	NR
Iga[13]	2014	TRA	68	83	32	53	52	NR	58	14	10	32
		TFA	70	72	44	64	32	NR	40	17	8	28
Kedev[14]	2014	TRA	57	60	35	45	37	NR	55	5	NR	NR
		TFA	63	46	31	54	31	NR	46	15	NR	NR
Roule[17]	2015	TRA	67	77	18	53	31	58	31	NR	12	19
		TFA	73	44	11	59	11	49	19	NR	19	44
Kubo[20]	2019	TRA	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
		TFA	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
CULPRIT-SHOCK TRIAL (Guedeney)[18]	2020	TRA	68	80	27	50	34	NR	33	NR	18	46
		TFA	69	76	34	62	35	NR	25	NR	17	55
Tehrani[19]	2020	TRA	64	75	43	NR	NR	NR	57	NR	16	23
		TFA	67	67	52	NR	NR	NR	35	NR	23	45
Zahn[21]	2020	TRA	69	78	30	NR	NR	NR	52	NR	19	NR
		TFA	68	70	31	NR	NR	NR	45	NR	27	NR
Tokarek[22]	2021	TRA	68	65	24	56	NR	NR	24	NR	17	30
		TFA	69	62	23	52	NR	NR	20	NR	20	47

TRA, transradial access; TFA, transfemoral access, DM, diabetes mellitus; HLD, hyperlipidaemia; HTN, hypertension; M, male; CAD, coronary artery disease; MI, myocardial infraction.

mortality [2/6, RR = 0.51 (0.42–0.63), $P < 0.0001$, $I^2 = 0$], 30-day mortality [3/6, RR = 0.60 (0.49—0.74), $P < 0.0001$, $I^2 = 51\%$], and mortality at long term [2/6, RR 0.72 (0.61–0.86), $P = 0.002$, $I^2 = 0$], respectively, when compared to TFA (Supplementary material online, Figure S3A, B, C). Similarly, TRA use in CS patients was associated with lower in-hospital major bleeding [3/6, RR 0.36 (0.23–0.55), $P < 0.00001$, $I^2 = 2\%$] and IABP use [3/6, RR 0.79 (0.73–0.86), $P < 0.00001$, $I^2 = 2\%$] (Supplementary material online, Figure S4A, B). Sensitivity analysis by the study exclusion method was performed to assess the effects of the largest study on the mortality outcomes. There was no significant change in the results for in-hospital all-cause mortality, 30-day all-cause mortality, and long-term all-cause mortality after the exclusion of studies by Kubo et al. and Guedeney et al., respectively (Supplementary material online, Figure S5A, B, C). Adjusted summary estimates with inverse variance analysis were calculated for in-hospital mortality, major bleeding, and 30-day mortality. The results of adjusted analyses were consistent with the main analyses (Supplementary material online, Figure S6A, B, C). Funnel plot distributions of RRs for 30-day all-cause mortality and IABP use showed a small degree of asymmetry. However, Egger's regression test and trim-and-fill models excluded the presence of significant publication bias (Supplementary material online, Figures S9A and S9B).

Meta-regression for mortality and IABP use

Random effects meta-regression analysis was performed to estimate the influence of IABP use on study outcomes. Our analysis showed that the difference in IABP use between TRA and TFA groups was not significantly associated with 30-day mortality ($P = 0.281$), access site bleeding ($P = 0.195$), or in-hospital major bleeding ($P = 0.130$) (Supplementary material online, Figure S7A, B, C). However, with a decrease in access site bleeding, the risk of all-cause mortality was significantly reduced as defined by the adjusted R^2 statistics with up to 90% of mortality explained by access site bleeding [$R^2 = 89.7\%$, $P = 0.003$) (Supplementary material online, Figure S8A).

Cardiac arrest as covariate for 30-day mortality

Six studies reported the incidence of CA prior to PCI. Patients undergoing PCI via TRA had a lower incidence of CA as compared to

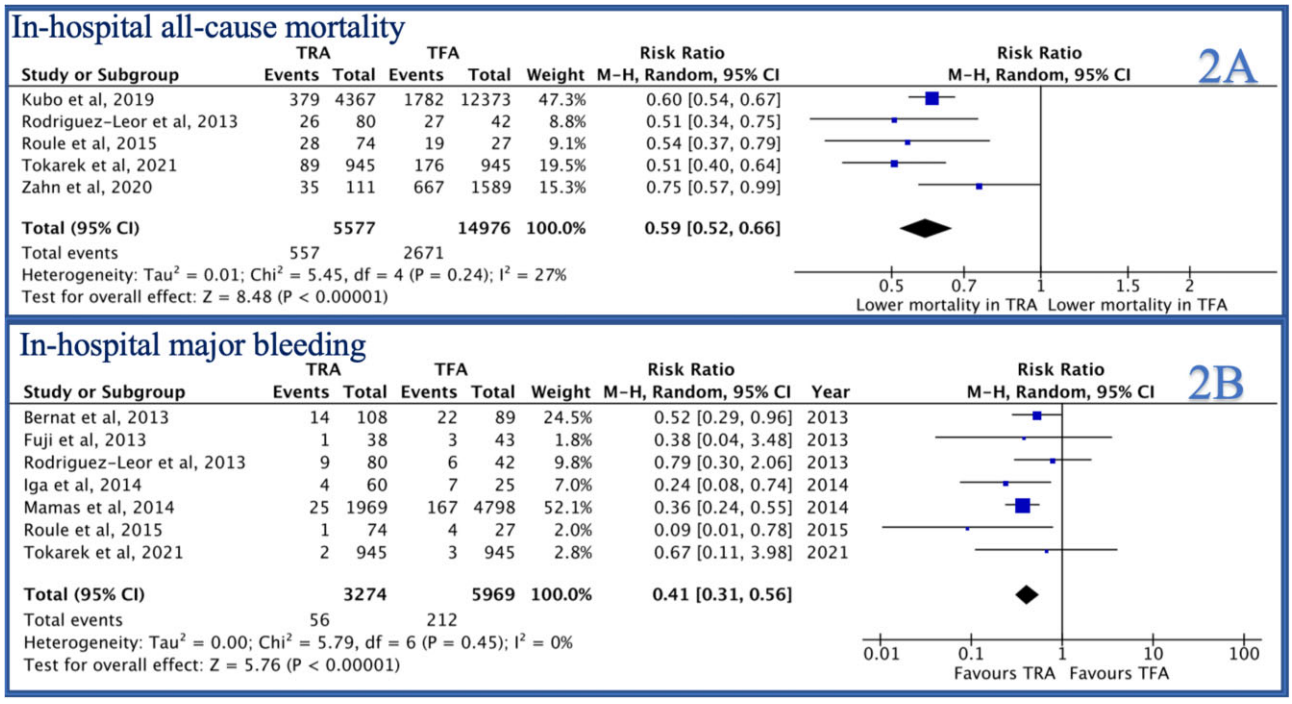


Figure 2 Forest plot comparing TRA vs. TFA for PCI in patients with STEMI complicated by cardiogenic shock (A: in-hospital all-cause mortality, B: in-hospital major bleeding).

the TFA group [RR 0.72 (0.59–0.87), $P = 0.001$, $I^2 = 52\%$]. Random effects meta-regression showed that the difference in the incidence of CA prior to PCI was not significantly associated with access site bleeding ($P = 0.13$) or in-hospital major bleeding ($P = 0.37$). However, CA had a significant effect on 30-day mortality ($R^2 = 79.08\%$, $P = 0.006$) (Supplementary material online, Figure S8B). Multivariate analysis showed that the combined difference in CA and access site bleeding could fully account for the observed variability in 30-day mortality ($R^2 = 100\%$, $P = 0.0008$).

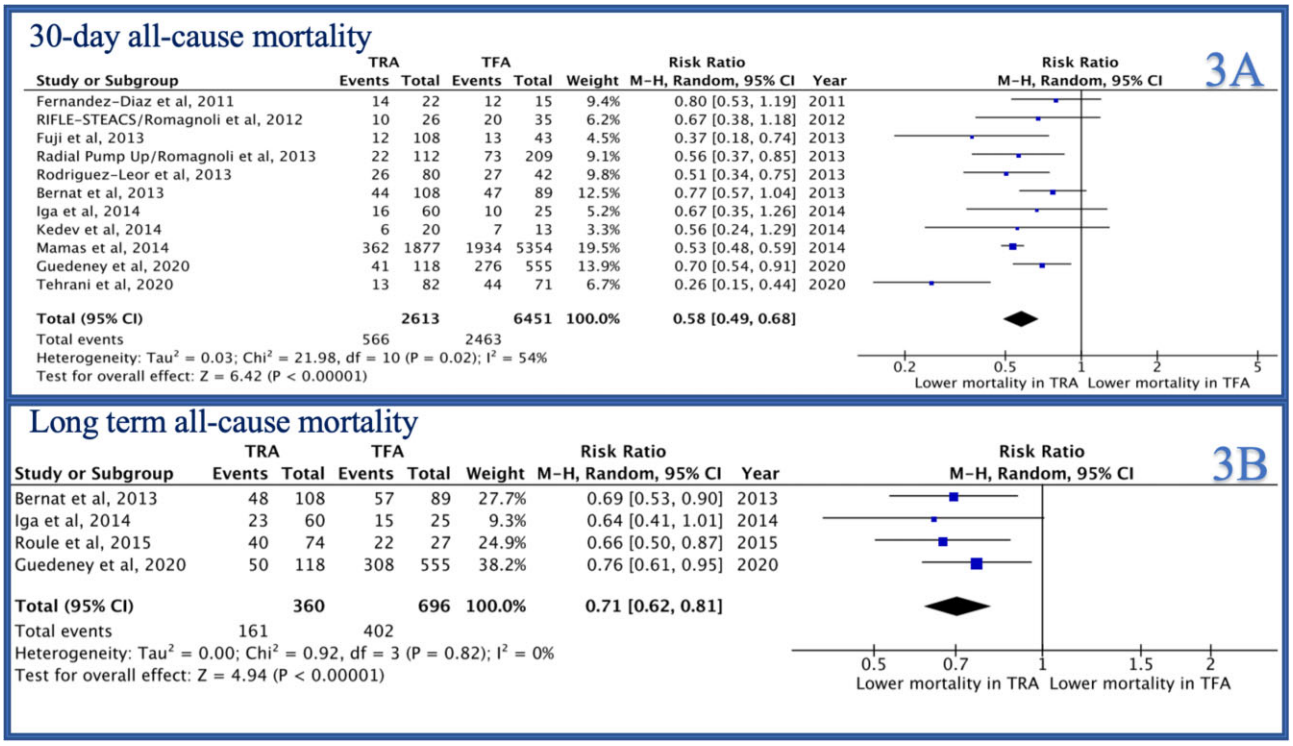
Discussion

We performed a systematic review and 14-study meta-analysis to compare periprocedural and clinical outcomes in patients with STEMI and CS undergoing PCI via TRA vs. TFA. We found that TRA was associated with lower all-cause mortality in the hospital, at 30-days and at long-term follow-up. Furthermore, TRA was associated with lower major bleeding, access site bleeding, MACCE, IABP utilization, procedure duration, and length of stay. There was no significant difference in post-PCI TIMI flow grade, procedural success, contrast volume, and fluoroscopy time between TRA and TFA.

Mortality

In the three decades since its first description, TRA has been increasingly used in clinical practice due to lower mortality compared with TFA for PCI in general. Specifically in STEMI with CS, our analysis showed TRA was associated with lower mortality than TFA at every time point. These findings are consistent with overall TRA vs. TFA use in STEMI PCI meta-analyses not specific to CS performed by Karrowni et al.[23] and Singh et al.,[24] respectively, but contradict the findings of the Minimizing Adverse Haemorrhagic Events by MATRIX (Transradial Access Site and Systemic Implementation of AngioX) trial[25] and SAFARI-STEMI (Safety and Efficacy of Femoral Access vs. Radial Access in STEMI),[26] which showed all-cause mortality was non-significantly different with TRA vs. TFA PCI in ACS patients. The benefit of TRA over TFA may be less pronounced in non-STEMI and unstable angina patients so that smaller trials with mixed ACS populations did not detect a difference.

Despite its mortality benefit, TRA is underutilized in STEMI patients with CS with significant operator and institutional variation.[27] Valle et al.[27] showed significant geographic, operator, and institutional variation in the use of TRA for STEMI PCI, but TRA use among all participating institutions was associated with mortality benefit. Reluctance to TRA adoption may also be due to the initial observational data, which showed lower procedural success and longer reperfusion time with TRA. These findings were also observed in analysis of the National Cardiovascular Disease Registry (NCDR) by Baklanov et al.,[28] which showed slightly increased door-to-balloon time (DTB) with TRA, but slightly increased DTB was balanced by the more favourable risk-adjusted mortality rates. Finally, not only short-term mortality, but even 1-year mortality may be influenced by the choice of access site. Non-fatal femoral site complications may leave patients with significant morbidity and deconditioning, which may not be fatal immediately but still potentiate 1-year mortality.



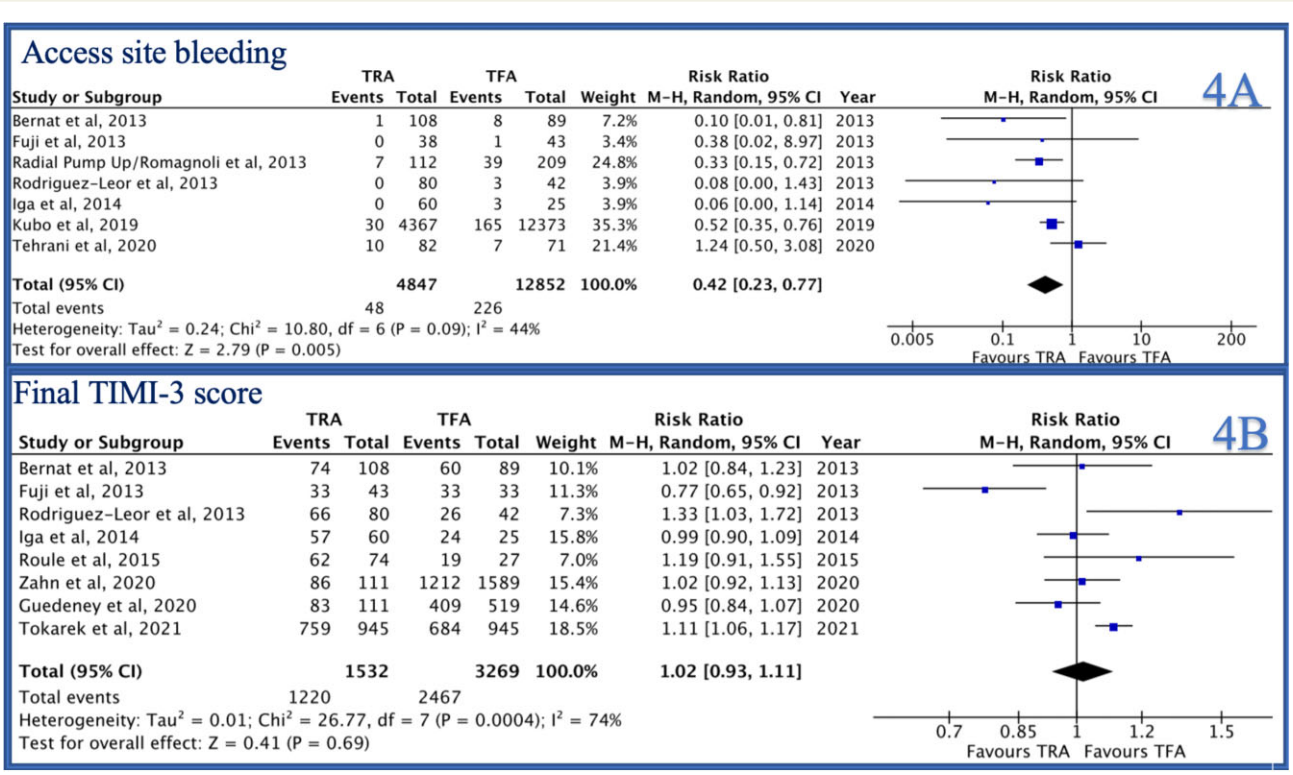
Study or Subgroup	TRA Events	TRA Total	TFA Events	TFA Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Fernandez-Diaz et al, 2011	14	22	12	15	9.4%	0.80 [0.53, 1.19]	2011
RIFLE-STEACS/Romagnoli et al, 2012	10	26	20	35	6.2%	0.67 [0.38, 1.18]	2012
Fuji et al, 2013	12	108	13	43	4.5%	0.37 [0.18, 0.74]	2013
Radial Pump Up/Romagnoli et al, 2013	22	112	73	209	9.1%	0.56 [0.37, 0.85]	2013
Rodriguez-Leor et al, 2013	26	80	27	42	9.8%	0.51 [0.34, 0.75]	2013
Bernat et al, 2013	44	108	47	89	12.5%	0.77 [0.57, 1.04]	2013
Iga et al, 2014	16	60	10	25	5.2%	0.67 [0.35, 1.26]	2014
Kedev et al, 2014	6	20	7	13	3.3%	0.56 [0.24, 1.29]	2014
Mamas et al, 2014	362	1877	1934	5354	19.5%	0.53 [0.48, 0.59]	2014
Guedeney et al, 2020	41	118	276	555	13.9%	0.70 [0.54, 0.91]	2020
Tehrani et al, 2020	13	82	44	71	6.7%	0.26 [0.15, 0.44]	2020
Total (95% CI)		**2613**		**6451**	**100.0%**	**0.58 [0.49, 0.68]**	
Total events	566		2463				

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 21.98$, df = 10 (P = 0.02); $I^2 = 54\%$
Test for overall effect: Z = 6.42 (P < 0.00001)

Study or Subgroup	TRA Events	TRA Total	TFA Events	TFA Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bernat et al, 2013	48	108	57	89	27.7%	0.69 [0.53, 0.90]	2013
Iga et al, 2014	23	60	15	25	9.3%	0.64 [0.41, 1.01]	2014
Roule et al, 2015	40	74	22	27	24.9%	0.66 [0.50, 0.87]	2015
Guedeney et al, 2020	50	118	308	555	38.2%	0.76 [0.61, 0.95]	2020
Total (95% CI)		**360**		**696**	**100.0%**	**0.71 [0.62, 0.81]**	
Total events	161		402				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.92$, df = 3 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 4.94 (P < 0.00001)

Figure 3 Forest plot comparing TRA vs. TFA for PCI in patients with STEMI complicated by cardiogenic shock (A: 30-day all-cause mortality, B: long-term all-cause mortality).



Study or Subgroup	TRA Events	TRA Total	TFA Events	TFA Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bernat et al, 2013	1	108	8	89	7.2%	0.10 [0.01, 0.81]	2013
Fuji et al, 2013	0	38	1	43	3.4%	0.38 [0.02, 8.97]	2013
Radial Pump Up/Romagnoli et al, 2013	7	112	39	209	24.8%	0.33 [0.15, 0.72]	2013
Rodriguez-Leor et al, 2013	0	80	3	42	3.9%	0.08 [0.00, 1.43]	2013
Iga et al, 2014	0	60	3	25	3.9%	0.06 [0.00, 1.14]	2014
Kubo et al, 2019	30	4367	165	12373	35.3%	0.52 [0.35, 0.76]	2019
Tehrani et al, 2020	10	82	7	71	21.4%	1.24 [0.50, 3.08]	2020
Total (95% CI)		**4847**		**12852**	**100.0%**	**0.42 [0.23, 0.77]**	
Total events	48		226				

Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 10.80$, df = 6 (P = 0.09); $I^2 = 44\%$
Test for overall effect: Z = 2.79 (P = 0.005)

Study or Subgroup	TRA Events	TRA Total	TFA Events	TFA Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bernat et al, 2013	74	108	60	89	10.1%	1.02 [0.84, 1.23]	2013
Fuji et al, 2013	33	43	33	33	11.3%	0.77 [0.65, 0.92]	2013
Rodriguez-Leor et al, 2013	66	80	26	42	7.3%	1.33 [1.03, 1.72]	2013
Iga et al, 2014	57	60	24	25	15.8%	0.99 [0.90, 1.09]	2014
Roule et al, 2015	62	74	19	27	7.0%	1.19 [0.91, 1.55]	2015
Zahn et al, 2020	86	111	1212	1589	15.4%	1.02 [0.92, 1.13]	2020
Guedeney et al, 2020	83	111	409	519	14.6%	0.95 [0.84, 1.07]	2020
Tokarek et al, 2021	759	945	684	945	18.5%	1.11 [1.06, 1.17]	2021
Total (95% CI)		**1532**		**3269**	**100.0%**	**1.02 [0.93, 1.11]**	
Total events	1220		2467				

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 26.77$, df = 7 (P = 0.0004); $I^2 = 74\%$
Test for overall effect: Z = 0.41 (P = 0.69)

Figure 4 Forest plot comparing TRA vs. TFA for PCI in patients with STEMI complicated by cardiogenic shock (A: access site bleeding, B: final TIMI-3 score).

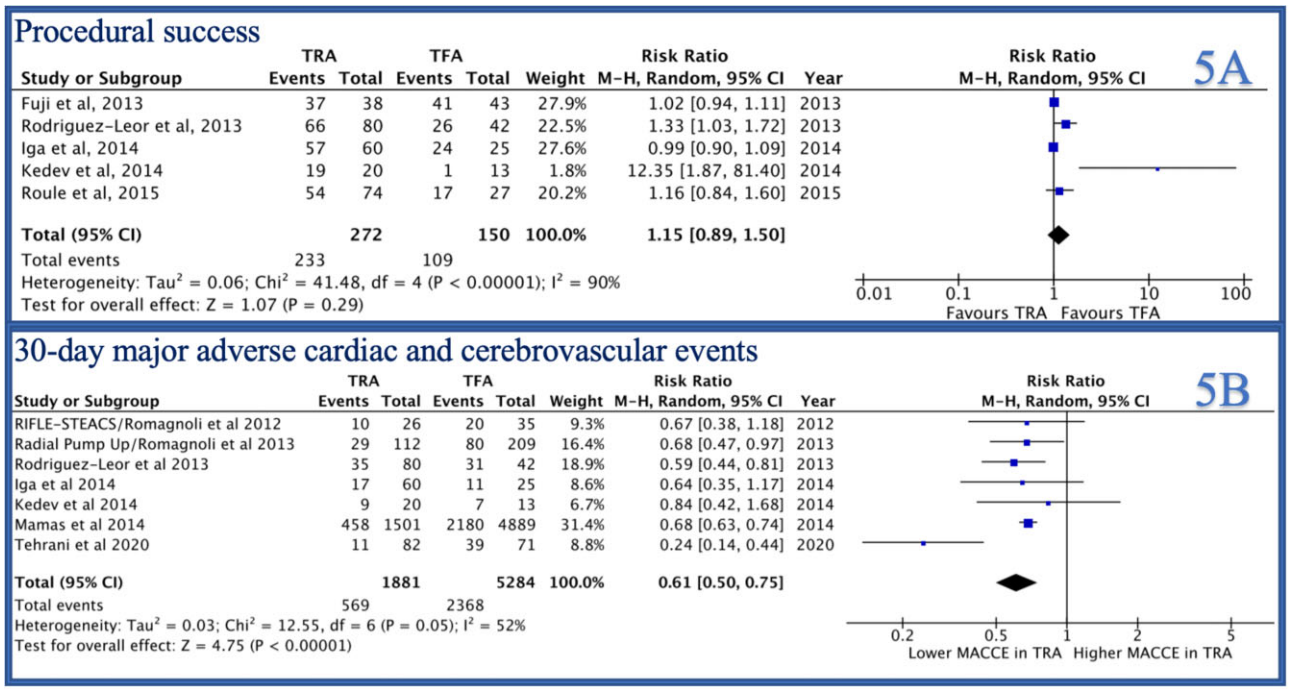


Figure 5 Forest plot comparing TRA vs. TFA for PCI in patients with STEMI complicated by cardiogenic shock (A: procedural success, B: 30-day MACCE).

Bleeding, stroke, and MACCE

Patients with STEMI and CS represent a high-risk population often treated with aggressive antithrombotic pharmacological and vascular interventions that convey benefits against ischaemia, albeit with higher vascular and bleeding complications. Our analysis showed TRA in STEMI with CS was associated with lower periprocedural bleeding than TFA, similar to the findings of the RIFLE-STEACS (Radial vs. Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) trial.[4] A prospective analysis by Nishihira et al.[29] demonstrated that periprocedural bleeding is associated with higher mortality in patients with STEMI and CS. Similarly, around 14% of noncardiac deaths reported in the Early Revascularization in Acute Myocardial Infarction Complicated by Cardiogenic Shock (SHOCK) trial were attributed to periprocedural bleeding.[18,30,31] To further this observation, our analysis showed a 30-day all-cause mortality benefit among TRA patients driven by the significant difference in access site bleeding between the groups. To help with access site bleeding, ultrasound guidance may be beneficial in patients with a weak pulse and hypotension such as STEMI patients with CS. The randomized RAUST trial (Radial Artery Access with Ultrasound Trial) demonstrated reduced time and number of attempts to achieve arterial access with ultrasound guidance.[32] Thus, TRA for PCI in STEMI patients with CS not only decreased periprocedural bleeding and thereby mortality, but also permitted safer utilization of robust antithrombotic therapies to improve overall ischemic outcomes in this high-risk patient population.[31]

There was no difference in stroke between TRA and TFA groups, which was consistent with the findings reported by Sirker et al.,[33] who concluded that radial access for cardiac catheterization was not associated with an increased risk of stroke. Although stroke risk was similar among the two groups, 30-day MACCE was lower in the TRA group, driven by the difference in mortality.

IABP Utilization

Patients with STEMI and CS are frequently treated with MCS devices, for which evidence is still accumulating. Our study found that IABP use was lower in the TRA group possibly suggesting preferential selection of TFA for patients who will receive post-PCI IABP, which may be inserted transfemorally through the access site used for PCI.[34] This could introduce selection bias, and the benefit of TRA on mortality and access site bleeding in our study could have been attributed to difference in the use of MCS. Therefore, we performed a meta-regression analysis based on the use of IABP and its association with 30-day mortality and access site bleeding. On meta-regression analysis, IABP use was not statistically associated with 30-day mortality or access site bleeding. Similar to IABP, newer left ventricular MCS devices including the Impella system (Abiomed, Danvers, MA, USA) also typically require femoral access for implantation,[34,35] further highlighting the importance of the radial-first approach in patients for whom post-PCI transfemoral MCS devices are planned to preserve the femoral site for that purpose.

Procedural parameters

Post-PCI TIMI flow grade, procedural duration and fluoroscopy time were similar with TRA and TFA in our analysis. This finding differed from the all-STEMI meta-analysis by Singh et al.[36] and reported increased fluoroscopy and DTB with TRA use in STEMI PCI, although these findings were associated with significant heterogeneity in their

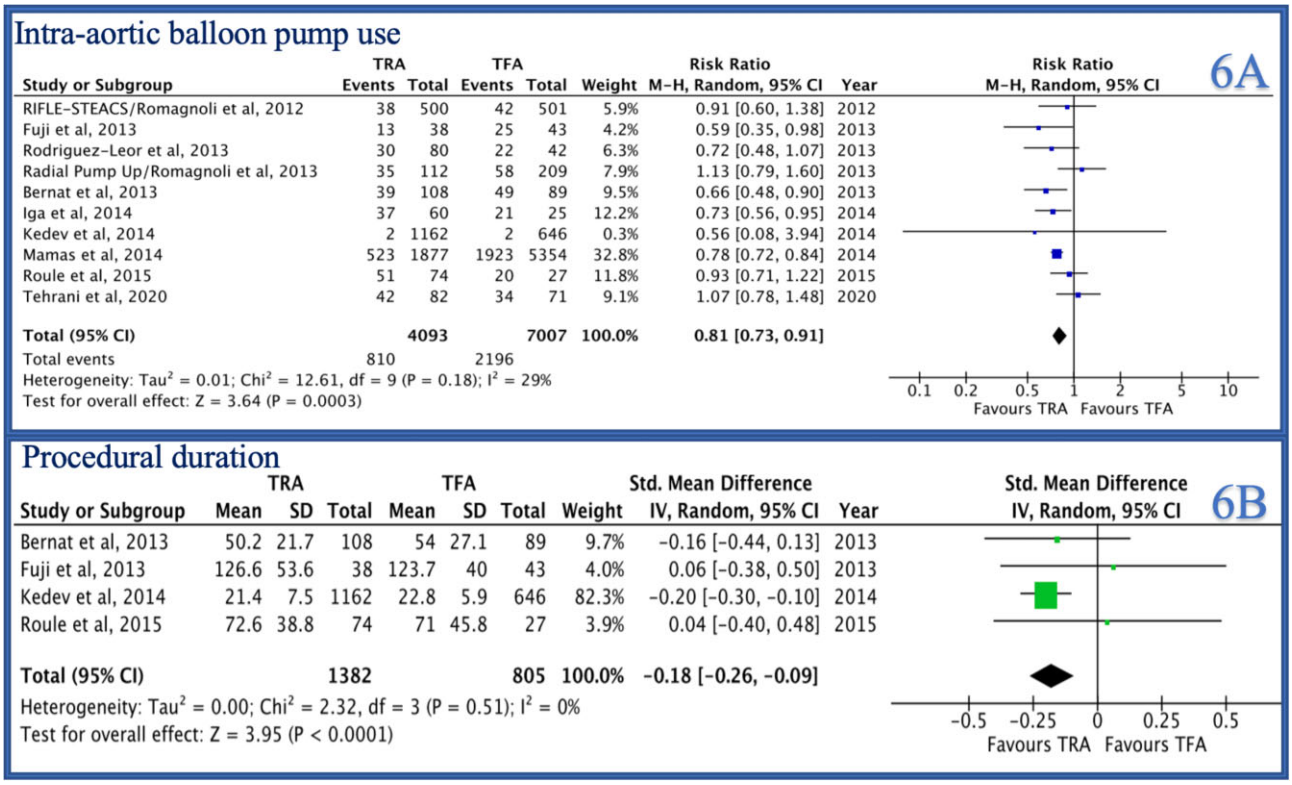


Figure 6 Forest plot comparing TRA vs. TFA for PCI in patients with STEMI complicated by cardiogenic shock (A: IABP, B: procedure duration).

analysis. Also, contrast volume and procedural success were similar in our study that was contrary to the results of Sciahbasi et al.,[37] who reported TRA PCI to be associated with higher contrast volume and difficulty in obtaining radial access successfully in patients with CS. These findings may reflect increasing proficiency in the TRA approach with growing adoption of TRA as a primary PCI approach. Consistent with this reasoning, Liam et al.[38] reported contrast volume to be lower in procedures performed by high-volume TRA operators than low-volume TRA operators. Finally, although TRA was not associated with difference in length of stay in this high-risk population, use of TRA has been established to be associated with improved patient comfort, early ambulation, and lower healthcare cost in broad PCI populations.[39–41]

Clinical implications

Although TRA PCI has been associated with lower vascular complications and better mortality, this finding is linked to both procedural volume and operator expertise.[42] Consequently, given better outcomes with increased operator proficiency, ESC has proposed >50 TRA cases to achieve TRA proficiency, and the Society for Cardiovascular Angiography and Interventions (SCAI) transradial working group has proposed >80 TRA cases to achieve proficiency.[43,44] Additionally, given the complexity of CS PCI and decision-making for MCS with the use of TFA and TRA, a randomized controlled trial with randomization to TRA vs. TFA following SCAI shock staging at time of index CS diagnosis could delineate more definitively the optimal access approach for these high-risk STEMI patients.[45] However, performing a randomized controlled comparison may itself present challenges of difficulty obtaining consent, operator proficiency and preference, and use of MCS.

Meta-analyses by Pancholy et al.,[6] Gandhi et al.,[46] and Del Rio-Pertuz et al.[47] evaluating TRA vs. TFA PCI in STEMI-CS were published previously. The analysis by Gandhi et al. was small, including only six studies, and reported only in-hospital outcomes. Del Rio-Perutz's work was a brief communication including only mortality as its outcome. In contrast to the analysis of eight studies by Pancholy et al., our contemporary meta-analysis adds to previous findings by including six additional studies. The previous meta-analyses differed substantially from ours by focusing only on 30-day all-cause mortality and 30-day MACCE and did not include details about periprocedural outcomes or long-term all-cause mortality. Additionally, our analysis reported details on procedural success, post-PCI coronary flow grade, procedural duration and use of IABP, which were not previously studied and are important considerations when choosing a PCI access site for STEMI patients with CS. As a result, the present study adds substantially to the literature.

Limitations

There are several important limitations of our meta-analysis. First, TRA use was highly operator-dependent with no specific selection criteria for PCI access site, leading to potential selection bias. Only one study reported when unsuccessful attempted TRA resulted

in TFA use. Second, only four studies reported patient outcomes data at ≥1 year, leading to limited applicability of our results over a longer follow-up period. However, a sensitivity analysis based on matched/randomized studies and study exclusion method was reported to further minimize the unmeasured confounding in the results. Third, data about ischemic outcomes such as recurrent MI, repeat revascularization, and crossover between access sites were not available. Finally, IABP was the most commonly reported MCS device in our analysis with limited information about the use of newer MCS devices such as Impella. Impella use was only reported explicitly by one study with less than 15 patients receiving the device. All studies either reported IABP as the only MCS device or reported MCS in aggregated, so specific data about Impella use were not available. However, since 9 of the 14 studies comprising this meta-analysis were conducted before the 2015 commercial release of Impella, Impella use was likely minimal. The on-going RECOVER-IV trial will report how Impella use affects mortality in patients with STEMI and CS.

Conclusions

In PCI for STEMI with CS, TRA is associated with significantly lower mortality and bleeding complications than TFA while achieving similar TIMI3 coronary flow and procedural success rates. A randomized controlled trial evaluating the optimal access for STEMI-CS should be pursued in accordance with SCAI shock staging to evaluate the role of a 'radial-first' approach in this high-risk population.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

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Conflict of interest

No authors report conflicts of interest to disclose.

Data availability

Data underlying this article are derived from a source in the public domain.

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