

Role of Aspiration and Mechanical Thrombectomy in Patients With Acute Myocardial Infarction Undergoing Primary Angioplasty

An Updated Meta-Analysis of Randomized Trials

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Objectives

This meta-analysis was designed to update data on clinical outcomes with aspiration thrombectomy or mechanical thrombectomy before primary percutaneous coronary intervention (PCI) compared with conventional primary PCI alone.

Background

The clinical efficacy of thrombectomy in acute myocardial infarction (AMI) remains uncertain.

Methods

Clinical trials that randomized AMI patients to aspiration (18 trials, n = 3,936) or mechanical thrombectomy (7 trials, n = 1,598) before PCI compared with conventional PCI alone were included.

Results

The weighted mean duration of clinical follow-up was 6 months. Aspiration thrombectomy vs. conventional primary PCI (18 trials, n=3,936): Major adverse cardiac events (MACE) (risk ratio [RR]: 0.76; 95% confidence interval [CI]: 0.63 to 0.92; p = 0.006) and all-cause mortality (RR: 0.71; 95% CI: 0.51 to 0.99; p = 0.049) were significantly reduced with aspiration thrombectomy. Beneficial trends were noted for recurrent MI (p = 0.11) and target vessel revascularization (p = 0.06). Final infarct size (p = 0.64) and ejection fraction (p = 0.32) at 1 month were similar. ST-segment resolution (STR) at 60 min (RR: 1.31; 95% CI: 1.16 to 1.48; p < 0.0001) and Thrombolysis In Myocardial Infarction blush grade (TBG) 3 post-procedure (RR: 1.37; 95% CI: 1.19 to 1.59; p < 0.0001) were both improved with aspiration thrombectomy. Mechanical thrombectomy vs. conventional primary PCI (7 trials, n = 1,598): there was no difference between the mechanical thrombectomy and conventional primary PCI arms in the incidence of MACE (RR: 1.10; 95% CI: 0.59 to 2.05; p = 0.77), mortality (p = 0.57), recurrent MI (p = 0.32), target vessel revascularization (p = 0.19), or final infarct size (p = 0.47). A benefit in STR at 60 min (RR: 1.25; 95% CI: 1.06 to 1.47; p = 0.007), but not TBG 3 (RR: 1.09; 95% CI: 0.86 to 1.38; p = 0.48) was noted.

Conclusions

Thrombectomy during AMI by manual catheter aspiration, but not mechanically, is beneficial in reducing MACE, including mortality, at 6 to 12 months compared with conventional primary PCI alone. (J Am Coll Cardiol 2013;62:1409-18) © 2013 by the American College of Cardiology Foundation

To reduce distal embolization, a number of adjunctive devices have been studied for use with primary percutaneous intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI). Broadly, they are

classified as aspiration thrombectomy (e.g., Export catheter, Medtronic, Minneapolis, Minnesota), mechanical thrombectomy (e.g., AngioJet, Medrad Interventional/Possis, Minneapolis, Minnesota), and embolic protection devices

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Guidelines Science Subcommittee; has received honoraria from the American College of Cardiology (Editor, Clinical Trials, *Cardiosource*), Duke Clinical Research Institute (clinical trial steering committees), Slack Publications (Chief Medical Editor, *Cardiology Today Intervention*), and WebMD (CME steering committees); is a Senior Associate Editor of the *Journal of Invasive Cardiology*; serves on the Data Monitoring Committee of the TOTAL trial; has received research grants from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, sanofi-aventis, and The Medicines Company; and participates in unfunded research with FlowCo, PLx Pharma, and Takeda. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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**Abbreviations
and Acronyms**

- CK** = creatine kinase
- CMR** = cardiac magnetic resonance imaging
- DE** = delayed enhancement
- MACE** = major adverse cardiac event(s)
- PCI** = percutaneous coronary intervention
- SPECT** = single-photon emission computed tomography
- STEMI** = ST-segment elevation myocardial infarction
- WMD** = weighted mean difference

(e.g., Percutaneous GuardWire, Minneapolis, Minnesota). In an earlier meta-analysis, we had demonstrated a salutary effect of aspiration thrombectomy devices on myocardial reperfusion parameters and mortality, whereas mechanical thrombectomy devices appeared to be associated with an increased risk of mortality (1).

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These findings were incorporated into the 2009 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for the management of patients with STEMI, and aspiration thrombectomy currently carries a Class IIa recommendation for use with primary PCI (2). However, the most recent trial on this topic showed no benefit on final infarct size at 30 days with routine aspiration thrombectomy in high-risk STEMI patients undergoing primary PCI (3). Similarly, the JETSTENT (AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting With Direct Stenting Alone in Patients With Acute Myocardial Infarction) trial (4) demonstrated a beneficial effect on major adverse cardiac events (MACE) with adjunctive mechanical thrombectomy over routine PCI in these patients. Because additional studies and prolonged follow-up of earlier trials have now been reported, we sought to perform an updated meta-analysis to determine the relative magnitude of benefit of adjunctive aspiration and mechanical thrombectomy devices on clinical and surrogate markers of reperfusion as compared with conventional primary PCI alone in patients presenting with STEMI.

Methods

Literature review. A computerized literature search of the Cochrane, Embase, and MEDLINE databases was conducted for randomized controlled trials published from January 1996 to December 2012, using the Medical Subject Heading and the key word search terms *thrombectomy*, *thrombus aspiration*, *thromboaspiration*, *aspiration*, *mechanical infarction*, and *myocardial infarction*. Only English-language studies were included. We also obtained recently presented data at national and international cardiology conferences. We also corresponded with authors when final results were not available and reviewed other meta-analyses on this topic. Additionally, we used Internet-based sources of information (<http://www.cardiosource.com>, <http://www.clinicaltrials.gov>, <http://www.theheart.org>, and <http://www.tctmd.com>).

Selection criteria. We selected studies that randomized patients within 12 h of acute myocardial infarction (AMI) to

either: 1) aspiration thrombectomy and primary PCI versus primary PCI alone or 2) mechanical thrombectomy and primary PCI versus primary PCI alone. We only included studies that reported clinical outcomes data and/or markers of myocardial reperfusion. We excluded studies that performed thrombectomy on saphenous vein grafts or that compared one thrombectomy device to another.

Outcomes/data abstraction. The primary clinical endpoint of interest was all-cause mortality. Secondary endpoints were recurrence of MI, target vessel revascularization, and MACE (composite of death, MI, and target vessel revascularization). Myocardial reperfusion was examined at 2 distinct time frames: immediately post-procedure (myocardial blush grade and ST-segment resolution) and at 1 to 3 months (change in infarct size and left ventricular ejection fraction after primary PCI). Definitions used to abstract outcomes are outlined in the [Online Appendix](#). Outcomes were tabulated by 2 independent reviewers (D.J.K., A.A.B.) and the number of events that occurred among each arm of a trial recorded. Discrepancies were resolved through discussion, and a third reviewer (D.L.B.) when necessary.

Statistical analysis. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was followed for this meta-analysis (5). For all clinical outcomes, an intention-to-treat analysis was utilized. For the reperfusion and infarct size outcomes, treatment-received (or per-protocol) analysis was utilized because there were generally fewer patients available for the determination of these outcomes. Summary relative risks (RRs) and their corresponding 95% confidence intervals (CIs) were computed for each dichotomous outcome using fixed- and random-effects (DerSimonian and Laird method) models (6). For outcomes with significant heterogeneity, the random-effects model is reported in the text and figures; for all others, the fixed-effects models are reported. If a study had no events in 1 group, we added 0.5 to each cell of the 2 × 2 table for that study to compute the summary RR. Heterogeneity between studies was assessed by calculating an I^2 statistic and publication bias with Begg's funnel plot method (7). For infarct size, the weighted mean difference (WMD) and corresponding 95% CIs were computed using random-effects modeling (8). Where these data were unavailable (4,9), they were imputed from available data using published approaches (10,11). Where significant heterogeneity was noted, the impact of important baseline covariates was examined using random-effects meta-regression, including baseline Thrombolysis In Myocardial Infarction (TIMI) flow grade 0/1, glycoprotein IIb/IIIa inhibitor use, direct stenting, and total ischemic time. As a form of sensitivity analysis, we repeated the aspiration thrombectomy versus conventional primary PCI analyses after exclusion of the TAPAS (Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) (12). A sensitivity analysis was also planned after removing studies of low methodologic quality based on bias assessment (13). Because the experimental arm was an interventional device, concealment

Table 1 Baseline Characteristics of the Patient Population

First Author/Study (Year) (Ref. #)	Device	Thrombectomy/Conventional Primary PCI							Follow-Up Duration, Months
		n	Age, Mean, Yrs	Baseline TIMI Flow Grade 0/1, %	Mean Ischemic Time, h*	GP IIb/IIIa Inhibitor, %	Clopidogrel Loading [†]	Direct Stenting in Thrombectomy Arm, %	
Aspiration thrombectomy vs. conventional primary PCI trials									
Dudek et al. (2004) (18)	Rescue	40/32	57/59	79/66	4.3/3.9	0/0	Yes	NA	H
REMEDIA (2005) (16)	Diver CE	50/49	61/60	86/90	4.6/5.0*	68/63	Yes	66	1
DEAR-MI (2006) (14)	Pronto	74/74	57/60	81/73	3.4/3.3	100/100	No	70	1
De Luca et al. (2006) (15)	Diver CE	38/38	67/65	100/100	7.2/7.6	100/100	No	92	6
Kaltoft et al. (2006) (9)	Rescue	108/107	65/63	68/69	4.0/3.5	96/93	Yes	81	1
TAPAS (2008) (12)	Export	535/536	63/63	55/60	3.2/3.1	93/90	Yes	55	12
Chao et al. (2008) (22)	Export	37/37	60/62	NA	5.6/5.9	19/32	Yes	51	6
EXPORT (2008) (21)	Export	120/129	59/61	99/100	6.0/5.1	4/14	NA	44	1
VAMPIRE (2008) (19)	TVAC	180/175	63/64	75/75	6.3/7.1	0/0	No	NA	8
EXPIRA (2009) (20)	Export	88/87	67/65	NA	6.2/6.1	100/100	Yes	76	9
Lipiecki et al. (2009) (24)	Export	20/24	59/59	100/96	7.1/7.4	30/74	Yes	50	H
Liistro et al. (2009) (25)	Export	55/56	64/65	69/76	3.2/3.5	100/100	Yes	21	6
PIHRATE (2010) (17)	Diver CE	100/96	61/59	97/98	NA	8/11	Yes	75	6
Ciszewski et al. (2011) (23)	Rescue/Diver CE	67/70	64/64	90/91	5.6/5.6	84/80	Yes	79	H
INFUSE-AMI (2012) (3)	Export	229/223	61/59	73/70	2.4/2.7	50/50	Yes	NA	1
MUSTELA (2012) (33)	Export	50/104	62/63 [‡]	95/81 [‡]	3.8/3/5 [‡]	100/100	Yes	NA	12
Noel et al. (abstr. 2005) (26)	Export	24/26	61	NA	4.7	NA	NA	83	H
NONSTOP (abstr. 2004) (27)	Rescue	129/129	64/66	NA	NA	NA	NA	NA	H
Mechanical thrombectomy vs. conventional primary PCI trials									
Beran et al. (2002) (32)	X-sizer	30/31	56/54	80/74	4.9/4.7	73/68	No	42	1
Napodano et al. (2003) (31)	X-sizer	46/46	61/64	74/85	4.0/3.4	43/41	No	61	1
Florence (2004) (30)	AngioJet	50/50	63/66	76/80	3.9/4.4	98/98	No	94	1
X AMINE ST (2005) (29)	X-sizer	100/101	61/62	NA	4.2/4.4	55/65	No	60	6
AIMI (2006) (28)	AngioJet	240/240	60/60	68/63	5.1/5.0	95/94	Yes	NA	6
JETSTENT (2010) (4)	AngioJet	256/245	63/64	84/84	2.7/2.8	97/98	Yes	94	12
MUSTELA (2012) (33)	AngioJet	54/104	62/63 [‡]	95/81 [‡]	3.8/3.5 [‡]	100/100	Yes	NA	12

*Defined as onset of ischemic symptoms until PCI, except where noted which is onset of symptoms until angiography. [†]Either pre- or post-procedure. [‡]Values for all thrombectomy (aspiration + mechanical) vs. conventional primary PCI alone.

AIMI = AngioJet Rheolytic Thrombectomy In Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction; DEAR-MI = Dethrombosis to Enhance Acute Reperfusion in Myocardial Infarction; EXPIRA = Thrombectomy With Export Catheter in Infarct-Related Artery During Primary Percutaneous Coronary Intervention; GP = glycoprotein; H = follow-up to hospital discharge; INFUSE-AMI = Infuse-Acute Myocardial Infarction; JETSTENT = AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting With Direct Stenting Alone in Patients With Acute Myocardial Infarction; MUSTELA = MULTidevice Thrombectomy in Acute ST-Segment Elevation Acute Myocardial Infarction; NA = not available; NONSTOP = Intracoronary Aspiration before coronary Stenting in Patients with Acute Myocardial Infarction; PIHRATE = Polish-Italian-Hungarian RAnomized ThrombEctomy Trial; PRISMA = Preferred Reporting Items for Systematic reviews and Meta-Analyses; REMEDIA = Randomized Evaluation of the Effect of Mechanical Reduction of Distal Embolization by Thrombus-Aspiration in Primary and Rescue Angioplasty; TAPAS = Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study; TIMI = Thrombolysis in Myocardial Infarction; VAMPIRE = VAcuum asPiration Thrombus REmoval; X AMINE ST = X-Sizer in AMI for Negligible Embolization and Optimal ST Resolution.

of allocation sequence was not possible. With the exception of a few studies (mostly abstracts) where it was unclear, outcome assessment was blinded in all trials. Thus, a sensitivity analysis based on quality was not pursued.

Mean follow-up was weighted according to the sample sizes of individual trials. All p values were 2-tailed, with statistical significance set at 0.05, and CIs were calculated at the 95% level. All analyses were performed using STATA software version 10.0 (STATA Corporation, College Station, Texas).

Results

A total of 25 trials in 5,534 patients met our selection criteria (3,4,9,12,14-33). Of these, 1,944 patients underwent adjunctive aspiration thrombectomy; 779, adjunctive mechanical thrombectomy; and 2,811, conventional primary PCI alone. The baseline characteristics of the included patients are listed in Table 1. The mean ischemic time ranged from 2.4 to 7.6 h. TIMI flow grade 0/1 at baseline was noted in 63% to 100% of patients. All patients received aspirin before

the procedure. Although the majority of patients received a thienopyridine pre- or post-procedure, this information was unavailable in 3 trials (26,27,33). Glycoprotein IIb/IIIa inhibitor use was variable. It was disallowed in the VAMPIRE (Vacuum Aspiration Thrombus Removal) trial (19) and in the trial by Dudek et al. (18); it was part of a 2 × 2 factorial design in the INFUSE-AMI (Infuse-Acute Myocardial Infarction) trial (50%) (3), and it was administered to all patients in 4 trials, either upstream (14,15,20) or intraprocedurally (25). Use of direct stenting ranged from 21% to 94%.

Aspiration thrombectomy versus conventional primary PCI (18 trials, n = 3,936). IMMEDIATE MYOCARDIAL REPERFUSION. The incidence of TIMI blush grade 3 post-procedure was 63.6% in the aspiration thrombectomy arm versus 48.5% with PCI alone (RR: 1.37, 95% CI: 1.19 to 1.59; p < 0.0001). There was evidence of high heterogeneity among the studies (I²: 87.8%). Similarly, the incidence of complete ST-segment resolution was higher in the aspiration thrombectomy arm (55.8% vs. 44.3%; RR: 1.31; 95% CI: 1.16 to 1.48; p < 0.0001). There was evidence of high heterogeneity

Table 2 Imaging Follow-Up

First Author/Study (Year) (Ref. #)	n	% of Clinical Follow-Up	Final Infarct Size, %		Final Ejection Fraction, %		Follow-Up, Months	Method of Assessment
			Thrombectomy	Conventional Primary PCI	Thrombectomy	Conventional Primary PCI		
Aspiration thrombectomy vs. conventional primary PCI								
Dudek et al. (2004) (18)	72	100	NA	NA	60.3 ± 9.2	55.3 ± 14.7	3	Echo
Kaltoft et al. (2006) (9)	189	88	15.0 ± 15.6	7.5 ± 11.9	51.0 ± 10.4	53 ± 8.2	1	SPECT
Chao et al. (2008) (22)	74	100	NA	NA	56.0 ± 10.0	57.0 ± 10.0	1	Echo
VAMPIRE (2008) (19)	216	61	NA	NA	57.1 ± 12.5	56.7 ± 12.3	6	Ventriculogram
EXPIRA (2009) (20)	72	41	9.0 ± 4.5	11.0 ± 8.7	49.0 ± 9.3	46.7 ± 10.6	3	CMR
Lipiecki et al. (2009) (24)	40	100	30.6 ± 15.8	28.5 ± 17.9	48.0 ± 12.0	45.0 ± 11.0	H	SPECT/CMR*
Liistro et al. (2009) (25)	111	100	NA	NA	55.0 ± 6.0	49.0 ± 8.0	6	Echo
Ciszewski et al. (2011) (23)	129	94	23.1 ± 13.3	28.9 ± 10.2	NA	NA	H	SPECT
INFUSE-AMI (2012) (3)	353	78	15.9 ± 9.7	16.7 ± 10.6	49.6 ± 10.0	49.5 ± 11.7	1	CMR
MUSTELA (2012) (33)	113	73	21.3 ± 11.3	19.3 ± 10.6	57.0 ± 10.0	59.0 ± 11.0	3	CMR
Noel et al. (abstr. 2005) (26)	50	100	12.9 ± 9.6	20.9 ± 7.8	NA	NA	H	CMR
Mechanical thrombectomy vs. conventional primary PCI								
Napodano et al. (2003) (31)	92	100	NA	NA	51.9 ± 7.7	49.9 ± 8.9	1	Echo
Florence (2004) (30)	100	100	13.0 ± 11.6	21.2 ± 18.0	NA	NA	1	SPECT
AIMI (2006) (27)	402	84	12.5 ± 12.1	9.8 ± 10.9	51.3 ± 11.5	52.3 ± 10.9	1†	SPECT
JETSTENT (2010) (4)	425	85	11.8 ± 15.2	12.7 ± 13.7	NA	NA	1	SPECT
MUSTELA (2012) (33)	116	75	17.5 ± 9.6	19.3 ± 10.6	NA	NA	3	CMR

*Final infarct size measured with SPECT, final ejection fraction measured by CMR. †21 days.

CMR = cardiac magnetic resonance imaging; H = hospital; SPECT = single-photon emission computed tomography; other abbreviations as in Table 1.

among the studies (I^2 : 60.9%) (Online Fig. 1). Meta-regression did not identify a difference based on baseline TIMI flow grade 0/1, glycoprotein IIb/IIIa inhibitor use, direct stenting, or total ischemic time for either of these outcomes.

FINAL INFARCT SIZE AND EJECTION FRACTION. Information on final infarct size was available in 7 studies ($n = 950$), and it was studied using delayed enhancement - cardiac magnetic resonance imaging (DE-CMR) in 4 studies (3,20,26,33) and using technetium-99m sestamibi in the other 3 (9,23,24) (Table 2). The mean duration of follow-up was 35.9 days (range: hospital discharge to 6 months). There was no difference in final infarct size between the aspiration thrombectomy and PCI-only arms (17.1% vs. 17.3%; WMD: -0.85% ; 95% CI: -4.37% to 2.67% ; $p = 0.64$). On restricting the analysis to DE-CMR studies only, there was still no difference in final infarct size between the 2 arms (WMD: -1.92% , 95% CI: -5.04% to 1.20% ; $p = 0.23$). Information on final ejection fraction was available in 9 studies and was obtained using CMR in 4 studies (3,20,24,33), SPECT in 1 (9), echocardiography in 3 (18,22,25), and cine-ventriculography in 1 (19) (Table 2). There was no difference in final ejection fraction between the 2 arms (53.0% vs. 52.8%; WMD: 1.09% ; 95% CI: -1.06% to 3.24% ; $p = 0.32$) (Online Fig. 2). Further, no difference was noted on restricting the analysis to studies assessing ejection fraction beyond 1 month ($n = 6$) (WMD: 2.32% ; 95% CI: -0.89% to 5.53% ; $p = 0.16$).

CLINICAL OUTCOMES. The weighted mean duration of follow-up was 5.9 months (range: hospital discharge to 12 months). The primary endpoint of all-cause mortality was significantly lower in the aspiration thrombectomy arm as compared with the PCI-only arm (2.7% vs. 3.9%; RR: 0.71; 95% CI: 0.51 to 0.99; $p = 0.049$). There was no evidence of heterogeneity (I^2 : 0%) or publication bias ($p = 0.60$). A random-effects model yielded similar results (RR: 0.73; 95% CI: 0.52 to 1.03; $p = 0.07$). On analyzing by duration of follow-up, there was no significant mortality benefit within 1 month (RR: 0.69; 95% CI: 0.43 to 1.08; $p = 0.11$), but mortality was significantly lower with aspiration thrombectomy at 6 to 12 months of follow-up (RR: 0.67; 95% CI: 0.45 to 1.00; $p = 0.05$). Reinfarction (1.6% vs. 2.4%; RR: 0.68; 95% CI: 0.42 to 1.10; $p = 0.11$) and target vessel revascularization (6.9% vs. 8.7%; RR: 0.79; 95% CI: 0.61 to 1.02; $p = 0.06$) were similar between the 2 arms, but numerically lower in the aspiration thrombectomy arm. The composite MACE outcome was significantly lower in the aspiration thrombectomy arm over the duration of follow-up (10.8% vs. 14.0%; RR: 0.76; 95% CI: 0.63 to 0.92; $p = 0.006$). All strokes were similar between the 2 arms (0.7% vs. 0.4%; RR: 1.31; 95% CI: 0.30 to 5.79; $p = 0.72$) (Fig. 1).

SENSITIVITY ANALYSIS. On excluding TAPAS, TIMI blush grade 3 (RR: 1.37; 95% CI: 1.18 to 1.59; $p < 0.0001$) and ST-segment resolution (RR: 1.33; 95% CI: 1.15 to 1.54; $p < 0.0001$) were still significantly improved with aspiration

thrombectomy over conventional primary PCI alone. MACE events remained significantly lower with aspiration thrombectomy (RR: 0.69; 95% CI: 0.51 to 0.93; $p = 0.016$), driven predominantly by a reduction in target vessel revascularization (RR: 0.66; 95% CI: 0.43 to 1.01; $p = 0.06$). There were no differences in mortality (RR: 0.83; 95% CI: 0.51 to 1.32; $p = 0.42$) or reinfarction (RR: 0.90; 95% CI: 0.45 to 1.81; $p = 0.76$) between the two arms.

Mechanical thrombectomy versus conventional primary PCI (7 trials, $n = 1,598$). **IMMEDIATE MYOCARDIAL REPERFUSION.** The incidences of TIMI blush grade 3 post-procedure were 48.8% in the mechanical thrombectomy arm versus 49.5% with PCI alone (RR: 1.09; 95% CI: 0.86 to 1.38; $p = 0.48$). There was evidence of high heterogeneity among the studies (I^2 : 75.0%). However, the incidence of complete ST-segment resolution was higher in the mechanical thrombectomy arm (74.9% vs. 63.7%; RR: 1.25; 95% CI: 1.06 to 1.47; $p = 0.007$). There was evidence of high heterogeneity among the studies (I^2 : 76.7%) (Online Fig. 3). Meta-regression did not identify a difference in outcomes based on baseline TIMI flow grade 0/1, glycoprotein IIb/IIIa inhibitor use, direct stenting, or total ischemic time for either of the 2 outcomes.

FINAL INFARCT SIZE AND EJECTION FRACTION. Data on final infarct size were available for 4 studies ($n = 1,043$), and studied using DE-CMR in 1 study (33) and with technetium-99m sestamibi in the other 3 (4,28,30) (Table 2). The mean duration of follow-up was 33.2 days (range: 21 to 90 days). There was no difference in final infarct size between the mechanical thrombectomy and PCI-only arms (12.7% vs. 13.3%; WMD: -1.34% ; 95% CI: -4.98 to 2.29 ; $p = 0.47$) (Online Fig. 4). Final ejection fraction could not be analyzed because data were available from 2 studies only.

CLINICAL OUTCOMES. The weighted mean duration of follow-up was 6.2 months (range: 1 to 12 months). The primary endpoint of all-cause mortality was similar between the mechanical thrombectomy and PCI-only arms (4.5% vs. 3.9%; RR: 1.20; 95% CI: 0.64 to 2.23; $p = 0.57$). There was evidence of moderate heterogeneity (I^2 : 30%), but no evidence of publication bias ($p = 1.0$). Meta-regression did not identify any difference in mortality based on baseline TIMI flow grade 0/1, glycoprotein IIb/IIIa inhibitor use, direct stenting, or total ischemic time. Reinfarction (0.8% vs. 1.4%; RR: 0.62; 95% CI: 0.23 to 1.62; $p = 0.32$), target vessel revascularization (4.0% vs. 5.1%; RR: 0.74; 95% CI: 0.48 to 1.16; $p = 0.19$), all strokes (1.3% vs. 0.4%; RR: 2.74; 95% CI: 0.93 to 8.01; $p = 0.07$), and the composite MACE outcome (10.1% vs. 10.9%; RR: 1.10; 95% CI: 0.59 to 2.05; $p = 0.77$) were all similar between the mechanical thrombectomy and PCI-only arms (Fig. 2).

Discussion

Our meta-analysis of data from 5,534 patients with AMI in 25 trials indicates that as compared with conventional

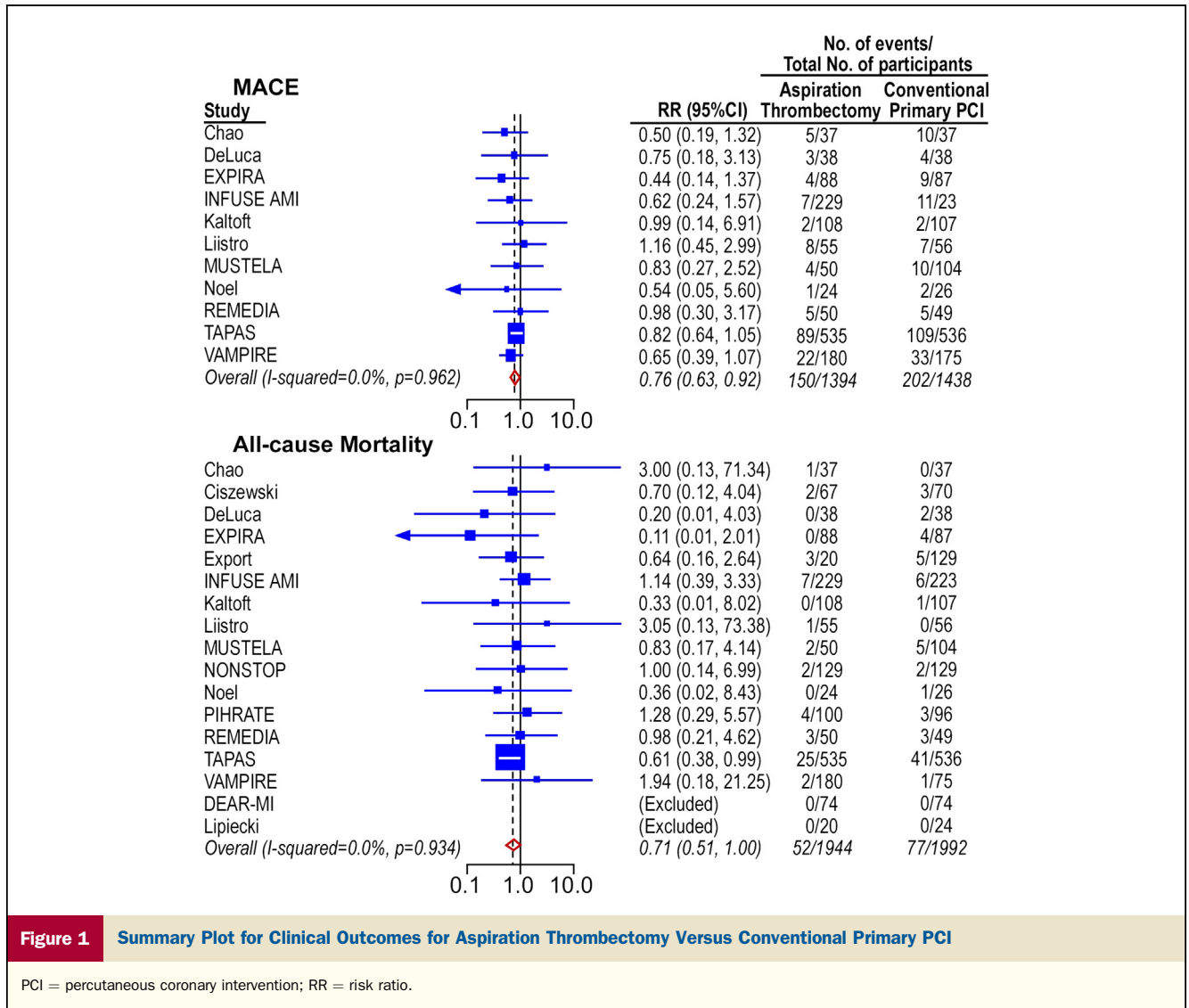


Figure 1 Summary Plot for Clinical Outcomes for Aspiration Thrombectomy Versus Conventional Primary PCI

PCI = percutaneous coronary intervention; RR = risk ratio.

primary PCI alone, aspiration thrombectomy was associated with a significant 24% reduction in MACE, including a 29% reduction in all-cause mortality at 6 months' median follow-up. Rates of reinfarction and target vessel revascularization were also numerically lower. On the other hand, mechanical thrombectomy had a neutral effect on clinical outcomes as compared with conventional primary PCI alone, with a consistent and concerning trend toward a higher incidence of stroke in all trials evaluated.

Given the importance of this topic and disparate results from the different clinical trials, a number of prior meta-analyses have been conducted (34–36). However, they have been limited by their duration of follow-up (30 days) and by combining all available devices into one thrombectomy category. Our findings extend findings from these prior meta-analyses, in that although no benefit in clinical outcomes was noted with aspiration thrombectomy at 30 days, we report a benefit at 6 to 12 months of follow-up. Our immediate reperfusion results are also similar to the only published head-

to-head trial (n = 99) between the 2 types of devices wherein aspiration thrombectomy resulted in superior reperfusion as compared with mechanical thrombectomy (37).

In the context of aspiration thrombectomy, 2 trials deserve special mention. On one hand, the results of the recent INFUSE-AMI trial may have caused uncertainty in the minds of some cardiologists regarding the utility of adjunctive thrombectomy for primary PCI patients. The primary endpoint for the INFUSE-AMI trial was final infarct size on DE-CMR, and was similar at 30 days between the aspiration thrombectomy and conventional primary PCI arms alone. Our findings are reassuring in that despite the inclusion of INFUSE-AMI, there remains a continued mortality benefit with aspiration thrombectomy at 6 to 12 months over conventional primary PCI. On the other hand, the only trial to show a mortality benefit with aspiration thrombectomy was TAPAS. This trial has been criticized for numerous reasons. These include possible selection bias (single-center study), unclear mechanism (no

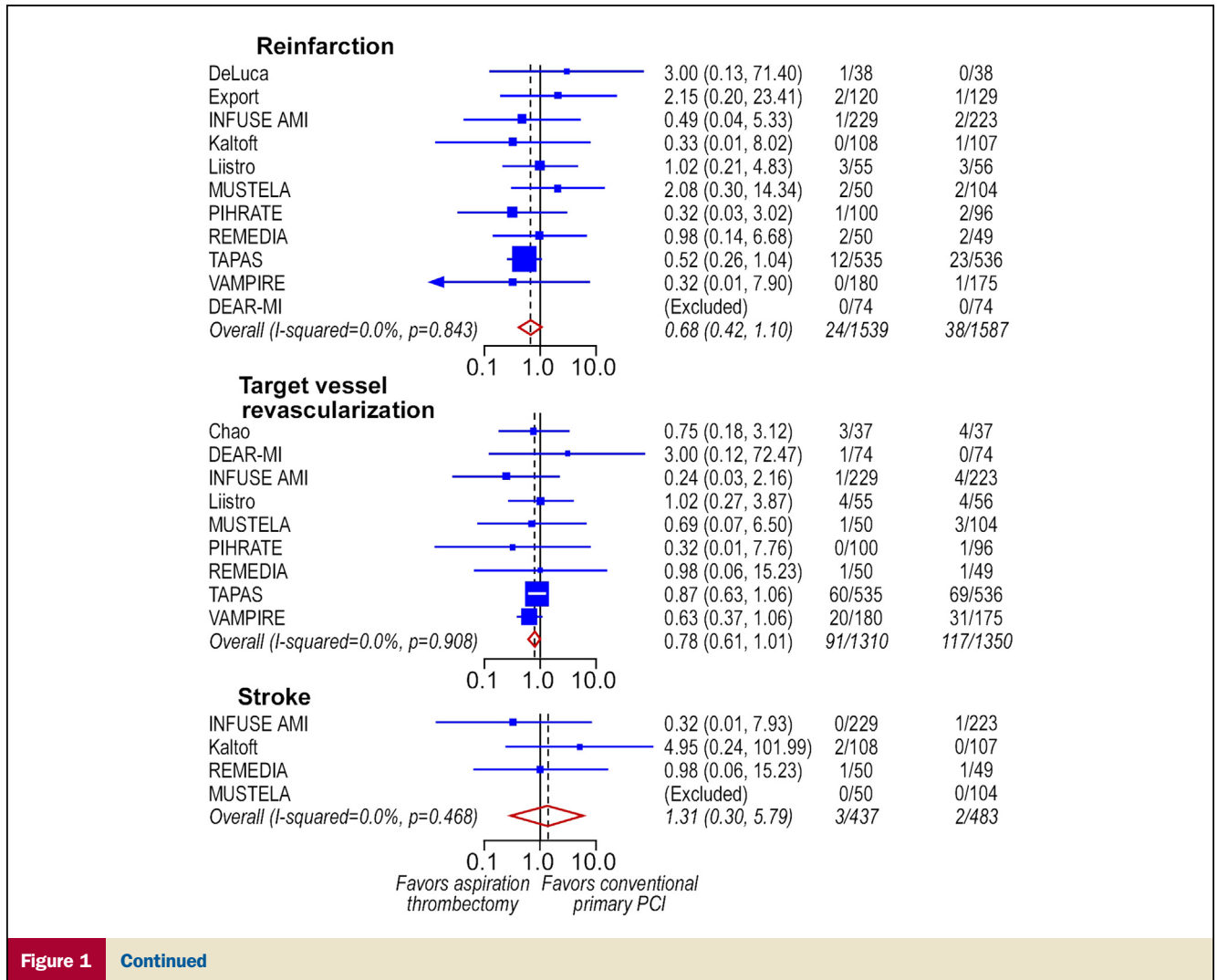
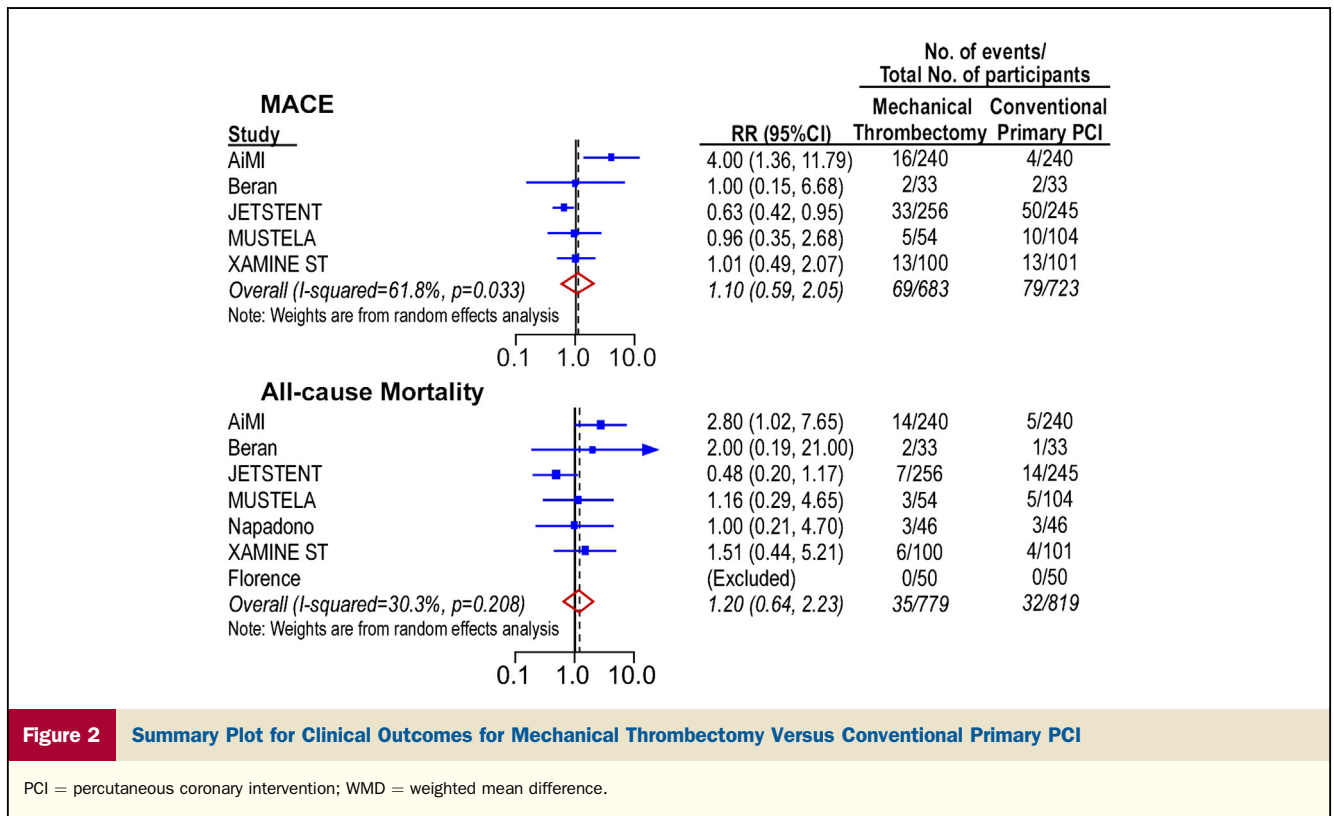


Figure 1 Continued

difference in enzymatic infarct size post-procedure but a significant difference in cardiovascular and all-cause mortality at 1 year), and the possibility of chance (the trial was not originally powered for mortality) (12). Our sensitivity analysis, however, suggests that even after exclusion of TAPAS from the analysis, there was still a significant reduction in MACEs at 6 months, driven predominantly by a reduction in target vessel revascularization rates. This could be due to better sizing of stents during the index procedure or less stent thrombosis as a result of thrombus removal (38).

Along these lines, it is interesting that numerically lower target vessel revascularization rates at 6 to 12 months were noted with both aspiration and mechanical thrombectomy compared with conventional primary PCI. Could thrombus extraction and less target vessel revascularization/late stent thrombosis thus represent an alternative mechanism for long-term clinical benefit with aspiration thrombectomy despite no difference in infarct size at 1 month compared with conventional primary PCI? This finding is hypothesis generating and needs further study. In a recent study, the reference vessel diameter and minimal lumen diameter

on dedicated quantitative angiographic analysis were both significantly greater with aspiration thrombectomy as compared with conventional primary PCI. Moreover, the mean stent area on optical frequency domain imaging was numerically larger with aspiration thrombectomy (39). An interesting finding in our analysis is the discrepancy between infarct size and left ventricular ejection fraction at 1 month and clinical outcomes at 6 to 12 months. What might explain this disconnect? As far as infarct size is concerned, it is widely appreciated that SPECT imaging has lower spatial resolution than does DE-CMR, especially for subendocardial infarcts (40). Thus, although SPECT studies were included to increase overall power, the addition of SPECT studies to DE-CMR studies to compare final infarct size estimates may have diluted the results. However, even after exclusion of the SPECT studies, we still noted that there was no difference in infarct size with aspiration thrombectomy. In the case of left ventricular ejection fraction, although there is good overall correlation between SPECT and CMR, discrepancies may be large for small changes (41). Two-dimensional echocardiography and cine-ventriculography do not have the same



accuracy as CMR for ejection fraction determination (42,43). Also, as outlined in Table 2, a significant proportion of patients clinically followed up in these trials did not have evaluable CMR studies (e.g., 22% in INFUSE-AMI and 59% in EXPIRA). This might have created selection bias and also a reduction in power to detect a true difference. From a technical standpoint, none of the DE-CMR studies reported image intensity thresholds utilized for infarct size quantification (44). Significant interstudy variability may have resulted if different definitions were used by different trials (45). Finally, surrogate endpoints do not always translate into clinically relevant outcomes, as has been noted several times before (46).

Our findings argue against a routine role for mechanical thrombectomy in patients undergoing primary PCI. A higher risk of stroke with mechanical thrombectomy, as we previously reported (1), and further confirmed in this study is also concerning. However, it should be noted that the combined sample size of the mechanical thrombectomy trials was <50% that of the aspiration thrombectomy trials. It is possible that the inclusion of larger mechanical thrombectomy trials in the future may show a different result.

Study Limitations. Because this was a meta-analysis, the validity of our results is dependent on the validity of the studies included. We did not include patient-level data. We also included data that have been reported only in conference presentations or in abstract form and so have not undergone peer review. This inclusion was necessary to maximize the utilization of all available data on this important topic. The

results of our sensitivity analysis suggest that results obtained by including data from abstracts did not differ significantly from results obtained from published manuscripts only (data not shown). We did not include other measures of infarct size, such as creatine kinase-myocardial band or troponin measurements, due to inconsistent reporting.

Two large multicenter trials comparing aspiration thrombectomy to conventional primary PCI, both powered for clinical endpoints, are currently ongoing (47,48). Until such time that these results are available, our current analysis supports the routine use of aspiration thrombectomy devices as adjunctive therapy in STEMI patients undergoing primary PCI over conventional primary PCI alone. The current IIa recommendation in the ACC/AHA STEMI guidelines also appears justified. Mechanical thrombectomy, on the other hand, does not appear to affect clinical outcomes and cannot be recommended for routine use in this patient population at this time.

Conclusions

Thrombectomy during AMI by manual catheter aspiration, but not mechanically, is beneficial in reducing MACE, including mortality, at 6 to 12 months compared with conventional PCI alone.

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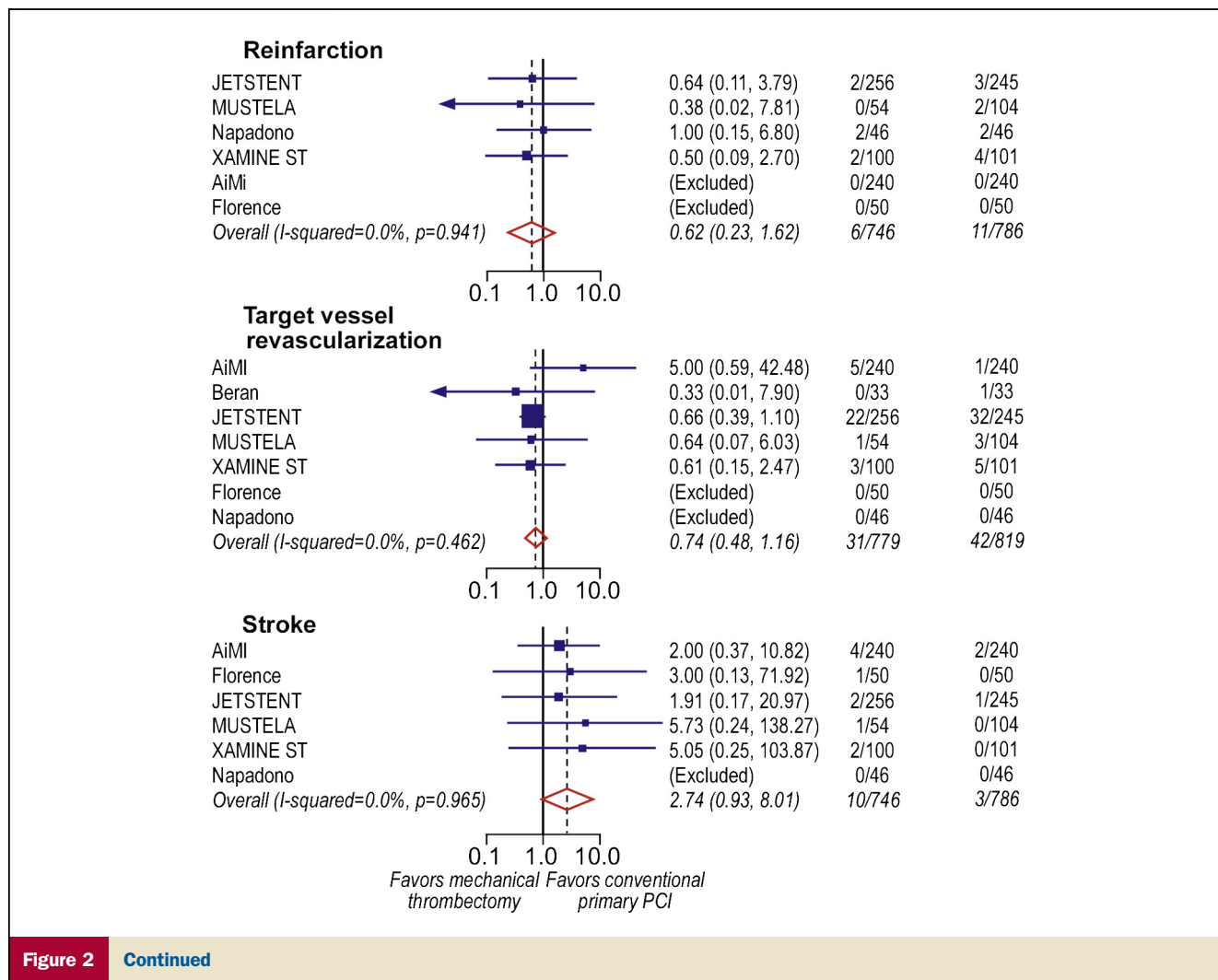


Figure 2 Continued

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Key Words: meta-analysis ■ mortality ■ myocardial infarction ■ outcomes ■ thrombectomy.

▶ APPENDIX

For a list of related acronyms and supplemental figures, please see the online version of this article.