Thrombus aspiration in patients with ST elevation myocardial infarction: Meta-analysis of 16 randomized trials

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ABSTRACT

Objective: The mortality rate is high in some patients undergoing primary percutaneous coronary intervention (PPCI) because of ineffective epicardial and myocardial perfusion. The use of thrombus aspiration (TA) might be beneficial in this group but there is contradictory evidence in current trials. Therefore, using PRISMA statement, we performed a meta-analysis that compares PPCI+TA with PPCI alone.

Methods: Sixteen studies in which PPCI (n=5262) versus PPCI+TA (n=5256) were performed, were included in this meta-analysis. We calculated the risk ratio (RR) for epicardial and myocardial perfusion, such as the Thrombolysis In myocardial Infarction (TIMI) flow, myocardial blush grade (MBG) and stent thrombosis (ST) resolution (STR), and clinical outcomes, such as all-cause death, recurrent infarction (Re-MI), target vessel revascularization/target lesion revascularization (TVR/TLR), stent thrombosis (ST), and stroke.

Results: Postprocedural TIMI-III flow frequency, postprocedural MBG II-III flow frequency, and postprocedural STR were significantly high in TA+PPCI compared with the PPCI alone group. However, neither all-cause mortality [6.6% vs. 7.4%, RR=0.903, 95% confidence interval (CI): 0.785-1.038, p=0.149] nor Re-MI (2.3% vs. 2.6%, RR=0.884, 95% CI: 0.693-1.127, p=0.319), TVR/TLR (8.2% vs. 8.0%, RR=1.028, 95% CI: 0.900-1.174, p=0.687), ST (0.93% vs. 0.90%, RR=1.029, 95% CI: 0.668-1.583, p=0.898), and stroke (0.5% vs. 0.5%, RR=1.073, 95% CI: 0.588-1.959, p=0.819) rates were comparable between the groups.

Conclusion: This meta-analysis is the first updated analysis after publishing the 1-year result of the "Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction" trial, and it showed that TA did not reduce the rate of all-cause mortality, Re-MI, TVR/TLR, ST, and stroke. *(Anatol J Cardiol 2015; 15: 175-87)*

Keywords: thrombus aspiration, meta-analysis, ST elevation myocardial infarction

Introduction

Primary percutaneous coronary intervention (PPCI) ensures both effective epicardial flow and has positive effects on short-long term survival in stent thrombosis (ST)-segment elevation myocardial infarction (STEMI) (1, 2). However, in some patients, although sufficient epicardial perfusion is achieved, impaired myocardial perfusion could be observed, and the incidence of adverse cardiovascular events is high, the recovery of left ventricular (LV) function is low, and the size of infarction is larger (3, 4). The mechanisms that might be responsible from impaired myocardial perfusion could be microvascular plugging that develops due to embolization of thrombotic or atheromatous debris (5, 6). Numerous adjunctive devices such as aspiration thrombectomy, mechanical thrombectomy, and embolic protec-

tion device were used to reduce embolization. Different results were found in comparison of manual thrombus aspiration (TA) with conventional PPCI; however, in most studies and meta-analysis, it was claimed that TA improves myocardial and epicardial perfusion and has positive effects on clinical outcomes (7-13). In a recently performed large-scale randomized controlled trial (RCT) "Thrombus Aspiration during Primary Percutaneous Coronary Intervention" (TAPAS) study (14, 15), it was indicated that TA is beneficial at both the 30-day and 1-year follow-up, and current guidelines remarked that the routine use of TA in patients admitted for STEMI could be done with Class-IIa recommendations (16, 17). However, the recently published "Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction" (TASTE) trial (18) is the largest study comparing TA and conventional PPCI until today, and it indicates that TA has no

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│  656 papers from databases search                    │
│  (PubMed and Cochrane library)                       │
│                                                       │
│           Papers excluded due to non-RCTs (Registries,│
│           reviews, case reports, editorials, etc.) (n=631)│
│                                                       │
│  25 potentially eligible RCT                          │
│                                                       │
│           One RCT was device comparison               │
│           Eight were related to mechanical thrombectomy│
│                                                       │
│  16 RCT included in the meta-analysis                 │
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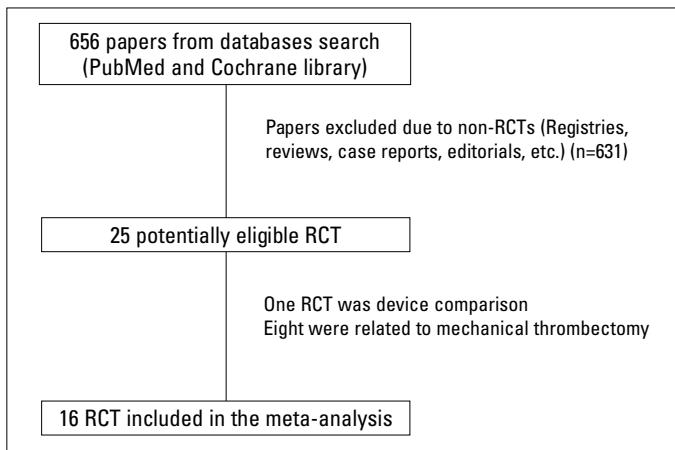
Figure 1. Flow chart of the trials included in the meta-analysis

effect on short- and long term-term mortality. However, a systematic review and meta-analysis that include the long-term outcomes of this study was not performed yet.

In this meta-analysis, we aimed to compare the beneficial effects of TA over conventional PPCI on epicardial and myocardial perfusion as well as the clinical outcomes of patients with STEMI undergoing PPCI.

Methods

Literature review

We searched the MEDLINE and Cochran Library for RCTs published from January 1996 to September 2014 in English and in humans. A computerized search using the terms "thrombectomy," "thromboaspiration," "aspiration thrombectomy," and "myocardial infarction" was made. Abstracts of national or international congress or unpublished trials were not included in the study.

Criteria for study selection

We chose the studies in which the patients admitted within 24 h of STEMI were randomized as PPCI+TA or PPCI alone. We excluded the studies that did not have clinical outcomes and/or myocardial perfusion symptoms as well as those in which mechanical thrombectomy was used.

In the first literature screening, 441 articles were obtained from MEDLINE and 215 from Cochrane Library. Only 25 of these were eligible for the analysis. Out of these 25, one RCT device comparison and 8 that were related to mechanical thrombectomy were excluded from the study. As a result, 16 RCTs were found to be suitable for the meta-analysis. Figure 1 displays the flow chart of trial selection.

Definitions of end-points

The primary end-point of the study is all-cause mortality. All-cause mortality was defined as death from any cause in most trials. In the trials that assessed only cardiovascular death, we accepted these as an all-cause mortality. The secondary end-points were reinfarction (Re-MI), target vessel revascularization/target lesion revascularization (TVR/TLR), stent thrombosis

Table 1. Berdeu scale (19) and frequency of endorsement (n=16)

Item	Yes (n)	No (n)
1. Obtained informed consent from patients	16	0
2. Approval by an regional ethical committee	16	0
3. Risk-Benefit ratio valuation	0	16
4. Respect for the principle of a priori equivalence	16	0
5. Refusal consent	1	15
6. Placebo ethical justification	0	16
7. Fairness of participant selection (inclusion/exclusion criteria)	16	0
8. Planned interim analysis	2	14
9. Prospectively defined stopping rules	0	16
10. Independent Monitoring Committee	4	12

(ST), stroke, major adverse cardiovascular events (MACE) (all-cause death, Re-MI, TVR/TLR), postprocedural myocardial blush grade (MBG), postprocedural Thrombolysis In myocardial Infarction (TIMI) flow grade, and postprocedural ST-segment resolution (STR).

Postprocedural myocardial perfusion signs were defined as follows: Final TIMI flow grade III, final MBG II or III, and ≥50% STR 60-90 min after PPCI were accepted as good myocardial perfusion.

Data extraction

Three independent reviewers (I.H.T, M.K., and A.K.) tabulated the following variables: 1) patient demographics, 2) angiographic characteristics, 3) the number of events, and 4) the duration of follow-up. Discrepancies were resolved by a fourth reviewer (E.A.).

To assess the methodological quality of included RCTs, the Berdeu scale was used (19). Findings are shown in Table 1.

Statistical analysis

The PRISMA statement was followed for this meta-analysis (20). The summary risk ratio (RR) and 95% confidence interval (CI) were calculated between TA+PPCI and PPCI alone regarding the clinical outcome using the fixed- and random-effects model. In figures and texts, the fixed-effects model was used. The analysis was performed by including and not including the TASTE study. The Cochrane Q statistic and I^2 statistic were used to evaluate heterogeneity. A funnel plot and Egger's regression test for funnel plot asymmetry were used to examine the likely presence of publication bias and small-study effects. Statistical significance was defined as p<0.05 (two-tailed tests). Analyses were performed using the Comprehensive meta-analysis software trial version 2 (Biostat, Englewood, NJ, USA).

We also applied Trial sequential analysis (TSA) to all RCTs included to meta-analysis. TSA was performed according to the monitoring boundaries approach for outcome measures such as all cause mortality, re-MI and TVR/TLR. TSA is a statistical method that combines an a priori information size calculation for a meta-analysis with adaptation of monitoring boundaries to

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Table 2. Baseline clinical characteristics of randomized controlled trials included in the meta-analysis (number of TA+PPCI or PPCI alone)

Study	Device	Center/Country	Year	Blinding	FU (m)	Number	Age	Male	DM	HT	Smoke	HL
Kaltoft (34)	Rescue	Denmark	2006	UB	1	108/107	65/63	82/86	9/6	33/22	59/69	10/10
Silva-Orrego (DEAR-MI) (32)	Pronto	Italy	2006	NA	1	74/74	57/59	62/56	16/11	28/32	38/43	26/18
Burzotta (REMEDIA) (31)	Diver CE	Italy	2005	UB	1	50/49	61/60	45/38	11/9	31/28	31/26	27/17
Dudek (PIHRATE) (23)	Diver CE	MC	2010	NA	6	100/96	61/59	80/78	13/9	58/52	62/61	43/47
De Carlo (MUSTELA) (29)	Export	MC	2012	NA	12	104/104	62/63	88/79	20/21	54/49	50/51	54/45
Lipiecki (30)	Export	France	2009	NA	-	20/20	59/59	12/18	1/2	5/8	7/9	6/5
Liistro (22)	Export	Italy	2009	UB	6	55/56	64/65	43/43	11/7	33/30	35/36	19/17
Chevalier (24)	Export	MC	2008	NA	1	120/129	59/61	97/105	20/17	50/57	51/46	44/54
Vlaar (TAPAS) (14)	Export	Netherlands	2008	UB	12	535/536	63/63	363/392	56/67	171/195	213/225	115/130
Lagerqvist (TASTE) (18)	Export/ Pronto/ Terumo eliminate	MC	2014	UB	12	3621/3623	66/66	2721/2703	448/453	1545/1527	1083/1173	753/762
De Luca (21)	Diver CE	Italy	2006	NA	6	38/38	67/65	27/21	9/7	15/19	7/10	NA
Stone (INFUSE-AMI) (33)	Export	MC	2012	SB	12	229/223	61/59	169/165	34/17	76/66	98/108	38/33
Sardella (EXPIRA) (26)	Export	Italy	2009	NA	9	88/87	68/65	57/48	21/16	59/43	43/23	NA
Ikari (VAMPIRE) (27)	Nipro's TVAC	MC	2008	NA	8	180/175	63/64	145/136	42/52	99/103	102/89	90/85
Ciszewski (28)	Rescue/ Diver CE	Poland	2011	UB	IH	67/70	64/64	48/50	7/12	41/37	29/28	52/47
Chao (25)	Export	Taiwan	2008	NA	6	37/37	60/62	31/32	12/8	21/21	15/17	22/21

DM - diabetes mellitus; FU - follow-up (months); HL - hyperlipidemia; HT - hypertension; IH - in-hospital; MC - multicenter; NA - not available; PPCI - primary percutaneous coronary intervention; SB - single blinded; TA - thrombus aspiration; UB - unblinded

evaluate the accumulating evidence. Our assumptions included two-sided testing, type 1 error=5%, power=80%. We chose a 20% relative risk reduction for outcome measures. The main result of TSA was expressed through a cumulative z-curve graph; the boundaries in this graph for concluding superiority or inferiority or futility were determined according to the O'Brien–Fleming alpha-spending function. All calculations were carried out using specific statistical software of TSA version 0.9 beta (TSA, User Manual for TSA, Copenhagen Trial Unit 2011, www.ctu.dk/tsa).

Results

Of a total of 16 studies, 10518 patients met our selection criteria (14, 18, 21-34). Of these, 5256 were in the TA+PPCI arm and 5262 in the PPCI alone arm. The basal characteristics of the patients included in the study are shown in Table 2. The end-point definitions and pharmacological and angiographic baseline characteristics are shown in Table 3.

In TSA, required information size was exceeded (required information size 8911) for all cause mortality, the cumulative Z-curve did not crossed the TSA boundary, indicating that sufficient evidence exist for a lack of 20% RRR of all cause mortality by TA plus PPCI compared to PPCI alone. In addition, the cumulative z-curve was ended in futility area, indicating that a lack of sufficient evidence of a benefit of TA plus PPCI for reduction re-MI and TVR/TLR (required information size 26534) (Fig.12-14).

Effect of aspiration thrombectomy on myocardial and epicardial perfusion

The frequencies of postprocedural TIMI-III flow (85.7% vs. 81.2%, RR=1.035, 95% CI: 1.013-1.058, p=0.002), postprocedural MBG II-III flow (83.0% vs. 72.6%, RR=1.113, 95% CI: 1.078-1.150, p<0.001), and postprocedural STR≥70% on ECG (54.5% vs. 44.7%, RR=1.222, 95% CI: 1.144-1.304, p<0.001) (only in the study by Chevalier et al. (24), ≥50%) in the TA+PPCI arm were significantly greater compared with the PPCI alone group. Results of postprocedural TIMI-III flow, MBG II-III, and STR are shown in Figure 2. Although there was no significant heterogeneity in the postprocedural TIMI-III flow (Q=22.1, df=13, I^2=41%, p=0.054), there was significant heterogeneity for MBG II-III (Q=26.5, df=12, I^2=54.8%, p=0.009) and for STR (Q=31, df=13, I^2=58%, p=0.003) between studies.

Effect of aspiration thrombectomy on clinical outcomes

The follow-up duration of the patients was between 1 and 12 months. Although there was no follow-up in the study by Lipecki et al. (30), the follow-up in the study by Ciszewski et al. (28) included only the in-hospital period.

The frequency of all-cause mortality was 6.6% in TA+PPCI, whereas it was 7.4% in the PPCI alone arm. There were no significant differences between the likelihood of all-cause mortality in TA+PPCI compared with PPCI alone (RR=0.903, 95% CI: 0.785-1.038, p=0.149) (Fig. 3, top panel). Similarly, the

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Table 3. Baseline characteristics and end-point definition of patients and trials

Study	Primary EP	Secondary EP	P2Y12 inhibitors loading (300 or 600 mg), n	GpIIb/IIIa inhibitors, n	Pain to Balloon time, n	Preprocedural TIMI II/III, n	TIMI thrombus grade IV-V, n
Kaltoft (34)	Myocardial salvage	Final infarct size, TIMI flow, cTFC, STR, cTnT, DE, Total procedure time, MACE, LVEF at 30-day, device success	300 mg Clp	104/100	242/208	33/23	NA
Silva-Orrego (DEAR-MI) (32)	STR>70%, MBG=3	DE, No reflow, Peak CK-MB, DS, Death, Re-MI, hospitalization for HF, Stroke, TVR, major bleeding	NA	74/74	206/199	14/20	NA
Burzotta (REMEDIA) (31)	STR≥70%, MBG≥2	Peak CK-MB, DS, DE, No reflow	300 mg Clp	50/49	274/300	7/5	NA
Dudek (PIHRATE) (23)	STR≥70% at 60 min	STR≥70% immediately after PCI, DS, DE, transient no reflow, slow flow, TIMI<3, final thrombus grade>1, MBG-3	600 mg Clp	NA	NA	3/2	47/34
De Carlo (MUSTELA) (29)	STR, infarct size	TIMI flow, MBG, infarct transmurality, microvascular obstruction, MACE	600 mg Clp	104/104	230/208	9/23	104/104
Lipiecki (30)	Infarct size	RWMA-Regional thickening and infarct transmurality scores, LV volumes, global EF, TIMI flow, DE, MBG, STR, cTnT, CK	300 mg Clp	6/18	426/444	0/1	NA
Liistro (22)	STR≥70%	TMPG≥2, TIMI 3 flow, cTFC, MCE score index, ST deviation, RWMA score, LV volumes	600 mg Clp	55/56	189/209	17/13	NA
Chevalier (24)	STR≥50%, MBG=3	Magnitude of STR, TIMI flow, cTFC, MACCE (Death, Re-MI), TVR-TLR, Emergent CABG, CVA, DE, Need for bail-out techniques	NA	79/90	271/322	NA	NA
Vlaar (TAPAS) (14)	Postprocedural MBG 0-1	Postprocedural TIMI flow 3, STR, TVR, Re-MI, Death	600 mg Clp	469/452	190/185	238/215	NA
Lagerqvist (TASTE) (18)	All-cause mortality	Hospitalization for Re-MI, ST, TVR, TLR, PCI complications, HF, Length of stay	NA	558/630	185/182	792/809	1138/1078
De Luca (21)	NA	NA	No	38/38	432/456	0/0	NA
Stone (INFUSE-AMI) (33)	NA	Infarct size, TIMI flow, MBG, STR, MACE (death, Re-MI, new onset HF, rehospitalization for HF)	600 mg Clp or 60 mg prasugrel	118/111	46/163	61/67	NA
Sardella (EXPIRA) (26)	MBG≥2, STR	NA	300 mg Clp	NA	NA	NA	78/79
Ikari (VAMPIRE) (27)	Final TIMI<3	MBG, cTFC, TIMI flow, CK, CK-MB, stent re-stenosis, LV function, BNP, MACE (death, Re-MI, TVR)	No	No	270/312	46/43	NA
Ciszewski (28)	Myocardial salvage index	In-hospital mortality, CK-MB, cTFC	300/600 mg Clp	NA	338/336	7/6	65/65
Chao (25)	ΔTIMI flow, ΔMBG	MACE (Death, Stroke, non-fatal Re-MI, TVR)	300 mg Clp	7/12	312/331	NA	NA*

BNP - brain natriuretic peptide; CABG - coronary artery bypass grafting; CK-MB - creatinine kinase-MB; Clp - clopidogrel; cTFC - corrected TIMI frame count; cTnT - cardiac troponin T; CVA - cerebrovascular accidents; DE - distal embolization; DS - direct stenting; EP - endpoint; HF - heart failure; LV - left ventricle; LVEF - left ventricular ejection fraction; MBG - myocardial blush grade; MACCE - major adverse cardiac and cerebral events; MACE - major adverse clinical events; NA - not available; PCI - percutaneous coronary intervention; Re-MI - recurrent myocardial infarction; STR - ST-segment resolution; TIMI - thrombolysis in myocardial infarction flow grade; TLR - target lesion revascularization; TVR - target vessel revascularization

frequencies of Re-MI (2.3% vs. 2.6%, RR=0.884, 95% CI: 0.693-1.127, p=0.319) (Fig. 3, bottom panel), TVR/TLR (8.2% vs. 8.0%, RR=1.028, 95% CI: 0.900-1.174, p=0.687) (Fig. 4, top panel), MACE (14.3% vs. 14.5%, RR=0.988, 95% CI: 0.902-1.082, p=0.795) (Fig. 4, bottom panel), stroke (0.5% vs. 0.5%, RR=1.073, 95% CI: 0.588-1.959, p=0.819) (Fig. 5, bottom panel), and ST (0.93% vs.

0.90%, RR=1.029, 95% CI: 0.668-1.583, p=0.898) (Fig. 5, top panel) in the TA+PPCI arm were comparable compared with the PPCI alone group.

There was no significant heterogeneity for all-cause mortality (Q=8.3, df=13, I²=0%, p=0.820), Re-MI (Q=5.6, df=10, I²=0%, p=0.847), TVR/TLR (Q=7.2, df=9, I²=0%, p=0.609), MACE (Q=19.5,
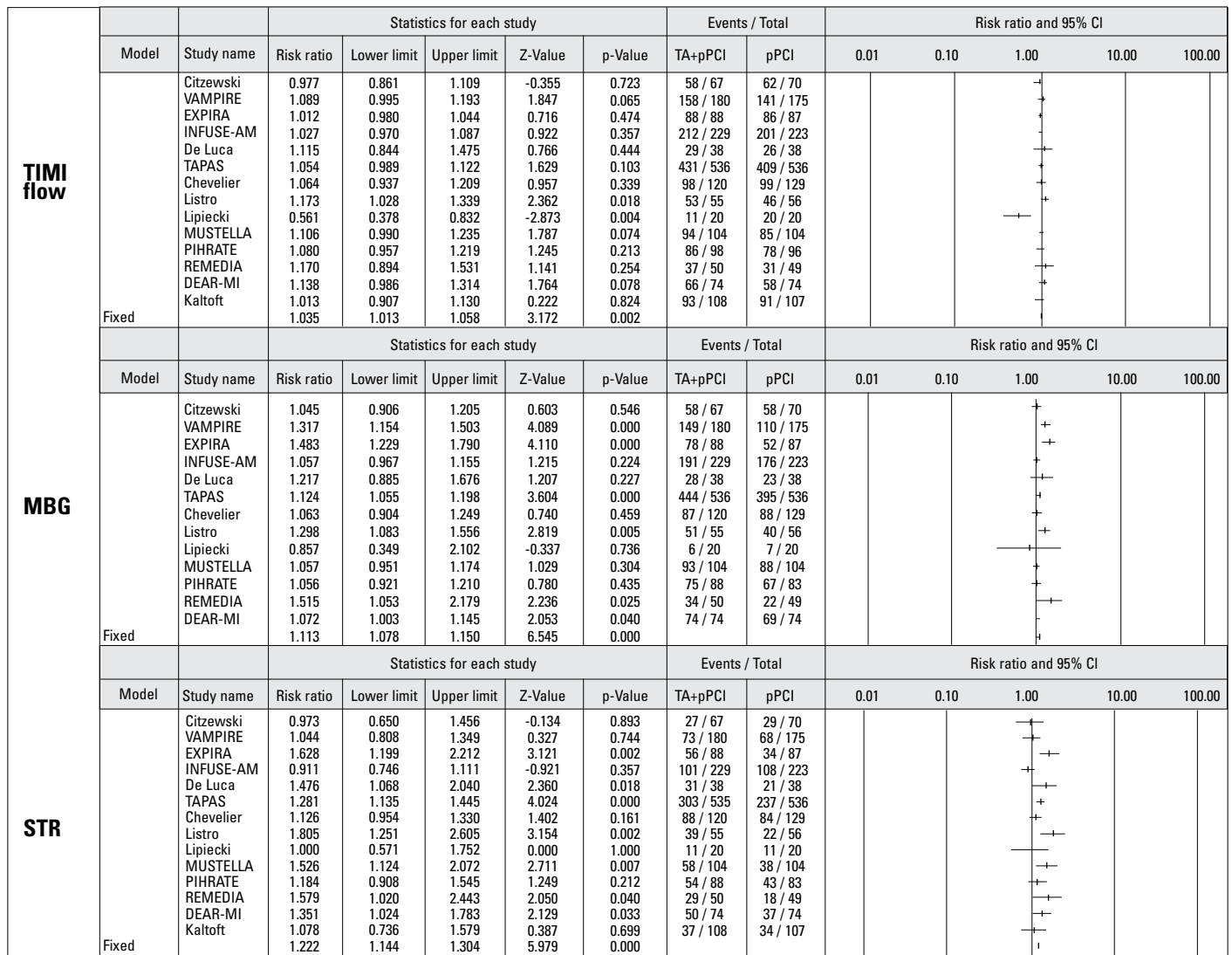
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	Model	Study name	Statistics for each study					Events / Total		Risk ratio and 95% CI				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	0.01	0.10	1.00	10.00	100.00
TIMI flow		Citzewski	0.977	0.861	1.109	-0.355	0.723	58 / 67	62 / 70					
		VAMPIRE	1.089	0.995	1.193	1.847	0.065	158 / 180	141 / 175					
		EXPIRA	1.012	0.980	1.044	0.716	0.474	88 / 88	86 / 87					
		INFUSE-AM	1.027	0.970	1.087	0.922	0.357	212 / 229	201 / 223					
		De Luca	1.115	0.844	1.475	0.766	0.444	29 / 38	26 / 38					
		TAPAS	1.054	0.989	1.122	1.629	0.103	431 / 536	409 / 536					
		Chevelier	1.064	0.937	1.209	0.957	0.339	98 / 120	99 / 129					
		Listro	1.173	1.028	1.339	2.362	0.018	53 / 55	46 / 56					
		Lipiecki	0.561	0.378	0.832	-2.873	0.004	11 / 20	20 / 20					
		MUSTELLA	1.106	0.990	1.235	1.787	0.074	94 / 104	85 / 104					
		PIHRATE	1.080	0.957	1.219	1.245	0.213	86 / 98	78 / 96					
		REMEDIA	1.170	0.894	1.531	1.141	0.254	37 / 50	31 / 49					
		DEAR-MI	1.138	0.986	1.314	1.764	0.078	66 / 74	58 / 74					
		Kaltoft	1.013	0.907	1.130	0.222	0.824	93 / 108	91 / 107					
	Fixed		1.035	1.013	1.058	3.172	0.002							

	Model	Study name	Statistics for each study					Events / Total		Risk ratio and 95% CI				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	0.01	0.10	1.00	10.00	100.00
MBG		Citzewski	1.045	0.906	1.205	0.603	0.546	58 / 67	58 / 70					
		VAMPIRE	1.317	1.154	1.503	4.089	0.000	149 / 180	110 / 175					
		EXPIRA	1.483	1.229	1.790	4.110	0.000	78 / 88	52 / 87					
		INFUSE-AM	1.057	0.967	1.155	1.215	0.224	191 / 229	176 / 223					
		De Luca	1.217	0.885	1.676	1.207	0.227	28 / 38	23 / 38					
		TAPAS	1.124	1.055	1.198	3.604	0.000	444 / 536	395 / 536					
		Chevelier	1.063	0.904	1.249	0.740	0.459	87 / 120	88 / 129					
		Listro	1.298	1.083	1.556	2.819	0.005	51 / 55	40 / 56					
		Lipiecki	0.857	0.349	2.102	-0.337	0.736	6 / 20	7 / 20					
		MUSTELLA	1.057	0.951	1.174	1.029	0.304	93 / 104	88 / 104					
		PIHRATE	1.056	0.921	1.210	0.780	0.435	75 / 88	67 / 83					
		REMEDIA	1.515	1.053	2.179	2.236	0.025	34 / 50	22 / 49					
		DEAR-MI	1.072	1.003	1.145	2.053	0.040	74 / 74	69 / 74					
	Fixed		1.113	1.078	1.150	6.545	0.000							

	Model	Study name	Statistics for each study					Events / Total		Risk ratio and 95% CI				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	0.01	0.10	1.00	10.00	100.00
STR		Citzewski	0.973	0.650	1.456	-0.134	0.893	27 / 67	29 / 70					
		VAMPIRE	1.044	0.808	1.349	0.327	0.744	73 / 180	68 / 175					
		EXPIRA	1.628	1.199	2.212	3.121	0.002	56 / 88	34 / 87					
		INFUSE-AM	0.911	0.746	1.111	-0.921	0.357	101 / 229	108 / 223					
		De Luca	1.476	1.068	2.040	2.360	0.018	31 / 38	21 / 38					
		TAPAS	1.281	1.135	1.445	4.024	0.000	303 / 535	237 / 536					
		Chevelier	1.126	0.954	1.330	1.402	0.161	88 / 120	84 / 129					
		Listro	1.805	1.251	2.605	3.154	0.002	39 / 55	22 / 56					
		Lipiecki	1.000	0.571	1.752	0.000	1.000	11 / 20	11 / 20					
		MUSTELLA	1.526	1.124	2.072	2.711	0.007	58 / 104	38 / 104					
		PIHRATE	1.184	0.908	1.545	1.249	0.212	54 / 88	43 / 83					
		REMEDIA	1.579	1.020	2.443	2.050	0.040	29 / 50	18 / 49					
		DEAR-MI	1.351	1.024	1.783	2.129	0.033	50 / 74	37 / 74					
		Kaltoft	1.078	0.736	1.579	0.387	0.699	37 / 108	34 / 107					
	Fixed		1.222	1.144	1.304	5.979	0.000							

Figure 2. Meta-analysis of postprocedural TIMI flow grade III (top panel), MBG II-III (middle panel), and STR≥50% (bottom panel)
MBG - myocardial blush grade; STR - ST resolution; TIMI - thrombolysis in myocardial infarction

Table 4. Publication bias and small-study effect for end-points

End-points	Egger's test, t value and two-tailed *P* value
All-cause death	0.575/0.575
Re-MI	0.807/0.440
TVR/TLR	1.556/0.158
MACE	1.287/0.890
Stroke	0.131/0.907
Stent thrombosis	0.092/0.931
Final TIMI flow	0.193/0.409
Final MBG	0.878/0.185
Postprocedural STR	0.636/0.311

MACE - major adverse cardiac events; MBG - myocardial blush grade; Re-MI - recurrent myocardial infarction; STR - ST-segment resolution; TIMI - thrombolysis in myocardial infarction; TLR - target lesion revascularization; TVR - target vessel revascularization

df=14, I²=28%, p=0.145), stroke (Q=1.5, df=3, I²=0%, p=0.676), and ST (Q=4, df=4, I²=1.1%, p=0.400).

Sensitivity analysis

The sensitivity analysis indicated that none of the studies had a significant influential effect on the overall estimate for all-cause death, Re-MI, TVR/TLR, MACE (Fig. 6), ST, and stroke (Fig. 7), except the TASTE trial, which had a significant influential effect on the overall estimate of MACE. All the studies had a significant influential effect on the overall estimate for postprocedural MBG, STR, and TIMI flow (Fig. 8).

When the meta-analysis was repeated without including the TASTE study, there were no significant differences in the likelihood of all-cause death (RR=0.74, 95% CI: 0.52–1.05, p=0.094), reinfarction (RR: 0.64 (0.39-1.07), p=0.092), and TVR/TLR (RR:0.79 (0.61-1.03) p=0.079) in TA+PPCI compared with PPCI alone. Moreover, the frequency of stroke (RR:1.20 (0.21-6.66) p=0.835) and ST (RR:0.72 (0.32-1.61) p=0.424) was similar (Fig. 9 and 10). Because the data of postprocedural TIMI flow, MBG, and STR were not present in the TASTE study, the analysis was not performed.
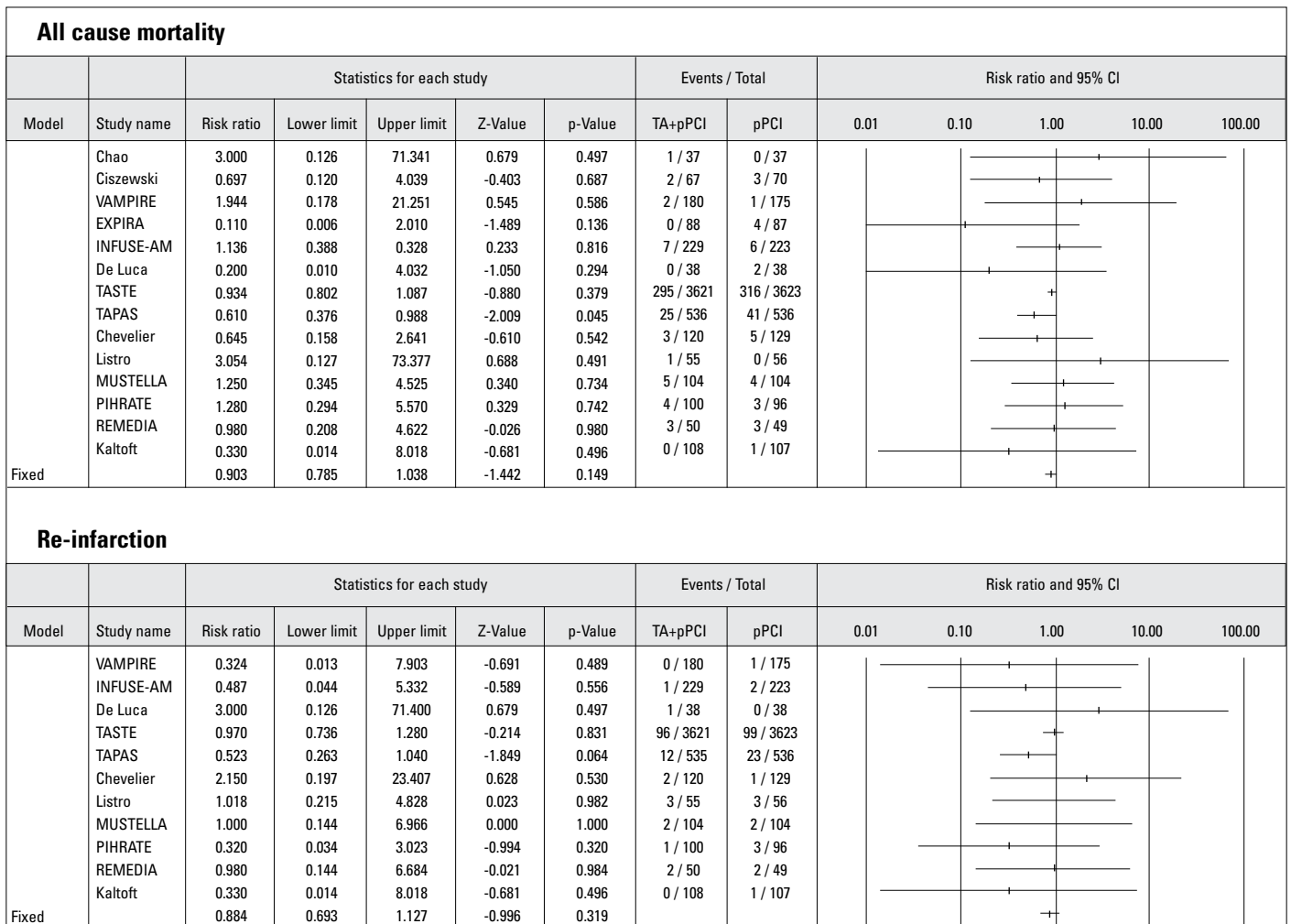
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All cause mortality

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	Risk ratio and 95% CI
			Statistics for each study				Events / Total		Risk ratio and 95% CI
	Chao	3.000	0.126	71.341	0.679	0.497	1 / 37	0 / 37	
	Ciszewski	0.697	0.120	4.039	-0.403	0.687	2 / 67	3 / 70	
	VAMPIRE	1.944	0.178	21.251	0.545	0.586	2 / 180	1 / 175	
	EXPIRA	0.110	0.006	2.010	-1.489	0.136	0 / 88	4 / 87	
	INFUSE-AM	1.136	0.388	0.328	0.233	0.816	7 / 229	6 / 223	
	De Luca	0.200	0.010	4.032	-1.050	0.294	0 / 38	2 / 38	
	TASTE	0.934	0.802	1.087	-0.880	0.379	295 / 3621	316 / 3623	
	TAPAS	0.610	0.376	0.988	-2.009	0.045	25 / 536	41 / 536	
	Chevelier	0.645	0.158	2.641	-0.610	0.542	3 / 120	5 / 129	
	Listro	3.054	0.127	73.377	0.688	0.491	1 / 55	0 / 56	
	MUSTELLA	1.250	0.345	4.525	0.340	0.734	5 / 104	4 / 104	
	PIHRATE	1.280	0.294	5.570	0.329	0.742	4 / 100	3 / 96	
	REMEDIA	0.980	0.208	4.622	-0.026	0.980	3 / 50	3 / 49	
	Kaltoft	0.330	0.014	8.018	-0.681	0.496	0 / 108	1 / 107	
Fixed		0.903	0.785	1.038	-1.442	0.149			

Re-infarction

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	Risk ratio and 95% CI
			Statistics for each study				Events / Total		Risk ratio and 95% CI
	VAMPIRE	0.324	0.013	7.903	-0.691	0.489	0 / 180	1 / 175	
	INFUSE-AM	0.487	0.044	5.332	-0.589	0.556	1 / 229	2 / 223	
	De Luca	3.000	0.126	71.400	0.679	0.497	1 / 38	0 / 38	
	TASTE	0.970	0.736	1.280	-0.214	0.831	96 / 3621	99 / 3623	
	TAPAS	0.523	0.263	1.040	-1.849	0.064	12 / 535	23 / 536	
	Chevelier	2.150	0.197	23.407	0.628	0.530	2 / 120	1 / 129	
	Listro	1.018	0.215	4.828	0.023	0.982	3 / 55	3 / 56	
	MUSTELLA	1.000	0.144	6.966	0.000	1.000	2 / 104	2 / 104	
	PIHRATE	0.320	0.034	3.023	-0.994	0.320	1 / 100	3 / 96	
	REMEDIA	0.980	0.144	6.684	-0.021	0.984	2 / 50	2 / 49	
	Kaltoft	0.330	0.014	8.018	-0.681	0.496	0 / 108	1 / 107	
Fixed		0.884	0.693	1.127	-0.996	0.319			

Figure 3. Meta-analysis of all-cause death (top panel) and Re-MI (bottom panel) (Re-MI-recurrent myocardial infarction)

The publication bias and small-study effects, assessed by Egger's tests, were not significant (all two-tailed, p>0.2) for all-cause death, Re-MI, MACE, and postprocedural MBG. However, Egger's test was significant for TVR/TLR, postprocedural TIMI flow, and STR (Table 4). Funnel plots for all-cause death, Re-MI, TVR/TLR, and MACE are shown in Figure 11.

Discussion

In our meta-analysis consisting of 16 studies that included 10518 patients, we observed that TA+PPCI did not reduce the rate of death, Re-MI, TVR/TLR, MACE, ST, and stroke compared with PPCI alone.

In numerous RCTs and meta-analyses, it was shown that the superiority of PPCI to thrombolytic therapy in STEMI patients is related to the achievement of better epicardial perfusion (35). However, in some patients in whom sufficient epicardial perfusion is provided, the restoration of myocardial perfusion becomes insufficient. Besides, the clinical outcomes in this group of patients are worse (2, 6). In this group of patients, distal embolization of plaque debris, vasoconstriction, and reperfusion injury were considered to be responsible (36, 37). Glycoprotein IIb/IIIa inhibitors, coronary vasodilators such as adenosine and verapamil, and thrombectomy devices are found to be effective in the prevention of this phenomenon (38).

Previous meta-analyses showed that TA improves epicardial and myocardial perfusion, and these findings are consistent with those of the present meta-analysis (7, 8, 10, 13). It is known that the patients with good epicardial and myocardial perfusion after PPCI have better clinical outcomes compared with those with poor epicardial and myocardial perfusion (1, 39). From this point of view, we can expect that improved epicardial and myocardial perfusion following thrombectomy may positively affect clinical outcomes. However, in the meta-analyses related to thrombus aspiration, there are conflicting results regarding clinical outcomes. In some studies, it was demonstrated that it decreased the rate of mortality (7-9), whereas in other studies, it did not (10, 11, 13). In the present meta-analysis, we demonstrated that TA was not related to the decrease in the likelihood of all-cause mortality, Re-MI, TVR/TLR, ST, and stroke.

This is the first meta-analysis to include the 12-month data of the TASTE trial, which is the largest trial till date (18). The TASTE trial is a large (over 7000 patients) multicenter study designed to
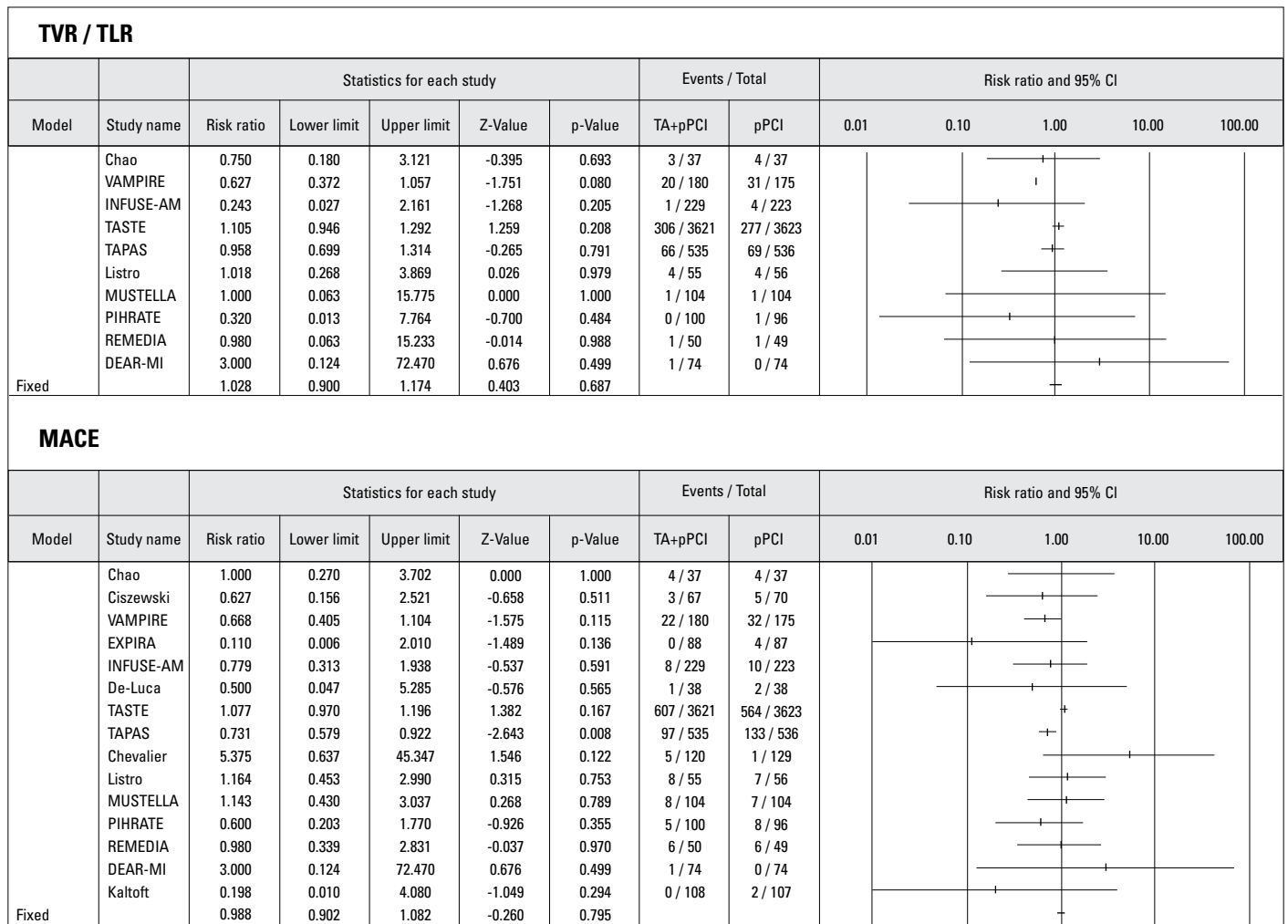
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TVR / TLR

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	Risk ratio and 95% CI
				Statistics for each study			Events / Total		
	Chao	0.750	0.180	3.121	-0.395	0.693	3 / 37	4 / 37	
	VAMPIRE	0.627	0.372	1.057	-1.751	0.080	20 / 180	31 / 175	
	INFUSE-AM	0.243	0.027	2.161	-1.268	0.205	1 / 229	4 / 223	
	TASTE	1.105	0.946	1.292	1.259	0.208	306 / 3621	277 / 3623	
	TAPAS	0.958	0.699	1.314	-0.265	0.791	66 / 535	69 / 536	
	Listro	1.018	0.268	3.869	0.026	0.979	4 / 55	4 / 56	
	MUSTELLA	1.000	0.063	15.775	0.000	1.000	1 / 104	1 / 104	
	PIHRATE	0.320	0.013	7.764	-0.700	0.484	0 / 100	1 / 96	
	REMEDIA	0.980	0.063	15.233	-0.014	0.988	1 / 50	1 / 49	
	DEAR-MI	3.000	0.124	72.470	0.676	0.499	1 / 74	0 / 74	
Fixed		1.028	0.900	1.174	0.403	0.687			

MACE

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	Risk ratio and 95% CI
				Statistics for each study			Events / Total		
	Chao	1.000	0.270	3.702	0.000	1.000	4 / 37	4 / 37	
	Ciszewski	0.627	0.156	2.521	-0.658	0.511	3 / 67	5 / 70	
	VAMPIRE	0.668	0.405	1.104	-1.575	0.115	22 / 180	32 / 175	
	EXPIRA	0.110	0.006	2.010	-1.489	0.136	0 / 88	4 / 87	
	INFUSE-AM	0.779	0.313	1.938	-0.537	0.591	8 / 229	10 / 223	
	De-Luca	0.500	0.047	5.285	-0.576	0.565	1 / 38	2 / 38	
	TASTE	1.077	0.970	1.196	1.382	0.167	607 / 3621	564 / 3623	
	TAPAS	0.731	0.579	0.922	-2.643	0.008	97 / 535	133 / 536	
	Chevalier	5.375	0.637	45.347	1.546	0.122	5 / 120	1 / 129	
	Listro	1.164	0.453	2.990	0.315	0.753	8 / 55	7 / 56	
	MUSTELLA	1.143	0.430	3.037	0.268	0.789	8 / 104	7 / 104	
	PIHRATE	0.600	0.203	1.770	-0.926	0.355	5 / 100	8 / 96	
	REMEDIA	0.980	0.339	2.831	-0.037	0.970	6 / 50	6 / 49	
	DEAR-MI	3.000	0.124	72.470	0.676	0.499	1 / 74	0 / 74	
	Kaltoft	0.198	0.010	4.080	-1.049	0.294	0 / 108	2 / 107	
Fixed		0.988	0.902	1.082	-0.260	0.795			

Figure 4. Meta-analysis of TVR/TLR (top panel) and MACE (bottom panel)
MACE - major adverse cardiac events; TVR/TLR - target vessel revascularization/target lesion revascularization

Table 5. Comparison of meta-analyses in patients with STEMI who used manual aspiration thrombectomy

	No. of RCT	No. Of pts.	Death	Re-MI	TVR/TLR	Stroke	ST
Kumbhani (7)	18	3941	0.71 (0.51-1.00)	0.68 (0.42-1.10)	0.78 (0.61-1.01)	1.31 (0.30-5.79)	NA
Costopoulos (8)	11	2293	0.57 (0.33-0.97)	NA	NA	NA	NA
Bavry (9)	13	3026	0.63 (0.43-0.93)	0.65(0.37-1.12)	0.83 (0.64-1.08)	3.43 (0.85-14.0)	NA
De Luca (10)	11	2311	0.65 (0.39-1.09)	0.78(0.39-1.58)	NA	3.1 (0.62-15.5)	NA
Mongeon (11)	16	3365	0.58 (0.28-1.22)	NA	NA	NA	NA
Tamhane (13)	8	1902	0.59 (0.35-1.01)	NA	NA	2.84 (0.51-15.6)	NA
Our (Tanboğa)	16	10518	0.86 (0.69-1.06)	0.63 (0.43-0.92)	0.79 (0.66-0.95)	1.07 (0.58-1.96)	0.58 (0.33-1.02)

NA - not available; RCT - randomized controlled trials; Re-MI - recurrent myocardial infarction; ST - stent thrombosis; STEMI - ST elevation myocardial infarction; TLR - target lesion revascularization; TVR - target vessel revascularization.
*De Luca, Tamhane, Costopoulos, and Mongeon et al. used OR in their meta-analysis; Kumbhani, Bavry, and Tanboğa used RR in their meta-analysis

have statistical power for the evaluation of adverse cardiovascular outcomes such as all-cause mortality, Re-MI, TVR, and ST. They found that the frequency of adverse cardiovascular outcomes were similar at 30 days and 12 months between TA+PPCI and PPCI alone. Our meta-analysis results might be driven mainly by the TASTE trial because of its weight. However, we performed sensitivity analysis by excluding the TASTE study and found that the results did not reach statistical significance. In the TAPAS study, the first largest study related to TA, it was demonstrated that the results of the 30-day follow-up had positive effects on clinical outcomes compared with the results of the 1-year follow-up (14, 15). However, in contrast to the TASTE
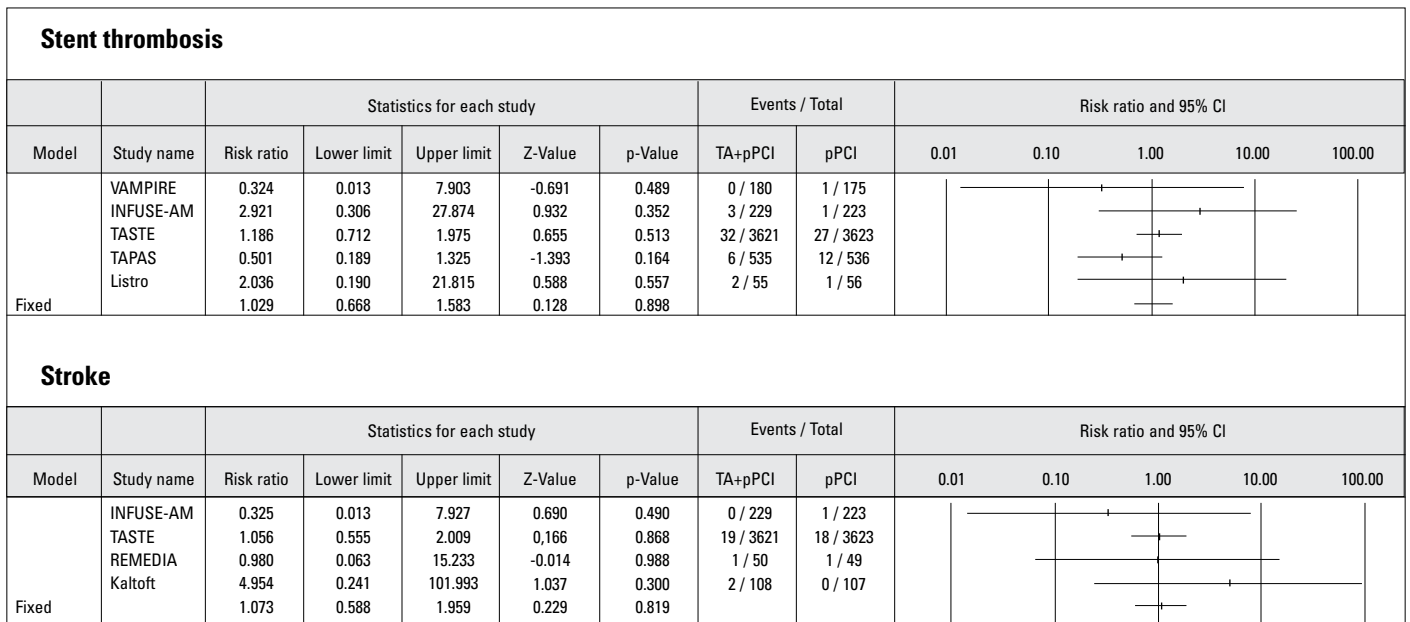
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Stent thrombosis

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	Risk ratio and 95% CI
	VAMPIRE	0.324	0.013	7.903	-0.691	0.489	0 / 180	1 / 175	
	INFUSE-AM	2.921	0.306	27.874	0.932	0.352	3 / 229	1 / 223	
	TASTE	1.186	0.712	1.975	0.655	0.513	32 / 3621	27 / 3623	
	TAPAS	0.501	0.189	1.325	-1.393	0.164	6 / 535	12 / 536	
	Listro	2.036	0.190	21.815	0.588	0.557	2 / 55	1 / 56	
Fixed		1.029	0.668	1.583	0.128	0.898			

Stroke

Model	Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	TA+pPCI	pPCI	Risk ratio and 95% CI
	INFUSE-AM	0.325	0.013	7.927	0.690	0.490	0 / 229	1 / 223	
	TASTE	1.056	0.555	2.009	0.166	0.868	19 / 3621	18 / 3623	
	REMEDIA	0.980	0.063	15.233	-0.014	0.988	1 / 50	1 / 49	
	Kaltoft	4.954	0.241	101.993	1.037	0.300	2 / 108	0 / 107	
Fixed		1.073	0.588	1.959	0.229	0.819			

Figure 5. Meta-analysis of stroke (top panel) and ST (bottom panel)
ST - stent thrombosis

Death

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
VAMPIRE	0.324	0.013	7.903	-0.691	0.489
INFUSE-AM	0.487	0.044	5.332	-0.589	0.556
De-Luca	3.000	0.126	71.400	0.679	0.497
TASTE	0.970	0.736	1.280	-0.214	0.831
TAPAS	0.523	0.263	1.040	-1.849	0.064
Chevalier	2.150	0.197	23.407	0.628	0.530
Listro	1.018	0.215	4.828	0.023	0.982
MUSTELLA	1.000	0.144	6.966	0.000	1.000
PIHRATE	0.320	0.034	3.023	-0.994	0.320
REMEDIA	0.980	0.144	6.684	-0.021	0.984
Kaltoft	0.330	0.014	8.018	-0.681	0.496
	0.884	0.693	1.127	-0.996	0.319

ReMI

Study name	Point	Lower limit	Upper limit	Z-Value	p-Value
VAMPIRE	0.889	0.697	1.134	-0.946	0.344
INFUSE-AM	0.889	0.697	1.135	-0.941	0.347
De-Luca	0.878	0.688	1.120	-1.051	0.293
TASTE	0.648	0.391	1.074	-1.683	0.092
TAPAS	0.953	0.735	1.235	-0.366	0.714
Chevalier	0.876	0.686	1.118	-1.065	0.287
Listro	0.881	0.689	1.126	-1.012	0.312
MUSTELLA	0.882	0.691	1.127	-1.004	0.316
PIHRATE	0.895	0.701	1.142	-0.893	0.372
REMEDIA	0.882	0.691	1.127	-1.001	0.317
Kaltoft	0.889	0.697	1.134	-0.947	0.344
	0.884	0.693	1.127	-0.996	0.319

TVR/TLR

Study name	Point	Lower limit	Upper limit	Z-Value	p-Value
Chao	1.031	0.902	1.178	0.442	0.658
VAMPIRE	1.063	0.927	1.220	0.878	0.380
INFUSE-AM	1.033	0.904	1.180	0.481	0.630
TASTE	0.847	0.656	1.092	-1.283	0.199
TAPAS	1.043	0.901	1.208	0.568	0.570
Listro	1.028	0.899	1.175	0.403	0.687
MUSTELLA	1.028	0.900	1.174	0.404	0.686
PIHRATE	1.030	0.902	1.176	0.433	0.665
REMEDIA	1.028	0.900	1.174	0.404	0.686
DEAR-MI	1.026	0.898	1.172	0.375	0.707
	1.028	0.900	1.174	0.403	0.687

MACE

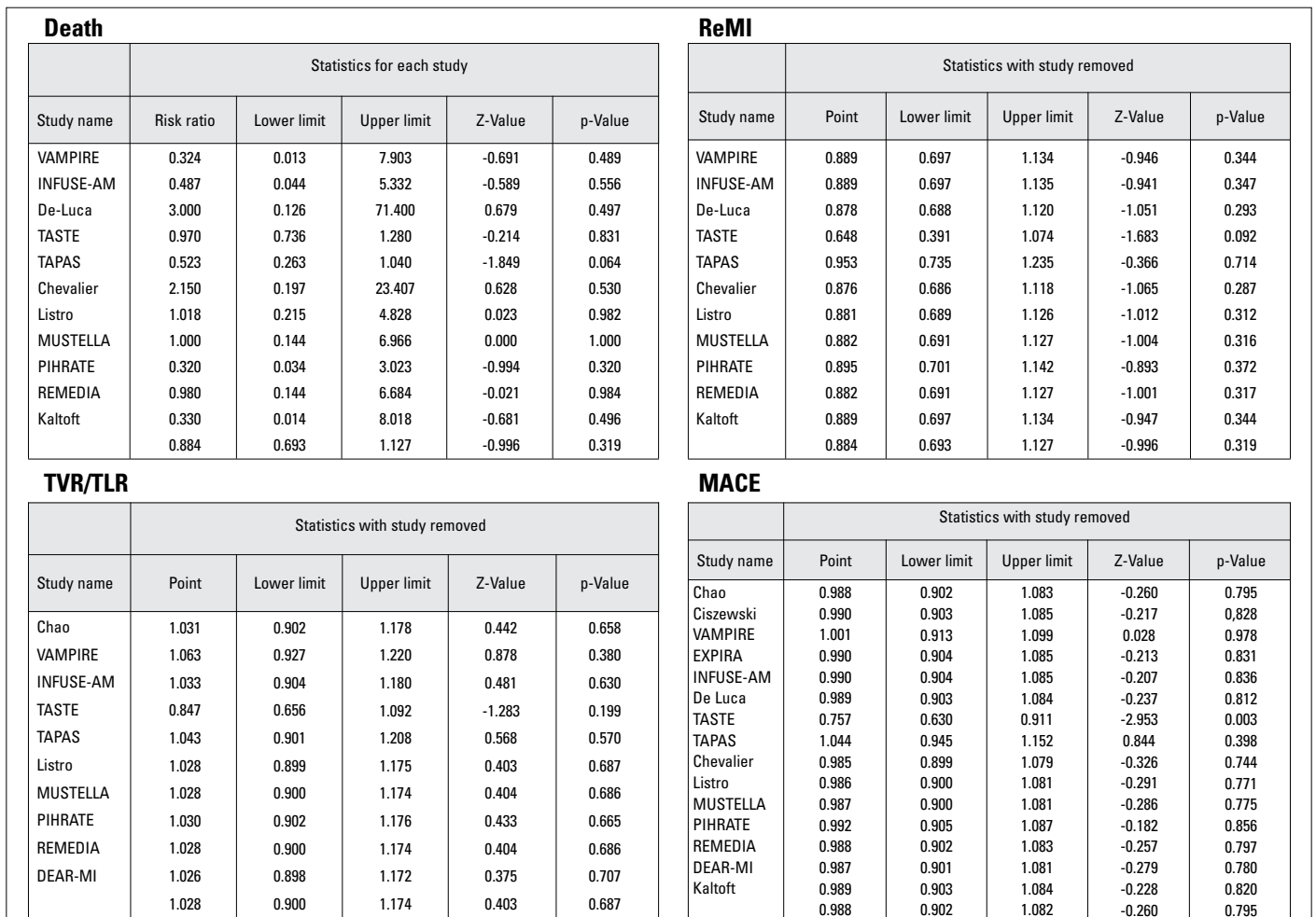| Study name	Point	Lower limit	Upper limit	Z-Value	p-Value
Chao	0.988	0.902	1.083	-0.260	0.795
Ciszewski	0.990	0.903	1.085	-0.217	0,828
VAMPIRE	1.001	0.913	1.099	0.028	0.978
EXPIRA	0.990	0.904	1.085	-0.213	0.831
INFUSE-AM	0.990	0.904	1.085	-0.207	0.836
De Luca	0.989	0.903	1.084	-0.237	0.812
TASTE	0.757	0.630	0.911	-2.953	0.003
TAPAS	1.044	0.945	1.152	0.844	0.398
Chevalier	0.985	0.899	1.079	-0.326	0.744
Listro	0.986	0.900	1.081	-0.291	0.771
MUSTELLA	0.987	0.900	1.081	-0.286	0.775
PIHRATE	0.992	0.905	1.087	-0.182	0.856
REMEDIA	0.988	0.902	1.083	-0.257	0.797
DEAR-MI	0.987	0.901	1.081	-0.279	0.780
Kaltoft	0.989	0.903	1.084	-0.228	0.820
	0.988	0.902	1.082	-0.260	0.795

Figure 6. Meta-analytic statistics with one study excluded for all-cause death (left top panel), Re-MI (right top panel), TVR/TLR (left bottom panel), and MACE (right bottom panel)
MACE - major adverse cardiac events; Re-MI - recurrent myocardial infarction; TVR/TLR - target vessel revascularization/target lesion revascularization

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Stent thrombosis

Study name	Statistics with study removed				
	Point	Lower limit	Upper limit	Z-Value	p-Value
VAMPIRE	1.052	0.678	1.633	0.226	0.821
INFUSE-AM	0.989	0.634	1.541	-0.050	0.960
TASTE	0.716	0.315	1.625	-0.800	0.424
TAPAS	1.229	0.756	1.996	0.831	0.406
Listro	1.006	0.646	1.566	0.025	0.980
	1.029	0.666	1.591	0.130	0.897

Stroke

Study name	Statistics with study removed				
	Point	Lower limit	Upper limit	Z-Value	p-Value
INFUSE-AM	1.121	0.607	2.070	0.366	0.715
TASTE	1.200	0.216	6.667	0.209	0.835
REMEDIA	1.078	0.581	1.998	0.238	0.812
Kaltoft	1.007	0.545	1.862	0.023	0.982
	1.073	0.588	1.959	0.229	0.819

Figure 7. Meta-analytic statistics with one study excluded for stroke (top panel) and stent thrombosis (bottom panel)

TIMI flow

Study name	Statistics with study removed				
	Point	Lower limit	Upper limit	Z-Value	p-Value
Ciszewski	1.037	1.015	1.060	3.301	0.001
VAMPIRE	1.032	1.010	1.055	2.838	0.005
EXPIRA	1.056	1.026	1.087	3.681	0.000
INFUSE-AM	1.037	1.013	1.061	3.073	0.002
De-Luca	1.035	1.013	1.058	3.144	0.002
TAPAS	1.033	1.010	1.057	2.784	0.005
Chevalier	1.035	1.012	1.057	3.076	0.002
Listro	1.032	1.010	1.055	2.849	0.004
Lipiecki	1.037	1.015	1.060	3.354	0.001
MUSTELLA	1.033	1.011	1.056	2.902	0.004
PIHRATE	1.034	1.012	1.057	3.021	0.003
REMEDIA	1.035	1.013	1.057	3.112	0.002
DEAR-MI	1.033	1.011	1.056	2.963	0.003
Kaltoft	1.036	1.014	1.059	3.212	0.001
	1.036	1.014	1.058	3.193	0.001

MBG

Study name	Statistics with study removed				
	Point	Lower limit	Upper limit	Z-Value	p-Value
Ciszewski	1.118	1.081	1.155	6.612	0.000
VAMPIRE	1.102	1.066	1.139	5.755	0.000
EXPIRA	1.104	1.069	1.141	5.963	0.000
INFUSE-AM	1.123	1.085	1.162	6.582	0.000
De-Luca	1.113	1.078	1.149	6.489	0.000
TAPAS	1.110	1.069	1.152	5.474	0.000
Chevalier	1.116	1.080	1.153	6.562	0.000
Listro	1.108	1.073	1.145	6.176	0.000
Lipiecki	1.114	1.079	1.151	6.594	0.000
MUSTELLA	1.120	1.083	1.158	6.578	0.000
PIHRATE	1.117	1.081	1.155	6.579	0.000
REMEDIA	1.111	1.076	1.148	6.405	0.000
DEAR-MI	1.127	1.086	1.169	6.382	0.000
	1.114	1.079	1.150	6.578	0.000

STR

Study name	Statistics with study removed				
	Point	Lower limit	Upper limit	Z-Value	p-Value
Ciszewski	1.229	1.150	1.314	6.082	0.000
VAMPIRE	1.235	1.154	1.322	6.098	0.000
EXPIRA	1.205	1.127	1.288	5.437	0.000
INFUSE-AM	1.266	1.181	1.357	6.655	0.000
De-Luca	1.212	1.133	1.296	5.618	0.000
TAPAS	1.197	1.107	1.295	4.517	0.000
Chevalier	1.240	1.155	1.332	5.905	0.000
Listro	1.206	1.128	1.289	5.504	0.000
Lipiecki	1.225	1.147	1.309	6.021	0.000
MUSTELLA	1.208	1.130	1.292	5.526	0.000
PIHRATE	1.224	1.144	1.310	5.852	0.000
REMEDIA	1.214	1.136	1.298	5.736	0.000
DEAR-MI	1.214	1.135	1.299	5.635	0.000
Kaltoft	1.226	1.147	1.311	6.002	0.000
	1.222	1.144	1.304	5.979	0.000

Figure 8. Meta-analytic statistics with one study excluded for postprocedural TIMI flow grade (top panel), MBG (middle panel), and STR (bottom panel)
MBG - myocardial blush grade; STR - ST resolution; TIMI - thrombolysis in myocardial infarction

study, the present study was a single center study and was not designed for the evaluation of adverse cardiovascular outcomes. The comparison of the previous meta-analysis with the current meta-analysis is shown in Table 5. The effect of TA on mortality is conflicting. In the meta-analysis by Costopoulos (8), Bavry (9), and Kumbhani et al. (7), TA was found to be associated with lower mortality; however, in the meta-analyses by Mongeon (11), Tamhane (13), and De Luca (10) as well as the present meta-analysis, it was found that TA did not decrease the mortality risk compared with PPCI alone. The duration of follow-up was determined as 30 days in the studies by Mongeon (11), Tamhane (13), and De Luca (10). TA, not reducing the mortality
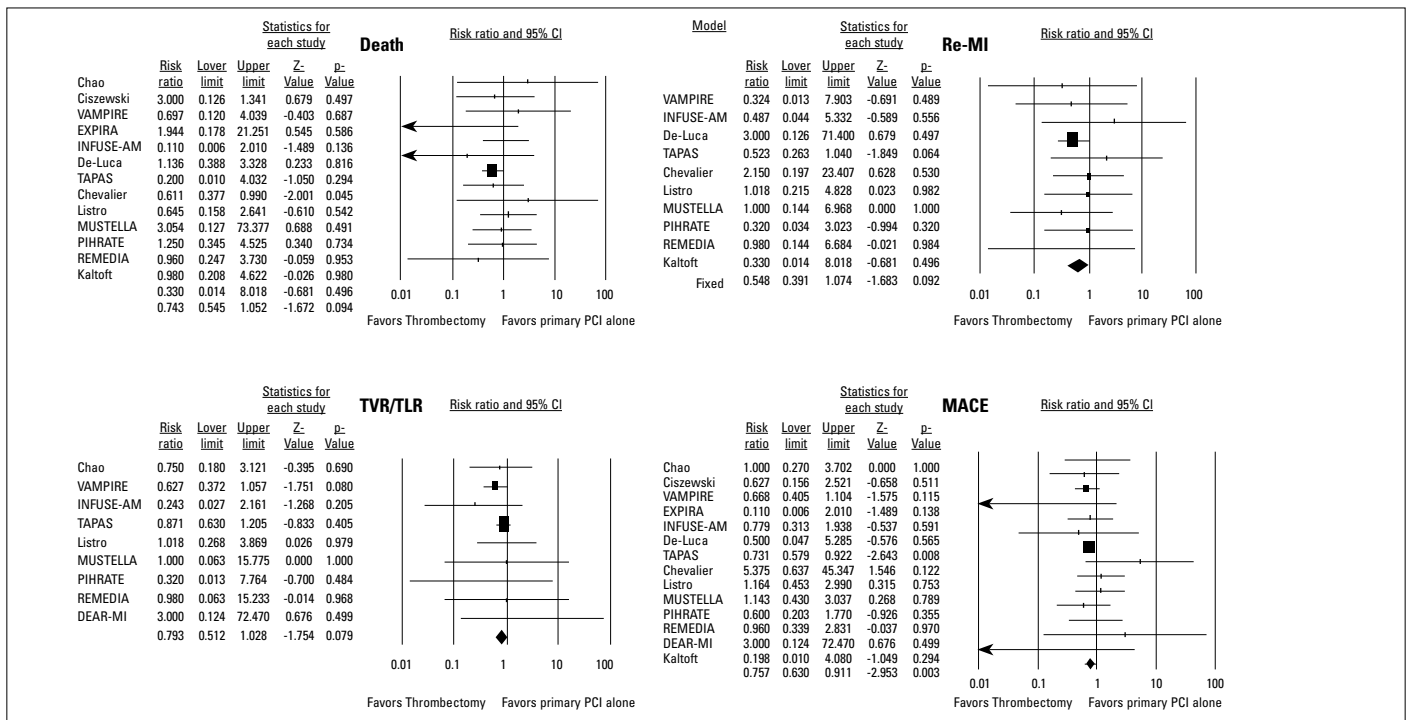
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Death — Statistics for each study — Risk ratio and 95% CI

	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Chao					
Ciszewski	3.000	0.126	1.341	0.679	0.497
VAMPIRE	0.697	0.120	4.039	-0.403	0.687
EXPIRA	1.944	0.178	21.251	0.545	0.586
INFUSE-AM	0.110	0.006	2.010	-1.489	0.136
De-Luca	1.136	0.388	3.328	0.233	0.816
TAPAS	0.200	0.010	4.032	-1.050	0.294
Chevalier	0.611	0.377	0.990	-2.001	0.045
Listro	0.645	0.158	2.641	-0.610	0.542
MUSTELLA	3.054	0.127	73.377	0.688	0.491
PIHRATE	1.250	0.345	4.525	0.340	0.734
REMEDIA	0.960	0.247	3.730	-0.059	0.953
Kaltoft	0.980	0.208	4.622	-0.026	0.980
	0.330	0.014	8.018	-0.681	0.496
	0.743	0.545	1.052	-1.672	0.094

Favors Thrombectomy — Favors primary PCI alone

Re-MI — Model — Statistics for each study — Risk ratio and 95% CI

Model	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
VAMPIRE	0.324	0.013	7.903	-0.691	0.489
INFUSE-AM	0.487	0.044	5.332	-0.589	0.556
De-Luca	3.000	0.126	71.400	0.679	0.497
TAPAS	0.523	0.263	1.040	-1.849	0.064
Chevalier	2.150	0.197	23.407	0.628	0.530
Listro	1.018	0.215	4.828	0.023	0.982
MUSTELLA	1.000	0.144	6.968	0.000	1.000
PIHRATE	0.320	0.034	3.023	-0.994	0.320
REMEDIA	0.980	0.144	6.684	-0.021	0.984
Kaltoft	0.330	0.014	8.018	-0.681	0.496
Fixed	0.548	0.391	1.074	-1.683	0.092

Favors Thrombectomy — Favors primary PCI alone

TVR/TLR — Statistics for each study — Risk ratio and 95% CI

	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Chao	0.750	0.180	3.121	-0.395	0.690
VAMPIRE	0.627	0.372	1.057	-1.751	0.080
INFUSE-AM	0.243	0.027	2.161	-1.268	0.205
TAPAS	0.871	0.630	1.205	-0.833	0.405
Listro	1.018	0.268	3.869	0.026	0.979
MUSTELLA	1.000	0.063	15.775	0.000	1.000
PIHRATE	0.320	0.013	7.764	-0.700	0.484
REMEDIA	0.980	0.063	15.233	-0.014	0.968
DEAR-MI	3.000	0.124	72.470	0.676	0.499
	0.793	0.512	1.028	-1.754	0.079

Favors Thrombectomy — Favors primary PCI alone

MACE — Statistics for each study — Risk ratio and 95% CI

	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Chao	1.000	0.270	3.702	0.000	1.000
Ciszewski	0.627	0.156	2.521	-0.658	0.511
VAMPIRE	0.668	0.405	1.104	-1.575	0.115
EXPIRA	0.110	0.006	2.010	-1.489	0.138
INFUSE-AM	0.779	0.313	1.938	-0.537	0.591
De-Luca	0.500	0.047	5.285	-0.576	0.565
TAPAS	0.731	0.579	0.922	-2.643	0.008
Chevalier	5.375	0.637	45.347	1.546	0.122
Listro	1.164	0.453	2.990	0.315	0.753
MUSTELLA	1.143	0.430	3.037	0.268	0.789
PIHRATE	0.600	0.203	1.770	-0.926	0.355
REMEDIA	0.960	0.339	2.831	-0.037	0.970
DEAR-MI	3.000	0.124	72.470	0.676	0.499
Kaltoft	0.198	0.010	4.080	-1.049	0.294
	0.757	0.630	0.911	-2.953	0.003

Favors Thrombectomy — Favors primary PCI alone

Figure 9. Meta-analysis of all-cause death (left top panel), Re-MI (right top panel), TVR/TLR (left bottom panel), and MACE (right bottom panel) when the TASTE trial was excluded

MACE - major adverse cardiac events; Re-MI - recurrent myocardial infarction; TASTE - Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction in Scandinavia; TVR/TLR - target vessel revascularization/target lesion revascularization

Stroke — Statistics for each study — Risk ratio and 95% CI

	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
INFUSE-AM	0.325	0.013	7.927	-0.690	0.490
REMEDIA	0.980	0.063	15.233	-0.014	0.988
Kaltoft	4.954	0.241	101.993	1.037	0.300
	1.200	0.216	6.667	0.209	0.835

Favors Thrombectomy — Favors primary PCI alone

Stent thrombosis — Statistics for each study — Risk ratio and 95% CI

	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
VAMPIRE	0.324	0.013	7.903	-0.691	0.489
INFUSE-AMI	2.921	0.306	27.874	0.932	0.352
TAPAS	0.501	0.189	1.325	-1.393	0.164
Liistro	2.036	0.190	21.815	0.588	0.557
	0.719	0.320	1.615	-0.799	0.424

Favors Thrombectomy — Favors primary PCI alone

Figure 10. Meta-analysis of stroke (top panel) and stent thrombosis (bottom panel) when the TASTE trial was excluded

TASTE - Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction in Scandinavia

risk might be related to the short duration of follow-up. To overcome this, we took the duration of follow-up as liberal.

In the previous European Society of Cardiology (ESC) Myocardial Revascularization guidelines (40), the routine use of TA was a Class-IIa indication. However, in the current ESC Myocardial Revascularization guidelines (41), the TASTE trial was taken into consideration; therefore, the role of TA was re-evaluted and the class of its recommendation was modified to

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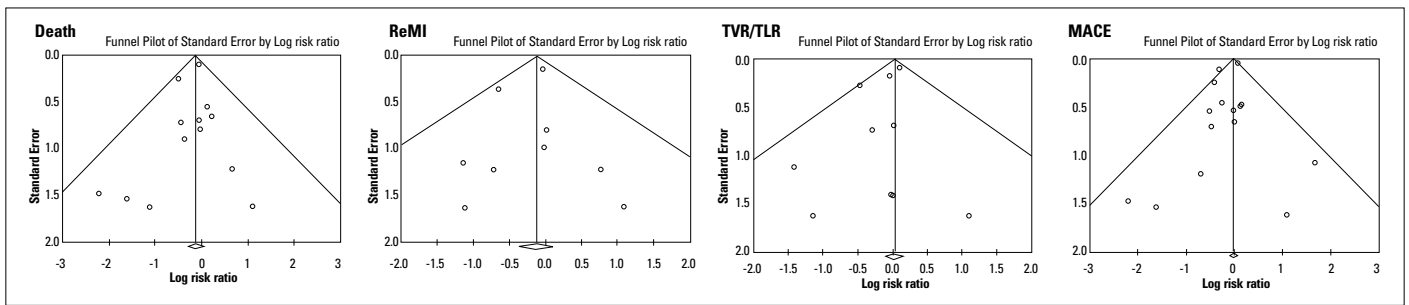
Figure 11. Funnel plot for all-cause death (left top panel), Re-MI (right top panel), TVR/TLR (left bottom panel), and MACE (right bottom panel) to assess publication bias

MACE - major adverse cardiac events; Re-MI - recurrent myocardial infarction; TVR/TLR - target vessel revascularization/target lesion revascularization
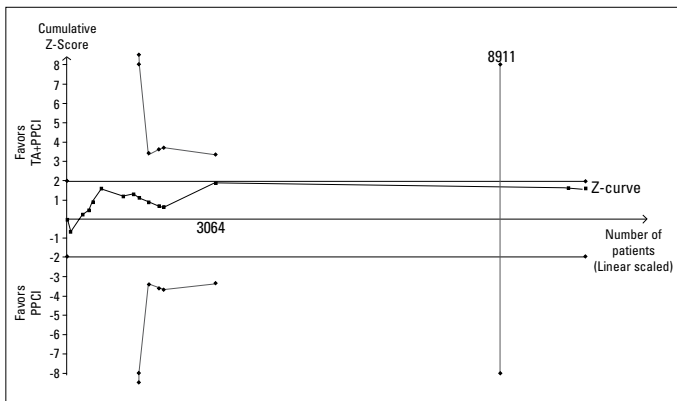
Figure 12. Trial sequential analysis evaluating trombus aspiration in terms of all cause death. The expected RRR was assumed to be 20%
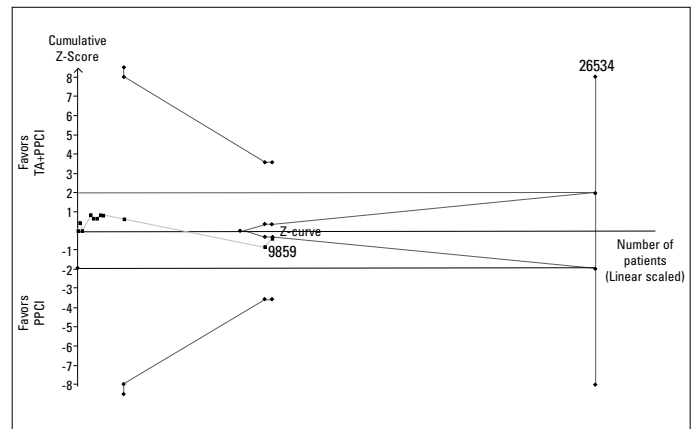
Figure 14. Trial sequential analysis evaluating trombus aspiration in terms of TVR/TLR. The expected RRR was assumed to be 20%

data, which were not put into the peer review process and abstracts of the congress.

Conclusion

In patients with STEMI, TA+PPCI might be related to better epicardial and myocardial perfusion. However, TA did not reduce the frequency of death, Re-MI, MACE TVR/TLR, ST, and stroke. These results do not support the routine use of TA in patients with STEMI.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - İ.H.T.; Design - İ.H.T., E.A.; Supervision - E.A., S.S.; Materials - M.K., A.K., S.T.; Data collection &/or processing - İ.H.T., M.K., A.K.; Analysis &/or interpretation - İ.H.T., V.O.; Literature search - İ.H.T., E.A., V.O.; Writing - İ.H.T., M.K., S.T.; Critical review - S.S., İ.H.T.

Figure 13. Trial sequential analysis evaluating trombus aspiration in terms of recurrent myocardial infarction. The expected RRR was assumed to be 20%

Class-IIb. This new ESC recommendation is compatible with our meta-analysis. However, for more accurate evidence in patients with STEMI, routine aspiration thrombectomy with percutaneous coronary intervention (PCI) versus PCI alone in patients with STEMI undergoing PPCI (TOTAL; ClinicalTrials.gov number: NCT01149044) will be performed.

Study limitations

Because this study is a meta-analysis, the accuracy of the results is related to the accuracy of the RCT included in the meta-analysis. Besides, we did not analyze the unpublished

References

1. Stone GW, Peterson MA, Lansky AJ, Dangas G, Mehran R, Leon MB. Impact of normalized myocardial perfusion after successful angioplasty in acute myocardial infarction. J Am Coll Cardiol 2002; 39: 591-7. **[CrossRef]**

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Aspiration thrombectomy in STEMI

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2. van 't Hof AW, Liem A, Suryapranata H, Hoorntje JC, de Boer MJ, Zijlstra F. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: myocardial blush grade. Zwolle Myocardial Infarction Study Group. Circulation 1998; 97: 2302-6. **[CrossRef]**

3. Ito H, Maruyama A, Iwakura K, Takiuchi S, Masuyama T, Hori M, et al. Clinical implications of the 'no reflow' phenomenon. A predictor of complications and left ventricular remodeling in reperfused anterior wall myocardial infarction. Circulation 1996; 93: 223-8. **[CrossRef]**

4. Claeys MJ, Bosmans J, Veenstra L, Jorens P, De Raedt H, Vrints CJ. Determinants and prognostic implications of persistent ST-segment elevation after primary angioplasty for acute myocardial infarction: importance of microvascular reperfusion injury on clinical outcome. Circulation 1999; 99: 1972-7. **[CrossRef]**

5. Topol EJ, Yadav JS. Recognition of the importance of embolization in atherosclerotic vascular disease. Circulation 2000; 101: 570-80. **[CrossRef]**

6. Kotani J, Nanto S, Mintz GS, Kitakaze M, Ohara T, Morozumi T, et al. Plaque gruel of atheromatous coronary lesion may contribute to the no-reflow phenomenon in patients with acute coronary syndrome. Circulation 2002; 106: 1672-7. **[CrossRef]**

7. Kumbhani DJ, Bavry AA, Desai MY, Bangalore S, Bhatt DL. Role of aspiration and mechanical thrombectomy in patients with acute myocardial infarction undergoing primary angioplasty: an updated meta-analysis of randomized trials. J Am Coll Cardiol 2013; 62: 1409-18. **[CrossRef]**

8. Costopoulos C, Gorog DA, Di Mario C, Kukreja N. Use of thrombectomy devices in primary percutaneous coronary intervention: a systematic review and meta-analysis. Int J Cardiol 2013; 163: 229-41. **[CrossRef]**

9. Bavry AA, Kumbhani DJ, Bhatt DL. Role of adjunctive thrombectomy and embolic protection devices in acute myocardial infarction: a comprehensive meta-analysis of randomized trials. Eur Heart J 2008; 29: 2989-3001. **[CrossRef]**

10. De Luca G, Navarese EP, Suryapranata H. A meta-analytic overview of thrombectomy during primary angioplasty. Int J Cardiol 2013; 166: 606-12. **[CrossRef]**

11. Mongeon FP, Belisle P, Joseph L, Eisenberg MJ, Rinfret S. Adjunctive thrombectomy for acute myocardial infarction: A bayesian meta-analysis. Circ Cardiovasc Interv 2010; 3: 6-16. **[CrossRef]**

12. Burzotta F, De Vita M, Gu YL, Isshiki T, Lefevre T, Kaltoft A, et al. Clinical impact of thrombectomy in acute ST-elevation myocardial infarction: an individual patient-data pooled analysis of 11 trials. Eur Heart J 2009; 30: 2193-203. **[CrossRef]**

13. Tamhane UU, Chetcuti S, Hameed I, Grossman PM, Moscucci M, Gurm HS. Safety and efficacy of thrombectomy in patients undergoing primary percutaneous coronary intervention for acute ST elevation MI: a meta-analysis of randomized controlled trials. BMC Cardiovasc Disord 2010; 10: 10. **[CrossRef]**

14. Vlaar PJ, Svilaas T, van der Horst IC, Diercks GF, Fokkema ML, de Smet BJ, et al. Cardiac death and reinfarction after 1 year in the Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS): a 1-year follow-up study. Lancet 2008; 371: 1915-20. **[CrossRef]**

15. Svilaas T, Vlaar PJ, van der Horst IC, Diercks GF, de Smet BJ, van den Heuvel AF, et al. Thrombus aspiration during primary percutaneous coronary intervention. N Engl J Med 2008; 358: 557-67. **[CrossRef]**

16. Steg PG, James SK, Atar D, Badano LP, Blomstrom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012; 33: 2569-619. **[CrossRef]**

17. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61: e78-140. **[CrossRef]**

18. Lagerqvist B, Fröbert O, Olivecrona GK, Gudnason T, Maeng M, Alström P, et al. Outcomes 1 year after thrombus aspiration for myocardial infarction. N Engl J Med 2014; 371: 1111-20. **[CrossRef]**

19. Meningaud JP, Berdeu D, Moutel G, Herve C. Ethical assessment of clinical research publications. Med Law 2001; 20: 595-603.

20. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009; 62: 1006-12. **[CrossRef]**

21. De Luca L, Sardella G, Davidson CJ, De Persio G, Beraldi M, Tommasone T, et al. Impact of intracoronary aspiration thrombectomy during primary angioplasty on left ventricular remodelling in patients with anterior ST elevation myocardial infarction. Heart 2006; 92: 951-7. **[CrossRef]**

22. Liistro F, Grotti S, Angioli P, Falsini G, Ducci K, Baldassarre S, et al. Impact of thrombus aspiration on myocardial tissue reperfusion and left ventricular functional recovery and remodeling after primary angioplasty. Circ Cardiovasc Interv 2009; 2: 376-83. **[CrossRef]**

23. Dudek D, Mielecki W, Burzotta F, Gasior M, Witkowski A, Horvath IG, et al. Thrombus aspiration followed by direct stenting: a novel strategy of primary percutaneous coronary intervention in ST-segment elevation myocardial infarction. Results of the Polish-Italian-Hungarian RAndomized ThrombEctomy Trial (PIHRATE Trial). Am Heart J 2010; 160: 966-72. **[CrossRef]**

24. Chevalier B, Gilard M, Lang I, Commeau P, Roosen J, Hanssen M, et al. Systematic primary aspiration in acute myocardial percutaneous intervention: a multicentre randomised controlled trial of the export aspiration catheter. Euro Intervention 2008; 4: 222-8. **[CrossRef]**

25. Chao CL, Hung CS, Lin YH, Lin MS, Lin LC, Ho YL, et al. Time-dependent benefit of initial thrombosuction on myocardial reperfusion in primary percutaneous coronary intervention. Int J Clin Pract 2008; 62: 555-61. **[CrossRef]**

26. Sardella G, Mancone M, Bucciarelli-Ducci C, Agati L, Scardala R, Carbone I, et al. Thrombus aspiration during primary percutaneous coronary intervention improves myocardial reperfusion and reduces infarct size: the EXPIRA (thrombectomy with export catheter in infarct-related artery during primary percutaneous coronary intervention) prospective, randomized trial. J Am Coll Cardiol 2009; 53: 309-15. **[CrossRef]**

27. Ikari Y, Sakurada M, Kozuma K, Kawano S, Katsuki T, Kimura K, et al. Upfront thrombus aspiration in primary coronary intervention for patients with ST-segment elevation acute myocardial infarction: report of the VAMPIRE (VAcuuM asPIration thrombus REmoval) trial. JACC Cardiovasc Interv 2008; 1: 424-31. **[CrossRef]**

28. Ciszewski M, Pregowski J, Teresinska A, Karcz M, Kalinczuk L, Pracon R, et al. Aspiration coronary thrombectomy for acute myocardial infarction increases myocardial salvage: single center randomized study. Catheter Cardiovasc Interv 2011; 78: 523-31. **[CrossRef]**

29. De Carlo M, Aquaro GD, Palmieri C, Guerra E, Misuraca L, Giannini C, et al. A prospective randomized trial of thrombectomy versus no

Anatol J Cardiol 2015; 15: 175-87

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thrombectomy in patients with ST-segment elevation myocardial infarction and thrombus-rich lesions: MUSTELA (MUltidevice Thrombectomy in Acute ST-Segment ELevation Acute Myocardial Infarction) trial. JACC Cardiovasc Interv 2012; 5: 1223-30. **[CrossRef]**

30. Lipiecki J, Monzy S, Durel N, Cachin F, Chabrot P, Muliez A, et al. Effect of thrombus aspiration on infarct size and left ventricular function in high-risk patients with acute myocardial infarction treated by percutaneous coronary intervention. Results of a prospective controlled pilot study. Am Heart J 2009; 157: 583 e1-7.

31. Burzotta F, Trani C, Romagnoli E, Mazzari MA, Rebuzzi AG, De Vita M, et al. Manual thrombus-aspiration improves myocardial reperfusion: the randomized evaluation of the effect of mechanical reduction of distal embolization by thrombus-aspiration in primary and rescue angioplasty (REMEDIA) trial. J Am Coll Cardiol 2005; 46: 371-6. **[CrossRef]**

32. Silva-Orrego P, Colombo P, Bigi R, Gregori D, Delgado A, Salvade P, et al. Thrombus aspiration before primary angioplasty improves myocardial reperfusion in acute myocardial infarction: the DEAR-MI (Dethrombosis to Enhance Acute Reperfusion in Myocardial Infarction) study. J Am Coll Cardiol 2006; 48: 1552-9. **[CrossRef]**

33. Stone GW, Maehara A, Witzenbichler B, Godlewski J, Parise H, Dambrink JH, et al. Intracoronary abciximab and aspiration thrombectomy in patients with large anterior myocardial infarction: the INFUSE-AMI randomized trial. JAMA 2012; 307: 1817-26. **[CrossRef]**

34. Kaltoft A, Bottcher M, Nielsen SS, Hansen HH, Terkelsen C, Maeng M, et al. Routine thrombectomy in percutaneous coronary intervention for acute ST-segment-elevation myocardial infarction: a randomized, controlled trial. Circulation 2006; 114: 40-7. **[CrossRef]**

35. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003; 361: 13-20. **[CrossRef]**

36. Niccoli G, Burzotta F, Galiuto L, Crea F. Myocardial no-reflow in humans. J Am Coll Cardiol 2009; 54: 281-92. **[CrossRef]**

37. Henriques JP, Zijlstra F, Ottervanger JP, de Boer MJ, van 't Hof AW, Hoorntje JC, et al. Incidence and clinical significance of distal embolization during primary angioplasty for acute myocardial infarction. Eur Heart J 2002; 23: 1112-7. **[CrossRef]**

38. Haeck JD, Verouden NJ, Henriques JP, Koch KT. Current status of distal embolization in percutaneous coronary intervention: mechanical and pharmacological strategies. Future Cardiol 2009; 5: 385-402. **[CrossRef]**

39. Mehta RH, Harjai KJ, Cox D, Stone GW, Brodie B, Boura J, et al. Clinical and angiographic correlates and outcomes of suboptimal coronary flow inpatients with acute myocardial infarction undergoing primary percutaneous coronary intervention. J Am Coll Cardiol 2003; 42: 1739-46. **[CrossRef]**

40. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. Eur Heart J 2010; 31: 2501-55. **[CrossRef]**

41. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2014; 35: 2541-619. **[CrossRef]**