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: 0.693-1.217, p=0.299), 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.

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-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 for 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 protection 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
effect on short- and long-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, Re-MI, TVR/TLR, postprocedural myocardial blush grade (MBG), postprocedural Thrombolysis In myocardial Infarction (TIMI) flow grade, and postprocedural ST-segment resolution (STR).

(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.

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     |
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, I²=41%, p=0.054), there was significant heterogeneity for MBG II-III (Q=26.5, df=12, I²=54.8%, p=0.009) and for STR (Q=31, df=13, I²=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

| 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-Orge (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 (PIHRAPE) (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  |
| Listro (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) | Nimpro’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 | IH       | 6      | 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

Table 2. Baseline clinical characteristics of randomized controlled trials included in the meta-analysis (number of TA+PPCI or PPCI alone)
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, MACE (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=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; MACE - 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.
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 was similar (Fig. 9 and 10).

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Because the data of postprocedural TIMI flow, MBG, and STR was similar (Fig. 9 and 10).
Aspiration thrombectomy in STEMI

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, and MACE (36, 37).

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...
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
### Stent thrombosis

| Model   | Study name | Risk ratio | Lower limit | Upper limit | Z-Value | p-Value | TA | pPCI | pPCI | 0.01 | 0.10 | 1.00 | 10.00 | 100.00 |
|---------|------------|------------|-------------|-------------|---------|---------|-----|------|------|------|------|------|--------|---------|
| VAMPIRE | 0.324      | 0.013      | 7.903       | -0.691      | 0.489   |         | 1 / 175 |    |     |      |     |      |      |        |         |
| INFUSE-AM | 2.921      | 0.306      | 27.874      | 0.932       | 0.352   |         | 1 / 223 |    |     |      |     |      |      |        |         |
| TASTE   | 1.186      | 0.712      | 1.976       | 0.655       | 0.513   |         | 27 / 3623 | 1 / 223 |    |     |      |     |      |      |        |         |
| TAPAS   | 0.501      | 0.169      | 1.325       | -1.393      | 0.164   |         | 12 / 535 | 1 / 56 |    |     |      |     |      |      |        |         |
| Listro  | 2.036      | 0.190      | 21.815      | 0.588       | 0.557   |         | 56 / 526 |    |     |      |     |      |      |        |         |

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

### Stroke

| Model   | Study name | Risk ratio | Lower limit | Upper limit | Z-Value | p-Value | TA | pPCI | pPCI | 0.01 | 0.10 | 1.00 | 10.00 | 100.00 |
|---------|------------|------------|-------------|-------------|---------|---------|-----|------|------|------|------|------|--------|---------|
| INFUSE-AM | 0.325      | 0.013      | 7.927       | 0.690       | 0.490   |         | 1 / 223 |    |     |      |     |      |      |        |         |
| TASTE   | 1.056      | 0.555      | 2.009       | 0.166       | 0.868   |         | 18 / 3623 | 18 / 3623 |    |     |      |     |      |      |        |         |
| REMEDIA | 0.980      | 0.063      | 15.233      | -0.014      | 0.988   |         | 1 / 50 | 1 / 49 |    |     |      |     |      |      |        |         |
| Katloft | 4.954      | 0.241      | 101.993     | 1.037       | 0.300   |         | 107 / 2 |    |     |      |     |      |      |        |         |

### 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   |
| PIHRITE    | 0.320      | 0.034       | 3.023       | -0.994  | 0.320   |
| REMEDIA    | 0.980      | 0.144       | 6.844       | -0.021  | 0.964   |
| Katloft    | 0.330      | 0.014       | 8.018       | -0.681  | 0.496   |
| DEAR-MI    | 0.884      | 0.093       | 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       | -0.386  | 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   |
| PIHRITE    | 0.895 | 0.701       | 1.142       | -0.693  | 0.372   |
| REMEDIA    | 0.862 | 0.691       | 1.127       | -1.001  | 0.317   |
| Katloft    | 0.889 | 0.697       | 1.134       | -0.947  | 0.344   |

### MACE

| Study name | Point | Lower limit | Upper limit | Z-Value | p-Value |
|------------|-------|-------------|-------------|---------|---------|
| VAMPIRE    | 0.888 | 0.902       | 1.083       | -0.290  | 0.795   |
| INFUSE-AM  | 0.900 | 0.903       | 1.085       | -0.217  | 0.828   |
| De-Luca    | 1.001 | 0.913       | 1.099       | 0.028   | 0.978   |
| TASTE      | 0.990 | 0.904       | 1.085       | -0.213  | 0.831   |
| TAPAS      | 0.816 | 0.904       | 1.085       | -0.207  | 0.836   |
| Chevalier  | 0.886 | 0.900       | 1.081       | -0.291  | 0.711   |
| Listro     | 0.987 | 0.900       | 1.083       | -0.286  | 0.775   |
| MUSTELLA   | 0.987 | 0.900       | 1.081       | -0.279  | 0.780   |
| PIHRITE    | 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       | 1.083       | -0.279  | 0.789   |
| Katloft    | 0.988 | 0.902       | 1.082       | -0.286  | 0.820   |
| DEAR-MI    | 0.988 | 0.902       | 1.082       | -0.286  | 0.820   |

**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
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

| Study name | Point | Lower limit | Upper limit | Z-Value | p-Value |
|------------|-------|-------------|-------------|---------|---------|
| VAMPIRE    | 1.052 | 0.678       | 1.633       | 0.228   | 0.821   |
| INFUSE-AM  | 0.989 | 0.634       | 1.541       | -0.500  | 0.600   |
| TASTE      | 0.716 | 0.315       | 1.625       | -0.800  | 0.424   |
| TAPAS      | 1.229 | 0.796       | 1.996       | 0.831   | 0.406   |
| Listro     | 1.006 | 0.646       | 1.566       | 0.025   | 0.980   |
| Lipiecki   | 1.032 | 0.615       | 1.560       | 3.301   | 0.001   |
| VAMPIRE    | 1.032 | 0.615       | 1.560       | 3.301   | 0.001   |
| EXPIRA     | 1.056 | 0.626       | 1.687       | 3.681   | 0.000   |
| INFUSE-AM  | 1.037 | 0.626       | 1.687       | 3.681   | 0.000   |
| De-Luca    | 1.035 | 0.626       | 1.687       | 3.681   | 0.000   |
| TAPAS      | 1.033 | 1.010       | 1.057       | 2.764   | 0.005   |
| Chevalier  | 1.035 | 1.012       | 1.057       | 2.764   | 0.005   |
| Lipiecki   | 1.032 | 0.615       | 1.560       | 3.301   | 0.001   |
| MUSTELLA   | 1.033 | 0.611       | 1.566       | 2.902   | 0.004   |
| PIHRATE    | 1.034 | 0.612       | 1.557       | 3.021   | 0.003   |
| REMEDIA    | 1.035 | 0.613       | 1.557       | 3.021   | 0.003   |
| DEAR-MI    | 1.033 | 1.011       | 1.056       | 2.963   | 0.002   |
| Lipiecki   | 1.036 | 1.014       | 1.059       | 3.212   | 0.001   |
| Listro     | 1.032 | 0.615       | 1.560       | 3.301   | 0.001   |
| Lipiecki   | 1.036 | 1.014       | 1.058       | 3.212   | 0.001   |

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

| Study name | 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   |
| Listro     | 1.007 | 0.545       | 1.862       | 0.023   | 0.982   |
| Lipiecki   | 1.073 | 0.588       | 1.959       | 0.229   | 0.819   |

Figure 8. Meta-analytic statistics with one study excluded for postprocedural TIMI flow grade (top panel), MBG (middle panel), and STR (bottom panel)
risk ratio and 95% Cl overcame this, we took the duration of follow-up as liberal.

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

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-evaluated and the class of its recommendation was modified to

| Risk ratio | Lower | Upper | p-value | Value |
|---|---|---|---|---|
| INFUSE-AM | 0.325 | 0.173 | 0.426 | 0.699 |
| REMEDIA | 0.980 | 0.980 | 1.000 | 1.000 |
| Kaltoft | 4.954 | 2.631 | 0.000 | 0.000 |
| VAMPIRE | 0.324 | 0.173 | 0.426 | 0.699 |
| INFUSE-AM | 2.931 | 2.931 | 1.000 | 1.000 |
| TAPAS | 0.501 | 0.501 | 1.000 | 1.000 |
| Listro | 2.036 | 2.036 | 1.000 | 1.000 |

| Risk ratio | Lower | Upper | p-value | Value |
|---|---|---|---|---|
| VAMPIRE | 0.324 | 0.173 | 0.426 | 0.699 |
| INFUSE-AM | 2.931 | 2.931 | 1.000 | 1.000 |
| TAPAS | 0.501 | 0.501 | 1.000 | 1.000 |
| Listro | 2.036 | 2.036 | 1.000 | 1.000 |

| Risk ratio | Lower | Upper | p-value | Value |
|---|---|---|---|---|
| VAMPIRE | 0.324 | 0.173 | 0.426 | 0.699 |
| INFUSE-AM | 2.931 | 2.931 | 1.000 | 1.000 |
| TAPAS | 0.501 | 0.501 | 1.000 | 1.000 |
| Listro | 2.036 | 2.036 | 1.000 | 1.000 |
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 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.

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