ST-Elevation Myocardial Infarction, Thrombus Aspiration, and Different Invasive Strategies. A TASTE Trial Substudy

Ole Fröbert, MD, PhD; Fredrik Calais, MD; Stefan K. James, MD, PhD; Bo Lagerqvist, MD, PhD

Background—The clinical effect of thrombus aspiration in ST-elevation myocardial infarction may depend on the type of aspiration catheter and stenting technique.

Methods and Results—The multicenter, prospective, randomized, open-label trial Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE) did not demonstrate a clinical benefit of thrombus aspiration compared to percutaneous coronary intervention alone. We assessed the effect of type of aspiration device, stent type, direct stenting, and postdilation on outcomes at 1 year. There was no difference in all-cause mortality, between the 3 most frequently used aspiration catheters (Eliminate [Terumo] 5.4%, Export [Medtronic] 5.0%, Pronto [Vascular Solutions] 4.5%) in patients randomized to thrombus aspiration. There was no difference in mortality between directly stented patients randomized to thrombus aspiration compared to patients randomized to percutaneous coronary intervention only (risk ratio 1.08, 95% CI 0.70 to 1.67, \( P=0.73 \)). Similarly, there was no difference in mortality between the 2 randomized groups for patients receiving drug-eluting stents (risk ratio 0.89, 95% CI 0.63 to 1.26, \( P=0.50 \)) or for those treated with postdilation (risk ratio 0.72, 95% CI 0.49 to 1.07, \( P=0.11 \)). Furthermore, there was no difference in rehospitalization for myocardial infarction or stent thrombosis between the randomized arms in any of the subgroups.

Conclusions—In patients with ST-elevation myocardial infarction randomized to thrombus aspiration, the type of aspiration catheter did not affect outcome. Stent type, direct stenting, or postdilation did not affect outcome irrespective of treatment with thrombus aspiration and percutaneous coronary intervention or percutaneous coronary intervention alone.


Key Words: angioplasty • myocardial infarction • stenting • thrombus aspiration

Coronary artery thrombus aspiration is a simple, intuitive adjunct to percutaneous coronary intervention (PCI) thought to alleviate microvascular obstruction and improve flow in ST-segment elevation myocardial infarction (STEMI). Earlier and small studies on thrombus aspiration showed promising results on a range of surrogate end points,\(^1\)\(^-\)\(^4\) although beneficial effects on myocardial blush grade and ST-segment resolution are not universal findings in thrombus aspiration trials.\(^5\)\(^-\)\(^7\) The 1071-patient single-center Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS) trial suggested a survival benefit in patients randomized to thrombus aspiration,\(^8\)\(^-\)\(^9\) while no overall clinical effect was documented in the 7244 patients in the Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE) trial after 30 days\(^10\) or after 1 year.\(^11\) Because TASTE was a large multicenter Registry-based Randomized Clinical Trial\(^12\) with liberal inclusion and few exclusion criteria, we speculated whether type of aspiration device, stent type, direct stenting, or postdilation could contribute to explain the neutral outcome of TASTE. We used 1-year data to analyze the impact of different invasive strategies on death, a new myocardial infarction, and stent thrombosis.

Methods

Study Design

The TASTE trial design has been described in detail previously.\(^12\) In brief, TASTE was a multicenter, prospective, randomized controlled clinical open-label trial in patients with STEMI undergoing PCI. The study hypothesis was that routine
Thrombus aspiration, as an adjunct to PCI, is associated with a better outcome compared to PCI alone. We used the national comprehensive Swedish angiography and angioplasty registry, which is part of the Internet-based Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies registry. All baseline and procedural data are entered directly online into the registry, and clinical end point parameters were obtained from national health registries and not centrally adjudicated. No study-specific clinical follow-up was done. Validation of Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies source data against electronic health records has been performed periodically in all hospitals by comparing 50 entered variables in 30 to 40 randomly selected patients per hospital and year with an overall agreement of 95%.

Individuals considered for inclusion were patients referred for PCI due to STEMI of between 30 minutes and 24 hours duration. In patients considered for inclusion, the following was required: correspondence between ECG findings and suspected culprit artery, a minimum visual estimate of 50% stenosis in the culprit artery, and feasibility of performing thrombus aspiration, as judged by the treating physician. Exclusion criteria included the need for emergency coronary artery bypass grafting, inability to provide informed consent, age below 18 years, and previous randomization in TASTE. Eligible patients were randomized online in a 1:1 ratio following oral consent. Within 24 hours all patients were asked to confirm participation by signature. In the TASTE trial, thrombus aspiration catheter type and stenting technique were at the operator’s discretion.

The regional ethical review board of Uppsala, Sweden approved the study (Dnr 2010/111).

### Invasive Procedures

The use of platelet inhibitors or anticoagulants was left to the discretion of the treating physician. After the restoration of antegrade flow, administration of intracoronary nitrates was encouraged. Stenting was encouraged with optional postdilatation. For patients randomized to thrombus aspiration, guidewire placement was followed by thrombus aspiration with a manual aspiration catheter. In lesions that could not be passed through, predilating was permitted with the smallest possible angioplasty balloon to a nominal diameter size of 2.0 mm. Thrombus aspiration catheters were required to be 6-F compatible, low profile in design, and intended for manual aspiration. The following catheters were recommended but other catheters fulfilling the criteria were allowed: Eliminate (Terumo; crossing profile, 0.068 in.), Export Aspiration Catheter (Medtronic; 0.067 in.), and Pronto extraction.

### Table 1. Baseline and Procedural Characteristics According to Aspiration Device

<table>
<thead>
<tr>
<th></th>
<th>Missing Information</th>
<th>Terumo Eliminate</th>
<th>Medtronic Export</th>
<th>Vascular Solutions Pronto</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1748</td>
<td>1291</td>
<td>380</td>
<td></td>
</tr>
<tr>
<td>Age (y), mean (±SD)</td>
<td>(0)</td>
<td>67.1 (11.6)</td>
<td>66.4 (11.2)</td>
<td>65.8 (11.6)*</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>(0)</td>
<td>452 (25.9)</td>
<td>330 (23.5)</td>
<td>98 (25.8)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>(0.5)</td>
<td>229 (13.1)</td>
<td>158 (12.2)</td>
<td>41 (10.8)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>(5.5)</td>
<td>535 (30.6)</td>
<td>386 (29.9)</td>
<td>101 (26.6)</td>
</tr>
<tr>
<td>Previous myocardial infarction, n (%)</td>
<td>(1.3)</td>
<td>197 (11.3)</td>
<td>140 (10.8)</td>
<td>42 (11.1)</td>
</tr>
<tr>
<td>Previous PCI, n (%)</td>
<td>(0)</td>
<td>160 (9.2)</td>
<td>125 (9.7)</td>
<td>35 (9.2)</td>
</tr>
<tr>
<td>Previous coronary artery bypass grafting, n (%)</td>
<td>(0)</td>
<td>38 (2.2)</td>
<td>20 (1.5)</td>
<td>8 (2.1)</td>
</tr>
<tr>
<td>On warfarin prior to PCI, n (%)</td>
<td>(0)</td>
<td>31 (1.8)</td>
<td>22 (1.7)</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Heparin prior to PCI, n (%)</td>
<td>(0)</td>
<td>840 (48.1)</td>
<td>397 (20.8)</td>
<td>146 (38.4)*</td>
</tr>
<tr>
<td>Symptom to PCI time (h), median (IQR)</td>
<td>(0)</td>
<td>3.11 (2.08 to 5.67)</td>
<td>3.08 (2.00 to 5.35)</td>
<td>3.75 (2.09 to 6.39)</td>
</tr>
<tr>
<td>Diagnostic ECG to PCI time (h), median (IQR)</td>
<td>(5.8)</td>
<td>1.12 (0.83 to 1.55)</td>
<td>1.08 (0.77 to 1.55)</td>
<td>1.15 (0.88 to 1.85)</td>
</tr>
<tr>
<td>Killip class ≥2, n (%)</td>
<td>(1.0)</td>
<td>97 (5.5)</td>
<td>75 (5.8)</td>
<td>53 (13.9)*</td>
</tr>
<tr>
<td>Radial access, n (%)</td>
<td>(0)</td>
<td>1349 (77.2)</td>
<td>750 (58.1)</td>
<td>300 (78.9)*</td>
</tr>
<tr>
<td>TIMI flow grade 0 or 1 before PCI, n (%)</td>
<td>(12.0)</td>
<td>1382 (79.1)</td>
<td>1019 (79.0)</td>
<td>263 (71.9)*</td>
</tr>
<tr>
<td>Bivalirudin during PCI, n (%)</td>
<td>(0)</td>
<td>1503 (86.0)</td>
<td>1012 (78.4)</td>
<td>197 (51.8)*</td>
</tr>
<tr>
<td>Glucoprotein IIb/IIIa inhibitor during PCI, n (%)</td>
<td>(0)</td>
<td>215 (12.3)</td>
<td>221 (17.1)</td>
<td>135 (35.5)*</td>
</tr>
</tbody>
</table>

ECG indicates electrocardiogram; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

*Baseline characteristics that differ at \( P<0.05 \).
catheter (Vascular Solutions; 0.070 in.). Direct stenting, stent type, postdilatation, and duration of P2Y12 inhibitor treatment was at physician discretion, while lifelong acetylsalicylic acid was recommended.

End Points, Outcomes, and Definitions

The primary end point of time to all-cause mortality at 30 days\(^\text{10}\) and secondary end points after 1 year have been reported previously.\(^\text{11}\) The 1-year end points used for this substudy on different invasive strategies, a substudy involving subgroups not defined a priori in the study protocol, were all-cause mortality using mortality data obtained from the national population registry and time to rehospitalization with myocardial infarction and time to stent thrombosis obtained from the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies registry and the national discharge registry. Myocardial infarction was defined as ICD codes I21 and I22. No study-specific clinical follow-up was done.

Statistics

The results were analyzed according to the intention-to-treat principle. Baseline characteristics were summarized with means and SDs for continuous variables and percentages for discrete variables. Cumulative event rates were estimated by the Kaplan–Meier method. The primary outcome variables were mortality, rehospitalization for myocardial infarction, and stent thrombosis. Adjusted cumulative risk ratios (RR) of outcomes with different aspiration catheter types were

![Figure 1. A, Kaplan–Meier curves showing cumulative probability of all-cause mortality up to 1 year in patients randomized to thrombus aspiration. Outcomes associated with different thrombus aspiration catheters are shown. B, Cumulative probability of reinfarction until 1 year. C, Cumulative probability of stent thrombosis until 1 year.](http://jaha.ahajournals.org/)

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calculated using a Cox proportional hazard regression model. We also performed multiple imputation of unknown or missing information regarding baseline and procedural variables. All background and procedural factors shown in Table 1 were forced into the Cox regression model for calculation of the adjusted mortalities for the different catheter types. For myocardial infarction, due to few events, only covariates demonstrating statistical significant differences were used in the model. For stent thrombosis, too few events precluded a meaningful regression analysis. All analyses were conducted with SPSS (version 22.0 for Mac; IBM Corp, Armonk, NY). A \( P\)-value <0.05 was considered statistically significant.

Results

Study Population

All 29 of Sweden’s PCI centers along with 1 in Iceland and 1 in Denmark participated in the trial. During the study period, 11 956 patients with STEMI underwent PCI and were registered in Swedish angiography and angioplasty registry and 7244 patients were randomized. No patients were lost to follow-up. However, due to withdrawal of consent from 6 patients, these patients were only included in the analysis until the date of withdrawal.

Procedural Data

Following randomization, 93.9% of patients in the thrombus aspiration group underwent thrombus aspiration while 4.9% of patients in the PCI-alone group underwent thrombus aspiration. Patients were treated according to international guidelines, with high proportions of patients receiving preprocedural platelet inhibition, procedural antithrombotic agents, and with a high proportion of radial access and use of drug-eluting stents.10

Aspiration Catheters

Selected baseline clinical and procedural characteristics subdivided per aspiration catheter type are listed in Table 1. In Figure 1, the cumulative probabilities of all-cause mortality, reinfarction, and stent thrombosis to 1 year in patients randomized to thrombus aspiration are shown. The Eliminate was the most frequently used aspiration catheter (1748 patients) and was chosen as reference in comparison with the other catheters. The Export catheter was used in 1291 patients and the Pronto in 380 patients (data on other catheter types [97 patients] and cases where catheter type was not stated [105 patients] are not reported here). There were no differences in outcome between the 3 different catheters regarding death, reinfarction, or stent thrombosis (Table 2).

Direct Stenting

Direct stenting was performed in 1388 of 3621 patients (38.3%) randomized to thrombus aspiration and in 843 of 3623 patients (23.3%) randomized to PCI only. Neither the risk of all-cause mortality (RR 1.08, 95% CI 0.70 to 1.67, \( P=0.73\)), reinfarction (RR 0.74, 95% CI 0.42 to 1.28, \( P=0.27\)), nor stent thrombosis (RR 0.74, 95% CI 0.30 to 1.78, \( P=0.50\)) differed between the 2 randomized treatments (Figure 2). Predilatation before stenting was performed in 2064 (57.0%) of patients randomized to thrombus aspiration and in 2613 (72.1%) randomized to PCI only. Neither the risk of all-cause mortality (RR 0.94, 95% CI 0.73 to 1.20, \( P=0.60\)), reinfarction (RR 1.03, 95% CI 0.73 to 1.46, \( P=0.87\)), nor stent thrombosis (RR 0.69, 95% CI 0.34 to 1.40, \( P=0.30\)) differed between the 2 randomized treatments. No statistical interaction between randomized treatment and predilatation/direct stenting was found for any of these 3 outcome measures.

Table 2. Aspiration Device and Outcome at 1 Year

<table>
<thead>
<tr>
<th>Aspiration Device</th>
<th>N (%)</th>
<th>All-Cause Death (%)</th>
<th>Hospitalization for a New Myocardial Infarction (%)</th>
<th>Stent Thrombosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terumo Eliminate</td>
<td>1748 (48.3)</td>
<td>5.4</td>
<td>2.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Medtronic Export</td>
<td>1291 (35.7)</td>
<td>Unadjusted 5.0 HR 0.93 (0.68 to 1.28, ( P=0.67))</td>
<td>2.6 HR 1.07 (0.68 to 1.68, ( P=0.77))</td>
<td>0.6 HR 0.72 (0.30 to 1.69, ( P=0.45))</td>
</tr>
<tr>
<td>Vascular Solutions Pronto</td>
<td>380 (10.5)</td>
<td>Unadjusted 4.5 HR 0.87 (0.49 to 1.39, ( P=0.47))</td>
<td>3.2 HR 1.27 (0.67 to 2.40, ( P=0.47))</td>
<td>0.5 HR 0.6 (0.14 to 2.63, ( P=0.50))</td>
</tr>
</tbody>
</table>

The Terumo Eliminate catheter was used as reference for hazard ratios (HR) and 95% CI. NA indicates not applicable.
Drug-Eluting and Bare Metal Stents

A total of 1703 patients (47.0%) randomized to thrombus aspiration and 1742 (48.1%) randomized to PCI only received drug-eluting stents. All-cause mortality (RR 0.89, 95% CI 0.63 to 1.26, P=0.50) did not differ between patients in the 2 groups (Figure 3). Also, all-cause mortality (RR 0.93, 95% CI 0.72 to 1.08, P=0.22) did not differ between patients receiving bare metal stents in the 2 groups. Reinfarction did not differ between patients randomized to thrombus aspiration or PCI only receiving drug-eluting (RR 0.86, 95% CI 0.54 to 1.37, P=0.53) or bare metal stents (RR 0.94, 95% CI 0.64 to 1.38, P=0.75) as was the case for stent thrombosis (RR 0.60, 95% CI 0.28 to 1.31, P=0.20 and RR 0.91, 95% CI 0.43 to 1.94, P=0.81, respectively). No statistical interaction between randomized treatment and the choice of drug-eluting/bare metal stent was found for any of the 3 outcome measures.

Postdilatation

Postdilatation was performed in 1183 patients (32.7%) randomized to thrombus aspiration and in 1153 patients (31.8%) randomized to PCI only. Neither the risk of all-cause mortality (RR 0.74, 95% CI 0.51 to 1.07, P=0.11), reinfarction (RR 0.86, 95% CI 0.51 to 1.46, P=0.57), nor stent thrombosis (RR 0.67, 95% CI 0.26 to 1.77, P=0.42) differed between the 2 patient groups (Figure 4).

No postdilatation was used in 2269 (62.7%) of patients randomized to thrombus aspiration and in 2305 (63.6%) of patients randomized to PCI only.
patients randomized to PCI only. Neither the risk of all-cause mortality (RR 1.03, 95% CI 0.80 to 1.33, \( P = 0.84 \)), reinfarction (RR 0.94, 95% CI 0.66 to 1.34, \( P = 0.73 \)), nor stent thrombosis (RR 0.78, 95% CI 0.40 to 1.49, \( P = 0.45 \)) differed between the 2 randomized treatments. No statistical interaction between randomized treatment and postdilatation/no postdilatation was found for any of the 3 outcomes.

**Discussion**

In this substudy to the 7244-patient TASTE registry-based randomized clinical trial on thrombus aspiration in patients with STEMI, we found no statistically significant differences in outcomes pertaining to thrombus aspiration catheter type, direct stenting, stent type, or postdilatation. Importantly, however, the TASTE trial was not powered for the post-hoc analyses presented in this substudy.

**Aspiration Catheters**

While meta-analyses have indicated that so-called mechanical thrombus aspiration devices with rotating cutters or water jets attached to vacuum systems are inferior to manual aspiration catheters in terms of clinical outcome,\(^{15,16}\) less is known about efficacy and safety between different kinds of manual aspiration catheters. Theoretically, a too-small internal lumen catheter may dislodge thrombus and brittle plaque material, thus impeding myocardial perfusion. Two clinical studies including a total of 263 patients with STEMI compared a large-internal-lumen catheter (Diver, Invatec) with a
medium-sized catheter (Export, Medtronic) and demonstrated less effective thrombus aspiration with the large-lumen catheter.\textsuperscript{17,18} Except for aspiration lumen area, which was slightly larger in the Pronto catheter, the specifications of the 3 main catheter types in TASTE were very similar.\textsuperscript{14} Our findings of comparable Kaplan–Meier event curves on all-cause death, myocardial infarction, and stent thrombosis indicate that performance is also similar.

**Direct Stenting**

There is a causality dilemma on direct stenting and thrombus aspiration in STEMI. Both techniques may reduce thrombus dislodgment and improve microcirculatory reperfusion during primary PCI. When coronary thrombus material has been removed, it is visually easier to estimate residual stenosis grade and calcification and thus easier to appropriately size a stent for direct implantation. This is reflected in findings from several studies, including TAPAS and TASTE, where direct stenting was used more frequently in patients undergoing thrombus aspiration.\textsuperscript{8,10,19} Although retrospective data indicate that direct stenting is an independent predictor of improved survival in patients undergoing primary PCI\textsuperscript{20} by nature, patients who can be treated with direct stenting most likely have a better prognosis due to simpler coronary lesions and the fact that thrombus can be removed or is absent. In the 501-patient JETSTENT study, patients with STEMI were randomized to mechanical rheolytic thrombectomy followed by direct stenting or to direct stenting alone.\textsuperscript{21} ST-segment resolution was more frequent, and the 6-month major adverse

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**Figure 4.** A, Kaplan–Meier curves showing cumulative probability of all-cause mortality to 1 year in patients treated with postdilatation and randomized to thrombus aspiration (TA) and percutaneous coronary intervention (PCI) or only PCI. B, Cumulative probability of reinfarction until 1 year. C, Cumulative probability of stent thrombosis until 1 year.
cardiovascular events rate was significantly lower in the thrombectomy arm than in the direct-stenting-alone arm. In a substudy from the 148-patient Dethrombosis to Enhance Acute Reperfusion in Myocardial Infarction study on thrombus aspiration or PCI-only in STEMI, direct stenting was associated with reduced distal embolization and improved myocardial reperfusion. In this study we found no differences in the analyzed 1-year clinical outcome parameters between patients in the thrombus aspiration group and patients in the PCI-only group treated by direct stenting and although no statistical comparison was done, the event rates were almost identical to our findings in the overall TASTE cohort.

Drug-Eluting and Bare Metal Stents

The presence of uncovered stent struts is associated with late stent thrombosis after drug-eluting stent implantation and in theory, thrombus aspiration could be expected to reduce stent undersizing due to thrombus dissolution and to improve apposition. However, no clinical outcome measures met statistical significance in this study.

Postdilatation

Hypothetically, stent undersizing in patients with STEMI not undergoing thrombus aspiration could be a contributing factor to why postdilatation was more infrequent after thrombus aspiration in 1 study, although no such difference was seen in the TASTE trial. In a retrospective study of more than 90,000 Swedish stent implantations, we found postdilatation to be associated with a higher restenosis risk but stent thrombosis did not differ statistically between procedures with or without postdilatation. While postdilatation is not without risks, no statistically significant effect on outcome measures between directly stented patients randomized to thrombus aspiration versus patients randomized to PCI only were found in this study.

Limitations

It is a limitation to this substudy that none of the studied invasive strategies were part of the randomization in the TASTE trial, and therefore prone to selection bias. Postdilatation in particular, where (a statistically nonsignificant) separation of survival curves was seen (Figure 4A), seems susceptible to this type of bias. Baseline and procedural differences in the use of anticoagulation and platelet inhibition agents and in Killip class were prominent with respect to aspiration catheter type and most likely reflect a combination of chance and variation in operator and institutional preferences. The sheer size of TASTE, in which more patients were included than in all previous randomized trials on thrombus aspiration in STEMI combined, to some extent compensates for this. Handling of aspiration catheters was not reported, and it cannot be excluded that 1 or more of the catheters was more frequently discarded and replaced by another type. A beneficial effect of thrombus aspiration on mortality may be limited to patients with viable myocardium and improving left ventricular function and could take several years to detect, but will be reported according to our scheduled 2, 5, and 10-year follow-up.12

Conclusions

In contrast to findings in many smaller trials, manual thrombus aspiration was not associated with a clinical benefit in the TASTE study. In this substudy we tried to tease out from the data whether the neutral findings could be explained in part by different invasive strategies. However, type of aspiration device did not affect outcome in patients randomized to thrombus aspiration. Stent type, direct stenting, or postdilatation did not confer a worse or better outcome on death, a new myocardial infarction, or stent thrombosis whether randomized to thrombus aspiration and PCI or to PCI only.

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Disclosures

Fröbert reports receiving consultant fees from Biosensors and Biotronik. James reports receiving payment for lectures from Medtronic. Calais and Lagerqvist have none declared.
References


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