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## **Thrombus Aspiration in Patients with ST-Elevation Myocardial Infarction Presenting Late after Symptom Onset**

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**Running title:** Thrombus aspiration in late presenting STEMI

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**ABSTRACT**

**Background** Thrombus aspiration is an established treatment option in patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). However, there are only limited data on the efficacy of thrombus aspiration in STEMI patients presenting  $\geq 12$  hours after symptom onset.

**Objectives** To examine whether manual thrombus aspiration reduces microvascular obstruction (MVO) assessed by cardiac magnetic resonance imaging (CMR) in patients with STEMI presenting late after symptom onset.

**Methods** Patients with subacute STEMI presenting  $\geq 12$  and  $\leq 48$  hours after symptom onset were randomized to primary PCI with or without manual thrombus aspiration in a 1:1 ratio. Patients underwent CMR 1 to 4 days after randomization. The primary endpoint was the extent of MVO.

**Results** A total of 152 patients underwent randomization. The time between symptom onset and PCI was  $28 \pm 12$  hours. Baseline characteristics were comparable between groups. The majority of patients (60%) showed at least a moderate amount of viable myocardium in the affected region. Extent of MVO was not significantly different between patients assigned to thrombus aspiration and the control group ( $2.5 \pm 4.0\%$  versus  $3.1 \pm 4.4\%$  of left ventricular mass,  $p=0.47$ ). There were also no significant differences in infarct size, myocardial salvage, left ventricular ejection fraction or angiographic and clinical endpoints between groups.

**Conclusions** In this first randomized trial on thrombectomy in patients with STEMI presenting late after symptom onset, routine thrombus aspiration before PCI failed to show a benefit on markers of reperfusion success.

**KEYWORDS:** Thrombus aspiration; ST-elevation myocardial infarction; cardiac magnetic resonance imaging; microvascular obstruction.

**CONDENSED ABSTRACT**

It is unclear whether routine manual thrombus aspiration reduces microvascular obstruction (MVO) in patients with subacute ST-elevation myocardial infarction (STEMI). 152 patients with STEMI presenting between 12 and 48 hours after symptom onset were randomized to primary percutaneous coronary intervention (PCI) with or without thrombus aspiration. The primary endpoint extent of MVO assessed by cardiac magnetic resonance imaging was not significantly different between groups. Routine thrombus aspiration before PCI thus failed to show a benefit on reperfusion success in patients with STEMI presenting late after symptom onset.

**ABBREVIATIONS**

<b>CMR</b>	Cardiac magnetic resonance imaging
<b>LV</b>	Left ventricular
<b>%LV</b>	Percentage of left ventricular mass
<b>MSI</b>	Myocardial salvage index
<b>MVO</b>	Microvascular obstruction
<b>PCI</b>	Percutaneous coronary intervention
<b>SPECT</b>	Single-photon emission computed tomography
<b>STEMI</b>	ST-elevation myocardial infarction
<b>TIMI</b>	Thrombolysis In Myocardial Infarction

## INTRODUCTION

Thrombus aspiration is an established treatment option in patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) although recent trials reported disappointing results with no reduction in mortality and possibly an increase in stroke (1,2). Current evidence is largely restricted to patients presenting within the first hours after symptom onset. Nevertheless, patients presenting  $\geq 12$  hours after the beginning of symptoms may display particularly high thrombus burden due to long dwelling times. Thus, thrombus aspiration might be a useful adjunct to conventional PCI in this subset of patients. A prior study suggested that thrombus aspiration may indeed be more effective in late presenting patients (3). On the other hand, thrombectomy could also be detrimental in this situation because of mechanical thrombus dislodgement and distal embolization with subsequent microvascular injury and expansion of the necrotic zone. Thrombus composition may also play a role. While in the initial stages of evolving infarction thrombotic material is relatively soft (low fibrin content, high platelet content), it becomes more organized (high fibrin content, low platelet content) and possibly less suited for aspiration at later stages (4). However, data on the efficacy of thrombus aspiration in the subgroup of STEMI patients presenting late after symptom onset are scarce. The current trial examined the effect of routine thrombus aspiration on microvascular obstruction (MVO) assessed by cardiac magnetic resonance imaging (CMR) in patients with subacute STEMI presenting between 12 and 48 hours after symptom onset.

## METHODS

### *Design overview*

The trial's main objective was to study whether manual thrombus aspiration reduces MVO in patients with subacute STEMI. Eligible patients were randomized to primary PCI with

or without manual thrombus aspiration. The main inclusion criteria were STEMI greater than or equal to 12 and less than or equal to 48 hours after symptom onset irrespective of signs of ongoing ischemia and age between 18 and 90 years. Exclusion criteria included prior thrombolysis, contraindications for CMR (known at the time of randomization) and severe comorbidities with limited life expectancy <6 months. Patients underwent CMR 1-4 days after randomization. The primary efficacy endpoint was the extent of MVO on late gadolinium enhancement CMR. All patients were enrolled at a single institution (University of Leipzig – Heart Center). The study was approved by the local Institutional Review Board and conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent before randomization.

The trial was registered under [www.clinicaltrials.gov](http://www.clinicaltrials.gov): NCT01379248.

#### *Randomization and blinding*

Eligible patients willing to take part in the study were assigned in a 1:1 ratio to the treatment groups by permuted block randomization with randomly changing block sizes via an internet-based system using a computer-generated list of random numbers. Randomization was performed before coronary angiography in the catheterization laboratory. The randomization list was generated and maintained by an information technology expert who was not involved in the clinical conduct of the study.

CMR and all other subsequent analyses were performed by readers blinded to treatment assignment. By design, physicians performing the invasive procedures were aware of randomization results. Patients were not informed about treatment allocation until completion of the study.

#### *Endpoints*

The primary efficacy endpoint was the extent of MVO assessed by CMR in the modified intention-to-treat population. Secondary CMR endpoints included infarct size, myocardial salvage as well as left ventricular (LV) volumes and ejection fraction. Furthermore, a central blinded analysis of angiographic markers of reperfusion success such as the Thrombolysis In Myocardial Infarction (TIMI) flow post-PCI and myocardial blush grade was performed. Coronary collateralization was graded according to the Rentrop classification (grade 0, no visible filling of any collateral channel; grade 1, filling of the side branches of the infarct-related artery; grade 2, partial filling of the epicardial vessel of the infarct-related artery; grade 3, complete collateral filling of the epicardial vessel) (5). For enzymatic infarct size determination, high-sensitivity troponin T after 24 and 48 h was evaluated. The clinical endpoints of all-cause and cardiovascular death, myocardial reinfarction, target vessel revascularization, stent thrombosis and stroke are reported up to 30 days after randomization. Clinical endpoints were defined according to guidelines (6).

#### *Percutaneous coronary intervention*

Thrombus aspiration had to be performed before the first balloon inflation using a manual aspiration catheter (Export® AP, 6 French, Medtronic Inc. Minneapolis, Minnesota, USA). A minimum of 2 aspiration passages across the lesion was recommended. Otherwise, PCI was performed according to current best practice.

#### *Cardiac magnetic resonance imaging*

Patients underwent CMR 1-4 days after randomization for the evaluation of the primary endpoint MVO and selected secondary endpoints (infarct size, myocardial salvage, LV ejection fraction and volumes). The scan protocol on a clinical 1.5 Tesla scanner has been used in several other randomized trials and has been described in detail previously (7). In brief, infarct size and

MVO were assessed in late gadolinium enhancement short-axis images covering the LV approximately 15 min after injection of gadolinium chelate. An inversion-recovery turbo gradient-echo sequence was used for image acquisition. A hypointense core within the hyperenhanced infarcted area was defined as MVO. For determination of infarct-related myocardial edema/area at risk, short-axis slices covering the LV using a T2-weighted triple-inversion recovery turbo spin-echo sequence before contrast administration were obtained. Assessment of LV function and volumes was performed in short-axis slices from base to apex acquired by a standard steady-state free precession technique.

CMR images were sent on storable media to the CMR core laboratory at the University Heart Center Lübeck, Germany, for assessment by fully blinded operators. For all quantitative analyses, certified CMR evaluation software was used (cmr42, Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada). Semiautomated computer-aided threshold detection was used to identify regions of edema, MVO, and infarcted myocardium. A myocardial region was regarded as affected if at least 10 adjacent myocardial pixels revealed a signal intensity of  $>2$  SDs of remote healthy myocardium for edema and  $>5$  SDs in late gadolinium enhancement images (Figure 1). MVO and infarct size were expressed as percentage of LV mass, given by the sum of the mass of MVO and late gadolinium enhancement regions for all slices divided by the overall mass of the LV myocardial cross-section slices (%LV). If present, MVO was included in the overall infarct size and was quantified separately. Myocardial salvage index (MSI) was calculated as area at risk minus infarct size divided by area at risk multiplied by 100 as previously described (8).

The core laboratory has vast experience in CMR image acquisition and post-processing (9,10).



### *Sample size*

Sample size was calculated for the between-group comparison with regard to the primary endpoint. From the results of a previous study and internal data, we expected a mean difference of 2.0%LV in the extent of MVO between the treatment arms with a standard deviation of 3.5 (11). Based on these assumptions, a total of 132 patients needed to be analyzed to reject the null hypothesis of equal means between the 2 groups with a statistical power of 90% (two-tailed t-test,  $\alpha=0.05$ ). To account for a presumed rate of 15% of patients not undergoing CMR or without analyzable examinations, a total of 152 patients were randomized. Sample size was calculated with the use of SiZ (Cytel Inc., Cambridge, Massachusetts, USA).

### *Statistical analysis*

Categorical variables are expressed as number and percentage of patients. Continuous data are reported as means and standard deviation as well as 95% confidence intervals when appropriate. Correlations were investigated using Spearman's correlation coefficient. Patient characteristics were compared using Fisher's exact test for categorical variables and independent samples t-tests as well as analysis of variance for continuous data. Data were analyzed for both a modified intention-to-treat (cohort for primary endpoint analysis) and a per-protocol population. The modified intention-to-treat cohort comprised all patients with subacute STEMI who underwent randomization irrespective of treatment actually received or protocol adherence. Based on angiographic, laboratory, and CMR imaging results (normal coronary arteries, no elevation of cardiac enzymes, no edema), patients with a final diagnosis other than STEMI were excluded (n=8). The per-protocol analysis included all patients with subacute STEMI who received treatment according to the initial allocation.

A two-tailed p-value <0.05 was considered statistically significant. Statistical analyses were performed with SPSS 17.0 (SPSS Inc., Chicago, Illinois).

## RESULTS

### *Baseline characteristics*

From March 2011 through November 2014, a total of 152 patients underwent randomization (Figure 2). Eight patients were excluded from the analysis due to a final diagnosis other than STEMI.

Baseline characteristics were well balanced between the two treatment groups (Table 1). The time between symptom onset and PCI was  $28 \pm 12$  hours for the overall cohort ( $p=0.17$  for between group comparison). The aspiration catheter could not be advanced to the culprit site in 5 patients. Three patients randomized to PCI alone underwent thrombus aspiration due to operator's choice (bailout situations due to unsatisfactory result after conventional PCI). Thrombectomy led to aspiration of macroscopic thrombus material in >60% of patients (Table 1). Administration of glycoprotein IIb/IIIa receptor inhibitors was similar between groups (18 [25%] patients in thrombus aspiration group versus 21 [28%] patients in control group,  $p=0.85$ ).

### *Impact of thrombectomy on cardiac magnetic resonance imaging parameters*

MVO was present in 59% ( $n=33$ ) and 64% ( $n=35$ ) of patients following thrombectomy and conventional PCI, respectively ( $p=0.69$ ). The primary endpoint extent of MVO was  $2.5 \pm 4.0$  %LV mass in patients assigned to thrombus aspiration and  $3.1 \pm 4.4$  %LV in patients randomized to the control group ( $p=0.47$ , Table 2 and Figure 3). There were also no significant differences in infarct size, MSI, LV volumes or ejection fraction between groups (Table 2). The results were consistent across all subgroups (Figure 4) and did not change substantially when analyzing only the per-protocol population.

*Angiographic and procedural outcome*

The majority of patients (n=90, 62.5%) displayed complete occlusion of the culprit vessel prior to PCI corresponding to thrombus grade 5 (Table 1). Coronary collaterals were present in 89 patients (62%) with no differences between the groups (p=0.23). In the thrombectomy group, significantly more patients underwent primary stenting without predilation of the lesion (Table 1, p<0.001).

Post-interventional TIMI flow grade 3 was achieved in 54 (78%) patients in the thrombectomy group and 50 (69%) patients in the control group with conventional PCI only (p=0.44). Myocardial blush grade after PCI was not significantly different between groups (grade 3: 70.0% versus 64.9%, p=0.83).

*Enzymatic infarct size*

Enzymatic infarct size assessed by high-sensitivity troponin T values was similar between the thrombectomy and the standard PCI group with  $3031 \pm 2189$  ng/l versus  $2588 \pm 1908$  ng/l at 24 hours (p=0.24) and  $2995 \pm 2395$  ng/l versus  $3150 \pm 2140$  ng/l (p=0.75) at 48 hours.

*Clinical outcome*

Follow-up at 30 days was completed in all patients. The clinical event rate was low (Table 3). Overall, 16 events were recorded. One patient who did not undergo thrombus aspiration suffered from stroke several hours after catheterization.

With respect to early clinical outcome, no significant differences between the groups could be observed (Table 3). The mortality rate at 30 days was 2.9% (n=2) in patients undergoing thrombectomy versus 5.4% (n=4) in those undergoing standard PCI only (p=0.68).

*Reperfusion success*

CMR was performed after a mean of  $2.3 \pm 2.0$  days after PCI with no significant difference between groups ( $p=0.66$ ). A total of 33 patients did not undergo CMR or had non-analyzable images (Figure 2).

LV ejection fraction was moderately impaired ( $45 \pm 11\%$ ). At an area at risk of  $38 \pm 16\%$  LV and a final infarct size of  $28 \pm 17\%$  LV, MSI was  $27 \pm 26$ . The majority of patients (60%) had a MSI  $>10$ . MSI did not differ between asymptomatic patients and those with ongoing ischemic symptoms ( $33 \pm 29$  versus  $26 \pm 25$ ,  $p=0.31$ ). MSI was higher in patients with preserved or residual epicardial flow of TIMI grades 3 and 2 prior to reperfusion versus those with severely compromised or absent flow of TIMI 1 and 0 ( $43 \pm 32$  versus  $21 \pm 20$ ,  $p<0.001$ ). Patients with at least a minimum of angiographically visible collaterals (Rentrop grades 1-3) displayed higher MSI in comparison to those without ( $37 \pm 30$  versus  $21 \pm 21$ ,  $p=0.004$ ). MSI, infarct size, and MVO showed no significant difference between patients in the shortest, intermediate and longest tertile of symptom onset to PCI times (Figure 5 a + b + c). There was no correlation of MSI ( $p=0.30$ ), infarct size ( $p=0.80$ ), and MVO ( $p=0.41$ ) with symptom-onset-to-balloon time.

## DISCUSSION

This is the first randomized controlled study to examine a possible beneficial effect of routine manual thrombus aspiration exclusively in patients with subacute STEMI. Further, it reports on the largest cohort of late presenting STEMI patients undergoing CMR imaging for the assessment of reperfusion success. The main findings can be summarized as follows: i) aspiration thrombectomy did not reduce the extent of MVO compared with standard PCI without thrombectomy, which is corroborated by a lack of benefit in secondary endpoints; and ii) STEMI patients with a symptom onset to reperfusion time  $>12$  hours display only moderate amount of salvageable myocardium.

*Thrombus aspiration in ST-elevation myocardial infarction*

Previous randomized trials evaluating the effects of thrombus aspiration in STEMI have mainly focused on patients within 12 hours of symptom onset. A medium-sized study showed a reduction in the extent of MVO and reduced infarct size after thrombectomy (11). In line with these results, the single-center Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study (TAPAS) found an improvement in angiographic as well as electrocardiographic markers of reperfusion success and even a reduction in all-cause and cardiac death at 1 year (12,13). These positive initial results were recently challenged by several large trials: The INFUSE-AMI study could not find a beneficial effect of thrombus aspiration on infarct size assessed by CMR in patients with anterior STEMI presenting very early after symptom onset (14). The multicenter Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE) study randomized 7244 patients to manual thrombus aspiration followed by PCI versus PCI only (1). There was neither a beneficial effect of thrombectomy on the primary endpoint of all-cause mortality nor on any other clinical endpoint. The largest trial to date („Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone [TOTAL]“) in 10.732 patients with acute STEMI confirmed these neutral results on mortality, however found an increased stroke rate at 30 days following thrombus aspiration (2). Consistent with these results, the most recent meta-analysis concludes that in STEMI aspiration thrombectomy before primary PCI is not associated with any benefit on clinical endpoints and might increase the risk of stroke (15). The same likely holds true for patients with non-STEMI (10). The results from TASTE and TOTAL have not yet found their way into treatment guidelines which still express a moderate recommendation for routine manual thrombectomy in all STEMI patients (16,17).

It is important to realize that there are only scarce data on the efficacy of thrombus aspiration in patients who present later than 12 hours after symptom onset. Although the aforementioned TASTE trial had a liberal inclusion window of 24 hours following initial symptoms, the vast majority of patients presented within the first hours (the median time between symptom onset and PCI was 3 hours).

Several hypotheses might serve to explain why thrombus aspiration failed in the majority of recent trials including ours despite being a theoretically sound concept. First, aspiration will remove thrombotic material in many patients (as verified by analysis of the aspirate), but manipulation with the catheter might also dislodge thrombotic material with subsequent embolization into the microcirculation. These opposing effects might balance each other resulting in neutral outcome.

Second, the magnitude of the presumed net effect of thrombus aspiration might not be enough to produce changes in the extent of MVO or other surrogate parameters of reperfusion success. This might be especially true in a late-presenting cohort where due to high thrombus burden the potential for significant iatrogenic distal embolization is likely higher than in patients presenting early after symptom onset. However, thrombus aspiration in the first hours of infarction revealed equally sobering results. In the INFUSE-AMI trial which randomized only patients with large anterior infarctions within 4 hours of symptom onset, manual thrombus aspiration did not affect infarct size measured by CMR (14). Subgroup analyses from the TASTE and TOTAL trials also found no reduction in clinical events in patients with the shortest symptom-onset-to-PCI times (1,2). Specific to subacute stages of STEMI, the amount of myocardium to be salvaged may also be too small for thrombus aspiration to effectively impact infarct size. The present trial explored the unselected routine use of thrombus aspiration before

PCI in patients with subacute STEMI. However, it is possible that thrombus aspiration might only be advantageous in specific subsets of patients such as those with large thrombus burden, total occlusion or reduced flow. However, almost 90% of patients in our trial displayed either complete vessel occlusion or high thrombus burden (thrombus grades 3 to 5) making this an unlikely explanation for the neutral results.

*Reperfusion success and primary PCI in subacute ST-elevation myocardial infarction*

There is general consensus that primary PCI is the treatment of choice for STEMI patients who present within 12 hours of symptom onset. Data are much less clear for patients presenting thereafter. Recent treatment guidelines recommend considering reperfusion therapy with primary PCI in STEMI patients with symptom duration of 12 to 48 hours (18).

The theoretical consideration favoring reperfusion over medical therapy in subacute STEMI is the hypothesis that a significant amount of viable myocardium that can still be salvaged despite prolonged ischemia is present. Factors such as a stuttering course with intermittent occlusion and recanalization, ischemic preconditioning, persistence of minimal flow in the infarct-related artery, or recruitment of collaterals may prevent complete necrosis and preserve some degree of myocardial viability (19-23). The current study is the first to study the hypothesis by means of CMR demonstrating a moderate amount of viable myocardium in patients presenting between 12 and 48 hours after symptom onset. However, these findings cannot be interpreted as being supportive for a beneficial effect of mechanical reperfusion, as all patients underwent PCI. There are only few prospective studies investigating the value of late mechanical reperfusion. The Beyond 12 hours Reperfusion Alternative Evaluation 2 (BRAVE 2) trial randomized 335 asymptomatic STEMI patients presenting 12 to 48 hours after symptom onset to immediate invasive or conservative treatment (23). Infarct size by SPECT was significantly smaller

following the invasive strategy which might translate into a reduction in mortality observed at long-term follow-up (24). The Occluded Artery Trial (OAT) randomized 2,166 late-presenting clinically stable post-STEMI patients with an occluded infarct-related artery to either PCI or medical treatment. PCI was not associated with a reduction in clinical events compared to conservative therapy (25). However, OAT is hardly comparable to the present trial as it differs in several key aspects. First, OAT enrolled patients presenting between 3 and 28 calendar days after symptom onset with only few patients enrolled in the very early period (26). In contrast, we randomized patients as soon as 12 and no later than 48 hours after symptom onset. Second, OAT enrolled stable patients without signs of ongoing ischemia upon presentation whereas in the current trial over 50% of patients had persistent ischemic symptoms. Third, OAT enrolled only patients with complete occlusion of the infarct-related artery while this was not a prerequisite in our trial.

### *Limitations*

While a total of 132 patients were to be analyzed according to the a priori sample size calculation, only 111 patients finally entered the primary endpoint analysis. The study did thereby not reach the planned statistical power of 90%. Second, the significantly lower percentage of predilation in patients assigned to thrombus aspiration might have introduced a certain degree of bias. Upfront thrombus aspiration may have more frequently led to decreased local thrombus burden and adequate visualization of the culprit site to perform direct stenting. Although evidence is limited, direct stenting in suitable lesions may result in a reduction of microvascular injury (27). The trial did not study the effect of thrombectomy as bailout therapy. Large residual thrombus, slow or absent flow after unsuccessful conventional PCI should thus be considered a differing clinical scenario. Interventionalists were not blinded to treatment



allocation. However, the potential for significant bias is limited since all endpoint analyses were performed by fully blinded investigators.

### **Conclusions**

In patients with subacute STEMI presenting between 12 and 48 hours after symptom onset, routine manual thrombus aspiration before PCI failed to show a significant reduction in the primary endpoint of MVO assessed by CMR, as compared to conventional PCI alone. These findings are supported by a lack of benefit in angiographic, enzymatic, and clinical secondary endpoints.

## **PERSPECTIVES**

### **What is Known?**

Patients with STEMI presenting within 12 hours after symptom onset do not benefit from routine manual thrombus aspiration in the infarct-related artery. It is unclear whether thrombectomy may be a treatment option in late presenting patients between 12 and 48 hours who often display particularly high thrombus burden.

### **What is New?**

Patients with STEMI presenting late after symptom onset do not benefit from routine manual aspiration thrombectomy prior to PCI.

### **What is Next?**

Treatment modalities other than routine thrombus aspiration are needed to further reduce microvascular injury in patients with STEMI.

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**FIGURE LEGEND****Figure 1*****Cardiac magnetic resonance imaging analysis***

Patient with subacute STEMI presenting 21 hours after symptom onset.

(A) Proximal occlusion of left anterior descending artery.

(B) Contrast-enhanced CMR showing transmural anteroseptal necrosis with a marked core of MVO.

(C) Computer-aided signal intensity analysis of MVO and infarct size. The yellow overlay (infarct size) indicates a signal intensity of >5 standard deviations compared to remote, healthy myocardium. The orange overlay within the infarct indicates the computer detected zone of MVO.

(STEMI=ST-elevation myocardial infarction; CMR=cardiac magnetic resonance imaging; MVO=microvascular obstruction)

**Figure 2*****Study flow***

Study flow chart showing the number of randomized patients and patients with primary endpoint assessment.

(STEMI=ST-elevation myocardial infarction; PCI=percutaneous coronary intervention; CMR=cardiac magnetic resonance imaging)

\*Of the 69 patients who received the allocated treatment, 18 did not undergo CMR.

**Figure 3*****Extent of microvascular obstruction with and without thrombus aspiration***

Shown is the mean extent of MVO between patients assigned to PCI with and without thrombus aspiration.

Error bars display 95% confidence intervals.

(%LV=percentage of left ventricular mass; PCI=percutaneous coronary intervention; MVO=microvascular obstruction)

**Figure 4*****Subgroup analysis for the primary endpoint extent of microvascular obstruction***

Mean difference and 95% confidence intervals in the primary endpoint of MVO between the standard PCI group and the thrombectomy group for predefined subgroups.

(MVO=microvascular obstruction; TIMI=Thrombolysis in Myocardial Infarction; PCI=percutaneous coronary intervention; GP=glycoprotein)

**Figure 5*****Cardiac magnetic resonance imaging parameters according to time from symptom onset to reperfusion***

Shown is the mean extent of MSI, infarct size, and MVO according to the time from symptom onset to reperfusion (12-24 hours, >24-36 hours, and >36-48 hours).

Error bars display 95% confidence intervals.

(CMR=cardiac magnetic resonance imaging; MSI=myocardial salvage index; MVO=microvascular obstruction; %LV=percentage of left ventricular mass)

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**Table 1** Baseline and procedural characteristics

Variable	Thrombus aspiration (n=70)	Standard PCI only (n=74)
Age (years)	66±12	66±15
Male	48/70 (69)	59/74 (80)
Hypertension	55/70 (79)	48/74 (65)
Current smoking	25/70 (36)	31/72 (43)
Hyperlipoproteinemia	11/70 (16)	17/74 (23)
Diabetes mellitus	22/70 (31)	25/74 (34)
Cardiogenic shock	2/70 (3)	4/74 (5)
Prior myocardial infarction	2/70 (3)	4/74 (5)
Prior coronary artery bypass surgery	2/70 (3)	0
Body mass index (kg/m <sup>2</sup> )	28.9±3.8	28.6±4.7
Glomerular filtration rate (ml/min/1.73 m <sup>2</sup> )	86±27	79±26
Ongoing signs of ischemia on admission	28/57 (49)	34/62 (55)
Door-to-balloon-time (min)	78±150	62±105
Symptom-onset-to-balloon-time (hours)	26±13	29±12
Infarct-related artery		
Left anterior descending	38/70 (54)	32/72 (44)
Left circumflex	11/70 (16)	9/72 (13)
Right coronary	21/70 (30)	31/72 (43)
TIMI flow before PCI		
0	44/70 (63)	46/74 (62)
1	3/70 (4)	2/74 (3)
2	14/70 (20)	13/74 (18)
3	9/70 (13)	12/74 (18)
TIMI thrombus grade before wire crossing		
0: No thrombus	5/70 (7)	12/74 (16)
1: Possible thrombus	1/70 (1)	1/74 (1)
2: Definite thrombus, <0.5 x vessel diameter	2/70 (3)	0/74
3: Definite thrombus, 0.5-2 x vessel diameter	8/70 (11)	4/74 (5)
4: Definite thrombus, >2 x vessel diameter	9/70 (13)	11/74 (15)
5: Total occlusion	44/70 (63)	46/74 (62)
Killip class at presentation		
1	63/70 (90)	64/74 (87)
2	5/70 (7)	9/74 (12)
3	2/70 (3)	1/74 (1)
4	0/70 (0)	0/74 (0)
Myocardial blush grade before PCI		
0		

1	52/70 (74)	
2	5/70 (7)	53/74 (72)
3	4/70 (6)	4/74 (5)
	9/70 (13)	6/74 (8)
Multivessel disease		11/74 (15)
Predilation*	38/70 (54)	
Postdilation	27/70 (39)	44/74 (60)
Visible thrombus in aspirate†	7/69 (10)	54/72 (75)
Drug-eluting stent	31/51 (61)	14/72 (19)
Number of stents	50/69 (73)	2/3 (67)
	1.6±0.9	44/72 (61)
Chronic medication prior to hospital admission		1.8±1.2
Aspirin		
Thienopyridine	61/70 (87)	
Statin	36/70 (51)	55/74 (74)
Beta blocker‡	11/70 (16)	33/74 (45)
ACE inhibitor/angiotensin receptor antagonist	38/70 (54)	15/74 (20)
Oral anticoagulant	36/70 (51)	27/74 (37)
	2/70 (3)	37/74 (50)
		4/74 (5)

Categorical data are presented as frequencies (percentages), continuous data as means ± standard deviation. \*estimated according to MDRD (modification of diet in renal disease) formula.

PCI=percutaneous coronary intervention; TIMI=Thrombolysis in Myocardial Infarction;

ACE=angiotensin converting enzyme.

\*p-value <0.001

†Three patients randomized to PCI alone underwent bailout thrombus aspiration (cross-over).

‡p-value 0.04

**Table 2** Results of cardiac magnetic resonance imaging

Variable	Thrombus aspiration (n=56)	Standard PCI only (n=55)	<i>p</i>
Time from PCI to CMR (days)	2.2±1.5	2.4±2.4	0.66
LV mass (grams)	147±45	140±36	0.36
Microvascular obstruction (grams)	4.2±7.8	4.7±7.5	0.77
Microvascular obstruction (%LV)	2.5±4.0	3.1±4.4	0.47
Infarct size (grams)	44.0±28.0	38.6±26.8	0.32
Infarct size (%LV)	29.5±16.6	27.2±16.7	0.49
Area at risk (grams)	57.0±28.6	49.6±23.9	0.17
Area at risk (%LV)	38.9±16.1	37.1±16.3	0.59
Myocardial salvage (grams)	12.5±8.5	11.8±12.7	0.77
Myocardial salvage index (%area at risk)	26.2±21.2	28.8±30.8	0.63
LV ejection fraction (%)	160±52	157±42	0.77
LV enddiastolic volume (mL)	88±38	89±34	0.89
LV endsystolic volume (mL)			

Data are presented as means ± standard deviation.

(PCI=percutaneous coronary intervention; CMR=cardiac magnetic resonance imaging; LV=left ventricular; %LV=percentage of left ventricular mass)

**Table 3** Clinical events at 30 days

<b>Variable</b>	<b>Thrombus aspiration (n=70)</b>	<b>Standard PCI only (n=74)</b>	<b><i>P</i></b>
All-cause death	2 (3)	4 (5)	0.68
Cardiovascular death	2 (3)	3 (4)	1.0
Reinfarction	0	0	-
Target vessel revascularization	2 (3)	0	0.24
Target lesion revascularization	2 (3)	0	0.24
Stent thrombosis	0	0	-
Stroke	0	1 (1)	0.24

Data are presented as frequencies (percentages).  
(PCI=percutaneous coronary intervention)











