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A Prospective Randomized Trial of Thrombectomy Versus No Thrombectomy in Patients With ST-Segment Elevation Myocardial Infarction and Thrombus-Rich Lesions

MUSTELA (MUltidevice Thrombectomy in Acute ST-Segment ELevation Acute Myocardial Infarction) Trial

Marco De Carlo, MD, PHD,* Giovanni D. Aquaro, MD,† Cataldo Palmieri, MD,‡ Elena Guerra, MD,* Leonardo Misuraca, MD,* Cristina Giannini, MD, PHD,* Massimo Lombardi, MD,† Sergio Berti, MD,‡ A. Sonia Petronio, MD*

Pisa and Massa, Italy

Objectives The aim of this study was to evaluate whether thrombectomy during primary percutaneous coronary intervention (pPCI) in patients with high thrombus burden improves myocardial reperfusion and reduces infarct size.

Background Thrombectomy aims at reducing distal thrombotic embolization during pPCI, improving myocardial reperfusion and clinical outcome.

Methods We randomized 208 patients with high thrombus burden in a 1:1 ratio to either pPCI with thrombectomy (Group T) or standard pPCI (Group S). Thrombectomy was performed with either rheolytic or manual aspiration catheters. Three-month magnetic resonance imaging was performed to assess infarct size and transmurality and microvascular obstruction (MVO). The primary endpoints were ST-segment elevation resolution (STR) >70% at 60 min and 3-month infarct size.

Results The baseline profile was similar between groups, except for a higher rate of initial Thrombolysis In Myocardial Infarction flow grade 3 in Group S ($p = 0.002$). Group T showed a significantly higher rate of STR (57.4% vs. 37.3%; $p = 0.004$) and of final myocardial blush 3 (68.3% vs. 52.9%; $p = 0.03$). Group T and Group S did not differ with regard to infarct size (20.4 ± 10.5% vs. 19.3 ± 10.6%; $p = 0.54$) and transmurality (11.9 ± 12.0% vs. 11.6 ± 12.7%; $p = 0.92$), but Group T showed significantly less MVO (11.4% vs. 26.7%; $p = 0.02$) and a higher prevalence of inhomogeneous scar ($p < 0.0001$). One-year freedom from major adverse cardiac events was similar between groups.

Conclusions Thrombectomy as an adjunct to pPCI in patients with high thrombus load yielded better post-procedural STR and reduced MVO at 3 months but was not associated with a reduction in infarct size and transmurality. Thromboaspiration in Patients With High Thrombotic Burden Undergoing Primary Percutaneous (Coronary Intervention; NCT01472718) (J Am Coll Cardiol Intv 2012;5: 1223–30) © 2012 by the American College of Cardiology Foundation

From the *Cardiac Catheterization Laboratory, Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; †Institute of Clinical Physiology C.N.R./G. Monasterio Foundation, Pisa, Italy; and the ‡Institute of Clinical Physiology C.N.R./G. Monasterio Foundation, Massa, Italy. Dr. Petronio has served as a clinical proctor for Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Primary percutaneous coronary intervention (pPCI) is highly effective in restoring a normal Thrombolysis In Myocardial Infarction (TIMI) flow in patients with ST-segment elevation acute myocardial infarction (STEMI), but a relevant proportion of patients shows a poor myocardial reperfusion, which strongly correlates with larger infarct size and worse clinical outcome (1). Thrombectomy devices aim at improving myocardial reperfusion by preventing distal thrombus embolization during pPCI. After controversial results of the initial studies, 2 recent randomized single-center studies (2,3) demonstrated a significant benefit of thrombus aspiration on clinical outcome although not on infarct size. Currently, magnetic resonance imaging (MRI) with late gadolinium enhancement (LGE) is the best method to assess infarct size (4) but was used only in a substudy of a single-center randomized trial on thrombectomy (5). Moreover, all thrombectomy studies until now included patients with variable degrees of thrombus load, leaving open the question of whether the benefits of routine thrombus aspiration could be obtained also with a strategy of selective thrombectomy in patients with large thrombus burden.

Our aim was to assess the impact of thrombectomy, either manual or rheolytic, on myocardial reperfusion and infarct size in patients with high thrombotic burden.

Abbreviations and Acronyms

cTFC = corrected TIMI frame count

LGE = late gadolinium enhancement

LV = left ventricular

MACE = major adverse cardiac events

MBG = myocardial blush grade

MRI = magnetic resonance imaging

MT = manual thrombectomy

MVO = microvascular obstructionp

pPCI = primary percutaneous coronary intervention

RT = rheolytic thrombectomy

STEMI = ST-segment elevation myocardial infarction

STR = ST-segment elevation resolution

TIMI = Thrombolysis In Myocardial Infarction

Methods

Study design and patients. The MUSTELA (MUltidevice thrombectomy in acute ST ELevation Acute myocardial infarction) trial was a multicenter prospective randomized study that assigned patients in a 1:1 ratio to either thrombectomy as an adjunct to pPCI (Group T) or standard pPCI without thrombectomy (Group S). Inclusion criteria were age ≥18 years; STEMI (new ST-segment elevation of >1 mm in at least 2 contiguous leads or new left bundle branch block) within 12 h of symptom onset; TIMI thrombus grade >3 after reclassification of initial grade 5 after coronary recanalization with a guidewire or small balloon according to Sianos et al. (6); and reference diameter of the infarct-related artery ≥3.0 mm at visual estimate. Exclusion criteria were previous infarct in the same ventricular wall; cardiogenic shock; severe liver/renal failure; contraindications to abciximab; and contraindications to MRI. Patients showing a TIMI thrombus grade >3 at diagnostic angiography underwent stratification for infarct location on the anterior versus non-anterior left ventricular (LV) wall and were randomized on the basis of computer-generated random sequence through a dedicated website.

The study was approved by the local Ethics Committee, and written informed consent was obtained from all patients before diagnostic angiography (clinical trial unique identifier: NCT01472718; see note after abstract).

PCI procedure. The PCI was performed with standard technique, with the radial approach as first choice. Thrombectomy was performed with either the manual aspiration Export catheter (Medtronic CardioVascular, Santa Rosa, California) or the RT AngioJet Ultra catheter (Possis Medical, Inc., Minneapolis, Minnesota) in a sequential alternating fashion. The thrombectomy catheter was activated just proximal to the culprit lesion and was slowly pushed across the lesion for at least 2 passages; additional passages were performed until no further reduction in thrombus load could be obtained. Pre-dilation with small balloons was performed only if the thrombectomy catheter failed to cross the lesion. Direct stenting was recommended, whereas choice of coronary stents was left at the discretion of the physician. Use of embolic protection devices was not allowed.

All patients received IV aspirin 250 mg and clopidogrel 600 mg oral load at time of STEMI diagnosis. In the catheterization laboratory, IV boluses of unfractionated heparin (60 U/kg body weight) and abciximab (0.25 mg/kg) were administered, followed by a12-h abciximab infusion at 0.125 μg/kg/min. The activated clotting time was kept in the 200- to 250-s range during pPCI.

Angiographic and electrocardiographic analysis. All angiograms were analyzed by 2 experienced investigators in our core laboratory in Pisa University Hospital. We assessed the initial and post-procedural TIMI flow grade, corrected TIMI frame count (cTFC), and myocardial blush grade (MBG) (7–8). Thrombotic burden was graded according to the TIMI thrombus classification modified according to Sianos et al. (6). Complete thrombus removal by thrombectomy was defined by a reduction in thrombus grade from grade 4 to grade 0 to 1. Procedural success was defined as a final TIMI flow grade 3 with a residual stenosis ≤20%.

The ST-segment elevation was measured 40 ms after the J point, and the sum of ST-segment deviations was determined on a 12-lead electrocardiogram before and 60 min after intervention. The ST-segment elevation resolution (STR) was categorized as complete (>70%), partial (30% to 70%), or absent (<30%) (9).

MRI protocol. Three months after PCI, MRI was performed with a 1.5-T scanner with an 8-element cardiac phased array receiver surface coil (CVi, HD release; GE Healthcare, Milwaukee, Wisconsin). Left ventricular functional parameters were obtained from short-axis cine images from mitral valve plane to the apex, with a steady-state free

precession pulse sequence. Rest myocardial perfusion images were acquired during 30 to 40 consecutive heartbeats, immediately after administration of a 0.1-mmol/kg bolus of Magnevist (Schering, Berlin, Germany); a CASH2 (Calibration Slice using Hybrid Acquisition) pulse sequence was used, and 3 short-axis planes (at basal, mid, and apical level) were acquired. An additional bolus of 0.1 mmol/kg of Magnevist was injected immediately after the acquisition of perfusion images. Early enhancement images were acquired in the same short- and long-axis slices used for cine-MRI, with a fast Gradient Echo Inversion Recovery sequence.

Late-enhancement images were obtained 10 min after the injection of contrast medium in the same acquisition planes. The inversion recovery time was optimized to nullify the signal from normal myocardium.

All MRIs were performed and analyzed in Pisa by 2 expert cardiologists blinded to the randomization status of the patient. We used a previously validated software to measure LV volumes and mass (Mass, MEDIS, Leiden, the Netherlands). To assess infarct size, in all short-axis images the myocardial contours and LGE boundaries were traced manually; when islands of viable myocardium were identified within the scar (see following), the extent of LGE was corrected by subtracting their area, measured with a semiautomatic, previously validated software (10) (Fig. 1). We expressed infarct size as percentage of LV mass.

To measure infarct transmurality, we divided the myocardium according to the standard 17-segment model. Each segment was then divided into 100 chordae, perpendicularly directed from the endocardial to the epicardial border; LGE was calculated automatically in each chorda and defined as transmural when it spanned ≥75% of myocardial thickness.

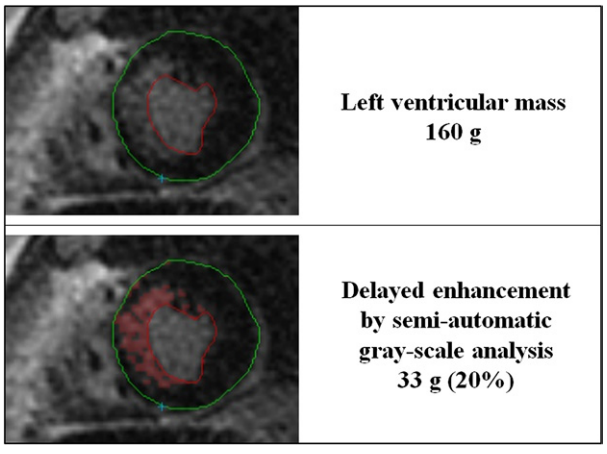

Figure 1. Infarct Size Measurement With Late Gadolinium-Enhancement Magnetic Resonance

(Top) Measurement of left ventricular mass by manual tracing. **(Bottom)** Semiautomatic gray-scale analysis of the transmural scar (**red** area within the interventricular septum).

Those segments with transmural LGE in most of their chordae were considered to have transmural LGE. The LGE extension and transmurality in the apical cap was calculated from long-axis images. Finally, transmurality was calculated as the percentage of segments with transmural LGE.

Microvascular obstruction (MVO) was defined as the presence of hypo-intense areas within the infarct core scar characterized by enhanced myocardium in LGE images. The presence of scar inhomogeneity in segments without MVO was assessed with a semiautomatic detection algorithm previously described (10). Briefly, we considered areas of unenhanced myocardium, defined with a signal-intensity threshold of <6 SD above mean reference signal intensity, inside the scar as islands of viable myocardium (Fig. 2). Infarct inhomogeneity was defined by the presence of islands of viable myocardium covering >5% of myocardial scar. Interobserver and intraobserver coefficients of variation, assessed in 25 consecutive patients, were 3% and 2% for both infarct size and MVO, respectively.

Follow-up. Follow-up visits were scheduled at 1, 6, and 12 months after pPCI. We assessed the 1-year rate of major adverse cardiac events (MACE), defined as a composite of death, reinfarction, and target vessel revascularization.

Study endpoints. The primary endpoints were: 1) the rate of complete STR at 60 min after pPCI, and 2) infarct size at 3 months.

The secondary endpoints were: 1) post-procedural TIMI flow grade; 2) post-procedural MBG; 3) infarct transmurality at 3 months; 4) MVO at 3 months; and 5) 1-year actuarial freedom from MACE.

Statistical analysis. Continuous variables are presented as mean ± SD or as median (interquartile range) and were compared with 2-tailed Student *t* test or Mann–Whitney test, as appropriate. Categorical variables were compared by $\chi 2$ or Fisher exact test, as appropriate. The cumulative incidences of MACE at follow-up were assessed with the Kaplan–Meier method, and the log-rank test was used for comparison between groups. The analysis was performed on the basis of the intention-to-treat. All probability values reported are 2-sided, and a probability value <0.05 was considered significant. To adjust for baseline TIMI flow grade 3, we performed a post hoc analysis of covariance on infarct size by randomization status, with baseline TIMI flow grade 3 as covariate.

Sample size calculation with regard to the first primary endpoint was based on an expected prevalence of complete STR of 58% in the thrombectomy group and of 37% in the control group (11); thus 85 patients were required in each group to detect such difference with a power of 80% and a 2-sided alpha value of 0.05. Concerning the second primary endpoint, we expected an infarct size of 15 ± 9% in the standard pPCI group (12) and an infarct size of 11 ± 9% in the thrombectomy group, assuming an infarct size reduction of 20%. Consequently, a sample size of 80 patients/group was required to detect the difference with a power of 80%

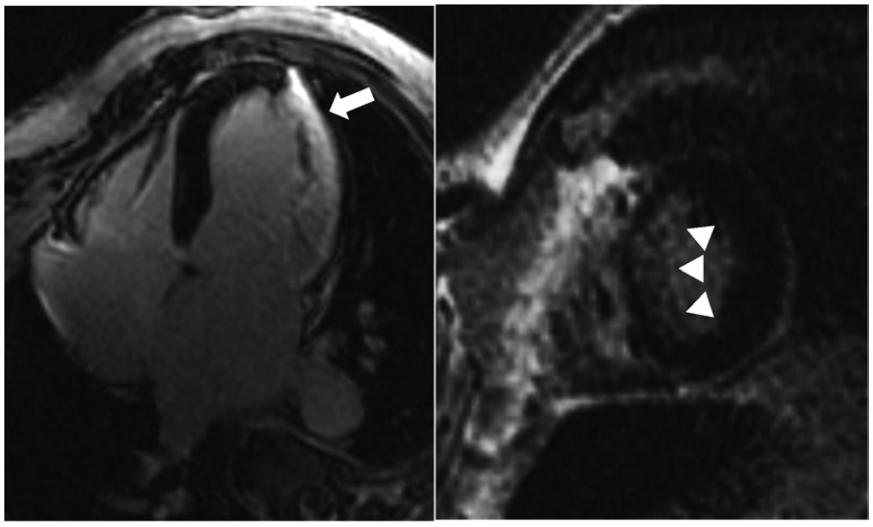

Figure 2. Scar Homogeneity Assessment With Late Gadolinium-Enhancement Magnetic Resonance

(Left) Large posterolateral transmural infarction containing only scar tissue ("homogeneous scar"; **arrow**). **(Right)** Septal transmural infarction with interspersed areas of viable myocytes within the scar ("inhomogeneous scar"; **arrowheads**).

and a 2-sided alpha value of 0.05. Assuming a 10% attrition rate for MRI, we scheduled to enroll 88 patients/group. All data were processed with the Statistical Package for Social Sciences (version 15; SPSS, Chicago, Illinois).

Results

Study population. We randomized 208 patients to either thrombectomy (n = 104) or standard pPCI (n = 104). The flow of participants through the study is represented in Figure 3. Baseline clinical characteristics were similar between groups (Table 1). Importantly, the rate of anterior wall STEMI was balanced, because of stratification before randomization, and also the rate of 3-vessel disease, the angiographic area at risk, and the LV ejection fraction were similar between groups. A trend to a shorter pain-to-balloon time in Group S was observed (p = 0.07). Of note, baseline TIMI flow grade 3 was significantly more frequent in Group S (16.3% vs. 3.8%, p = 0.002), with a lower cTFC (p = 0.005).

Procedural results. The radial approach was used in 95.2% of patients. Fifty-four patients (51.9%) in Group T underwent rheolytic thrombectomy (RT), and 50 (48.1%) underwent manual thrombectomy (MT). Balloon pre-dilation of the culprit lesion was necessary to allow lesion crossing with the thrombectomy catheter in only 4 patients (3.8%), 2/group. The thrombectomy catheter could not be delivered to the culprit lesion because of vessel tortuosity only in 1 MT patient, who was then successfully treated with RT. No thrombectomy catheter-associated complications were observed; in particular, there was no need for temporary pacing with RT. Among patients undergoing MT, atherothrombotic material was retrieved in 41 (82.0%).

The use of thrombectomy allowed a significantly higher rate of direct stenting in Group T (74.8% vs. 47.6%; p < 0.0001), with no difference in stent number and length. Group T showed a significantly higher rate of final MBG 3 (68.3% vs. 52.9%; p = 0.03), a lower rate of final TIMI flow grade 2 (6.7% vs. 15.4%; p = 0.04), and a trend to a higher rate of final TIMI flow grade 3 (90.4% vs. 81.7%; p = 0.07) (Table 2). Final cTFC was similar between groups but improved more in Group T with respect to baseline (p = 0.006).

The primary endpoint of complete STR was reached in a significantly higher proportion of patients in Group T (57.4% vs. 37.3%; p = 0.004).

MRI results. Seventy-nine patients (76.0%) of Group T and 75 (72.1%) of Group S underwent 3-month MRI; the most common reasons for missing MRI analysis were withdrawal of consent and death before 3 months (Fig. 3). Infarct size was similar between groups (20.4 ± 10.5% vs. 19.3 ± 10.6%, Group T vs. Group S, respectively; p = 0.54) as well as transmurality (11.9 ± 12.0% vs. 11.6 ± 12.7%; p = 0.92) (Fig. 4, Table 3). However, a lower prevalence of MVO was found in Group T (11.4% vs. 26.7%; p = 0.02), together with a higher rate of inhomogeneous myocardial scar (35.4% vs. 2.7%; p < 0.0001). Left ventricular ejection fraction, end-diastolic volume, and stroke volume were similar between groups.

In the present study, a higher baseline TIMI flow was associated with a smaller infarct size (p = 0.03); this fact could have favored Group S patients, who showed a significantly

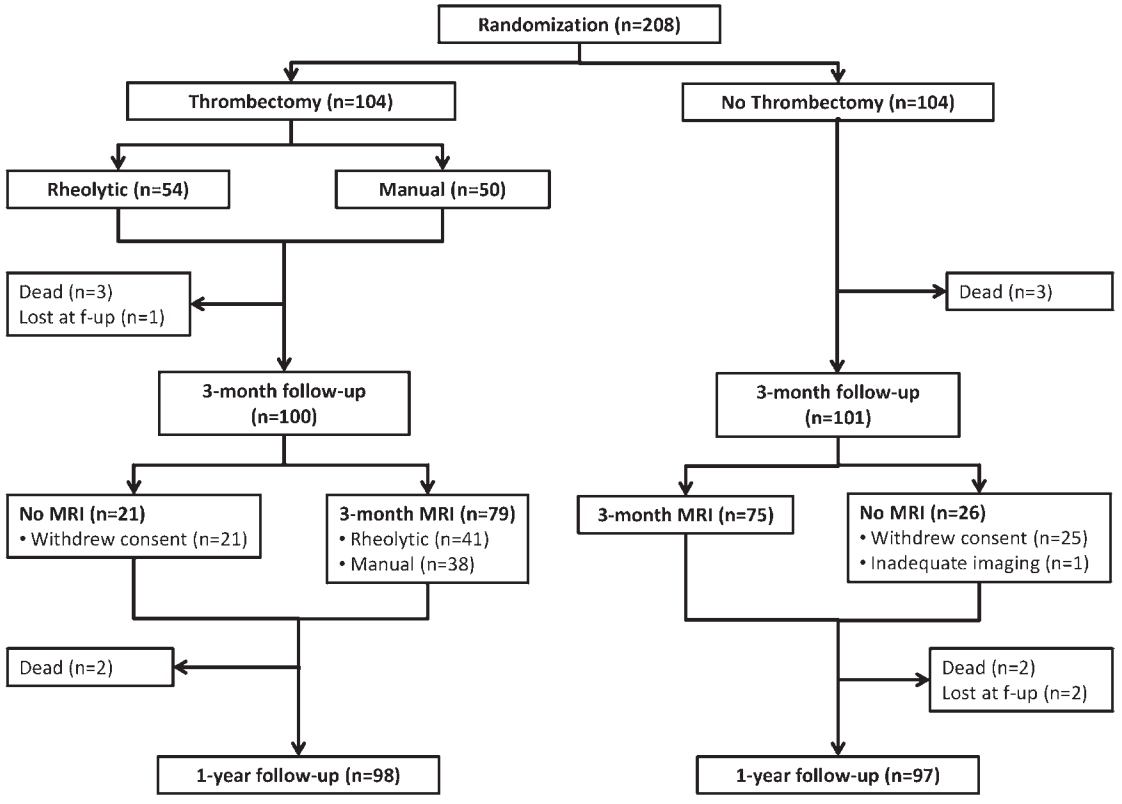

Figure 3. Study Design

MRI = magnetic resonance imaging.

higher baseline TIMI flow, masking a potentially significant reduction in infarct size with thrombectomy. However, after adjustment for baseline TIMI flow by means of analysis of covariance, the esteemed infarct size was still similar between groups (20.3% vs. 19.7%, Group T vs. Group S; p = 0.88).

MT versus RT. The rate of complete thrombus aspiration was higher with RT versus MT (94.4% vs. 78.0%; p = 0.02). No statistically significant differences were observed between the 2 devices with regard to the primary and secondary study endpoints; however, a trend toward a smaller infarct size was observed in the 41 patients treated with RT who underwent 3-month LGE-MRI versus the 38 treated with MT (17.5 ± 9.6% vs. 21.3 ± 11.3%; p = 0.10).

One-year outcome. One-year follow-up was 98.6% complete, with only 1 patient of Group T and 2 of Group S being lost. Ninety-eight patients of Group T and 97 of Group S reached the 1-year follow-up. In Group T, 5 patients died because of cardiac causes, 2 suffered reinfarction (treated with PCI in 1 case), and 1 underwent target vessel revascularization. In Group S, 4 patients died because of cardiac causes, 1 died because of hepatic cancer, 2 suffered reinfarction (treated with PCI in both cases), and 1 underwent target vessel revascularization. The actuarial freedom from MACE was 91.4 ± 2.8% in Group T versus 90.2 ± 2.9% in Group S (p = 0.97) (Fig. 5).

Discussion

The present study is the first to assess the impact of thrombus aspiration on infarct size assessed with MRI in a large cohort of patients with high thrombotic burden. Although such patients are the best candidates to benefit most from thrombectomy, we did not observe a significant advantage of thrombus aspiration over standard pPCI in terms of infarct size and transmurality at 3-month follow-up. However, thrombectomy was associated with better myocardial reperfusion in terms of STR, MBG, and MVO.

Thrombectomy during pPCI. Distal thrombotic embolization, occurring in approximately 15% of patients undergoing pPCI (13), is 1 of the mechanisms leading to unsuccessful myocardial reperfusion after pPCI, and numerous types of thrombectomy devices have been developed to prevent it. Initial single-center studies reported positive results with thrombectomy devices when "soft" endpoints, such as post-PCI TIMI flow, MBG, or STR were used (11,14,15). However, the first multicenter randomized studies failed to

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Table 1. Baseline Characteristics

	Thrombectomy (n = 104)	Standard (n = 104)	p Value
Age, yrs	62.4 (54.4–69.6)	63.0 (52.9–71.4)	0.72
Male sex	88 (88.4)	79 (76)	0.83
Diabetes	20 (19.2)	21 (20.4)	0.83
Hypertension	54 (51.9)	49 (47.6)	0.53
Dyslipidemia	54 (51.9)	45 (43.7)	0.23
Current smoker	50 (48.1)	51 (49.5)	0.81
Chronic renal failure	3 (2.9)	5 (4.9)	0.46
Pain-to-balloon-time, min	230 (134–294)	208 (148–271)	0.07
Maximum ST-segment elevation, mm	4 (3–5)	4 (3–5)	0.25
Total ST-segment elevation, mm	12 (8–15)	10 (7–15)	0.21
Anterior myocardial infarction	49 (47.1)	48 (46.2)	0.89
3-vessel disease	14 (13.5)	9 (8.7)	0.27
Killip class 3	4 (3.8)	9 (8.7)	0.10
Left ventricular ejection fraction, %	46 ± 8	46 ± 10	0.92
Initial TIMI flow: 0–1	95 (91.3)	81 (77.9)	0.007
2	5 (4.8)	6 (5.8)	0.70
3	4 (3.8)	17 (16.3)	0.002
Initial cTFC	95 ± 17	86 ± 28	0.005

Values are n (%), median (interquartile range), or mean ± SD.
cTFC = corrected TIMI frame count; TIMI = Thrombolysis In Myocardial Infarction.

demonstrate positive outcomes in terms of "hard" clinical endpoints and also with regard to infarct size (12,16,17). More recently, the single-center TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study) (2) and JETSTENT (AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting in Patients Undergoing Primary PCI for Acute Myocardial Infarction) (3) randomized studies demonstrated a significant benefit of aspiration thrombectomy on

Table 2. Procedural Results

	Thrombectomy (n = 104)	Standard (n = 104)	p Value
Direct stenting	77 (74.8)	49 (47.6)	<0.0001
Total stent length, mm	19 (16–24)	20 (16–24)	0.95
Stent/patient	1.22 ± 0.50	1.17 ± 0.38	0.76
Final TIMI flow: 0–1	3 (2.9)	3 (2.9)	0.68
2	7 (6.7)	16 (15.4)	0.04
3	94 (90.4)	85 (81.7)	0.07
Final cTFC	18 (12–29)	21 (14–33)	0.22
cTFC reduction from baseline	80 (65–87)	71 (34–83)	0.006
Final MBG: 0–1	11 (10.6)	16 (15.4)	0.41
2	22 (13.5)	33 (31.7)	0.12
3	71 (68.3)	55 (52.9)	0.03
Procedural success*	94 (90.4)	85 (81.7)	0.07
ST-segment resolution >70%	58 (57.4)	38 (37.3)	0.004

Values are n (%) or median (interquartile range). *Residual stenosis <30% and TIMI flow grade 3.
cTFC = corrected TIMI frame count; MBG = myocardial blush grade; TIMI = Thrombolysis In Myocardial Infarction.

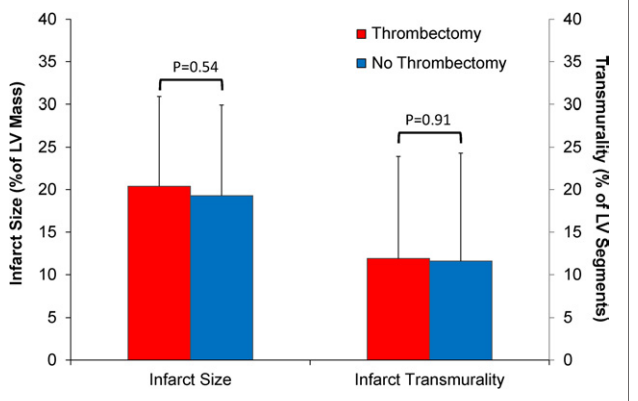

Figure 4. Infarct Size and Transmurality

Infarct size and transmurality at 3 months, Thrombectomy **(red bars)** versus No Thrombectomy **(blue bars)**. LV = left ventricular.

clinical outcomes, although no significant reduction in infarct size was demonstrated. Based mainly on the TAPAS trial, MT is currently recommended in all patients undergoing pPCI (18), although it is reasonable to assume that thrombus aspiration can be useful mainly in patients with large thrombus burden, which is an independent predictor of distal embolization during pPCI (13).

The correct assessment of infarct size in trials investigating thrombectomy during pPCI is of paramount importance, because the mechanism leading to a reduced mortality presumably should be a favorable effect on infarct size (4). Interestingly, all randomized trials failed to demonstrate a significant reduction in infarct size with thrombectomy, whatever the technique used for its assessment (2,3,5,12,16,17). Currently, LGE-MRI is the best technique for the assessment of infarct size and also allows measurement of transmurality and MVO (4,19,20). The only randomized study on thrombectomy that used LGE for infarct size was the single-center EXPIRA (thrombectomy with export catheter in infarct-related artery during primary percutaneous coronary intervention) trial (5), where

Table 3. MRI Results

	Thrombectomy (n = 79)	Standard (n = 75)	p Value
Infarct size, % of LV mass	20.4 ± 10.5	19.3 ± 10.6	0.54
Transmural infarct, % of LV segments	11.9 ± 12.0	11.6 ± 12.7	0.92
Microvascular obstruction, n	9 (11.4)	20 (26.7)	0.02
Inhomogeneous scar, n	28 (35.4)	2 (2.7)	<0.0001
LV ejection fraction, %	56 ± 12	59 ± 11	0.10
LV end-diastolic volume, ml/m^2	82 ± 24	79 ± 20	0.47
LV stroke volume, ml/m^2	45 ± 11	45 ± 12	0.75

Values are n (%) or mean ± SD.
LV = left ventricular; MRI = magnetic resonance imaging.

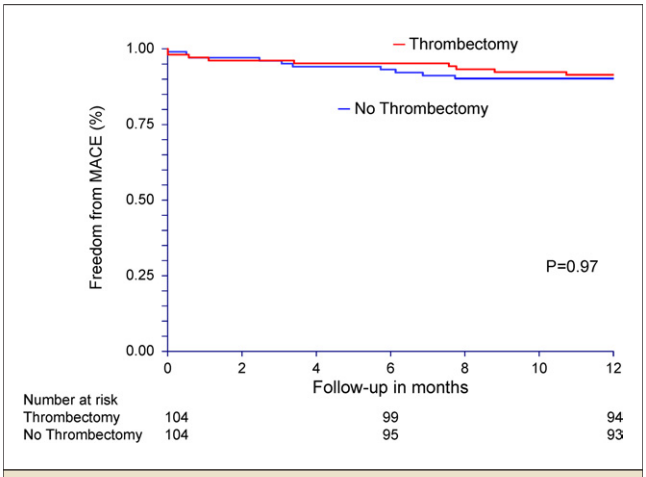

Figure 5. Freedom From MACE

Kaplan-Meier estimates of 1-year freedom from major adverse cardiac events (MACE). **Red line** indicates Thrombectomy group; **blue line** indicates No Thrombectomy group.

a subgroup a 72 patients underwent MRI at 3 days and 3 months after pPCI.

Procedural results. Compared with standard pPCI, adjunctive thrombectomy was associated with a significant reduction in the rate of final TIMI flow grade 2 ($p = 0.04$) and with a higher improvement in cTFC with respect to baseline ($p = 0.006$), possibly reflecting a better myocardial reperfusion. Moreover, by clearing up the culprit lesion, thrombectomy allowed a higher rate of direct stenting ($p < 0.0001$), although we did not confirm the slight reduction in the number of stents/patient previously reported (3).

Myocardial reperfusion. Our study showed a clear advantage of thrombectomy on surrogate markers of reperfusion at tissue level, with a complete STR of 57.4% of Group T patients versus 37.3% of Group S ($p = 0.004$), in agreement with previous studies reporting complete STR between 56.6% and 67.6% (5,14,21). Final MBG 3 was also significantly improved in Group T ($p = 0.03$), with a 68% rate falling within the wide range of 46% to 88% previously described (3,5,14,21). The range of MBG 3 rates reported in thrombectomy trials underlines the high interobserver variability of this method.

LGE-MRI. Our trial was designed to maximize the potential benefits of thrombectomy on infarct size, overcoming some limitations of previous trials. To this aim, we enrolled only patients with a high thrombus load, stratified patients according to infarct location, used a uniform antiplatelet regime and procedural technique, and assessed infarct size with LGE. Moreover, we assessed infarct size at 3 months after pPCI, when myocardial edema has resolved, whereas previous studies measured LGE at 2 to 5 days, when myocardial edema is relevant and might be misjudged as necrotic myocardium (5). However, infarct size and transmurality in our trial were similar between groups. Although all previous randomized trials on thrombectomy failed to demonstrate a significant reduction in infarct size (2,3,5,12,16,17), we expected to find an advantage in high-thrombus-load patients. To explain our findings, we can advance 2 hypotheses: 1) thrombectomy gives no real reduction in infarct size when added on top of full antiplatelet therapy (clopidogrel 600 mg and abciximab bolus), even in patients with high thrombus load, at least in case of a median pain-to-balloon time over 3 h; and 2) the possible reduction in infarct size with thrombectomy was masked by the less favorable clinical profile of the thrombectomy group with regard to initial TIMI flow grade 3 ($p = 0.002$) and pain-to-balloon time ($p = 0.07$). These findings seriously question the hypothesis that the benefit of thrombectomy on clinical outcome might derive from a significant reduction in infarct size and weaken the recommendation for its routine use in pPCI.

The presence of MVO early after STEMI has been recently demonstrated to be an independent predictor of LV remodeling (19) and of adverse clinical events (20), with incremental value above traditional prognostic markers, such as STR, TIMI flow, infarct size, and transmurality. In our study, MVO occurred in a significantly lower proportion of patients in the thrombectomy group ($p = 0.02$), reflecting a less-severe microvascular injury. The absolute rates of MVO at 3 months were much lower than those reported when MRI is performed a few days after pPCI, probably because of scar shrinkage, but still unexpectedly high, reflecting a persistent microvascular derangement late after STEMI. Finally, we observed for the first time that thrombectomy was associated with scar inhomogeneity in areas without MVO ($p < 0.0001$). However, the clinical relevance of the presence of islands of viable myocytes inside necrotic areas is unknown and warrants further investigation.

Clinical outcome. The 1-year actuarial freedom from MACE was similar between groups ($p = 0.97$), at variance with the results of the TAPAS and JETSTENT trials (2,3). However, the lack of clinical benefit from thrombectomy in our trial agrees with the lack of benefit on infarct size.

MT versus RT. Our trial was not designed to compare RT versus MT, but the balanced use of the 2 devices allows exploring the potential differences between them. We describe for the first time a significantly higher rate of complete thrombus removal with RT versus MT ($p = 0.02$) as well as a trend to a smaller infarct size at 3-month LGE ($p = 0.10$). However, larger randomized studies are mandatory to verify these preliminary findings. Importantly, no thrombectomy-related complications were observed with either device, confirming the high safety profile already reported for MT (21) and RT (3).

Study limitations. Our study has some limitations. First, the trial was single-blind, with the operator knowing the randomization assignment; however, the physicians reading LGE were unaware of randomization assignment. Second, we enrolled only 65% of the screened STEMI patients, because of selection criteria. However, excluding patients

with low thrombotic burden is very unlikely to have masked the benefits of thrombectomy. Third, infarct size assessment by LGE was performed in only 159 of 208 patients (76.4%), mainly because of patient withdrawal and patient death before 3 months. Nevertheless, ours is the thrombectomy trial with the largest population of patients undergoing LGE-MRI. Fourth, we did not choose the thrombectomy device in a randomized fashion, so that inferences on the comparison between devices can only be hypothesis-generating. Finally, the imbalance in initial TIMI flow grade 3 might have disadvantaged the thrombectomy group, possibly masking a potential benefit; however, after adjustment for this imbalance, we still could not find a significant reduction in infarct size with thrombectomy.

Conclusions

Thrombectomy as an adjunct to pPCI in patients with high thrombus load was associated with better myocardial reperfusion, in terms of better TIMI flow, higher STR, and reduced MVO but was not associated with a reduction in infarct size and transmurality at 3-month MRI or with better clinical outcome at 1 year. Rheolytic thrombectomy was more effective than MT in removing thrombus and showed a nonsignificant reduction in infarct size.

Reprint requests and correspondence: Dr. Marco De Carlo, Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Pisana, Cardiac Catheterization Laboratory, Ospedale Cisanello, Via Paradisa 2, 56124 Pisa, Italy. E-mail: marcodecarlo@gmail.com.

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