Catheter Aspiration after Every Stage during Primary Percutaneous Angioplasty; ADMIT Trial

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Abstract

We assess the epicardial and microcirculation flow characteristics, and clinical outcome by using catheter aspiration after each stage of primary percutaneous coronary intervention (PPCI). Conflicting data are reported regarding early and late benefit of using aspiration catheter in the initial phase PPCI.

A total of 100 patients with ST-segment elevation acute myocardial infarction (STEMI) were included: 51 underwent PPCI without using an aspiration device (SA group) and 49 underwent PPCI by activating an aspiration catheter after each stage of procedure; wiring, ballooning and stenting, respectively (MA group). Thrombolysis in myocardial infarction (TIMI) flow grade, TIMI frame counts and myocardial blush grade (MBG) were evaluated in each group during every stage of procedure. Major adverse cardiac events were evaluated in the index hospitalization and during 30 and 180 days of follow-up. A TIMI flow grade 2–3 was more prevalent in the MA group compared with the SA group only after wiring: 65.9 versus 39.1% ($p = 0.01$), but TIMI frame counts were lower in the MA versus SA group throughout all procedural steps. MBG 2–3 was statistically higher in the MA group compared with the SA group mainly after wiring. After stenting there were no significant changes in both epicardial and microcirculation flow parameters. There were no significant differences between the groups in early and late clinical outcomes. Improved flow parameters were noticed in the MA group only by activating the aspiration device after wiring. This early advantage disappeared after stenting. The initial better flow characteristic in the MA group was not translated into a better early or late clinical outcome.

Keywords

- ▶ primary PCI
- ▶ aspiration catheter
- ▶ TIMI flow
- ▶ TIMI frame counts
- ▶ myocardial blush grade
- ▶ stenting

Primary percutaneous coronary intervention (PPCI) is considered as a class I indication for replenished epicardial coronary flow in the setup of ST-segment elevation acute myocardial infarction (STEMI).¹ After crossing the lesion with a wire either direct stenting or ballooning followed by stenting are the main procedural therapeutic steps. One of the Achilles heels of this mechanical approach is discrepancy between epicardial versus microcirculation rate of reperfusion.²

Failure to establish normal intramyocardial perfusion in acute myocardial infarction patients is still common and occurs with up to 60% of patients who are “successfully” treated by different catheter based techniques.³ This phenomenon mainly results from distal atherothrombotic embolization into the microcirculation.⁴ Microvascular obstruction is generally associated with increased infarct size, poor left ventricular (LV) recovery and increased late mortality.⁵

Recently, several studies have shown that early aspiration after initial wiring during PPCI has some advantages over the standard technique by getting improved myocardial perfusion and clinical outcome^{6,7}. However, despite performing this maneuver myocardial blush grade (MBG) < 3 and failure of early-ST-segment resolution were still found among 50% and 43% of the patients, respectively.⁸ This phenomena was attributed to the initial delivery of the aspiration device in the thrombotic milieu and/or reappearance of atherothrombotic material in the involved vascular lumen during the consecutive steps of the procedure.

Previous reports have indicated that distal embolization may occur after every stage of angioplasty procedure.⁹ Moreover, intravascular ultrasound (IVUS) studies showed that up to 25% of stenting procedures are associated with prolapsing material through the stent struts into the affected lumen.¹⁰ The success rate of aspiration in thrombotic lesions ranged between 70 and 86%.¹¹ Therefore, the aim of our study was to evaluate the hypothesis that using aspiration after every stage of PPCI compared with the standard technique improves epicardial and microcirculation flow in patients with STEMI.

Methods

End Points

The primary end point of this study was first to assess the quality of both epicardial and microcirculation perfusion during PPCI, while performing an aspiration maneuver after each stage of procedure compared with the standard technique.

Secondary end points were to find out differences in LV function, ischemic mitral regurgitation and major adverse cardiac events (death, reinfarction, target vessel revascularization [TVR]) during index hospitalization and follow-up between the aspiration and nonaspiration groups.

Study Population

The Aspiration Device Myocardial Infarction Trial (ADMIT) approved by the local Institutional Review Board (Ha'Emek Medical Center) was a single center, prospective, randomized open trial comparing the standard PPCI technique versus an approach whereby aspiration was undertaken after every stage in the infarct related artery.

All patients admitted within a time frame of 12 hours of onset of symptoms of STEMI, regardless, of the initial thrombolysis in myocardial infarction (TIMI) flow were included. Patients who were treated by intravenous (IV) lytic agents in other hospitals and referred for rescue PCI were also included. Patients with a known allergy to either aspirin or clopidogrel, or having diseases with a life expectancy of less than 6 months, or unable to sign an informed consent, or in cardiogenic shock, were excluded. The first patient was enrolled in July 2007 and the last one was enrolled in September 2008.

Randomization and Treatment Arms

Informed consent was obtained before coronary angiography. Patients were randomized either to the standard arm (SA) or the multiaspiration arm (MA) by an out of hospital blinded statistical core center using a computerized system.

The SA group was characterized by performing conventional PPCI without using any aspiration device, whereas the MA group was defined as PPCI where aspiration was undertaken after every step of the procedure by means of after wiring, ballooning, and stenting, respectively. Crossover from the SA to the MA was left to the operator's decision in the presence of procedure related complications.

Assessing Epicardial and Microcirculation Perfusion by Invasive and Noninvasive Parameters

Angiographic Assessment

Both epicardial and microcirculation perfusion were determined in each infarct related artery by using the TIMI flow grade (0–3),¹² TIMI frame counts¹³ and MBG (0–3),¹⁴ respectively. These data were recorded in every infarct related artery in each patient during every stage of the procedure. To assess whether the MA technique is a time consuming approach compared with the standard approach, every step since the initial chest pain through emergency room arrival until the end of procedure were recorded. For the purpose of time definitions, initiation of PPCI was determined, while PCI's wire crossed the lesion, and end of procedure was defined when PCI related wire was retrieved from the infarct related artery. Since January 2005, our institute adopted the policy of direct transportation of patients with STEMI to the catheterization laboratory by bypassing the emergency room.

Noninvasive Parameters

A 12-lead echocardiography (ECG) was undertaken at admission for initial diagnosis and baseline reference for ST-segment dynamics. ST-segment resolution as a marker for reperfusion was evaluated, 90 minutes and 6 hours after PPCI. The degree of ST-segment resolution was categorized as complete (> 70%), partial (30–70%), or none (< 30%) relative to the presentation record.¹⁵

Transthoracic two-dimensional (2D) was undertaken at the catheterization laboratory before PPCI, 24 hours later and during 30 and 180 days of follow-up for evaluating global LV ejection fraction (LVEF), and the presence of either old or newly appearing ischemic mitral regurgitation. LV volumes were calculated by the modified Simpson biplane method. Mitral regurgitation severity was graded as: mild, moderate, or severe based on color Doppler and vena contracta criteria.¹⁶ Serum markers CK and Troponin T level were evaluated at presentation, 6 and 24 hours post PPCI. All angiographic parameters, ECG and echocardiographic data were analyzed by an independent team who were blinded to the treatment allocation.

Preprocedure Antithrombotic Therapeutic Regimen

Based on European guidelines,¹⁷ preprocedure antithrombotic therapy included oral aspirin 300 mg as a loading dose (or only 100 mg if the patient was on aspirin therapy) continued by 100 mg/day indefinitely, 600 mg clopidogrel loading dose continued by 75 mg/day for 1 year and IV 60 mg/kg unfractionated heparin as loading dose to keep activating clotting time during procedure > 250 second. Heparin was

Fig. 1 Kaplan-Meier: 180 days survival curve of multiaspiration arm versus standard arm.

continued for 12 hours post procedure in a dose of 500 units/hour parallel to Glycoprotein IIb/IIIa inhibitors infusion.

Only after wire crossing, all patients were treated by intracoronary 200 µg nitroglycerine, 36 µg of adenosine and IV eptifibatide (Integrilin): 180 µg/kg as a bolus followed by 2 µg/kg/min for 12 hours. These dosages were adjusted to renal function. In both group β blockers, angiotensin converting enzyme (ACE) inhibitors and statins were initiated after PPCI according to the guideline recommendations.¹⁷

PPCI Technique

The PPCI procedure was undertaken by either the radial or femoral approach using 6F guiding catheter. The aspiration was undertaken by using the "Export" Medtronic aspiration device (crossing profile of 0.0068). Direct stenting after wiring was possible to perform in each arm. In the presence of severe coronary narrowing associated with aspiration catheter propagation difficulties, slight dilatation with 1.5 to 2 mm balloon was possible to perform. All procedures were terminated by coronary stenting. Type of the implanted stent, either bare metal or drug eluting, was left for the operator's to decide. Per protocol, in the presence of multivessel disease only the infarct related artery was treated.

Aspiration Failure

Failure of aspiration procedure was defined as device related dissection, slow flow or no reflow after aspiration or last recorded TIMI or MBG of 0 or 1 or ST segment resolution (STR) < 30% after 90 minutes.

Follow-Up

In hospital, 30 and 180 days clinical follow-up were undertaken for assessing New York Heart Association (NYHA) functional class, major adverse cardiac events: death, rein-

farcion and TVR. At the same visit a transthoracic 2D ECG was undertaken for evaluating global LVEF and degree of ischemic mitral regurgitation.

Statistical Methods

Categorical variables where warranted were compared with the use of chi-square test or Fisher exact test were warranted. Continuous variables were compared with the use of a two-tailed student *t*-test for normally distributed variables and by the Wilcoxon test for non-normally distributed variables. Kaplan-Meier survival analysis was performed in comparing mortality between the two procedures. Adjustment for diabetes mellitus was performed as the treatment groups differed in the prevalence of diabetes mellitus at baseline. Primary analyses were conducted according to the intention to treat principle, as this approach minimizes the risk of selection bias. Secondary analyses were conducted according to the treated procedure to determine the effect of aspiration at each point in time on patient outcome. Paired *t*-tests were used to compare TIMI frame count pre- and postaspiration and the McNemar-Bowker test to compare changes in categorical data (MBG, TIMI flow grade) pre- and postaspiration at each procedural stage. A value of $p < 0.05$ was interpreted as statistically significant. Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, IL).

Results

Baseline Characteristics

During 14 months of enrolment 100 patients were included in the study; 51 in the SA group and 49 in the MA group (► **Table 1**). The two treatment groups did not differ in their demographic or clinical variables, except that the SA group had a higher percentage of patients with diabetes mellitus (45.1% vs. 26.5%, $p < 0.5$). In addition, the two groups tended to differ in the distribution of Killip class at presentation. Forty four of 51 (86.3%) patients from the SA group were in Functional Capacity –I (FC–I) whereas only 34 of 49 (69.4%) patients from the MA group were in FC–I ($p < 0.6$). After correction for diabetes, the two groups did not differ in demographic characteristics or clinical presentation except for Killip class ($p < 0.5$).

Crossover Patients

Seven of the patients in the SA group (13.7%) crossed over to the MA group (► **Table 2**). Reasons for crossover were: appearance of thrombus (3 out of 7 patients) and slow flow (4 out of 7 patients) in the infarct related artery after stenting. These patients were characterized by previous myocardial infarctions, PCI, and coronary stenting in the past and they tended to use acetylsalicylic acid (ASA) prior to hospitalization. The systolic blood pressure on admission was significantly lower and their heart rate was significantly higher. Excluding the subjects who crossed over from the SA to the MA group, the two treatment groups did not differ in their demographic or clinical variables except that the SA group had a higher percentage of patients with diabetes mellitus (50% vs. 26.5%, $p < 0.5$) and they differed in the distribution of Killip class ($p < 0.04$).

Table 1 Demographic and clinical characteristics according to intention to treat protocol

					Adjust for diabetes
Demographic variables	Standard arm (N = 51)	Multiaspiration arm (N = 49)	Test statistic	p	P
Age	57.2 ± 12.1	57.5 ± 12.4	$t = -0.145$	0.88	0.65
Gender (%male)	42 (82.4)	44 (89.8)	$\chi^2 = 1.15$	0.28	0.23
BMI	29.08 ± 6.49	28.00 ± 5.16	$t = 0.92$	0.92	0.46
Risk factors, N (%)					
Current smoking (% yes)	34 (66.7)	35 (71.4)	$\chi^2 = 0.26$	0.61	0.59
Diabetes	23 (45.1)	13 (26.5)	$\chi^2 = 3.74$	0.05	–
Hypertension	48 (94.1)	42 (85.7)	$\chi^2 = 1.96$	0.20	0.35
Hypercholesterolemia	50 (98.0)	48 (98.0)	$\chi^2 = 0.00$	1.00	0.86
Family history	22 (43.1)	18 (36.7)	$\chi^2 = 0.43$	0.51	0.59
Previous MI	10 (19.6)	9 (18.4)	$\chi^2 = 0.02$	0.87	0.97
Past PCI	11 (21.6)	9 (18.4)	$\chi^2 = 0.16$	0.69	0.82
Previous stent	9 (17.6)	6 (12.2)	$\chi^2 = 0.57$	0.45	0.56
S/P CABG	2 (3.9)	0 (0.0)	$\chi^2 = 1.96$	0.50	1.00
PVD	4 (7.8)	4 (8.2)	$\chi^2 = .00$	1.00	0.47
CRF	10 (19.6)	5 (10.2)	$\chi^2 = 1.73$	0.19	0.34
COPD	6 (11.8)	5 (10.2)	$\chi^2 = 0.06$	0.80	0.80
Blood disorder	2 (3.9)	6 (12.2)	$\chi^2 = 2.35$	0.16	0.07
Past CVA/TIA	5 (9.8)	3 (6.1)	$\chi^2 = 0.46$	0.72	0.60
GI bleeding	10 (19.6)	5 (10.2)	$\chi^2 = 1.73$	0.19	0.14
Prior noncardiac operations (any)	14 (27.5)	8 (16.3)	$\chi^2 = 1.80$	0.18	0.12
Prior medications					
ASA	20 (40.0)	13 (26.5)	$\chi^2 = 2.02$	0.16	0.34
Plavix	1 (2.0)	2 (4.1)	$\chi^2 = 0.36$	0.62	0.42
Beta-blocker	14 (28.0)	9 (18.4)	$\chi^2 = 1.29$	0.26	0.37
ACE I	15 (30.0)	16 (32.7)	$\chi^2 = 0.08$	0.78	0.20
Lipid L	21 (42.0)	19 (38.8)	$\chi^2 = 0.11$	0.74	0.89
Coumadin	0 (0.0)	1 (2.1)	$\chi^2 = 1.05$	0.49	1.00
Clinical presentation					
Systolic BP	127.7 ± 25.5	122.9 ± 28.5	$t = 0.89$	0.38	0.47
Diastolic BP	75.4 ± 13.0	75.5 ± 18.2	$t = -0.038$	0.97	0.94
Heart rate	78.7 ± 18.5	78.0 ± 16.1	$t = 0.197$	0.84	0.82
Killip			$\chi^2 = 5.56$	0.06	0.05
1	44 (86.3)	34 (69.4)			
2	7 (13.7)	12 (24.5)			
3	0 (0.0)	3 (6.1)			

Abbreviations: ACE, angiotensin converting enzyme; ASA, acetylsalicylic acid; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CVA, cerebrovascular accident; CX, circumflex GI, gastrointestinal; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack.

Time Scheme and Procedural Data by Treatment Group

Time from chest pain to emergency room (ER) and time from ER to the end of the procedure were not different between the groups, but the mean time from wire crossing to end of ballooning was significantly longer in the MA group (9 ± 8

minutes) compared with the SA group (4 ± 3 minutes) ($p = 0.004$) (► **Table 3**).

There were no differences between the arms in vascular approach, vessel type or the number of stents implanted. Seven patients (13.7%) in the SA group and eight (16.7%) in the

Table 2 Demographic and clinical variables between patients in the standard treatment group who crossed over to the multiaspiration treatment group

	Standard treatment			
	Crossover			
Demographic variables	Yes (N = 7)	No (N = 44)	Test statistic	p
Age	55.1 ± 9.6	57.5 ± 12.5	$t = -0.476$	0.64
Gender (% male)	7 (100.0)	35 (79.5)	$\chi^2 = 1.74$	0.33
BMI	28.71 ± 8.38	29.1 ± 6.26	$t = -0.163$	0.87
Risk factors, N (%)				
Current smoking (% yes)	6 (85.7)	28 (63.6)	$\chi^2 = 1.32$	0.40
Diabetes	1 (14.3)	22 (50.0)	$\chi^2 = 3.11$	0.11
Hypertension	6 (85.7)	42 (95.5)	$\chi^2 = 1.03$	0.36
Hypercholesterolemia	7 (100.0)	43 (97.7)	$\chi^2 = 0.16$	1.00
Family history	3 (42.9)	19 (43.3)	$\chi^2 = 0.00$	1.00
Past MI	4 (57.1)	6 (13.6)	$\chi^2 = 7.25$	0.02
Past PCI	4 (57.1)	7 (15.9)	$\chi^2 = 6.07$	0.01
Previous stents	4 (57.1)	5 (11.4)	$\chi^2 = 8.71$	0.01
Past CABG	1 (14.3)	2 (2.3)	$\chi^2 = 2.31$	0.26
PVD	1 (14.3)	3 (6.8)	$\chi^2 = 0.47$	0.46
CRF	3 (42.9)	7 (15.9)	$\chi^2 = 2.78$	0.13
COPD	2 (28.6)	4 (9.1)	$\chi^2 = 2.21$	0.19
Blood disorder	0 (0.0)	2 (4.5)	$\chi^2 = 0.33$	1.00
Past CVA/TIA	0 (0.0)	5 (11.4)	$\chi^2 = 0.88$	1.00
GI bleeding	0 (0.0)	10 (22.7)	$\chi^2 = 1.98$	0.32
Prior noncardiac operations (any)	2 (28.6)	12 (27.3)	$\chi^2 = 0.01$	1.00
Prior medications				
ASA	5 (71.4)	15 (34.9)	$\chi^2 = 3.35$	0.10
Plavix	0 (0.0)	1 (2.3)	$\chi^2 = 0.17$	1.00
Beta-blocker	3 (42.9)	11 (25.6)	$\chi^2 = 0.89$	0.38
ACE I	2 (28.6)	13 (30.2)	$\chi^2 = 0.01$	1.00
Lipid L	4 (57.1)	17 (39.5)	$\chi^2 = 0.77$	0.43
Coumadin	0 (0.0)	0 (0.0)	–	–
Clinical Presentation				
Systolic BP	110.0 ± 10.0	130.5 ± 26.1	$t = -3.76$	0.001
Diastolic BP	82.0 ± 11.0	74.4 ± 13.0	$t = 1.46$	0.15
Heart Rate	96.6 ± 20.1	75.9 ± 16.8	$t = 2.95$	0.005
Killip			$\chi^2 = 1.51$	0.24
1	5 (71.4)	39 (88.6)		
2	2 (28.6)	5 (11.4)		
3	0 (0.0)	0 (0.0)		

Abbreviations: ACE, angiotensin converting enzyme; ASA, acetylsalicylic acid; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CVA, cerebrovascular accident; CX, circumflex; GI, gastrointestinal; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack.

Table 3 Time scheme and procedure characteristics (data that pertained to aspiration were ignored in patients who crossed over from the standard to the aspiration group)

	Arm			
Variable	Standard (51)	Multiaspiration (49)	Test statistic	P
Time frame				
Time from chest pain to ER (N) Median (range)	2:50 ± 2:39 (51) 1:53 (0:16–11:49)	3:06 ± 3:09 (48) ^a 1:53 (0:28–14:29)	–0.45	0.66
Time from ER to wire (N) Median (range)	1:14 ± 1:50 (48) ^b 0:53 (0:00–12:43)	0:52 ± 0:26 (44) ^c 0:49 (0:10–2:06)	1.27	0.21
Time from wire to balloon (N) Median (range)	0:04 ± 0:03 (44) ^d 0:04 (0:00–0:17)	0:09 ± 0:08 (35) ^e 0:07 (0:00–0:50)	–3.10	0.004
Time from wire to stent (N) Median (range)	0:11 ± 0:06 (41) ^f 0:10 (0:02–0:27)	0:14 ± 0:08 (35) 0:12 (0:00–0:40)	–1.80	0.08
Time from ER to end of procedure	1:26 ± 1:55 (45) ^g	1:14 ± 0:29 (43) ^h	0.63	0.53
Procedure characteristics				
Direct stenting (%)	3 (7.0%)	9 (21.4%)	3.66	0.06
Rescue (%)	1 (2.0%)	3 (6.1%)	1.13	0.36
Approach	(N = 44)	(N = 44)	3.79	0.22
Femoral	24 (54.6%)	30 (68.2%)		
Radial	19 (43.2%)	13 (29.6%)		
Ulnar	0 (0.0%)	1 (2.2%)		
Brachial	1 (2.2%)	0 (0.0%)		
IIB/IIIA	42 (85.7%)	46 (93.9%)	1.78	0.32
Drug eluting stents	5 (12.2%)	4 (10.3%)	0.08	1.00
Number of stents/patient	1.15 ± 0.37 (39)	1.23 ± 0.48 (39)	–0.79	0.43
Treated vessel	–	–	0.24	0.96
LAD	29 (56.9%)	26 (53.1%)		
RCA	15 (29.4%)	15 (30.6%)		
CX	4 (7.8%)	5 (10.2%)		
Other	3 (6.9%)	3 (7.1%)		
Urgent CABG	7 (13.7%)	8 (16.7%)	0.17	0.78

Abbreviations: CABG, coronary artery bypass grafting; CX, circumflex artery; ER, emergency room; LAD, left anterior descending; RCA, right coronary artery.

^aOne (32) had no time of arrival at ER and had an urgent CABG

^bTwo^{11,20} had urgent CABG

^cOne (47) had urgent CABG; one failed wire,⁵ one did not do PCI (86), one missing all times (63)

^dOne² had urgent CABG and three went directly to stent.

^eNine (1, 4, 27, 37, 45, 64, 92, 94, 97) went directly to stent.

^fExcludes six who underwent urgent CABG (2, 11, 20, 39, 40, 71), one lacking times (50), one failed PCI (69) and two lacking a stent (21, 67); includes one who subsequently underwent CABG (85)

^gExcludes five who underwent urgent CABG (2, 11, 20, 39, 71) and one lacking times (50)

^hExcludes three who underwent urgent CABG (32, 47, 66), one failed wire,⁵ one who did not need the procedure (86) and one lacking data (63); includes 5 who subsequently underwent CABG (22, 24, 27, 33, 88)

MA group underwent urgent coronary angiography bypass graft. Three patients (7%) in the SA group and nine (21.4%) in the MA group underwent direct stenting. These rates showed a trend toward a statistically significant difference ($p = 0.06$).

Angiographic Data

There were no statistically significant differences in angiographic data between the groups before the procedure began

(► **Table 4**). TIMI flow grade 2–3 was higher among the MA group after wiring only: 65.9% versus 39.1%, respectively ($p = 0.01$). However, the TIMI frame count (TFC) were lower in the MA group during the entire procedural steps compared with the SA group, but the main statistically significant difference was noticed after wire crossing: 32.9 ± 32.4 in the MA group versus 58.4 ± 45.2 in the SA group ($p = 0.007$). The percentage of MBG level 2–3 was statistically higher in

Table 4 Angiographic parameters: TIMI flow grade, TFC, MBG in the multiaspiration versus standard arm

Measurement Time					
Group	TIMI	Time 0	Wire	Balloon	Stent
Multiaspiration	TIMI 0	27 (57.4%)	1 (2.4%)	1 (2.8%)	1 (2.5%)
	TIMI 1	1 (2.1%)	13 (31.7%)	3 (8.3%)	2 (5.0%)
	TIMI 2	11 (23.4%)	9 (22.0%)	9 (25.0%)	7 (17.5%)
	TIMI 3	8 (17.0%)	18 (43.9%)	23 (63.9%)	30 (75.0%)
Standard	TIMI 0	34 (68.0%)	11 (23.9%)	3 (6.7%)	0 (0.0%)
	TIMI 1	3 (6.0%)	17 (37.0%)	4 (8.9%)	3 (7.3%)
	TIMI 2	8 (16.0%)	13 (28.3%)	21 (46.7%)	3 (7.3%)
	TIMI 3	5 (10.0%)	5 (10.9%)	17 (37.8%)	35 (85.4%)
P	–	0.42	0.001	0.12	0.52
Adjusted p	–	0.39	0.001	0.14	0.38
Measurement Time					
Group	TIMI frame count	Wire	Balloon	Stent	
Multiaspiration		32.9 ± 32.4	31.3 ± 23.1	23.8 ± 12.0	
Standard		58.4 ± 45.2	40.0 ± 26.8	27.8 ± 17.5	
P		0.007	0.16	0.25	
Adjusted p		0.009	0.15	0.26	
Measurement Time					
Group	MBG	Time 0	Wire	Balloon	Stent
Multiaspiration	0	31 (70.5%)	16 (39.0%)	4 (11.4%)	1 (2.4%)
	1	8 (18.2%)	12 (29.3%)	10 (28.6%)	7 (17.1%)
	2	4 (9.1%)	9 (22.0%)	10 (28.6%)	12 (29.3%)
	3	1 (2.3%)	4 (9.8%)	11 (31.4%)	21 (51.2%)
Standard	0	41 (83.7%)	36 (81.8%)	13 (30.2%)	2 (5.1%)
	1	4 (8.2%)	5 (11.4%)	18 (41.9%)	7 (17.9%)
	2	4 (8.2%)	3 (6.8%)	9 (20.9%)	12 (30.8%)
	3	0 (0.0%)	0 (0.0%)	3 (7.0%)	18 (46.2%)
P		0.31	0.001	0.01	0.05
Adjusted p		0.17	0.001	0.01	0.06

the MA compared with the SA group mainly after wiring and ballooning. This difference disappeared after stenting. At the end of procedure both MA and SA groups showed MBG level 3 only among 50% of the patients. Aspiration failure determined by angiographic criteria showed a TIMI 0–1 of 7.5% in the MA group versus 7.3% in the SA group ($P = \text{NS}$). MBG 0–1 was 19.5% in the MA group and 23% in the SA group ($P = \text{NS}$).

ECG and Echocardiographic Data

At 90 minutes after PPCI a greater percentage of patients in the MA group had STR > 70% (63.8% vs. 38.0%; $p = 0.03$) (► **Table 5**). This finding was also maintained for diabetic patients ($p = 0.05$). However, by 6 hours there was no statistically significant difference in STR (78.7% vs. 62.0%) between the groups. There were no significant differences in mitral regurgitation (MR) grade between the groups before PPCI, at 24 hours, and after 30 days of follow-up. After 180 days of follow-up the rate of moderate MR in the MA

group was 6.2% versus 10% in the SA group ($p = \text{NS}$). Although there was some trend of higher ejection fraction in the MA group compared with the SA group during the follow-up period, these differences were not found to be statistically significant ($53.3 \pm 11\%$ vs. $49.4 \pm 11\%$, $p = 0.16$).

Cardiac serum markers (► **Table 6**) levels were not statistically different between the groups during the different phases of hospitalization. However, 24 hours post procedure the mean CK level in the SA group was 864.86 ± 652.43 versus 1469.78 ± 1548.34 units in the MA group ($p = 0.02$).

Clinical Follow-Up

There was no difference in NYH functional class, cardiac arrhythmias, mechanical complications, reinfarction and major adverse events between the two groups under clinical follow-up (► **Table 7**). These findings remain unchanged at 30 and 180 days follow-up. During 180 days three patients from the SA group were lost to follow-up (both 30 and 180 days

Table 5 ECG and echocardiographic data: Standard versus multiaspiration arm

	Standard Arm (N = 51)	Multiaspiration (N = 49)	Test statistic	P	DM Adjusted P
ECG					
STR 90 minutes	–	–	7.18	0.03	0.05
≤ 30	11 (22.0%)	5 (10.6%)	–	–	–
30–70	20 (40.0%)	11 (23.4%)	–	–	–
> 70%	19 (38.0%)	30 (63.8%)	–	–	–
STR 6 hours	–	–	3.24	0.23	0.27
≤ 30	6 (12.0%)	3 (6.4%)	–	–	–
30–70	13 (26.0%)	7 (14.9%)	–	–	–
> 70%	31 (62.0%)	37 (78.7%)	–	–	–
ECHO					
MR	–	–	2.08	0.36	0.48
Before PCI					
None	34 (70.8%)	27 (57.4%)	–	–	–
Mild	11 (22.9%)	17 (36.2%)	–	–	–
Moderate	3 (6.2%)	3 (6.4%)	–	–	–
24h Post	–	–	1.58	0.71	0.61
None	36 (73.5%)	31 (66.0%)	–	–	–
Mild	11 (22.4%)	12 (25.5%)	–	–	–
Moderate	2 (4.1%)	3 (6.4%)	–	–	–
Severe	0 (0.0%)	1 (2.1%)	–	–	–
30 days	–	–	0.19	0.91	0.89
None	30 (68.2%)	23 (63.9%)	–	–	–
Mild	9 (20.5%)	8 (22.2%)	–	–	–
Moderate	5 (11.4%)	5 (13.9%)	–	–	–
180 days	–	–	3.61	0.20	0.19
None	26 (65.0%)	27 (84.4%)	–	–	–
Mild	9 (25.0%)	3 (9.4%)	–	–	–
Moderate	5 (10.0%)	2 (6.2%)	–	–	–
Ejection Fraction					
Before PCI	46.5 ± 9.9%	44.7 ± 8.8%	0.92	0.36	0.18
24h P	47.0 ± 10.4%	46.0 ± 8.4%	0.54	0.59	0.40
30d	51.2 ± 10.3%	49.6 ± 12.6%	0.63	0.53	0.36
180d	49.4 ± 11.4%	53.3 ± 11.4%	–1.44	0.16	0.16

and four patients from the MA were lost to follow-up. In the Kaplan-Meier analysis these patients were censored at 30 days. Two of the patients from the standard treatment group and four in the aspiration group died during the follow-up period. There was no statistically significant difference in survival time between the aspiration and standard treatment arms (log-rank test $p > 0.32$).

Discussion

By activating thrombus aspiration catheter after every stage of PPCI we demonstrated that the main improvement of both

epicardial and microcirculation flow is by using this device at the first stage of procedure, which means immediately after wiring. Although the SA group showed poor perfusion indices at the beginning of procedure, a significant catch up and improvement of these parameters were shown immediately after stenting the infarct related artery. In our study the epicardial and microcirculation perfusion parameters were equivocal in both groups toward the end of the procedure. Unfortunately, there was no significant translation of this concept into a better early- or late-clinical outcome.

Although this is a primary PCI study, five rescue PCI patients were included (two in the SA and three in the MA

Table 6 Laboratory results: Standard versus multiaspiration arm

	Standard arm	Multiaspiration arm	Test statistic	p	Adjust for DM
CK 0 Median	1494.34 ± 1599.99 789.5 (N = 32)	1123 ± 932 690.7 (42)	1.14	0.26	0.20
CK 6h Median	1895.02 ± 1403.88 1465 (N = 44)	2569.98 ± 2517.16 1626 (N = 45)	-1.57	0.12	0.11
CK 24h Median	864.86 ± 652.43 778 (N = 43)	1469.78 ± 1548.34 943 (N = 41)	-2.31	0.02 ^a	0.02
Trop 0 Median	1.55 ± 2.97 0.025 (N = 34)	0.70 ± 1.74 0.05 (N = 35)	1.43	0.16	0.25
Trop 6 hour Median	3.59 ± 4.08 1.82 (N = 22)	4.80 ± 4.80 2.90 (N = 23)	-0.92	0.36	0.30
Trop 24h Median	1.36 ± 1.15 1.45 (N = 10)	3.18 ± 3.13 2.53 (N = 11)	-1.79	0.10	0.12

^aMann-Whitney Z = -1.82, *p* < 0.07

arm). Separate analysis by excluding these patients did not change our results.

Rationale

Several observations and previous reports motivated us to test a hypothesis of whether there is any benefit of activating thrombus aspiration after every stage of PPCI. Napodano et al reported that thromboembolic phenomena may occur after every stage of PPCI,⁹ prolapsing material were recorded by IVUS after coronary stenting¹⁰ and lastly, the reported success rate of retrieving thrombotic material after wiring is only 73%.⁸

Although this was a single center trial, we investigated all comers with STEMI, whereas randomization was performed prior to angiography. Compared with other trials^{8,18} our population had a relatively high percentage of diabetes (SA approximately 45%, MA approximately 26.5%) and patients from the MA group were sicker at presentation, whereby 30% of them were in FC II-III NYHA classification.

In spite of performing aspiration after every stage of procedure, we did not notice a significant difference related to the total time from ER to end of the procedure. However, time from wire to balloon was significantly longer in the MA group compared with the SA group.

By analyzing pattern and quality of coronary flows, both at the epicardial and microcirculation level, our study showed that the main improvement in perfusion parameters occurred mainly at the first stage of procedure. TIMI 3 flow, TIMI frame count and MBG were significantly better in the MA group compared with the SA group, only after the first aspiration. These differences practically disappear after stenting (► **Table 4**). This observation clarifies that the quality of both epicardial and intramyocardial coronary flow are multifactorial, whereas enlarging vessel diameter and stabilization of plaque by metal scaffolding have significant contribution to these phenomena.

Similar to other studies, the benefit of reducing microvascular obstruction by thrombus aspiration did not translate into early or late clinical positive outcomes. Using contrast ECG, Galiuto et al demonstrated that thrombus aspiration significantly reduces the extent of microvascular obstruction, but does not have a favorable effect upon LV remodeling.¹⁹ A meta-analysis of 21 trials evaluating the effectiveness of an embolic protection device including thrombectomy in PPCI, performed by De Luca et al, did not show improved survival.²⁰ One of the limitations of our study is that it does not take into account the size of the angiographic thrombus. Aspiration of large visible thrombus with AngioJet (Possis Medical Inc. Minneapolis, MN), for instance, did correlate with better outcomes in myocardial infarction patients.²¹

After a 6 month follow-up, our study did not show any benefit of the MA concept compared with the standard procedure regarding death, LVEF or ischemic mitral regurgitation. By analyzing the groups as treated, rather than by intention to treat, the same trend was observed.

In conclusion, significant improved angiographic parameters during PPCI using aspiration catheter were demonstrated only after wiring. The concept of performing aspiration after every stage during procedure did translate into a positive clinical outcome compared with the standard technique.

Study Limitations

Our study has some limitations. It is a single center experience. No angiographic evaluation of thrombus size and histologic structure were undertaken. Another limitation is the use of aspiration catheters. These are limited in their ability to aspirate thrombi because of their relatively small internal lumen diameter. Therefore, one of the potential reasons for the negative results is the inability to aspirate a significant amount of thrombotic material.

Table 7 In hospital including 30 and 180 days outcome

	Standard arm	Multiaspiration arm	p
Hospitalization			
FC	–	–	0.32
1	44 (86.3%)	37 (77.1%)	–
2	6 (11.8%)	10 (20.8%)	–
3	1 (2.0%)	0 (0.0%)	–
4	0 (0.0%)	1 (2.1%)	–
Arrhythmia	1 (2.0%)	1 (2.1%)	1.00
Mechanical complications	1 (2.0%)	1 (2.1%)	1.00
Reinfarction	0 (0.0%)	1 (2.1%)	0.48
TVR/TLR	3 (5.9%)	1 (2.1%)	0.62
CHF	4 (7.8%)	7 (14.9%)	0.34
Death	1 (2.0%)	2 (4.1%)	0.61
MACE	4 (7.8%)	3 (6.1%)	1.00
30 days			
NYHA	–	–	0.73
1	29 (63.0%)	24 (57.1%)	–
2	16 (34.8%)	16 (38.1%)	–
3	1 (2.2%)	2 (4.8%)	–
GXT	4 (8.7%)	5 (11.9%)	0.73
SPECT imaging	1 (2.2%)	2 (4.8%)	0.60
Angiography	1 (2.2%)	4 (9.5%)	0.19
Reinfarction ^a	0 (0.0%)	2 (4.8%)	0.22
TVR ^a	4 (8.7%)	3 (7.1%)	1.00
Death ^b	1 (2.1%)	3 (6.4%)	0.62
MACE ^c	5 (10.6%)	6 (13.6%)	0.75
180 days			
NYHA			0.80
1	28 (68.3%)	25 (65.8%)	–
2	11 (26.8%)	12 (31.6%)	–
3	2 (4.9%)	1 (2.6%)	–
GXT	2 (4.8%)	5 (12.8%)	0.25
SPECT imaging	1 (2.4%)	2 (5.1%)	0.61
Angiography	9 (21.4%)	5 (12.8%)	0.38
Reinfarction ^d	3 (7.1%)	3 (7.6%)	1.00
TVR ^e	9 (20.9%)	5 (13.2%)	0.39
Death ^f	2 (4.7%)	4 (9.8%)	0.43
MACE ^g	11 (25.0%)	8 (19.5%)	0.61

Abbreviations: GXT, graded exercise testing; NYHA, New York Heart Association; MACE, major adverse cardiac events; SPECT, single photon emission computed tomography; TLR, target lesion revascularization; TVR, target vessel revascularization.

^aN = 46 in standard arm, N = 42 in aspiration arm

^bN = 47 in standard arm, N = 47 in aspiration arm

^cN = 47 in standard arm, N = 44 in aspiration arm

^dN = 42 in standard arm, N = 39 in aspiration arm

^eN = 43 in standard arm, N = 38 in aspiration arm

^fN = 43 in standard arm, N = 41 in aspiration arm

^gN = 44 in standard arm, N = 41 in aspiration arm

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