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Thrombus aspiration in ST-elevation myocardial infarction: Does it actually impact long-term outcome?

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Abstract

Background: *The effect of thrombus aspiration on mortality is still controversial, with results which are often inconsistent in different randomized trials, real world registries and different follow-up duration. The aim of this analysis was to assess the effect on 30-day and 1-year mortality of thrombus aspiration during primary percutaneous coronary intervention (pPCI) for ST-elevation myocardial infarction (STEMI) compared with conventional PCI.*

Methods: *We used data from all the consecutive STEMI patients treated either with conventional PCI or thrombus aspiration between January 1, 2004 and January 1, 2012. Propensity matching score was calculated on the basis of several baseline and procedural characteristics in order to predict the probability for each patient of having been treated with thrombus aspiration. This propensity score analysis was used in order to select a cohort of patients treated with thrombus aspiration matched one-to-one with patients treated with conventional PCI.*

Results: *In total, 744 (53.1%) patients out of 1,400 enrolled were treated with thrombus aspiration. In the matched cohort, at 30-day follow-up 6.3% of patients in the conventional PCI group died compared to 4.7% in the thrombus aspiration group. The unadjusted hazard ratio (HR) for 30-day mortality was 1.01 (95% CI 0.33–3.14, p = 0.985). In the same cohort, 10.7% of patients died at 1-year in the conventional PCI group compared to 5.2% in the thrombus aspiration group. The 1-year unadjusted hazard ratio for mortality was 0.47 (95% CI 0.25–0.90, p = 0.025). The HR changed and was no longer significant after adjustment for differences in the use of glycoprotein (GP) IIb/IIIa inhibitors, lesion pre-dilatation and pre-procedural TIMI flow: 0.71 (95% CI 0.36–1.39, p = 0.322).*

Conclusions: *Thrombus aspiration does not influence 30-day mortality, however it is associated with 1-year survival benefit. GP IIb/IIIa inhibitors and thrombus aspiration may have an important synergistic role in leading to this long-term benefit.* (Cardiol J 2015; 22, 3: 306–314)

Key words: thrombus aspiration, percutaneous coronary intervention, ST elevation myocardial infarction, glycoprotein IIb/IIIa inhibitors

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Introduction

Primary percutaneous coronary intervention (pPCI) has become a treatment of choice for ST--elevation myocardial infarction (STEMI) since studies have demonstrated its superiority over conventional thrombolytic treatment [1]. Coronary stents and adjunctive pharmacologic agents have improved the effect of PCI [2, 3] restoring a normal anterograde blood flow in the vast majority of patients. However, dislodgement of atherothrombotic material from coronary lesions during PCI can result in distal embolization, termed the "no-reflow phenomenon, in 12–39% of patients" [4, 5]. Numerous adjunctive devices and drugs have been developed to remove thrombi or protect against distal embolization during PCI [6, 7]. Though studies so far have failed to demonstrate a benefit for distal protection devices, evidence to date appears to be more promising for thrombectomy devices as recognized by international guidelines [8, 9].

Nevertheless, the recent TASTE trial showed no benefit on 30-day mortality rate with routine thrombus aspiration in STEMI patients undergoing PCI [10]. Similarly, the INFUSE-AMI (Intracoronary Abciximab and Aspiration Thrombectomy in Patients with Large Anterior Myocardial Infarction) [11] showed no differences in final infarct size at 30-day between STEMI patients treated with pPCI alone or pPCI and thrombus aspiration. In these trials, despite broad inclusion criteria, the highest-risk patients, such as those with cardiogenic shock, were underrepresented. Moreover, as pointed out by Byrne and Kastrati [12] the potential benefits of thrombus aspiration mediated through enhanced myocardial salvage and favorable remodeling may not be captured at 30-day but may be expected to emerge during the first year after infarction.

We therefore investigated the effect of adjunctive thrombus aspiration on 30-day and 1-year mortality in a large propensity matched STEMI patient cohort.

Methods

The data analyzed in this study were obtained from STEMI patients (within 12 h from the onset of symptoms, without restriction based on age or clinical status at presentation) who underwent pPCI at the Careggi Hospital, University of Florence between January 1, 2004, and January 1, 2012. Data were collected in a prospective registry.

In the urban area of Florence, Acute Myocardial Infarction operative model assumes that patients are first evaluated by the medical emergency system staff in the pre-hospital setting and then directly admitted to the catheterization laboratory of our tertiary center (Cath Lab) or transferred there after a rapid stabilization in Emergency Department. After pPCI, they are admitted to our Intensive Cardiac Care Unit (ICCU).

The diagnosis of STEMI was based on the criteria of the American College of Cardiology/ /American Heart Association [9].

According to our Cath Lab's protocol, thrombus aspiration was performed in presence of the following conditions: (1) Thrombolysis In Myocardial Infarction (TIMI) grade 0 to 1 flow; (2) An infarction-related artery minimal reference diameter of at least 2.5 mm.

Mechanical (Export Medtronic Device) or Rheolytic (AngioJet Rheolytic Thrombectomy System, Medrad Interventional/Possis, Minneapolis, Minnesota) thrombus aspiration was performed according to the interventional cardiologist's discretion [13, 14]. As a general rule, rheolytic thrombus aspiration was preferred to mechanical thrombus aspiration in presence of a large thrombus burden in a proximal segment of a large coronary artery.

All patients were pretreated with aspirin 300 mg orally or 500 mg *i.v.* and clopidogrel 600 mg or prasugrel 60 mg or ticagrelor 180 mg orally. Heparin was given as an initial bolus of 70 U/kg *i.v.*, and additional boluses were administered during the procedure to achieve an activated clotting time of 200 to 250 s. Glycoprotein (GP) IIb/IIIa inhibitors were administered according to the interventional cardiologist's discretion during revascularization in the Cath Lab. After the procedure, patients were treated with aspirin (100 to 325 mg daily orally indefinitely) and clopidogrel (75 mg daily orally for 12 months) or prasugrel (10 mg orally for 12 months) or ticagrelor (90 mg orally twice daily for 12 months). Other drugs such as beta-blockers, angiotensin-converting enzyme inhibitors, and statins were used in accordance with standard guidelines.

Primary PCI was performed according to standard clinical practice using a femoral artery access with a 6 F sheath insertion in most of patients; in about one third of patients radial approach was used. Procedural success was defined as a post-procedure infarct stenosis < 20% together with TIMI grade 3 flow. Failure PCI was defined as a procedure resulting in TIMI grade 0–2 flow, regardless of the residual stenosis [15]. A 12-lead electrocardiogram was performed 60 min after the procedure in order to evaluate ST-segment resolution > 50%.

On ICCU admission, after PCI, in a fasting blood sample, the following parameters were measured:

troponin I [ng/mL] and hemoglobin [g/L]. Creatinine [mg/dL] was also measured in order to calculate glomerular filtration rate (GFR) [mL/min/1.73 m^2]. Troponin I (TnI) was measured 3 times a day throughout ICCU stay and peak TnI was considered. Transthoracic 2-dimensional echocardiography was performed in order to measure left ventricular ejection fraction (LVEF) on admission and at discharge.

Major bleedings were defined according to the TIMI criteria [16]. Patients were diagnosed with acute kidney injury if they had a serum creatinine value increase of ≥ 1.5-fold over the admission value within ICCU-stay [17].

The primary study outcomes were the mortality at 30-day and at 1-year follow-up. Post discharge mortality was computed as the ratio of the number of patients who died between discharge, 30-day and 1-year, and the total number of those discharged alive [18]. Most of patients were examined in the outpatient clinic at 30-day, 6-month and 1-year since the discharge otherwise they were contacted via telephone.

The study protocol was set up in accordance with the Declaration of Helsinki and approved by the local Ethics Committee. An oral informed consent for PCI was obtained in all the conscious patients and a written consent in the vast majority of patients according to their clinical conditions.

Statistical analysis

Statistical analysis was conducted with IBM SPSS 20.0 for Windows software (SPSS Inc, Chicago, IL). The primary outcome for the current analysis was 30-day and 1-year all cause mortality. To determine the effect of thrombus aspiration on the primary outcome, we first undertook an unadjusted Kaplan-Meier comparison. Cox regression analysis was performed to determine the hazard ratio (HR) for 30-day and 1-year mortality. Since patients were not randomly assigned to either adjunctive thrombus aspiration or conventional PCI, we applied propensity score matching to adjust for differences in baseline characteristics between patients treated with and without thrombus aspiration. The propensity score is a conditional probability of receiving thrombus aspiration given a set of observed co-variables. A multivariate logistic regression model was used to estimate propensity scores, with the two groups (i.e., thrombus aspiration vs. conventional PCI) as dependent variable and potential confounders as covariates. We identified 14 candidate variables potentially related to the use of thrombus aspiration [19]. All these variables were included in the propensity score estimation model: age, culprit vessel, number of vessels diseased, TIMI flow pre PCI, Killip class, total ischemic time, stent diameter, stent length, LVEF, admission troponin, hypertension, diabetes, smoking habit, chronic renal failure. Patients with one or more missing variables were excluded. Ultimately, the propensity model was derived in a cohort of 1,400 patients. We used the coefficients returned by the model to calculate a propensity score for all patients enrolled. The propensity-matched cohort was established by matching each individual case treated with thrombus aspiration in random order to the patient from the control group with the closest propensity score.

Results

Our series comprises 1,493 consecutive STEMI patients all submitted to pPCI. Of these, 93 were removed from the analysis because they had at least one missing data among variables used for matching. This resulted in a final study cohort of 1,400 patients. Of these, 744 (53.1%) were treated with adjunctive thrombus aspiration.

Characteristics of the full cohort

Patients treated with adjunctive thrombus aspiration differed significantly in clinical and procedural characteristics from those treated with conventional PCI (Table 1, left columns). Patients treated with thrombus aspiration were younger and had a lower LVEF at ICCU admission. The median TnI peak was almost double in the thrombus aspiration group. The infarct-related artery was more often occluded in the thrombus aspiration while the incidence of multivessel disease was higher in the conventional PCI group. Lesion predilatation was more often performed in the conventional PCI group where patients were treated with a smaller stent diameter while there was no difference in the total stent length. Finally, manual thrombus aspiration using Export was used in 594 (79.8) patients out of the 744 who underwent thrombectomy.

Characteristics of the propensity matched cohort

The propensity model yielded 6 statistically significant independent predictors for thrombus aspiration (Table 2). The c-statistic for the model was 0.86 (95% CI 0.83–0.90, $p < 0.001$). The propensity score analysis selected 724 well-matched pairs. The clinical and procedural characteristics are showed in Table 1 (right columns). The only baseline difference was the persistence of a higher incidence of total occluded vessels in the thrombus

Table 1. Clinical, angiographic and procedural characteristics of patients before and after propensity score matching.

	Before propensity score matching (n = 1,400)			After propensity score matching (n = 724; 51.7%)		
	Conventional PCI N = 656 (46.9%)	Thrombus aspiration N = 744 (53.1%)	P	Conventional PCI N = 362 (55.2%)	Thrombus aspiration N = 362 (48.7%)	P
Clinical characteristics						
Age [years]	68.7 ± 12.6	65.2 ± 12.8	< 0.001	67.0 ± 12.4	66.6 ± 12.4	0.709
Gender (male/female)	463/193 (70.6/29.4)	564/180 (75.8/24.2)	0.027	268/94 (74.0/26.0)	268/94 (74.0/26.0)	1
Body mass index [kg/m^2]	26.1 ± 3.6	26.4 ± 3.7	0.305	26.3 ± 3.5	26.5 ± 3.6	0.347
Admission LVEF [%]	44.2 ± 10.2	42.8 ± 9.6	0.007	44.0 ± 9.8	43.9 ± 9.0	0.941
Discharge LVEF [%]	44.8 ± 9.7	43.8 ± 9.1	0.039	44.8 ± 9.4	45.2 ± 8.4	0.547
Admission SAP [mm Hg]	131 ± 26	126 ± 24	< 0.001	130 ± 25	130 ± 24	0.977
Admission heart rate [bpm]	77 ± 16	79 ± 17	0.017	78 ± 16	78 ± 17	0.972
Comorbidities:						
Diabetes	169 (25.8%)	174 (23.4%)	0.302	81 (22.4%)	76 (21.0%)	0.652
Hypertension	380 (57.9%)	360 (48.4%)	< 0.001	193 (53.3%)	189 (52.2%)	0.766
Dyslipidemia	230 (35.1%)	270 (36.3%)	0.632	125 (34.5%)	130 (35.9%)	0.697
Previous acute MI	99 (15.1%)	96 (12.9%)	0.238	45 (12.4%)	37 (10.2%)	0.348
Previous PCI	89 (13.6%)	104 (14.0%)	0.824	45 (12.4%)	38 (10.5%)	0.414
Previous CABG	15 (2.3%)	14 (1.9%)	0.596	5 (1.4%)	10 (2.8%)	0.192
Ever smoke	377 (57.5%)	490 (65.9%)	0.001	228 (63.0%)	235 (64.9%)	0.588
Chronic renal failure	37 (5.6%)	27 (3.6%)	0.072	16 (4.4%)	14 (3.9%)	0.709
Chronic obstructive pulmonary disease	66 (10.1%)	58 (7.8%)	0.137	36 (9.9%)	31 (8.6%)	0.521
Laboratory findings:						
Peak troponin I [ng/mL], median (IQR)	55.8 (26.5–126.6)	110.0 (51.4–228.0)	< 0.001	66.4 (32.3–145.0)	88.6 (42.0–182.0)	0.003
Admission hemoglobin [g/L]	13.3 ± 1.8	13.6 ± 1.8	0.009	13.5 ± 1.8	13.6 ± 1.8	0.232
Nadir eGFR [mL/min/1.73 m^2]	68 ± 27	73 ± 26	< 0.001	71 ± 28	74 ± 27	0.060
Glycated hemoglobin [%]	6.4 ± 1.3	6.2 ± 1.2	0.060	6.4 ± 1.4	6.2 ± 1.3	0.264
Admission WBC (10^3/μL]	11.2 ± 4.0	11.9 ± 4.2	0.002	11.4 ± 4.2	11.5 ± 3.9	0.716
Killip class:			0.595			0.996
I	538 (81.9%)	596 (80.2%)		299 (82.6%)	300 (82.9%)	
II	49 (7.5%)	67 (9.0%)		28 (7.7%)	28 (7.7%)	
III	21 (3.2%)	19 (2.6%)		9 (2.5%)	8 (2.2%)	
IV	49 (7.5%)	61 (8.2%)		26 (7.2%)	26 (7.2%)	

→

Table 1. (cont.) Clinical, angiographic and procedural characteristics of patients before and after propensity score matching.

	Before propensity score matching (n = 1,400)			After propensity score matching (n = 724; 51.7%)		
	Conventional PCI N = 656 (46.9%)	Thrombus aspiration N = 744 (53.1%)	P	Conventional PCI N = 362 (55.2%)	Thrombus aspiration N = 362 (48.7%)	P
Angiographic and procedural characteristics						
TIMI flow pre-PCI:	n = 630	n = 734	< 0.001	n = 351	n = 354	< 0.001
0	357 (56.7%)*	607 (82.7%)		236 (67.2%)	269 (76.0%)	
1	176 (27.9%)*	83 (11.3%)		93 (26.5%)*	50 (14.1%)	
2	83 (13.2%)*	35 (4.8%)		20 (5.7%)	29 (8.2%)	
3	14 (2.2%)	9 (1.2%)		2 (0.6%)	6 (1.7%)	
STEMI location:			0.016			0.875
Anterior	340 (51.8%)	399 (53.6%)		183 (50.6%)	189 (52.2%)	
Inferior	249 (38.0%)	300 (40.3%)		145 (40.1%)	142 (39.2%)	
Other	67 (10.2%)*	45 (6.0%)		34 (9.4%)	31 (8.6%)	
Door to balloon time [min], median (IQR)	240 (165–338)	215 (150–300)	0.008	240 (150–300)	210 (150–310)	0.526
Culprit vessel:			0.005			0.221
Left anterior descending	335 (51.1%)	393 (52.8%)		179 (49.4%)	185 (51.1%)	
Circumflex	102 (15.5%)*	76 (10.2%)		56 (15.5%)	45 (12.4%)	
Right coronary artery	205 (31.2%)	261 (35.1%)		117 (32.3%)	123 (34.0%)	
Left main	11 (1.7%)	5 (0.7%)		8 (2.2%)	3 (0.8%)	
By-pass	3 (0.5%)	9 (1.2%)		2 (0.6%)	6 (1.7%)	
Diseased vessels:			< 0.001			0.830
1-vessel	204 (31.1%)*	343 (46.1%)		134 (37.0%)	141 (39.0%)	
2-vessels	229 (34.9%)	244 (32.8%)		130 (35.9%)	123 (34.0%)	
3-vessels	223 (34.0%)*	157 (21.1%)		98 (27.1%)	98 (27.1%)	
Pre-dilatation	512 (84.8%)	419 (60.0%)	< 0.001	304 (85.4%)	215 (59.6%)	< 0.001
Post-dilatation	137 (22.8%)	169 (24.5%)	0.474	93 (26.2%)	88 (24.6%)	0.635
Coronary angioplasty:			< 0.001			0.726
POBA	62 (9.5%)	76 (10.2%)		2 (0.6%)	3 (0.8%)	
BMS	282 (43.0%)	369 (49.6%)		169 (46.7%)	182 (50.3%)	
DES	282 (43.0%)	287 (38.6%)		181 (50.0%)	169 (46.7%)	
BMS + DES	16 (2.4%)	12 (1.6%)		10 (2.8%)	8 (2.2%)	
Mean stent diameter [mm], median (IQR)	2.75 (2.50–3.00)	3.00 (2.75–3.50)	< 0.001	3.00 (2.75–3.12)	3.00 (2.75–3.25)	0.198
Total stent length [mm], median (IQR)	23 (16–32)	23 (18–30)	0.759	23 (16–32)	23 (16–30)	0.875
Thrombus aspiration system:			N/A			N/A
Manual	–	594 (79.8%)		–	293 (80.9%)	
Rheolytic	–	135 (18.1%)		–	61 (16.9%)	
Combined	–	15 (2.0%)		–	8 (2.2%)	
PCI failure	42/643 (6.5%)	44/744 (5.9%)	0.634	12 (3.3%)	12 (3.3%)	1

*Z score test p value < 0.05 vs. others; CABG — coronary artery by-pass graft; CAD — coronary artery disease; eGFR — estimated glomerular filtration rate; BMS — bare metal stent; DES — drug eluting stent; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial Infarction; N/A — not assessed; PCI — percutaneous coronary intervention; POBA — plain old balloon angioplasty; SAP — systolic arterial pressure; STEMI — ST elevation myocardial infarction; TIMI — Thrombolysis In Myocardial Infarction; WBC — white blood cells

Table 2. Predictors of thrombus aspiration.

	Odds ratio	95% confidence interval	P
Age	0.99	0.98–1.00	0.193
Culprit vessel*	0.90	0.76–1.06	0.208
Number of vessels diseased**	0.55	0.46–0.66	< 0.001
TIMI flow pre PCI (1 unit step)	0.44	0.36–0.54	< 0.001
Killip class (1 class step)	0.95	0.79–1.14	0.595
Total ischemic time (1 min step)	0.999	0.999–1.000	0.169
Average stent diameter (1 mm step)	4.69	3.20–6.87	< 0.001
Average stent length (1 mm step)	1.00	0.99–1.01	0.823
Admission LVEF (1% step)	0.98	0.96–1.00	0.016
Troponin I (10 ng/μL step)	1.03	1.02–1.04	< 0.001
Hypertension	0.84	0.63–1.11	0.211
Diabetes	1.01	0.72–1.40	0.957
Ever smoking	1.21	0.90–1.63	0.203
Chronic renal failure	0.41	0.21–0.81	0.010

*Coded as follows: RCA = 1, LCX = 2, LAD = 3, LM = 4, GRAFT = 5; **Coded as follows: 1 vessel = 1, 2 vessels = 2, 3 vessels = 3; RCA — right coronary artery; LCX — left circumflex; LAD — left anterior descending; LM — left main; TIMI — Thrombolysis In Myocardial Infarction; PCI — percutaneus coronary intervention; LVEF — left ventricular ejection fraction

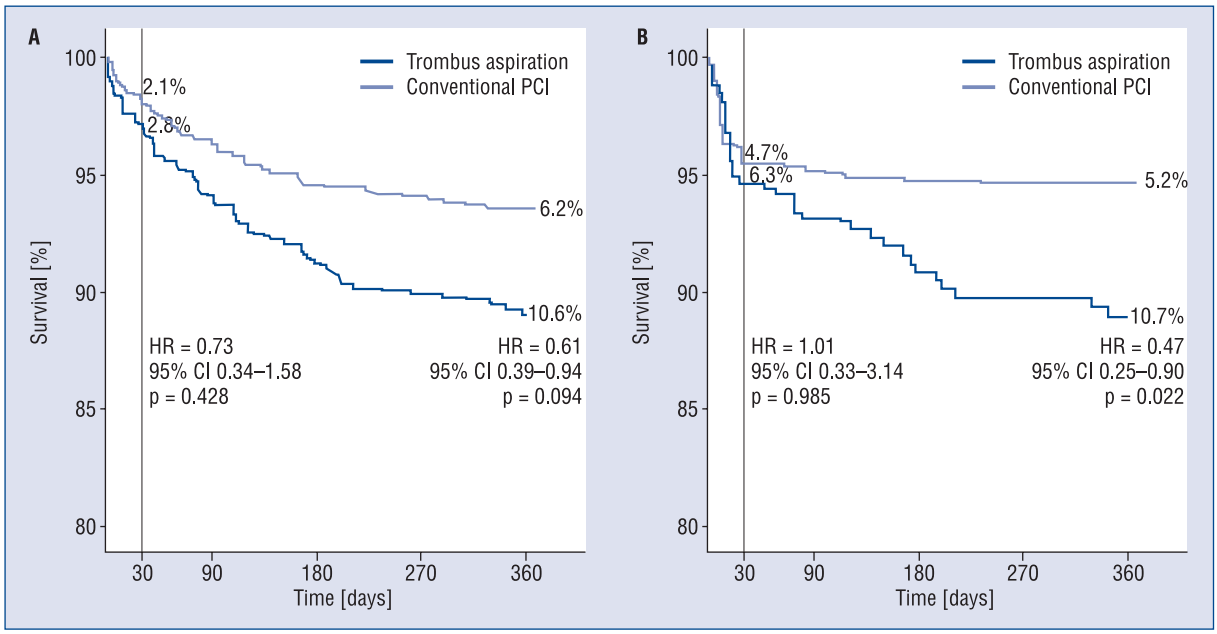

Figure 1. Time-to-event curves in patients treated with thrombus aspiration or conventional percutaneous coronary intervention (PCI); **A.** Survival analysis in the overall population; **B.** Survival analysis in the propensity matched cohort; HR — hazard ratio; CI — confidence interval.

aspiration group and a higher TnI peak during ICCU stay. Lesion predilatation was still more frequent in the conventional PCI group while GP IIb/IIIa inhibitors were more often used in the thrombus aspiration group.

Outcome in the full cohort

The Kaplan-Maier curves are given in Figure 1A. Sixty-six (4.7%) patients died during ICCU stay (conventional PCI: n = 33, 5.0% vs. thrombus aspiration: n = 33, 4.4%; p = NS) and 58 (4.3%)

Table 3. Adjusted Cox regression analysis for 1-year post discharge mortality in the propensity matched cohort.

	Adjusted hazard ratio	95% confidence interval	P
Thrombus aspiration	0.71	0.36–1.39	0.322
Balloon predilatation	1.40	0.65–3.05	0.386
Pre procedural TIMI flow	1.18	0.61–2.27	0.633
Glycoprotein IIb/IIIa inhibitors	0.25	0.13–0.45	0.001

TIMI — Thrombolysis In Myocardial Infarction

patients were lost at follow-up (conventional PCI: n = 26, 4.2% vs. thrombus aspiration: n = 32, 4.5%; p = NS). Therefore, follow-up analysis was performed on 597 patients in the conventional PCI group and 679 in the thrombus aspiration group. At 30-day 2.8% of patients in the conventional PCI group died compared to 2.1% in the thrombus aspiration group while at 1-year the corresponding figures were 10.6% and 6.2%, respectively. The unadjusted HR for 30-day mortality was 0.73 (95% CI 0.34–1.58, p = 0.428).

At 1-year follow-up the unadjusted HR for mortality was 0.61 (95% CI 0.39–0.94, p = 0.025) while the adjusted HR for age, admission TnI, diabetes, estimated GFR, admission hemoglobin and number of vessels diseased was 0.67 (95% CI 0.42–1.07, p = 0.094).

Outcome in the propensity matched cohort

In the propensity matched cohort, 22 (3.0%) patients died during ICCU stay (conventional PCI: n = 13, 3.6% vs. thrombus aspiration: n = 9, 2.5%; p = NS). Twenty-five (3.6%) patients were lost at follow-up (conventional PCI: n = 14, 4.0% vs. thrombus aspiration: n = 11, 3.1%; p = NS). The follow-up analysis was performed over 335 patients in the conventional PCI group and 342 in the thrombus aspiration group. At 30-day follow--up 6.3% of patients in the conventional PCI group died compared to 4.7% in the thrombus aspiration group. The unadjusted HR for 30-day mortality in the propensity matched cohort was 1.01 (95% CI 0.33–3.14, p = 0.985) (Fig. 1B). At 1-year, among the conventional PCI group 10.7% of patients died compared to 5.2% in the thrombus aspiration group. The 1-year unadjusted HR for mortality was 0.47 (95% CI 0.25–0.90, p = 0.022). The HR changed significantly and was no more significant after adjustment for differences in the use of GP IIb/IIIa inhibitors, lesion pre-dilatation and pre-procedural TIMI flow: 0.71 (95% CI 0.36–1.39, p = 0.322) (Table 3).

Discussion

The main finding of the present investigation is that adjunctive thrombus aspiration was not associated with any significant effect at 30-day follow-up, although 1-year mortality was significantly lower in the adjunctive thrombus aspiration PCI group than in the conventional PCI group. In a propensity matched cohort, adjunctive treatment with thrombus aspiration resulted in an unadjusted HR of 0.47 for 1-year mortality. However, this value was considerably altered by the concomitant administration of GP IIb/IIIa inhibitors.

These results need to be considered in the context of previous studies. Data either from large real world STEMI registries or randomized trials have not provided conclusive results so far. In a recent investigation [20] including 1,035 consecutive patients, manual aspiration, performed in the 18.3%, was associated with no difference in outcome at 30-day and 1-year, respectively. Similar results were reported by Kilic et al. [21]. On the contrary, in two large real world registries, thrombus aspiration was associated with long-term clinical benefit [22, 23]. Data from randomized trials are even more inconclusive and meta-analyses are not able to shed light on the real efficacy of thrombectomy. Some are showing mortality benefit [24, 25], whereas others have shown no significant effect [26, 27]. Moreover, in the recent TASTE trial [10], performed in a large sample size (7,244 STEMI patients), routine thrombus aspiration before PCI as compared with PCI alone did not reduce 30-day mortality among patients with STEMI. However, it may be supposed that the potential benefit of thrombus aspiration may not be captured at 30-day but may be expected to emerge during the first year after infarction. Indeed, it was not until 1-year follow-up that a significant difference in mortality emerged in TAPAS trial [28].

In this context, our study confirmed the lack of short-term benefit from adjunctive thrombus aspiration. The fact that mortality was not reduced with

thrombus aspiration within the first 30-days but only afterwards suggests that the initial myocardial insult may dictate the early prognosis (as a result of heart failure and arrhythmic complications) due to the large amount of myocardium at risk, as suggested by the almost double value of TnI peak in the thrombectomy group. A similar conclusion is also suggested by the fact that the propensity score matching selected a population with an higher 30-day overall mortality rate (5.5% vs. 2.4%) not affected by adjunctive thrombus aspiration. On the contrary, in this population, at high short-term risk, thrombus aspiration may improve the late survival mainly by preventing distal embolization and permanent microvessel damage. The role of microvessel salvage has been recently highlighted by Cuculi et al. [29] who demonstrated that positive changes of the coronary microcirculation in the first day after pPCI, as assessed using invasive index, are associated with myocardial salvage and better 6-month ejection fraction.

The role of GP IIb/IIIa inhibitors in determining the late survival benefit observed in our study among patients treated with thrombus aspiration should not be underestimated. The propensity matching selection was aimed at avoiding any pretreatment confounder [19] and was not performed in order to highlight the effects of different treatments. However, the multivariate analysis, which was performed in order to assess the impact of concomitant treatments on the long-term benefit, showed an important role of GP IIb/IIIa inhibitors. Both thrombus aspiration and GP IIb/IIIa inhibitors may have a role in preventing capillary block of the distal vascular bed due to embolization of thrombus and friable atheromatous debris which is thought to be ubiquitous after pPCI in STEMI. In the INFUSE AMI trial [11, 30], intralesional abciximab resulted in a modest reduction in infarct size, whereas infarct size was unaffected by thrombus aspiration and no significant differences in either ischemic or heart failure event rates were present with either therapy at 30-day follow-up. However, intralesional abciximab, thrombus aspiration, or both therapies before stent implantation were strongly associated with reduced 1-year rates of heart failure, stent thrombosis, and death compared with stenting alone. Consistently with these results, our study suggests a possible synergistic effect of the two treatments. Although caution is warranted given the retrospective nature of our study and the small INFUSE-AMI's sample size, these observations suggest that different synergistic mechanisms may underlie the potential clinical benefit of thrombus aspiration and GP IIb/IIIa inhibitors. In perspective, the micronet mesh-covered stent [31] is a promising third option in the prevention of distal embolization and a large-scale pivotal trial with this device has recently begun (NCT01869738).

Limitations of the study

Our study has several limitations. First, the study design was a non-randomized observational cohort study. We used rigorous adjustments for confounding factors, such as propensity score matching and multivariate analyses. While these statistical methods were used to eliminate differences in observed confounders that affected a patients' risk profile, they are unable to account for differences in unobserved confounders. A second limitation of our study is that we had no data on surrogate endpoints such as myocardial blush grade, ST-segment resolution, or infarct size. Such parameters could have reflected the assumed mode of action of aspiration catheters and could have supported the hypothesis that the observed mortality benefit was attributable to adjunctive thrombus aspiration. Finally, we did not take into account the possible modifications in the clinical treatment during the period of enrollment. The results from ongoing large-scale trials powered for mortality will determine whether thrombus aspiration before pPCI is indeed of clinical benefit (NCT01093404 and NCT01149044).

Conclusions

Adjunctive thrombus aspiration does not influence 30-day mortality while it is associated with 1-year survival benefit. This effect seems more evident in patients at higher short-term risk. GP IIb/IIIa inhibitors and thrombus aspiration may have an important synergistic role in leading to the long-term benefit. Our observations merit confirmation in currently enrolling large randomized trials powered for detecting a difference in mortality.

Conflict of interest: None declared

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