Heart Vessels (2010) 25:275–281
DOI 10.1007/s00380-009-1198-2

ORIGINAL ARTICLE

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Manual versus nonmanual thrombectomy in primary and rescue percutaneous coronary angioplasty

Received: May 17, 2009 / Accepted: August 14, 2009

Abstract Although many thrombectomy devices have been tested in ST-segment elevation acute myocardial infarction (STEMI), there are no comparative data on safety or effectiveness in thrombectomy or ST-segment resolution. This study compares manual versus nonmanual thrombectomy devices in patients undergoing primary or rescue percutaneous coronary intervention in a tertiary care center. We identified 232 consecutive patients with STEMI and time from symptom onset to emergency room contact of ≤12 h undergoing percutaneous coronary intervention with coronary thrombectomy devices. Primary end point was ST-segment resolution of ≥70%. Several angiographic, procedural and clinical secondary end points were also evaluated. The manual thrombectomy group included 110 patients and the nonmanual group 122 patients. Both groups were similar in their clinical characteristics. The primary end point occurred with similar frequency in patients treated with manual versus nonmanual thrombectomy (67.9% vs 60.0%, P = 0.216). No significant differences were found in the two groups with regard to procedural complications, angiographic reperfusion parameters, in-hospital major adverse cardiac events, or infarct size, whereas manual thrombectomy was associated with a better left ventricle ejection fraction at discharge. Furthermore, treatment with a manual thrombectomy device was associated with significantly shorter procedural times (69 min vs 95 min, $P < 0.001$) and lower procedural costs (2981 euros vs 7505 euros, $P < 0.001$). The use of manual thrombus-aspiration catheters appeared equivalent to nonmanual thrombectomy devices in the setting of primary or rescue percutaneous intervention in terms of clinical efficacy, and led to shorter procedures and cost savings.

Key words Acute myocardial infarction · Percutaneous transluminal coronary angioplasty · Thrombectomy

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Introduction

Acute myocardial infarction is mainly caused by a total or subtotal thrombotic occlusion of an epicardial coronary artery.[1] Percutaneous coronary intervention (PCI) with the use of stents, when logistically and technically feasible, has become the treatment of choice for patients with acute myocardial infarction.[2,3] However, the presence of extensive thrombosis may increase the risk of distal embolization during balloon inflation or during stent deployment. Indeed, distal embolization occurs in 15% of patients treated with primary PCI, and is associated with more extensive myocardial damage and a worse prognosis.[4]

To reduce the incidence of distal embolization during primary or rescue PCI, in recent years many thrombectomy devices have been tested and proved to be effective both for thrombus removal and improvement in myocardial perfusion. The first available thrombectomy devices actively removed the thrombus burden with mechanical systems, and most of them were technically complex and needed a long learning curve.[5–9] These facts probably led to controversial clinical results.[10,11] More recently, a series of easy-to-use manual thrombus-aspiration catheters.[12–15] showed thrombus burden reduction and myocardial reperfusion when compared with stand-alone primary PCI. Since only single-arm registries or controlled comparisons with standard PCI as control arm have been published to date, there is no comparative clinical study of thrombectomy devices.

The aim of this study was to compare manual thrombus aspiration catheters versus nonmanual thrombectomy devices in patients with ST-segment elevation acute myo-

cardial infarction (STEMI) treated at a high-volume tertiary care centre.

Patients and methods

We identified 232 consecutive patients with STEMI, treated between August 2000 and December 2007, undergoing primary or rescue PCI in whom a thrombectomy device was used. The only inclusion criterion was a time from symptom onset to first emergency room contact time of ≤12 h. Exclusion criteria were an epicardial Thrombolysis in Myocardial Infarction (TIMI) flow grade 3, without any evidence of intraluminal thrombus at baseline coronary angiography, an infarct-related artery <2 mm, or a culprit lesion on a saphenous vein graft.

Thrombectomy devices were defined as nonmanual if the thrombus removal was guaranteed by an electrically generated force and manual if it was obtained by an aspiration catheter connected to a syringe in which the vacuum was manually created. Thrombectomy was further defined as elective when the device was used up-front, or bail-out if used after predilatation with an undersized balloon leading to suboptimal result or thrombus persistence.

Between August 2000 and September 2005, the following nonmanual thrombectomy devices were used: Angiojet (Possis Medical, Minneapolis, MN, USA) in 57 cases, X-Sizer (ev-3, White Bear Lake, MN, USA) in 25 cases, and Rescue (Boston Scientific/Scimed, Mapple Groove, MN, USA) in 40 cases. Between August 2005 and December 2007, the following manual thrombectomy devices were used: Export (Medtronic, Minneapolis, MN, USA) in 100 cases and Diver CE (Invatec, Roncadelle, Italy) in 10 cases. All patients signed informed consent forms and the study complied with local ethics committee requirements.

Procedures

All percutaneous interventions were performed via the femoral approach. The culprit coronary was engaged with 6- or 8-F guide catheters according to the employed devices. After diagnostic angiography showing thrombosis in a vessel >2 mm, the patient received thrombectomy.

Since cardiac rhythm disturbances (high-grade atrioventricular block, asystole) requiring temporary pacing have been reported to occur in patients treated with Angiojet, the insertion of a temporary pacemaker catheter was carried out in almost all Angiojet patients.

After a 0.014-inch guidewire crossed the target lesion, the thrombectomy device was slowly advanced. Two to four passages in slow progress and retraction, across the lesion, with the device switched on were performed at the discretion of the operator or to achieve a satisfactory angiographic result. Subsequently, direct stenting was attempted in most cases unless not possible. In such cases, predilatation with an undersized balloon was recommended. All patients were treated with unfractioned heparin (initial weight adjusted intravenous bolus then further boluses administered with the aim of maintaining an activated clotting time of 250–300 s in patients treated with abciximab and >300 s in the remaining subjects) and with double antiplatelet therapy with aspirin and clopidogrel (loading dose of 300 mg followed by 75 mg/day) for at least 4 weeks. Unless contraindicated, abciximab (0.25 mg/kg bolus plus infusion of 0.125 μg/kg per minute for 12 h) was intravenously administered in all patients.

Procedural complications were considered as any coronary damage caused by the devices used for the PCI: abrupt closure, dissection, or perforation. Procedural time was computed from the patient's arrival at the catheterization laboratory up to his exit, and costs were automatically calculated by summing the prices of each interventional device used in the procedure. A dedicated database (Cardioplanet V.3.0, Ebit Aet, Genoa, Italy) collected all relevant information and data generated during a cath-lab procedure, including costs.

Angiographic analysis

Angiographic analysis was performed on the culprit lesion from the first and last angiogram acquired in the worst stenosis projection. Thrombus burden was assessed by using the TIMI thrombus score.[16] Stent thrombosis was defined as angiographic occlusion within 5 mm from the edges of a previously implanted stent. Angiographic reperfusion was evaluated by grading epicardial TIMI flow, TIMI myocardial perfusion grade, and measuring the corrected TIMI frame count.[17–20] Distal embolization was defined as the migration of a filling defect or the distal occlusion of the target vessel or one of its branches with diameter ≥1 mm at the end of or during the procedure. No reflow was defined as epicardial TIMI flow grade <2 not attributable to dissection, occlusive thrombosis, or epicardial spasm. The score suggested by Cohen et al.[21] was used for quantification of collateral flow. All angiographic analyses were performed off-line by independent operators unaware of used device.

Electrocardiographic analysis

Standard 12-lead electrocardiograms were acquired before PCI, defined as baseline, after 60 min from the procedure, after 6 h and 24 h in the first day, then every 24 h until discharge. The total sum of ST segment elevation was calculated at 60 ms from J in the leads V1–V6, I, and aVL for anterior STEMI and in the leads I, II, III, aVF, V5, and V6 for nonanterior STEMI. Myocardial reperfusion was evaluated by comparing the sums of the ST-segment elevation between the baseline with 60 min postprocedure ECG. All ECG analyses were performed off-line by independent operators unaware of angiographic data or used device.

Enzymatic infarct size and left ventricular function

Infarct size was estimated by measurement of enzyme activity by using creatine kinase mass band fraction (CK-MB).

The enzymatic activity was reported as μg/l, and assessed every 6 h in the first 48 h after admission. Peak release values from eight serial measurements up to 48 h after admission were reported.

All surviving patients underwent two-dimensional-transthoracic echocardiogram examination at hospital discharge. Left ventricular ejection fraction was calculated using the area–length method in the apical four-chamber view and the apical two-chamber view. All measures were given as mean value of two views.

End points

ST-segment resolution (STR) at 60 min was identified as the primary end point, since it has been proved to be the most clinically relevant yet practical predictor of myocardial reperfusion response and its absence is associated with a significantly greater myocardial damage, a lower recovery of left ventricular function, and a higher mortality.[22] Reperfusion was considered complete when STR was ≥70%, partial when it was between 50% and 69%, and absent if it was <50%.

Secondary end points were the following: procedural complications; procedural time and cost; postprocedural angiographic reperfusion parameters; procedural distal embolization; in-hospital major adverse cardiac events (including death, recurrent infarction, repeat urgent revascularization, and TIMI major bleedings); infarct size; left ventricular ejection fraction at discharge.

Statistical analysis

Categorical variables were reported as *n* (%) and were compared with chi-square or Fisher exact test, as appropriate. Continuous variables were reported as mean ± standard deviation or median (1st–3rd quartile), and were compared with Student *t*, Mann–Whitney *U*, or Wilcoxon tests, as appropriate. To account for potential differences between the manual and nonmanual thrombectomy groups, a multivariable binary logistic regression analysis with backward selection (0.20 cut-off for entry) was performed for the primary study end point (i.e., STR ≥70%), forcing as well a parsimonious propensity score as covariate in the final model, testing for its discrimination by means of a receiver operating characteristic curve.[23,24] The following variables were thus included in the propensity score: age, gender, hypertension, prior myocardial infarction, anterior myocardial infarction, shock, door to balloon time, pain onset to balloon time, left anterior descending as infarct-related artery, in-stent thrombosis as culprit lesion, number of diseased vessels, bail-out indication for thrombectomy device, corrected TIMI frame count at baseline, TIMI myocardial perfusion grade at baseline, and Rentrop collateral grade at baseline. Results were reported as odds ratios (OR) with associated 95% confidence intervals (CI). A *P* value of less than 0.05 was considered to be statistically significant, and all reported *P* values are two-sided. Statistical analysis was performed using SPSS version 11.5 (SPSS, Chicago, IL, USA).

Results

During the enrollment period, 1230 patients with STEMI were admitted to our institution. A total of 232 out of 575 patients with STEMI undergoing either primary or rescue PCI were analyzed. The manual thrombectomy group included 110 patients and the nonmanual thrombectomy group 122 subjects. Principal clinical characteristics were similar in the two groups, except for a longer door to balloon time in the nonmanual group, a feature likely due to the longer procedural time needed in the nonmanual group for device preparation (nearly 90 min versus 65 min in the manual thrombectomy group) (Table 1).

Unadjusted analysis showed that the primary end point (STR ≥70%) occurred with similar frequency in both groups ($P = 0.216$) (Fig. 1). Even at propensity-adjusted multivariable analysis (area under the curve for the propensity score = 0.76 [95% CI 0.70–0.82]), the two types of thrombectomy device led to similar rates of STR ≥70%: OR = 0.81 (95% CI 0.46–1.449, $P = 0.474$) for manual versus nonmanual thrombectomy. Similar results were obtained in a sensitivity analysis separating ST resolution into three classes (<50%, 50%–69%, ≥70%) and based on multinomial logistic regression ($P = 0.473$).

Procedural and angiographic results

Procedural and angiographic data are reported in Tables 2 and 3. The left anterior descending artery was more commonly involved in the nonmanual group than in the manual group ($P = 0.037$), whereas elective thrombectomy was more frequent in the manual group ($P < 0.001$), a finding

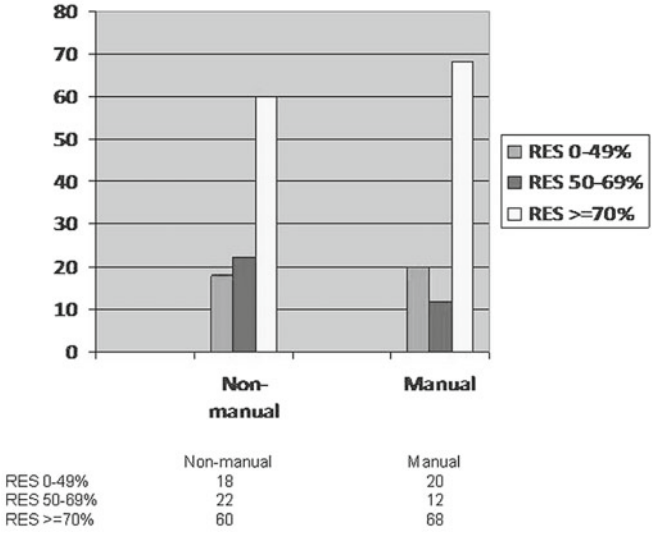

Fig. 1. ST segment resolution between manual and nonmanual thrombectomy groups

Table 1. Baseline patient characteristics

	Manual thrombectomy (n = 110)	Nonmanual thrombectomy (n = 122)	P value
Age (years)	60.2 ± 12.7	59.4 ± 12.4	0.607
Male gender	95 (86.4%)	104 (85.2%)	0.808
Family history of coronary artery disease	28 (25.5%)	31 (25.4%)	0.994
Smoking history	66 (60.0%)	75 (61.5%)	0.818
Arterial hypertension	41 (37.3%)	58 (47.5%)	0.114
Dyslipidemia	39 (35.5%)	58 (47.5%)	0.062
Diabetes mellitus	22 (20.0%)	30 (24.6%)	0.403
Insulin-dependent diabetes mellitus	10 (9.1%)	7 (5.7%)	0.328
Previous stroke	3 (2.7%)	6 (4.9%)	0.388
Peripheral artery disease	8 (7.3%)	8 (6.6%)	0.830
Previous myocardial infarction	14 (12.7%)	21 (17.2%)	0.340
Previous percutaneous coronary intervention	21 (19.1%)	20 (16.4%)	0.591
Previous coronary artery bypass grafting	0	3 (2.5%)	0.249
Preinfarction angina	17 (15.5%)	27 (22.3%)	0.185
Infarct location			0.043
Anterior	48 (43.6%)	70 (57.4%)	
Nonanterior	62 (56.4%)	52 (42.6%)	
Rescue angioplasty	25 (22.7%)	33 (27.0%)	0.448
Number of ECG derivations with ST elevation	4.4 ± 1.9	4.8 ± 1.9	0.113
Killip class			0.214
I	71 (64.5%)	81 (66.4%)	
II	26 (23.6%)	23 (18.9%)	
III	8 (7.3%)	5 (4.1%)	
IV	5 (4.5%)	13 (10.7%)	
Admission heart rate (beats/min)	75.4 ± 21.5	77.4 ± 21.9	0.490
Admission systolic blood pressure (mmHg)	125.5 ± 23.6	126.1 ± 26.8	0.869
Admission diastolic blood pressure (mmHg)	77.7 ± 13.2	77.1 ± 14.1	0.712
Patients transferred from other hospitals	30 (27.2%)	38 (31.1%)	0.517
Time from symptom onset to first medical contact (min)	101.5 (5.15–180)	70 (46.5–132)	0.094
Door to balloon time (min)	120 (82.8–225)	140 (100–220.5)	0.047
Total ischemic time (min)	242.5 (165.8–390.5)	246 (169–351)	0.824

Values are reported as n (%), mean ± standard deviation or median (1st–3rd quartile)

Table 2. Procedural characteristics

	Manual thrombectomy (n = 110)	Nonmanual thrombectomy (n = 122)	P value
Multivessel disease	55 (50%)	48 (39.3%)	0.103
Infarct-related artery			0.037
Left anterior descending	42 (38.2%)	67 (54.9%)	
Left circumflex	19 (17.3%)	14 (11.5%)	
Right coronary artery	49 (44.5%)	41 (33.6%)	
Indication for thrombectomy			<0.001
Elective	99 (90%)	85 (69.7%)	
Bail-out	11 (10%)	37 (30.3%)	
In-stent thrombosis	17 (15.5%)	13 (10.7%)	0.277
Balloon-only PTCA	12 (10.9%)	17 (13.9%)	0.487
Stenting	97 (88.2%)	98 (80.3%)	0.103
Direct stenting	61 (55.%)	55 (45.1%)	0.115
Drug-eluting stenting	17 (15.5%)	4 (3.3%)	0.001
No. of implanted stents >1	10 (9.1%)	7 (5.7%)	0.090
Maximum balloon diameter (mm)	3.16 ± 0.47	3.23 ± 0.68	0.337
Maximum balloon length (mm)	24.5 ± 9.6	18.9 ± 8.5	<0.001
Maximum balloon pressure (atm)	16.2 ± 3.5	13.9 ± 3.4	<0.001
Intra-aortic balloon pump	11 (10.0%)	11 (9.0%)	0.798
Temporary pacemaker	3 (2.7%)	49 (40.2%)	<0.001
Intravenous glycoprotein IIb/IIIa inhibitors	99 (90.8%)	117 (95.9%)	0.118
Procedural complications	2 (1.8%)	7 (5.7%)	0.123
Procedural time (min)	69 ± 21	95 ± 30	<0.001
Procedural cost (euros)	2981 ± 1372	7505 ± 2472	<0.001

Values are reported as n (%), mean ± standard deviation
PTCA, percutaneous transluminal coronary angioplasty

Table 3. Angiographic analysis

	Manual thrombectomy (n = 110)	Nonmanual thrombectomy (n = 122)	P value
Preprocedural analysis			
Collateral grade 0–1	100 (90.9%)	111 (90.9%)	0.984
Thrombus score	4.4 ± 1.2	4.5 ± 0.9	0.875
TIMI epicardial flow 0–1	85 (78.2%)	106 (86.9%)	0.055
TIMI myocardial perfusion grade 0–1	97 (88.2%)	110 (90.2%)	0.379
Corrected TIMI frame count	82 ± 33	86 ± 27	0.292
Reference vessel diameter (mm)	3.06 ± 0.59	3.02 ± 0.48	0.519
Minimum lumen diameter (mm)	0.15 ± 0.31	0.18 ± 0.46	0.521
Diameter stenosis (%)	94.9 ± 10.4	95.6 ± 9.2	0.613
Post-thrombectomy analysis			
Thrombus score	1.9 ± 1.4	1.6 ± 1.1	0.078
TIMI epicardial flow 0–1	27 (24.4%)	33 (27.1%)	0.664
Corrected TIMI frame count	34 ± 29	35 ± 24	0.119
TIMI myocardial perfusion grade 0–1	47 (42.7%)	59 (48.4%)	0.389
Lesion length (mm)	16.9 ± 7.6	14.7 ± 7.1	0.021
Postprocedural analysis			
Thrombus score	0.3 ± 0.8	0.2 ± 0.6	0.641
TIMI epicardial flow 0–1	8 (7.2%)	11 (9.1%)	0.629
Corrected TIMI frame count	21 ± 20	27 ± 19	0.092
TIMI myocardial perfusion grade 0–1	32 (29.1%)	37 (30.3%)	0.837
Distal embolization	15 (13.6%)	16 (13.1%)	0.907
No reflow	27 (24.5%)	35 (28.7%)	0.476
Reference vessel diameter (mm)	3.18 ± 0.54	3.18 ± 0.51	0.990
Minimum lumen diameter (mm)	2.77 ± 0.71	2.81 ± 0.65	0.648
Diameter stenosis (%)	11.2 ± 14.8	10.5 ± 12.3	0.712

Values are reported as n (%), mean ± standard deviation
TIMI, Thrombolysis in Myocardial Infarction

Table 4. Secondary end points

	Manual thrombectomy (n = 110)	Nonmanual thrombectomy (n = 122)	P value
Peak creatine kinase-mass (ng/ml)	307.8 ± 263.4	372 ± 289.3	0.093
Major adverse cardiac events	14 (12.7%)	15 (12.3%)	0.966
Death	11 (10%)	10 (8.2%)	0.633
Recurrent myocardial infarction	1 (0.9%)	2 (1.6%)	1.0
Repeat urgent revascularization	1 (0.9%)	0	0.474
Stroke	0	1 (0.8%)	1.0
Major bleeding	1 (0.9%)	2 (1.6%)	0.623
Left ventricular ejection fraction at discharge as measured by transthoracic echocardiography (%)	48.1 ± 9.2	45.1 ± 9.1	0.018

Values are reported as n (%), mean ± standard deviation

which may reflect a different approach to thrombotic lesions in the two groups. Culprit lesion length was longer in the manual group than in the nonmanual group (P = 0.021), leading to a longer balloon length in the manual thrombectomy group (P < 0.001).

There was a trend toward fewer procedural complications in the manual group: one patient in the manual group had guidewire-induced perforation and another had transient abrupt closure of the left main. In the nonmanual group, one patient had cardiac perforation due to right ventricular pacing, one had a large perforation of left anterior descending artery requiring sealing with two covered stents, one had abrupt closure of left anterior descending artery, two had a coronary hematoma for a large dissection treated with two bare metal stents, and two had thrombectomy device-induced coronary perforation.

Treatment with a manual thrombectomy device was associated with significantly shorter procedural times (69 min vs 95 min, P < 0.001) and lower procedural costs (2981 euros vs 7505 euros, P < 0.001).

Postprocedural epicardial TIMI 3 flow occurred with similar frequency in both groups (86 patients [78.1%] in the manual group versus 88 [72.0%] in the nonmanual group, P = 0.288), similarly to postprocedural myocardial blush grade 3 (62 [56.3%] vs 57 [43.1%], P = 0.142). Distal embolization rate was not significantly different in the groups, occurring indeed before device advancement in three patients in both groups.

We found no significant differences between groups in terms of infarct size, major adverse cardiac events, stroke, or major bleedings (Table 4). Specifically, all deaths occurred out of the catheterization laboratory and they all

had a cardiac cause, and all recurrent myocardial infarctions were non-Q. Manual thrombectomy devices were associated with higher discharge left ventricular ejection fraction as measured by transthoracic echocardiography (P = 0.018).

When a comparison was carried out between Angiojet and Export catheters, the results were similar to those obtained in the main analysis with regard to both the primary end point (67% for Export versus 63% for Angiojet, P = 0.322) and secondary end points. However, there was a trend toward fewer major adverse cardiac events in the Export group (12% vs 22.8% for Angiojet, P = 0.161).

Discussion

The present single-center retrospective study was the first to compare two different thrombectomy techniques: the manual and the nonmanual, in unselected patients with large coronary thrombus burden undergoing PCI for STEMI. No significant differences were found in the two groups with regard to several end points, i.e., myocardial reperfusion assessed with STR, procedural complications, angiographic reperfusion parameters, in-hospital major adverse cardiac events, and infarct size. Patients undergoing nonmanual thrombectomy had a lower left ventricular ejection fraction at discharge. This result can in part be explained with the higher frequency of anterior STEMI in the nonmanual group, probably due to the fact that in the early phase the mechanical devices were used only on nontortuous vessels such as the left anterior descending artery.

A recent meta-analysis showed that among patients with STEMI treated with PCI the use of adjunctive manual thrombectomy devices was associated with better epicardial and myocardial perfusion, less distal embolization, and significant reduction in 30-day mortality.[25] In our study, in-hospital mortality was higher (10% in the manual group and 8.2% in the mechanical group) than that reported by other similar studies. Two explanations may be proposed: first, we included unselected patients with cardiogenic shock, pulmonary edema, or in-stent thrombosis and secondly, in both groups the door-to-balloon time was over 90 min, as recommended in ACC/AHA guidelines,[26] likely due to the prolonged time required to transfer the patients from other remote hospitals in the catchment area.

Procedural time was significantly longer in the nonmanual thrombectomy device group compared to the manual group, with a difference of 26 min. This delay resulted in significant lengthening of door-to-balloon time. This might lead to a detrimental effect since Cannon reported that the door-to-balloon time over 120 min is related to a higher risk of in-hospital mortality, ranging from 41% to 62%.[27] In addition, procedural costs with an active device were €4524 higher, due almost exclusively to the device price.

Some limitations of the present study should be noted: (1) enrollment periods for nonmanual and manual devices were quite different, with an increasing use of adjunctive thrombectomy in patient with STEMI in recent years with user-friendly manual devices; (2) in the nonmanual thrombectomy group, devices were used with different techniques to dissolve the coronary thrombus. In conclusion, in our retrospective study in patients with large coronary thrombus burden undergoing primary or rescue PCI for STEMI, the use of manual thrombus-aspiration catheters appeared equivalent to nonmanual thrombectomy devices in terms of clinical efficacy, and led to shorter procedures and cost savings.

Acknowledgment We acknowledge all the catheterization laboratory staff of San Carlo Hospital, Potenza, Italy.

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