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Rheolytic Thrombectomy Does Not Prevent Slow-, No-Reflow During Percutaneous Coronary Intervention in Acute Myocardial Infarction

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Abstract. Percutaneous coronary intervention (PCI) in acute myocardial infarction (MI) has been associated with a high incidence of slow-, no-reflow. The slow-, no-reflow phenomenon is known to complicate both thrombolytic therapy and PCI. Removing intracoronary thrombus before PCI in acute MI patients may reduce the incidence of slow-, no-reflow phenomena. We studied the procedural outcome of 21 patients who underwent rheolytic thrombectomy using Possis® rheolytic thrombectomy catheter in the setting of acute MI as compared to twenty-eight patients who underwent PCI in the setting of acute MI using other modalities (PTCA with or without stenting) without thrombectomy. The study included 49 consecutive patients with 21 patients in the rheolytic thrombectomy group, and 28 patients in the no-rheolytic thrombectomy group. There was no significant difference between the two groups as regards to gender, age, and prevalence of coronary artery risk factors. The left ventricular ejection fraction was 44.7 ± 12 in the rheolytic thrombectomy group, and 37.6 ± 10.8 in the no-rheolytic thrombectomy group ($p = 0.08$). Thirty eight percent of the patients in the rheolytic thrombectomy group experienced slow flow, no-reflow, while 28.6% of the patients in the no-rheolytic thrombectomy group experienced slow flow, no-reflow ($p = 0.5$). In this matched series of patients with acute MI undergoing PCI, rheolytic thrombectomy by the Possis rheolytic thrombectomy catheter device does not appear to reduce the risk of slow flow, no-reflow, or in-hospital death, compared to standard PTCA and stenting of the infarct-related artery.

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Introduction

Coronary reperfusion by the use of thrombolysis and/or angioplasty has been established as an essential therapy of acute myocardial infarction (MI). Reperfusion of the epicardial coronary arteries does not necessarily guarantee adequate myocardial tissue reflow or salvage in patients with acute MI [1,9,19]. Some studies [12] have documented that scintigraphic evidence of no-reflow may occur suggesting that micro vascular injury may be angiographically inapparent in some patients. No-reflow manifests as acute reduction in coronary flow (TIMI grade 0–1) in the absence of dissection, thrombus, or high-grade residual stenosis at the original target lesion. Potential etiologies may include vasospasm, free radical induced endothelial dysfunction, macro- and micro debris/thrombus distal embolization, capillary plugging by platelet aggregates and neutrophils, and cellular edema with intramural hemorrhage [10,11]. We and others [3,18] have previously shown that thrombus containing lesions, detected by angioscopy, were associated with a very high incidence of both early and late adverse events. This no-reflow phenomenon is associated with myocardial damage, progressive left ventricular dilation and a high frequency of post-MI complications including pericardial effusion, cardiac tamponade, and congestive heart failure [5,7]. No-reflow is uncommon (2%) after elective catheter intervention in native coronaries, but it has been shown to complicate PCI of thrombus containing lesions such as in patients with acute coronary syndromes, acute MI (11–50%) [6,14,15,20] or degenerated saphenous vein grafts. This suggests that direct thrombus extraction before definitive PCI may reduce the risk of slow flow, no-reflow. The Possis® rheolytic thrombectomy (Possis Medical Inc, Minneapolis, Minnesota) is a catheter-based thrombectomy system that employs the concept of rheolytic thrombectomy to macerate and aspirate thrombi [16]. The aims of this study were to describe the safety of coronary thromb-

Table 1. Patient characteristics (Mean ± SD)

	Rheolytic thrombectomy (n = 21)	No-rheolytic thrombectomy (n = 28)
Age (years)	54.4 ± 13.1	55.5 ± 12.8
Gender (male/female)	14/7	22/6
Risk factors		
Hypertension	14 (66%)	18 (64%)
Current smoking	11 (52%)	13 (46%)
Diabetes mellitus	4 (19%)	8 (29%)
Hyperlipidemia	14 (66%)	13 (46%)
AMI location		
Anterior	11 (50%)	15 (54%)
Inferior	10 (48%)	12 (43%)
Lateral	1 (2%)	1 (3%)
LVEF* (%)	44.7 ± 12	37.6 ± 10.8 (p = 0.08)
Time to intervention (hours)	13.2 ± 9.4	6.5 ± 5.9 (p = 0.03)
Primary intervention	9 (42.8%)	14 (50%)
Rescue intervention	12 (57.2%)	14 (50%)
Cardiogenic shock	2 (9%)	3 (11%)

*LVEF = left ventricular ejection fraction.

ectomy by the rheolytic thrombectomy Possis system and evaluate the potential of this modality for preventing the slow-, no-reflow in patients with acute myocardial infarction undergoing PCI.

Material and Methods

Patient Population

We performed a retrospective analysis of the Memorial Hermann Heart Center interventional Cardiology database. We identified 21 AMI patients in whom rheolytic thrombectomy performed followed by PTCA or stenting was used. These were compared to 28 AMI patients treated by PCI without the use of rheolytic thrombectomy or intracoronary adenosine (previously proven to reduce the risk of slow-, no-reflow).

Rheolytic Thrombectomy

Possis rheolytic thrombectomy was performed using standard percutaneous techniques via the femoral artery. (Using 8 French guiding catheters). Temporary pacemakers were used in 52% of cases. In all cases, 0.014'' extra-support wires were used to deliver the thrombectomy catheter to the target lesion. In 12 patients, predilatation was performed to allow for delivery of the rheolytic thrombectomy distal to the target site. The rheolytic thrombectomy catheter was then delivered to the thrombus-containing lesion, passed through the obstruction, and activated, with slow pull back through the thrombus. If necessary, several passes were made to remove all visible thrombus.

PTCA Coronary Stent Implantation

PTCA and intracoronary stent implantation were performed using standard percutaneous techniques via the femoral artery. After stent implantation, angiographic optimization was usually performed by using high-pressure balloon dilatation to achieve a good angiographic result, with <20% residual stenosis by visual estimate. Ultrasound-guiding coronary stenting was not performed in the majority of cases. Each operator relied on his own judgment or on other objective measurements, such as online QCA, to assess stent expansion. All patients received pre-procedural oral aspirin and intravenous heparin to achieve an activated clotting time between 200 and 350 seconds. GP IIb/IIIb inhibitors and intra aortic balloon pump were used at the discretion of the operator. On completion of the procedure, the patients were moved to a monitored unit, and the arterial sheath was removed in the usual manner. During the procedure, patients' hemodynamics, ECG and symptoms were monitored.

Definitions

Slow Flow: TIMI flow = 2, not explained by dissection, thrombus, spasm, or severe residual stenosis at the original target lesion.

No-reflow: an acute and substantial impairment of antegrade blood flow (≤TIMI 1 flow), which was unrelated to recognizable anatomic vessel obstruction (e.g., dissection, spasm, thrombus, or residual stenosis >50%) at the original lesion site or distal to the lesion.

Acute myocardial infarction: chest pain lasting >30 minutes and evolving characteristic electrocardiogram abnormalities that included ST segment elevations of >1 mm in at least two contiguous leads, and an increase in serum creatine kinase levels to more than twice the upper limit of normal.

Primary intervention: percutaneous intervention as a primary reperfusion without previous thrombolytic therapy.

Rescue intervention: percutaneous intervention is performed when thrombolysis has failed to reperfuse the infarct related artery.

Statistical Analysis

Categoric variables are presented as mean ± SD. Differences between groups were evaluated by chi-square analysis or Fisher exact test for categoric variables and Student t test for continuous variables. Probability values <0.05 (2-tailed) were considered significant.

Results

Patient Characteristics

Table 1 summarizes patient characteristics. The study included 21 consecutive acute MI patients in the rheolytic thrombectomy group, and 28 consecutive patients in the no rheolytic thrombectomy group. The majority of these patients were men. There was no significant difference between the two groups as to gender, mean age, prevalence of coronary artery risk factors. The location of the MI (anterior, inferior) was

Table 2. Angiographic characteristics

	Rheolytic thrombectomy (n = 21)	No-rheolytic thrombectomy (n = 28)	p value
Lesion characteristics			
% Stenosis	82.1 ± 29.3	85.2 ± 10.8	0.4
Diameter (mm)	3.7 ± 0.52	3.2 ± 0.37	0.2
Length (mm)	12.2 ± 5.6	11.7 ± 5.1	0.3
Culprit artery			0.3
LAD*	11 (52.3%)	15 (53.5%)	
RCA†	3 (14.3%)	8 (28.5%)	
LCX‡	7 (33.3%)	5 (18%)	
Lesion site			0.05
Ostial	1 (4.7%)	1 (3.5%)	
Proximal	12 (57%)	8 (28.5%)	
Middle	8 (38%)	16 (57%)	
Distal	0 (0%)	3 (11%)	
Vein Grafts	5 (24%)	6 (21.5%)	
≥2 vessel disease	10 (47.6%)	9 (32%)	0.3
Baseline TIMI flow	1.28 ± 1.35	1.71 ± 1.01	0.5

*LAD = left anterior descending artery; †RCA = right coronary artery; ‡LCX = left circumflex artery.

similar in the groups as well as the procedure type (primary versus rescue). The left ventricular ejection fraction was 44.7 ± 12 in the rheolytic thrombectomy group, and 37.6 ± 10.8 in the no rheolytic thrombectomy group (p = 0.08).

Procedural Outcome

Table 2 summarizes angiographic data. There were no significant differences in lesion location between groups. The mean percent stenosis was 82.1 ± 29.3% in the rheolytic thrombectomy group, and 85.2 ± 10.8 in the no rheolytic thrombectomy group (p = 0.4). The rheolytic thrombectomy group has a higher frequency of multivessel disease (47.6% versus 32%; p = 0.3). Procedural characteristics are shown in Table 3. Glycoprotein IIb/IIIa inhibitors were used in 20 patients (95%) in the rheolytic thrombectomy group, and in 9 patients (32%) in the no rheolytic thrombectomy group (p = 0.0001). The use of IABP was deemed necessary in 2 patients in the rheolytic thrombectomy group (9%), while it was used in 8 patients (29%) in the no rheolytic thrombectomy group (p = 0.15).

Baseline TIMI flow was 1.28 ± 1.35 in the rheolytic thrombectomy group, and 1.71 ± 1.01 in the no rheolytic thrombectomy group (p = 0.5). Complete resolution of thrombus, evident angiographically, was seen in 14 patients in the rheolytic thrombectomy group (66.6%). The mean numbers of stents/patient deployed were 0.95 ± 0.56 in the rheolytic thrombectomy group and 1.08 ± 0.29 in the other group. No statistically significant difference was observed in the final TIMI flow. Perforation occurred in one patient in the rheolytic thrombectomy group (4.7%), which did not require emergency surgery [managed by perfusion balloon and discontinuation of IIb/IIIa inhibitors]. The incidence of slow, no-reflow was: 38% in the rheolytic thrombectomy and 28.6% in the no rheolytic thrombectomy groups, respectively (p = 0.5).

Clinical Outcome

See Table 3. Cardiac arrest during the procedure occurred in 1 patient (4%) in the rheolytic thrombectomy group (slow flow, no-reflow was not observed in this patient), compared to 3 (11%) in the no rheolytic thrombectomy group, (p = 0.6). The culprit arteries in the no rheolytic thrombectomy patients who had a cardiac arrest were the left anterior descending in all 3 patients, while it was the proximal right coronary artery in the one rheolytic thrombectomy patient. Two patients (7%) in the no rheolytic thrombectomy group died during hospitalization compared to 2 patients in the rheolytic thrombectomy group (9%) (p = 0.6).

The two reported deaths in the rheolytic thrombectomy group were related to multiple organ failure syndrome in one patient, while the other patient developed post procedure (24 hours) cardiac arrest (bradycardia and asystole). Autopsy was done in the latter case, and revealed patent culprit artery, and extensive anterior wall necrosis.

Re-MI occurred, and hence re-intervention was required in one patient in the rheolytic thrombectomy group (4.7%) due to subacute stent thrombosis occurring 24 hours following the procedure. The patient subsequently developed cardiac arrest 24 hours following the re-intervention. None of the patients is the no-rheolytic thrombectomy group developed subacute stent thrombosis.

Discussion

The major finding of our study is that rheolytic thrombectomy using Possis rheolytic thrombectomy does not reduce the incidence of slow, no-reflow in the setting of percutaneous intervention for Acute myocardial infarction. The reported incidence of slow, no-reflow after percutaneous coronary intervention ranges from 0.6–42%, depending on the definition used and the clinical setting [13]. Previous studies showed that

Table 3. Procedural characteristics in the two study groups

	Rheolytic thrombectomy (n = 21)	No-rheolytic thrombectomy (n = 28)	p value
No-reflow	8 (38%)	8 (28.6%)	0.5
Final TIMI flow	2.76 ± 0.52	2.81 ± 0.63	0.5
Residual stenosis	6.7 ± 11.2	6.2 ± 8.1	0.7
Type of			0.6
PTCA	5 (24%)	5 (18%)	
PTCA + stent	16 (74%)	23 (82%)	
Stents/lesion	0.95 ± 0.59	1.08 ± 0.29	0.6
Total fluoroscopy time (min)	30.15 ± 8.8	21.01 ± 11.3	0.004
IIb/IIIa inhibitor	20 (95%)	9 (32%)	0.000
IABP*	2 (9%)	8 (29%)	0.5
Intra-procedural cardiac arrest	1 (4%)	3 (11%)	0.6
In-hospital death	2 (9%)	2 (7%)	0.6

*LABP = intra aortic balloon pump.

predictors of no-reflow include: thrombus, emergency procedure, prior MI, and prior CABG. Slow flow was related to lesion length, recent unstable angina, and the use of beta-blockers [17].

The available evidence that distal embolization may play a role in the genesis of this phenomenon, and the fact that percutaneous intervention techniques in acute myocardial infarction are targeted towards restoring flow in the culprit artery, rather than extracting thrombus in the target lesion (mechanically compressing the thrombus in PTCA and/or stenting versus removing the thrombus mechanically) may be a potential ground for possible benefit of direct thrombus extraction techniques in reducing the incidence of slow flow, no-reflow.

The use of TEC® (Transluminal Extraction Catheter) atherectomy (InterVentional Technologies, San Diego, CA) in the setting of acute myocardial infarction has been associated with disappointing results, with a reported mortality rate of 5%, emergency bypass surgery in 4% and need for blood transfusion in 18% (8). In addition, no-reflow complicating this procedure (19%) is usually irreversible with persistent flow impairment. This study was designed to examine the possible role of the rheolytic thrombectomy device (Possis) in a patient population in whom the incidence of no-reflow is higher (acute MI, thrombus containing lesion). The rheolytic thrombectomy is a catheter-based thrombectomy system that employs the concept of rheolytic thrombectomy to macerate and aspirate thrombi [21].

The data showed that despite the fact that rheolytic thrombectomy device was used successfully to extract thrombus in patients with acute myocardial infarction, the incidence of slow, no-reflow in this patient population was not significantly reduced in comparison to the no rheolytic thrombectomy group. There are scanty data, to date, on the benefit of rheolytic thrombectomy in reducing the incidence of no-reflow in the setting of acute MI. Data from the PAMI (Primary Angioplasty in Myocardial Infarction) stent trial [4] show that stenting in the setting of acute MI may result in a decline in coronary flow, which may presumably be due to distal embolization of thrombus and/or plaque contents elicited by high pressure deployment of the stent. Mechanical extraction of thrombus, prior to stent deployment, would presumably reduce the extent of distal embolization caused by stent deployment. The mechanisms that interact to cause no-reflow remain speculative. One mechanism, which is widely proposed, is distal embolization of thrombi or other debris. Other mechanisms include oxygen free radical- mediated endothelial injury, capillary plugging by platelet aggregates and neutrophils, and intracellular/interstitial edema with intramural hemorrhage [2].

The failure to show any statistically significant benefit of rheolytic thrombectomy in reducing the incidence of slow, no-reflow in this study population may be due to the fact that in 12 patients (57%) predilatation was performed. This might have been a factor contributing to distal embolization and in turn no-reflow. In this study 43% of patients had total occlusion of the culprit vessel (19% were vein grafts and 24% were native coronary arteries). The presence of a totally occluded artery makes it almost impossible to appreciate the intracoronary thrombus angiographically. This might account for the relatively frequent need to predilate culprit vessels before delivery of the rheolytic thrombectomy. The use of Glycoprotein IIb/IIIa antagonists has been shown to decrease procedural complication rates in patients with acute coronary syndromes undergoing balloon angioplasty or stenting. The majority of patients in the rheolytic thrombectomy group (95%) received IIb/IIIa antagonists on elective basis, compared to a smaller percentage (32%) in the no rheolytic thrombectomy group. This observation is largely related to the growing use of these agents in the last 2 years, during which time most of the rheolytic thrombectomy cases were performed in our catheterization laboratory. Despite their use in 95% of the cases, no-reflow was not reduced in the rheolytic thrombectomy group. No definitive conclusions can be drawn from this study due to the relatively small number of patients. The limitations of the study include the retrospective non-randomized nature of the analysis, and the relatively small sample size.

Conclusion

Percutaneous coronary interventions in acute myocardial infarction are associated with high incidence of slow, no-reflow with negative prognostic implications.

Moreover, the presence of an angiographically evident thrombus in the culprit vessel clearly predicts a higher rate of complications. Available pharmacological and technical interventions have demonstrated modest reductions in the incidence of this phenomenon during coronary interventions. This study suggests that, despite adequate thrombus resolution following rheolytic thrombectomy in a considerable number of patients, the incidence of slow, no-reflow showed no statistically significant improvement when compared to other percutaneous modalities in acute MI. Larger scale studies are needed to evaluate the effect of rheolytic thrombectomy on the incidence of slow flow, no-reflow in the setting of acute myocardial infarction.

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