

# No-reflow in Patients with ST Elevation Acute Anterior Myocardial Infarction

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**Objective:** The aim of this study was to assess the prevalence of no-reflow after coronary recanalization in anterior acute myocardial infarction with ST-T segment elevation.

**Methods:** In a cohort of 80 consecutive patients with anterior acute myocardial infarction who were treated with primary angioplasty, we analysed angiographic and clinical characteristic of patients and the prevalence of pre-infarction angina. Successful angioplasty was defined as Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow and residual stenosis less than 50% after the angioplasty procedure. The phenomenon of no-reflow is defined as inadequate myocardial perfusion through a given segment of the coronary circulation without angiographic evidence of mechanical vessel obstruction.

**Results:** Successful angioplasty was achieved in 63 patients (78.75%). Mean age and gender were not different from patients with and without TIMI grade 3 flow. The no-reflow phenomenon was more frequently observed in patients with diabetes (29.41% vs 4.76%,  $p = 0.0001$ ). TIMI grade III flow was higher in the patients with pre-infarction angina (42.86% vs 11.76%  $p = 0.02$ ).

**Conclusion:** The no reflow phenomenon in patients with anterior acute myocardial infarction treated with primary angioplasty is present in 21.25% of patients. Pre-infarction angina is associated with preservation of the microvasculature, reflected by reduced no-reflow.

**Keywords:** primary coronary angioplasty, myocardial infarction, TIMI grade flow

## Introduction

In the acute phase of myocardial infarction, myocardial salvage can be achieved by reopening the infarct-related artery and re-establishing tissue-level perfusion within the jeopardised myocardium. Myocardial reperfusion limits infarct size and preserves left ventricular function, improving early and late outcome after acute myocardial infarction [1,2]. However, despite epicardial artery patency, myocardial tissue perfusion may be inadequate. This lack of intramyocardial reflow despite restoration of epicardial artery patency has been named the 'no-flow phenomenon' and is mainly related to extensive microcirculatory damage [3]. Temporary occlusion of the artery, a prerequisite condition for no-reflow, may be produced in the experimental setting or occur during reperfusion of an infarct-related artery or following percutaneous coronary intervention. No re-flow implies abnormal tissue perfusion and persistent no-reflow is associated with higher clinical complication rates [4].

We evaluated the retrospective the coronarographies of 80 patients with acute anterior myocardial infarction who were treated with primary angioplasty. The aim of this study was to assess the prevalence of no-reflow after coronary recanalization of infarct-related artery and to assess whether pre-infarction angina is associated with decreased no-reflow after successful angioplasty.

## Methods

We studied patients admitted with acute anterior myocardial infarction less than 12 h after symptom onset or in first 24 hours if there is ongoing ischaemia. The diagnosis of acute myocardial infarction was based on typical chest pain lasting more than 30 min, resistant to sublingual or

intravenous nitrates, and associated with ST segment elevation  $\geq 0.2$  mV in at least two contiguous leads. The diagnosis was confirmed in every case by elevation of creatine kinase to at least twice the normal value. The patients have not signed informed consent.

All the patients underwent coronary angiography on admission. Flow in the infarct-related artery were graded using the Thrombolysis In Myocardial Infarction (TIMI). Emergency PTCA was attempted when the stenosis were  $>70\%$  there and when flow in the infarct-related artery was  $<$  TIMI 3. All patients received during procedures, treatment with heparin 100U/Kg IV bolus before the procedure, then the one bolus of 2500U at every 30 minutes if the procedure has been extended. In addition, all patients received treatment with aspirin and clopidogrel 75-125mg/zi loading dose 600mg/zi then 75mg/zi daily dose for 9-12 months. Successful angioplasty was defined as Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow and residual stenosis less than 50% after the angioplasty procedure.

In a cohort of 80 consecutive patients with anterior acute myocardial infarction who were treated with primary angioplasty, we analysed angiographic and clinical characteristic of patients and the prevalence of pre-infarction angina. Pre-infarction angina was prospectively defined as at least one episode of typical chest or left arm or jaw pain, either at rest or during exercise, less than 7 days before acute myocardial infarction. The latter was defined by the onset of chest pain lasting more than 30 min leading to the hospital admission. No reflow phenomenon was defined as inadequate myocardial perfusion (TIMI  $< 3$ ) through a given segment of the coronary circulation without angio-

**Table I. Clinical variables of patients with acute anterior myocardial infarction**

Clinical variables	TIMI III		p
	Yes (n = 63)	No (n = 17)	
Age (years)	56±11	57±12	0.59
Male (%)	51 (81)	14 (82.35%)	0.98
Hypertension (%)	30 (47.6%)	10 (58.82%)	0.90
Diabetes (%)	3 (4.76%)	5 (29.41%)	< 0.0001
Dislipidemia (%)	28 (44.44%)	11 (64.70%)	0.17
Smoking (%)	24 (38.1%)	7 (35.29%)	1.0
Preinfarction angina (%)	27 (42.86%)	2 (11.76%)	0.02
Multivessel disease (%)	18 (28.57%)	5 (29.41%)	1.0
Ischaemic time (min)	300±173	433±237	0.03
CK (U/l)	2420±1150	3600±1950	0.02
Cardiogenic shock (%)	1 (1.58%)	1 (5.88%)	0.38
LVEF (%)	50±11%	41±12%	< 0.002
LVEF ≤ 40% (%)	55 (38.19%)	12 (66.66%)	0.02
Death (%)	4 (2.77%)	1 (5.55%)	0.44

graphic evidence of mechanical vessel obstruction. Infarct-related artery flow was quantified using the TIMI flow grade: 0 (no perfusion) = no flow beyond the occlusion; 1 (penetration without perfusion) = slow and incomplete opacification of the vascular bed by contrast material; 2 (partial perfusion) = slow but complete opacification of the vascular bed by contrast material, with slower clearance; 3 (complete perfusion) = prompt and complete opacification of the vascular bed, with rapid clearance, as in an uninvolved artery. Assessment of ST-T segment elevation was performed before and 90 minutes after primary coronary angioplasty. The peak value of CK were estimated for each patient. 2D echocardiography was performed before discharge (usually at seven days), left ventricular ejection fraction measurement by echocardiographic, using Simpsons method.

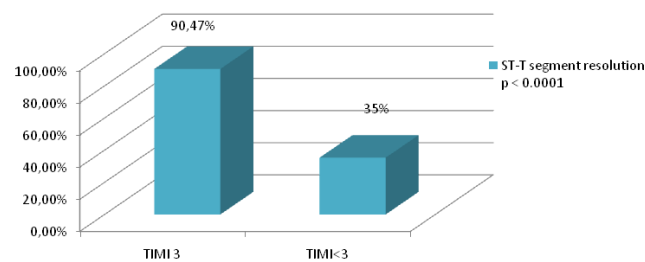
### Statistical analysis

All continuous values are expressed as mean\_standard deviation. Differences between group means were tested by two-tailed unpaired t-test with Welch correction. A chi-square statistic was calculated to test differences between proportions, with calculation of relative risks and exact 95% confidence intervals. Fisher's exact test was used for discrete variables. Statistical significance was defined as a P-value of less than 0.05.

### Results

Eighty patients with ST-T elevation acute anterior myocardial infarction underwent primary angioplasty. The no reflow phenomenon was observed in 17 patients (21.25%). Clinical characteristics of patients are shown in table I.

There were no differences between the two groups in age, gender, incidence of hypertension, dislipidemia, smoking, in patients with multivessel disease. No reflow phenomenon was more often observed in patients with diabetes, in patients with prolonged ischaemic time. Patients with TIMI<3 had a larger enzymatic infarct size (3600±1950 vs

**Fig. 1. Incidence of ST-T segment elevation resolution < 50% at 90 min after primary angioplasty**

2420±1150,  $p < 0.02$ ) and a lower left ventricular ejection fraction at discharge (41±12% vs 50±11%,  $p < 0.002$ ).

The incidence of ST-T segment elevation resolution < 50% at 90 minutes after infarct related artery recanalization was lower in patients with no reflow (35.29% vs 90.47%,  $p < 0.0001$ ).

In the patients with pre-infarction angina, sixteen patients had had angina for more than 1 week, including nine patients with known coronary artery disease. None of the patients had a history or evidence of previous myocardial infarction in the territory of the ongoing myocardial infarction. TIMI > 3 was more frequently observed in patients with preinfarction angina (42.86% vs 11.76%,  $p < 0.02$ ).

### Discussion

In this study, we defined the no-reflow phenomenon as a TIMI grade < 3 flow not attributable to epicardial spasm or obstruction after intervention. This conventional angiographic criterion clearly identifies a subset of patients with no-reflow resulting from severe microvascular dysfunction but does not identify those patients with no-reflow and impaired microvascular function but having a normal angiographic flow.

Brief episodes of myocardial ischaemia prior to experimental infarction are associated with decreased infarct size and improved wall motion recovery. In humans, pre-infarction angina is associated with improved prognosis after acute myocardial infarction. Several mechanisms may explain this benefit, such as enhanced collateral circulation towards the ischaemic myocardium, increased sensitivity to thrombolysis, or myocardial ischaemic preconditioning [5,6].

Improved perfusion of the area at risk after coronary recanalization may be related to ischaemic preconditioning of the vasculature. In humans, vascular injury following ischaemia and reperfusion results in myocardial no-reflow (reduced myocardial perfusion despite complete epicardial coronary recanalization). Preinfarction angina may reduce no-reflow by protecting against ischaemia/reperfusion-induced microvascular injury.

The no-reflow phenomenon in patients with anterior acute myocardial infarction treated with primary angioplasty is present in 21.25% of patients. Patients with no reflow had a lower left ventricle ejection fraction and much more myocardial necrosis. Pre-infarction angina is associ-

ated with a higher prevalence of TIMI 3 coronary flow in primary angioplasty. The cardioprotective role of pre-infarction angina may be explained by several mechanisms, such as opening of collateral circulation, increased sensitivity to thrombolysis, or myocardial pre-conditioning. Preconditioning may also protect the coronary arteriolar endothelium from ischaemia–reperfusion injury [2,7].

## Conclusions

In conclusion, preinfarction angina is associated with decreased no-reflow in patients with anterior infarctions and recanalization of the infarct vessel. Such decreased no-reflow may reflect preconditioning of the microvasculature by pre-infarction angina and provides an additional hypothetical mechanism for the clinical benefit of pre-infarction angina.

There are no conflicts of interest. The coauthors have performed interventional procedures.

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