

# Percutaneous Coronary Interventions in Patients with ST-segment Elevation Myocardial Infarction and Totally Occluded Culprit Artery after Pre-hospital Thrombolysis

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## Abstract

**The aim** of this study was to evaluate in-hospital outcomes of percutaneous coronary intervention (PCI) in patients with acute STEMI with completely occluded culprit artery after pre-hospital thrombolysis (PT).

**Methods:** Altogether 1,103 consecutive patients with STEMI admitted to the coronary care unit and submitted to PCI from January 2005 to January 2015 were included in the analysis. The clinical and angiographic characteristics, in-hospital outcomes, as well as predictors of no-reflow phenomenon were analyzed.

**Results:** Altogether 708 patients (64.2%) with a completely occluded culprit artery (initial TIMI flow  $\leq 1$ ) were included in the analysis. Overall, 78(11%) patients who received PCI after PT (PT-group) were compared with 630(89%) patients who received primary PCI (PPCI-group). The rates of no-reflow (14.1% vs 6.8%;  $P=0.02$ ) and recurrent MI (5.1% vs 1.3%;  $P=0.03$ ) were significantly higher in the PT-group. The rates of death (5.2% vs 5.1%;  $P=0.61$ ) and stent thrombosis (3.8% vs 1.3%;  $P=0.11$ ), as well as MACE (9.0% vs 7.0%;  $P=0.52$ ), were comparable between the groups. After univariate analysis, several clinical and procedural characteristics were associated with no-reflow, but only PT was associated with recurrent MI (OR=4.20; 95% CI 1.24-14.3;  $P=0.02$ ). After multivariate analysis, PT remained an independent predictor of no-reflow (OR=2.53; 95% CI 1.17-5.46;  $P=0.015$ ).

**Conclusion:** PCI in patients with STEMI and completely occluded culprit artery after PT was associated with higher levels of no-reflow and recurrent MI. Completely occluded culprit artery after PT was an independent predictor of no-reflow during PCI. (International Journal of Biomedicine. 2018;8(1):15-19.)

**Key Words:** STEMI • percutaneous coronary intervention • pre-hospital thrombolysis • totally occluded culprit artery

## Abbreviations

**BMI**, body mass index; **CAD**, coronary artery disease; **CKD**, chronic kidney disease; **CABG**, coronary artery bypass grafting; **MI**, myocardial infarction; **MACE**, major adverse cardiac events; **PCI**, percutaneous coronary intervention; **PT**, pre-hospital thrombolysis; **STEMI**, ST-segment elevation MI.

## Introduction

Despite the reduction in time to reperfusion with pre-hospital thrombolysis (PT), about 40% of patients do not achieve culprit artery patency.<sup>(1)</sup> In such cases, rescue percutaneous coronary interventions (PCI) reduce the risks of

recurrent MI and death compared to conservative therapy.<sup>(2,3)</sup> Some studies show no differences between rescue and primary PCI in reducing the composite of death, shock, congestive heart failure, or reinfarction.<sup>(4,5)</sup> However, the results of PCI in patients with a completely occluded culprit artery after PT are still insufficiently explored. We hypothesized that persistent infarct-related artery occlusion after PT can worsen the prognosis. The aim of this study was to evaluate in-hospital outcomes of PCI in patients with acute STEMI with completely occluded culprit artery after PT.

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## Materials and Methods

### Study population

Altogether 1,103 consecutive patients with STEMI admitted to the coronary care unit and submitted to PCI at our center from January 2005 to January 2015 were included in the analysis. Some patients underwent ambulance-based, full-dose tenecteplase thrombolysis, and since 2008, PT has been performed. The decision to conduct treatment with PT was taken by an ambulance physician according to the local standard. All patients received aspirin, 300 mg, and a loading dose of the clopidogrel (300 mg or 600 mg) before catheterization. Patients were anticoagulated with unfractionated heparin (100 IU/kg). Coronary angiography and PCI were performed from either the femoral or radial arterial access, according to the operator's decision. Patients were managed with standard post-PCI care and appropriate secondary prevention (aspirin, clopidogrel,  $\beta$ -blockers, angiotensin-converting-enzyme inhibitors and statins) was commenced unless otherwise contraindicated.

### Clinical and procedural data

Clinical data were obtained from the local hospital database, containing information on each PCI in STEMI patients, including demographics, baseline clinical and procedural details as well as in-hospital outcomes. All angiograms of the included patients were reviewed. An occluded culprit artery was defined as a culprit vessel with TIMI 0 to 1 flow, indicating no dye penetration or minimal dye penetration without complete vessel opacification. In patients after PT, non-invasive markers of reperfusion were evaluated and documented within 90 min after thrombolytic administration, according to hospital standard. In cases when ST resolution was partial or absent along with prolonged chest pain and absent of reperfusion arrhythmias, rescue PCIs were performed. The demographic, clinical, angiographic and in-hospital outcomes were analyzed. The composite of in-hospital death, recurrent MI and stent thrombosis were defined as MACE. Recurrent MI was defined as acute MI that occurs following the initial MI within hospitalization. Periprocedural MI was considered as a part of recurrent MI.

### Statistical analysis

All analyses were performed with SPSS v21.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables are presented as mean  $\pm$ SD and as medians (interquartile ranges). Continuous variables were compared by use of Student's unpaired t-test, or Mann-Whitney U test when data were not normally distributed. Categorical variables were expressed as numbers (percentages) and compared by Chi-squared test or Fisher's exact. To determine relationship between PT with no-reflow and recurrent MI univariate analysis was performed. To assess the impact of PT on no-reflow, multivariate logistic analysis was used. Variables reaching significance, or tendency to significance, on univariate analysis ( $p \leq 0.1$ ) were subsequently incorporated into a multivariate model. Independent variables are presented as odds ratios (OR) with 95% confidence intervals (CI). P-values  $< 0.05$  were considered statistically significant.

## Results

Out of 1,103 patients who underwent PCI for STEMI, 207(18.8%) received PT and 395(35.8%) were excluded—381 because initial TIMI flow  $\geq 2$  and 14 for failure of guidewire lesion crossing or stent delivery. The remaining 708 patients were included in the final analysis. Overall, 78(11%) patients who received PCI after PT (PT-group) were compared with 630(89%) patients who received primary PCI (PPCI-group).

### Clinical and procedural data

The characteristics of both patient groups are presented in Table 1. There were no differences in age, BMI, hyperlipidemia, incidence of diabetes, hypertension or CKD.

Table 1.

Baseline patient characteristics

Variable	PT-group	PPCI-group	P-value
Age, years	58.3 $\pm$ 10.6	59.0 $\pm$ 11.6	0.49
Males, gender, n (%)	63 (80.8%)	451 (71.6%)	0.09
BMI, kg/m <sup>2</sup>	29.3 $\pm$ 4.2	28.9 $\pm$ 4.9	0.26
Current smoker, n (%)	38 (48.7)	243 (38.6)	0.08
Hyperlipidemia, n (%)	66 (84.6)	555 (88.1)	0.37
Diabetes mellitus, n (%)	10 (12.8)	110 (17.5)	0.30
Hypertension, n (%)	58 (74.4)	505 (80.2)	0.23
Previous CAD, n (%)	25 (32.1)	229 (36.3)	0.46
Previous MI, n (%)	18 (23.1)	99 (15.7)	0.10
Previous PCI, n (%)	10 (12.8)	58 (9.2)	0.31
Previous CABG, n (%)	1 (1.3)	2 (0.3)	0.30
Previous stroke, n (%)	2 (2.6)	40 (6.3)	0.14
CKD, n (%)	4 (5.1)	39 (6.2)	0.48
Glycemia on admission, (mmol/l)	8.6 $\pm$ 3.0	8.5 $\pm$ 3.6	0.19
Killip class on admission, n (%)	I	66 (84.6)	576 (91.4)
	II	7 (9.0)	32 (5.1)
	III	1 (1.3)	3 (0.5)
	IV	4 (5.1)	19 (3)
			0.25

Angiographic and procedural data are summarized in Table 2. There were no differences between the groups with regard to infarct-related arteries, number of stents implanted, incidence of multivessel disease, use of thrombus aspiration, predilation and a transradial approach. Glycoprotein IIb/IIIa inhibitors were used more often in the PT-group. In the PT-group, pain-to-thrombolysis time was shorter than pain-to-door time in the PPCI-group. The median time from receiving thrombolysis to PCI was 220 (105-480) minutes. The rate of no-reflow was higher in the PT-group.

For PT-group, non-invasive markers of reperfusion were analyzed (Table 3). The absence of post-thrombotic resolution of ST elevation was detected in most patients. One-third of patients had prolonged chest pain and reperfusion arrhythmias.

Table 2.

## Angiographic and procedural outcomes

Variable	PT-group	PPCI-group	P-value
Infarct artery:			
Left anterior descending, n (%)	34 (43.6)	279 (44.3)	0.91
Left circumflex, n (%)	85 (13.5)	8 (10.3)	0.43
Right, n (%)	240 (38.1)	33 (42.3)	0.47
Left main, n (%)	5 (0.8)	1 (1.3)	0.51
Multi-vessel disease, n (%)	26 (33.3)	183 (29)	0.43
Number of stents implanted, n (%)	1.0±0.5	1.1±0.5	0.08
Predilatation, n (%)	46 (59)	404 (64.1)	0.37
Drug-eluting stent, n (%)	22 (31.4)	161 (27.5)	0.49
Transradial approach, n (%)	43 (55.1)	330 (52.4)	0.65
MT, n (%)	4 (5.1)	43 (6.8)	0.57
GPI, n (%)	3 (3.8)	4 (0.6)	0.03
Pain-to-door/pain-to-thrombolysis time*, min	80 [50;225]	120 [64;235]	0.03
No-reflow, n (%)	11 (14.1)	43 (6.8)	0.02

MT - manual thrombus aspiration; GPI - glycoprotein IIb/IIIa inhibitor; \*-Pain-to-door time calculated for PPCI-group, pain-to-thrombolysis time calculated for PT-group.

Table 3.

## Non-invasive markers of reperfusion in PT-group

Variable	n (%)	
Relative ST-segment resolution at 90 minutes	Complete (>70%)	6 (7.7)
	Partial (30%-70%)	17 (21.8)
	Absent (<30%)	55 (70.5)
Chest pain	Prolonged	28 (35.9)
	Absent	50 (64.1)
Reperfusion arrhythmias	AIVR	1 (1.3)
	VPB	19 (24.4)
	VF	5 (6.4)
	Absent	53 (67.9)

AIVR - accelerated idioventricular rhythm; VPB - ventricular premature beats; VF - ventricular fibrillation.

## In-hospital clinical outcomes

The rate of recurrent MI was significantly higher in the PT-group (Table 4). All recurrent MIs were due to stent thrombosis in the PPCI-group. In the PT-group, one patient had a recurrent MI without stent thrombosis. A recurrent MI in this case was diagnosed by the presence of typical symptoms of acute myocardial ischemia and a fivefold re-rise of troponin T. The rates of death and stent thrombosis, as well as MACE,

were comparable between the groups. After univariate analysis, several clinical and procedural characteristics were associated with no-reflow, but only PT was associated with recurrent MIs (Table 5). After multivariate analysis (Fig.1), PT remained an independent predictor of no-reflow (OR=2.53; 95% CI 1.17-5.46), along with age, body mass index, previous coronary artery disease, glycemia on admission, cardiogenic shock, left main PCI, multivessel disease and pre-dilatation.

Table 4.

## In-hospital clinical outcomes

Variable	PT-group	PPCI-group	P-value
Death, n (%)	4 (5.1)	33 (5.2)	0.61
Recurrent MI, n (%)	4 (5.1)	8 (1.3)	0.03
Stent thrombosis, n (%)	3 (3.8)	8 (1.3)	0.11
MACE, n (%)	7 (9.0)	44 (7.0)	0.52

Table 5.

## Univariate logistic analysis for no-reflow and recurrent MI

Variable	No-reflow			Recurrent MI		
	OR	95% CI	P	OR	95% CI	P
Age (years)	1.04	1.01-1.06	0.05	1.00	0.95-1.05	0.95
Male sex	1.02	0.55-1.90	0.95	0.53	0.11-2.42	0.41
BMI	1.07	1.01-1.12	0.02	0.90	0.78-1.03	0.12
Current smoker	0.68	0.37-1.23	0.20	1.53	0.49-4.80	0.47
Hyperlipidemia	0.68	0.32-1.43	0.47	0.70	1.15-3.23	0.64
Diabetes mellitus	1.62	0.84-3.13	0.15	0.98	0.21-4.53	0.98
Hypertension	1.31	0.63-2.75	0.47	0.77	0.21-2.88	0.70
Previous CAD	2.21	1.27-3.87	0.01	1.28	0.40-4.08	0.67
Previous MI	1.50	0.76-2.93	0.24	2.58	0.76-8.71	0.13
Previous PCI	0.74	0.26-2.11	0.57	0.85	0.12-6.71	0.88
CKD	2.56	1.08-6.06	0.03	3.20	0.69-15.06	0.14
Glycemia on admission	1.15	1.08-1.22	<0.001	0.96	0.79-1.16	0.64
Pain-to-door/pain-to-thrombolysis time*	1.00	0.99-1.01	0.76	0.99	0.94-1.03	0.64
Cardiogenic shock	7.41	2.99-18.38	<0.001	2.79	0.34-22.53	0.34
Left anterior descending PCI	1.01	0.58-1.77	0.97	1.79	0.56-5.68	0.33
Left circumflex PCI	0.66	0.26-1.69	0.38	0.60	0.08-4.68	0.62
Right PCI	0.86	0.48-1.53	0.60	1.14	0.36-3.63	0.82
Left main PCI	12.77	2.51-64.86	0.03	-		
Multi-vessel disease	2.03	1.16-3.56	0.02	1.72	0.54-5.49	0.36
Pre-dilatation	3.07	1.48-6.40	0.001	1.74	0.47-6.47	0.41
PT	2.24	1.10-4.55	0.03	4.20	1.24-14.30	0.02

\*-Pain-to-door time calculated for PPCI-group, pain-to-thrombolysis time calculated for PT-group.

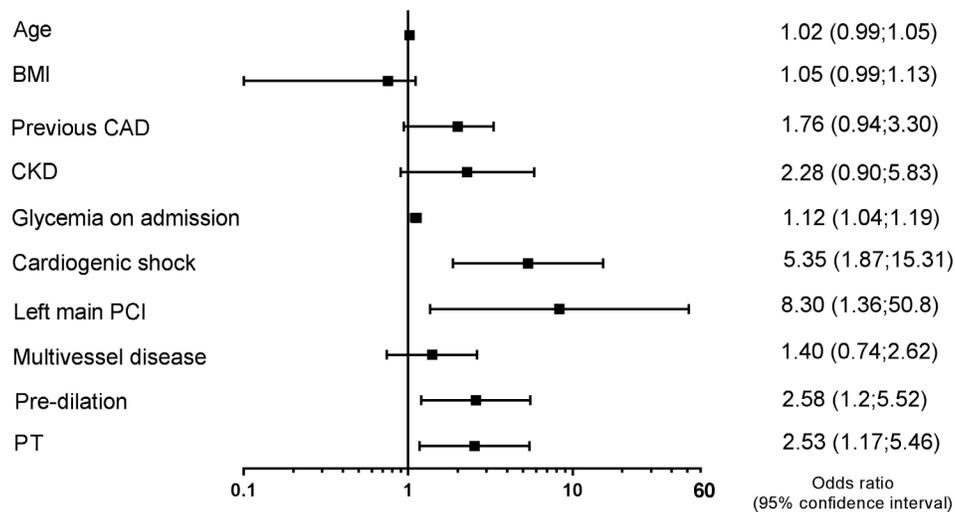


Fig. 1. Multivariate logistic analysis for no-reflow.

## Discussion

Recent studies have confirmed that a pharmacoinvasive strategy in patients with STEMI may be comparable to PPCI. In a CAPTIM trial, pre-hospital fibrinolysis followed by early transfer to PCI led to 5-year survival rates similar to those of PPCI.<sup>(6)</sup> In the 5-year analysis of the French Registry of Acute Coronary Syndrome (FAST-MI-2005), survival with a pharmacoinvasive strategy was comparable to survival with PPCI.<sup>(7)</sup> In the registry from Belgium, the results were similar for in-hospital mortality and 1-year survival.<sup>(8)</sup> In the STREAM study, the 30-day primary composite outcome (death, shock, congestive heart failure, or recurrent MI) was similar in the PPCI and pharmacoinvasive groups.<sup>(4)</sup> A combined analysis of the CAPTIM and WEST trials shows the advantages of the pharmacoinvasive strategy for 1-year outcomes.<sup>(9)</sup> In analysis of the Mayo Clinic STEMI database, fibrinolysis followed by transfer for PCI was found to be a reasonable alternative when PPCI is not readily available.<sup>(10)</sup> But in all of these studies, cases with successful and failed thrombolysis were not analyzed separately. A pharmacoinvasive approach can be more effective than PPCI in cases when culprit artery patency is achieved. In this situation, pharmacoinvasive strategy can reduce the reperfusion time, which is especially important for patients presenting early after the onset of symptoms.<sup>(11,12)</sup> But the incidence of complete culprit artery patency (TIMI grade 3 flow) occurred in only 55% to 60% of patients treated with PT.<sup>(1)</sup> In our study, patients with a totally occluded culprit artery after PT had higher rates of recurrent MI and incidence of no-reflow during PCI. Potentially all of these patients could receive a primary PCI at an acceptable time. Thrombolysis in these cases increased the time to PCI.

According to our data, unsuccessful PT was an independent predictor of no-reflow during PCI. Negative effects of the no-reflow phenomenon on clinical outcomes in patients with STEMI were demonstrated in several studies. No-reflow was associated with higher mortality, poor healing

of the infarct zone, and adverse remodeling with an increase in left ventricular failure.<sup>(13)</sup> The pathological mechanisms of no-reflow include injury related to ischemia, reperfusion, endothelial dysfunction, and distal thromboembolism.<sup>(14)</sup> Probably as a result of unsuccessful thrombolysis, components of the thrombus and atherosclerotic materials can produce small distal emboli, causing a further reduction in the coronary flow during PCI.

Several studies and meta-analyses have shown that early, routine, post-thrombolysis angiography with subsequent PCI can improve results, compared to a strategy of performing angiography and revascularization only in patients without ST-segment resolution or ongoing chest pain.<sup>(15-17)</sup> Our data confirm this statement. After PT, 8% of patients with persistent culprit artery occlusion had complete ST-segment resolution and 22% had partial ST-segment resolution. Moreover, most of the patients had no ongoing chest pain. An early routine post-thrombolysis strategy can be particularly effective in these cases.

Our study has several limitations. Firstly, this study was retrospective, nonrandomized and had the potential of selection bias. The number of patients in the PT-group was significantly lower than in the PPCI-group. Moreover, the number of events of recurrent MI and no-reflow were rather small. The multivariable models are not particularly strong with such a limited number of events. The study duration was over 10 years, and practice could change during this time. In addition, the long-term results were not assessed in this study.

**In conclusion,** PCI in patients with STEMI and completely occluded culprit artery after PT was associated with higher levels of no-reflow and recurrent MI. Completely occluded culprit artery after PT was an independent predictor of no-reflow during PCI.

## Competing interests

The authors declare that they have no competing interests.

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