Acute Myocardial Infarction with Spontaneous Reperfusion: Clinical Characteristics and Optimal Timing for Revascularization

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Abstract

Background: Spontaneous coronary reperfusion occurs in 7–27% of patients with ST elevation myocardial infarction, and is an independent predictor of myocardial salvage, percutaneous coronary intervention success, and improved outcome.

Objectives: To determine the optimal PCI time for patients admitted to the hospital due to STEMI with SCR.

Methods: We performed a retrospective analysis of all patients admitted to the coronary care unit between July 2002 and November 2004 with a diagnosis of STEMI with SCR.

Results: The study group comprised 86 patients. There was not a single reinfarction episode during an observation period of 6579 patient hours. Cardiac catheterization was executed early (< 24 hours from pain onset) in 26 patients and late (> 24 hours) in 55. Pre-PCI angiographic TIMI flow 2–3 was seen in > 95% in both groups. PCI was performed more frequently in the "early" group (P = 0.024), while multi-vessel coronary artery disease (P = 0.094) requiring coronary bypass surgery (P = 0.056) was observed more frequently in the "late catheterization" group. Myocardial infarction and angina pectoris at 30 days occurred more frequently in the early catheterization group (P = 0.039), however no difference in any major adverse cardiac events was detected during long-term follow-up (491 ± 245 days).

Conclusions: Reinfarction after STEMI with SCR is a rare event. Early PCI in patients with STEMI and SCR, even when executed with aggressive antiplatelet therapy, seems to result in an excess of early MACE without any long-term advantage. Prospective randomized trials should determine the optimal PCI timing for these patients.

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Spontaneous coronary reperfusion of the infarct-related artery occurs in 7–27% of patients experiencing acute ST elevation myocardial infarction [1-7]. This cohort seems to have smaller infarcts and patients are discharged from the hospital with apparently better left ventricular function and a more favorable prognosis [1-4,6-9].

Data collected from the four Primary Angioplasty in Myocardial Infarction (PAMI) studies [4] showed that patients undergoing primary percutaneous coronary intervention in whom TIMI-3 flow is present before angioplasty are less likely to develop complications related to left ventricular failure, and have improved early and late survival. Topol et al. [10] compared the outcome in patients subjected to immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction (TAMI-1). They reported that in patients with initially successful thrombolysis and a suitable coronary artery anatomy, immediate angioplasty offers no clear advantage over delayed elective angioplasty. The TAMI-1 trial revealed that 14% of the patients with tight coronary stenosis 90 minutes after thrombolysis had < 50% residual lesion by 7 days, obviating the need for angioplasty. Steg and colleagues [8] examined the in-hospital outcome of patients (n=47) with angiographically proven spontaneous reperfusion of the IRA who were all managed conservatively without emergency PCI, and found an excellent prognosis, but recurrent ischemia requiring emergency intervention was frequent. Little data are available on the optimal treatment strategy for these patients. No trial has ever examined the role of glycoprotein IIb/IIIa antagonists in these patients, and controversy still remains as to whether intervention should be delayed or performed immediately.

This study analyzed the data collected on all patients admitted with STEMI and SCR to the coronary care unit. Special attention was paid to revascularization timing, the use of GP-IIb/IIIa antagonists, and their effects on short- and long-term outcome.

Patients and Methods

This was a retrospective analysis of all patients admitted to the coronary care unit at Assaf Harofeh Medical Center between July 2002 and November 2004 with the diagnosis of STEMI with SCR. Data were obtained from the chart reviews, medical records,

PCI = percutaneous coronary intervention
STEMI = ST elevation myocardial infarction
SCR = spontaneous coronary reperfusion
IRA = infarct-related artery
GP = glycoprotein

electrocardiographic analysis, and a film review of cardiac catheterizations. Post-discharge outcome data were obtained from the cardiology clinic, hospital records and telephone interviews. The study group comprised all STEMI patients with typical chest pain lasting > 30 minutes and ST segment elevation > 1 mm in two contiguous ECG leads. Clinical criteria for SCR included all of the following:

- Spontaneous, partial or complete (> 50%) resolution of ST segment elevation as diagnosed by serial ECGs obtained before and during hospitalization, within 6 hours since permanent pain began.
- Significant relief of chest pain, within 6 hours since permanent pain began.
- Early inversion of T-waves in the infarct-related ECG leads; within 6 hours since permanent pain began.

Statistical analysis

Statistical analysis was executed by an independent statistician, using SPSS 12 software (SPSS Inc., Chicago, IL, USA). Data are expressed as mean ± SD for continuous variables, and frequencies and percentage for categorical variables. The chi-square test was used to compare categorical variables. Student's *t*-test and the Mann-Whitney test were used for the comparison of continuous variables. As for the difference in survival time between the groups, we used the Cox regression model in which we examined the effect of angiographic timing (treatment type) and IIb/IIIa antagonist treatment on patients' survival, controlled for the possible confounders. Using this model the hazard ratio was evaluated and presented with its *P* value and 95% confidence interval.

Results

Clinical and demographic data

Of the 1095 (7.84%) patients with MI (STEMI and non-STEMI), 81 fulfilled the criteria for SR [Table 1]. Most patients were in stable clinical condition on admission, as reflected by their vital signs. ECG revealed a maximal ST elevation score of 7 ± 5.7 mm and reciprocal ST depression score of 3.5 ± 3.5 mm. The location of STEMI according to admission ECG was inferior in 57%, posterior in 36%, anterior in 35%, and the lateral wall in 20%. The mean duration of chest pain (time from the start of chest pain to SCR) was 101 ± 96 minutes. Early cardiac catheterization (< 24 hours from onset of pain) was performed in 26 patients, and late (> 24 hours) in 55 patients. The decision when to perform cardiac catheterization was taken by the ICCU team based on clinical parameters and availability. There were more males and anterior wall myocardial infarctions in the "early" arm.

Hospital medical therapy [Table 2]

All patients were treated with aspirin; clopidogrel was used in 98.8%, and heparin or low molecular weight heparin in 97.7%. GP-IIb/IIIa antagonists were used in only 38.4% of patients. GP-IIb/IIIa was employed more frequently in the "early" arm both on admission and during hospitalization.

Table 1. Baseline demographic and clinical characteristics

	All	Early (n=26)	Late (n=55)	*P*
Age (yrs)	60 ± 11	57 ± 10.5	60.98 ± 11	0.135
Male gender	71 (82.6)	25 (96)	44 (80)	0.056
Body mass index (kg/m^2)	27	27.524	26.346	0.213
Angina pectoris	19 (22.1)	3 (11.53)	13 (23.63)	0.202
S/P myocardial infarction	13 (15.1)	3 (11.53)	8 (14.54)	0.712
S/P PCI	13 (13)	3 (11.53)	7 (12.72)	0.879
Congestive heart failure	1(1.2)	0	1 (1.81)	0.489
Atrial fibrillation	1 (1.2)	0	1 (1.81)	0.489
Valvular heart disease	1 (1.2)	0	1 (1.81)	0.489
Peripheral vascular disease	2 (2.3)	2 (7.69)	0	0.037
Diabetes mellitus	25 (29.1)	10 (38.46)	13 (23.63)	0.167
Stroke	5 (5.8)	1 (3.84)	4 (7.27)	0.55
Venous thromboembolism	1 (1.2)	1 (3.84)	0	0.147
Hypertension	43 (50)	11 (42.3)	27 (49.09)	0.568
Hypercholesterolemia	38 (44.2)	11 (42.3)	24 (43.63)	0.91
Family history	24 (27.9)	7 (26.92)	15 (27.27)	0.974
Current smoker	44 (54.3)	13 (50)	31 (56.36)	
Past smoker	16(19.8)	9 (34.61)	7 (12.72)	
Renal failure	4 (4.7)	0	3 (5.45)	0.225

The numbers in parentheses signify the percentage of patients.

Table 2. Medications during hospital stay

	All	Early	Late	*P*
Aspirin	86 (100)	26 (100)	55 (100)	1
ADP antagonist	85 (98.8)	26 (100)	54 (98.18)	0.489
Heparin	84 (97.7)	26 (100)	53 (96.36)	0.325
Statins	75 (87.2)	26 (100)	45 (81.81)	0.02
Beta-blockers	69 (80.2)	20 (76.92)	45 (81.81)	0.605
GP-IIb/IIIa antagonist	33 (38.4)	17 (65.38)	15 (27.27)	0.001
ACE inhibitors	55 (64)	15 (57.69)	38 (69.09)	0.314
Oral antidiabetic	13 (15.1)	4 (15.38)	7 (12.72)	0.744
Insulin	7 (8.1)	2 (7.69)	5 (9.09)	0.834
Nitrate	12 (14)	5 (19.23)	6 (10.9)	0.307
Calcium channel blockers	10 (11.6)	1 (3.84)	7 (12.72)	0.211
Diuretics	10 (11.6)	1 (3.84)	8 (14.54)	0.153
Anti-arrhythmic drugs	6 (7)	2 (7.69)	4 (7.27)	0.946
Angiotensin receptor blockers	3 (3.5)	1 (3.84)	2 (3.63)	0.963

The numbers in parentheses signify the percentage of patients
ACE = angiotensin converting enzyme

Angiographic data [Table 3]

Cardiac catheterization was performed in 94.2% of the patients. Pre-PCI angiographic TIMI flow was 2 and 3 in 12.9% and 83.9% respectively. Pre-PCI angiographic TIMI flow 2–3 was seen in > 95% in both early and late arms. Multi-vessel coronary artery disease ($P = 0.094$) and coronary bypass surgery ($P = 0.056$) tended to occur more frequently in the late catheterization group. PCI was performed in 75.3%, and more frequently in the early catheterization arm ($P = 0.024$). Stents were implanted in 95.3% of the percutaneous coronary interventions. Procedural success

Table 3. Percutaneous coronary intervention

	All	Early	Late	*P*
Cardiac catheterization	81 (94.2)	26 (32.09)	55 (67.9)	
No. of vessels involved				
0	4 (4.9)	1 (3.84)	3 (5.45)	0.094
1	29 (35.4)	13 (50)	16 (29.09)	
2	29 (35.4)	10 (38.46)	19 (34.54)	
3	20 (24.4)	2 (7.69)	17 (30.9)	
PCI	64 (75.3)	25 (96.15)	38 (69.09)	0.024
No. of stents				
0	3 (4.7)	2 (7.69)	1 (2.63)	0.452
1	49 (76.6)	18 (69.23)	31 (81.57)	
2	12 (18.8)	6 (23.07)	6 (15.78)	
Bare stent	51 (79.68)	18 (72)	33 (86.84)	
Cypher stent	10 (15.62)	6 (24)	4 (10.52)	
TIMI score pre-intervention				
0	2 (3.2)	0	2 (5)	0.148
2	8 (12.9)	5 (22.72)	3 (7.5)	
3	52 (83.9)	17 (77.27)	35 (87.5)	
Mean TFC pre-intervention	26.27			
TIMI score post-intervention				
0	1 (1.7)	0	1	0.549
2	1 (1.7)	0	1	
3	58 (96.7)	22 (100)	36 (94.73)	
Mean TFC post-intervention	22.25			

TIMI = thrombolysis in myocardial infarction, TFC = TIMI flow count.

was excellent; none of the patients had persistent no-reflow phenomenon. Pre- and post-PCI angiographic TIMI flow and TIMI frame count were similar for both arms.

Outcome [Table 4]

During the first month only 2.4% suffered from any MACE (myocardial infarction, recurrent cardiac catheterization, stroke, death). Myocardial infarction and angina pectoris at 30 days occurred more frequently in the early catheterization group ($P = 0.039$), with a trend toward GP-IIb/IIIa antagonist-treated patients ($P = 0.075$). However, no difference in any MACE was found during long-term follow-up (491 ± 245 days). During long-term follow-up 22.6% experienced angina and 26.2% experienced MACE, driven mostly by recurrent cardiac catheterizations (16.7%) and myocardial infarctions (7.1%).

Discussion

In this report clinical and angiographic characteristics of patients with STEMI and SCR of the IRA were found to resemble the general STEMI population, although the early and late outcomes seem to be more favorable. To date, no study to determine the optimal treatment for this population has been conducted, and the question whether the classic treatment that we provide for patients with STEMI is applicable to patients with SCR remains controversial.

Patients presenting with clinical features of SCR have a better prognosis [1-4,6-8] and an excellent in-hospital outcome,

MACE = major adverse cardiac event

Table 4. Early and late outcome

	All	Early	Late	*P*
Early outcome, 1 month				
Ejection fraction		47	44	0.148
Peak creatine phosphokinase		546	729	0.341
Angina pectoris	2	2 (7.69)	0	0.039
Myocardial infarction	13 (15.1)	2 (7.69)	0	0.039
Recurrent cardiac catheterization	12 (14)	1 (3.84)	0	0.147
Cerebrovascular accident	3 (3.5)	0	0	1
Death	1 (1.2)	0	0	1
Any MACE	2 (2.4)	2 (7.69)	0	0.039
Late outcome				
Angina pectoris	19 (22.6)	7 (26.92)	11 (20.37)	0.511
Myocardial infarction	6 (7.1)	3 (11.53)	2 (3.7)	0.175
Recurrent cardiac catheterization	14 (16.7)	6 (23.07)	8 (14.81)	0.362
Cerebrovascular accident	1 (1.2)	0	0	1
Death	2 (2.4)	0	1 (1.85)	0.485
Any MACE	22 (26.2)	9 (34.61)	10 (18.51)	0.113

The numbers in parentheses signify the percentage of patients.

with evidence of less myocardial damage than patients in whom reperfusion therapy was required to achieve TIMI-3 patency.

The major threat to these patients is considered to be reinfarction due to reocclusion of the IRA [8], since the large area of viable myocardium is potentially at risk. However, this event occurred in none of our patients (over an observation period of 6579 patient hours). This is in contrast with the 10–20% reocclusion of the IRA observed in patients with STEMI, post-thrombolysis [11].

No trial has addressed the question whether patients with clinical diagnosis of STEMI and SCR benefit from early cardiac catheterization or whether cardiac catheterization should be delayed. It is possible that delayed PCI may be safer, after a "cooling down" period, potential thrombus resolution and plaque stabilization.

Numerous studies found a better prognosis for patients with STEMI who had undergone cardiac catheterization, and TIMI flow 2-3 was found in the IRA prior to PCI (angiographic evidence of SCR) [12,13]. In this report we divided the patients with STEMI and clinical markers for SCR into two groups: patients who underwent cardiac catheterization less than 24 hours since pain had started (early) and those after 24 hours (late). There was a tendency to perform early catheterization in male patients with anterior wall MI. These patients were treated with GP-IIb/IIIa antagonists more often. The early and late outcome in these patients was excellent with no statistical difference between groups. Early outcome, one month after the STEMI, showed a trend for fewer major cardiac events in the late cardiac catheterization group. Thus, it would seem that angiography and PCI can be delayed and executed a few days later with minimal use of adjunctive pharmacotherapy. The procedure may be easier and even safer, and may have a better short-term outcome [10].

The role of IIb/IIIa antagonists in acute STEMI with SCR has

not yet been examined in the literature. We found that 38.4% of our patients received a GP-IIb/IIIa antagonist. As with early cardiac catheterization, the majority of patients treated with GP-IIb/IIIa antagonists had anterior wall MI and underwent early cardiac catheterization. No statistical difference was observed between patients treated with a IIb/IIIa antagonist and those who were not. The exact role of IIb/IIIa antagonists in acute STEMI with SCR should be examined in a large-scale prospective study.

Study limitations

This study should be analyzed with caution since non-randomized retrospective data may be subject to selection bias. Nevertheless, we believe that with the current antiplatelet and anticoagulant therapy, acute reocclusion of the IRA is a rarity in this cohort. Therefore, cardiac catheterization can be safely delayed in this group of patients.

Conclusions

Clinical diagnosis of STEMI with SCR correlates with the angiographic finding of an open (TIMI 2–3) IRA. Reinfarction is rare, while PCI results in high procedural success and favorable short and long-term outcome. Early PCI in these patients seems to result in excessive early MACE, without any long-term advantage. The treatment with GP-IIb/IIIa antagonists in patients with STEMI and SCR does not seem to yield any significant advantage. Prospective randomized trials will be required to determine the optimal PCI timing and the role of GP-IIb/IIIa antagonists in this cohort.

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Capsule

IQ in childhood and vegetarianism in adulthood

Gale et al. examined the relation between IQ in childhood and vegetarianism in adulthood, by a prospective cohort study in which IQ was assessed by tests of mental ability at age 10 years and vegetarianism by self-report at age 30. The 1970 British cohort study, a national birth cohort, included 8170 men and women aged 30 years. Of these participants, 366 (4.5%) said they were vegetarian, although 123 (33.6%) admitted eating fish or chicken. Vegetarians were more likely to be female, to be of higher social class (both in childhood and currently), and to have attained higher academic or vocational qualifications, although these socioeconomic advantages were not reflected in their income. Higher IQ at age 10 years was associated with an increased likelihood of being vegetarian at age 30. IQ remained a statistically significant predictor of being vegetarian as an adult after adjustment for social class (both in childhood and currently), academic or vocational qualifications, and gender (1.20, 1.06–1.36). Exclusion of those who said they were vegetarian but ate fish or chicken had little effect on the strength of this association.

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