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Comparison of the improvement in myocardial perfusion and function in cases of rapid and slow electrocardiographic stage dynamics between patients with TIMI-3 flow after primary angioplasty for acute myocardial infarction

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ABSTRACT

Background and objective: Post-PCI TIMI flow grade 3 in infarct-related artery not always is associated with follow-up improvement in myocardial perfusion and function. We compared the improvement in myocardial perfusion and function in cases of rapid and slow electrocardiographic (ECG) stage dynamics between patients with TIMI-3 flow after primary angioplasty for acute myocardial infarction (MI).

Materials and methods: Ten patients with post-PCI TIMI-3 flow were divided into group A (n = 50, no rapid change of ECG stages) and group B (n = 50, with a ≥2 ECG stages per 2 days change rate).

Results: There were no significant changes after 3 months in scintigraphic (ejection fraction 44.6 ± 9.3% vs. 42.0 ± 3.4%, P = 0.4; perfusion deficit severity 3.0 ± 0.7 vs. 2.3 ± 0.8, P = 0.1) and echocardiographic (dysfunction score 1.9 ± 0.2 vs. 1.6 ± 0.5, P = 0.2) data in group A. Scintigraphic data improved (ejection fraction 34.6 ± 3.9% vs. 52.0 ± 7.3, P = 0.03; perfusion deficit severity 2.8 ± 0.6 vs. 1.5 ± 0.8, P = 0.03) and changes in echocardiographic data were of borderline significance (dysfunction score 1.8 ± 0.2 vs. 1.4 ± 0.4, P = 0.06) in group B.

Conclusions: There was not any change in myocardial perfusion and function in a case of slow change of ECG stages after reached post-PCI TIMI flow grade 3, while myocardial perfusion improved and function tended to improve in a case of the rate at least two ECG stages in 2 days after primary angioplasty for acute MI.

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1. Introduction

Primary percutaneous coronary intervention (PCI) has become accepted as the preferred reperfusion strategy in acute ST-elevation myocardial infarction (MI) [1]. It is because primary angioplasty results in better function of the left ventricle (LV) and improved survival in large patient groups, but prediction of improvement in myocardial perfusion and function in individual patients may be more difficult. The primary angioplasty causes usually an early and complete myocardial reperfusion, but incomplete reperfusion is associated with an increased risk of death and LV dysfunction [2]. The additional therapy may be beneficial for such patients with suboptimal reperfusion.

Recently, Brener et al. [3] have showed that post-PCI thrombolysis in myocardial infarction (TIMI) 3 flow [4] strongly correlated with 3-year survival. However, in another study, neither post-PCI TIMI myocardial perfusion grade nor TIMI flow grade was significantly associated with 90 day death/chronic heart failure/shock [5]. There is considerable disparity between the angiographic appearance of restored TIMI flow in the infarct-related artery (IRA) and the electrocardiographic (ECG) signs of myocardial tissue reperfusion insufficiency manifested by persistent ST segment elevation after recanalization [6]. The reasons for this are speculative but might include the prolonged dilatation of the vessels impairing autoregulation, the release of vasoconstrictor substances from the angioplasty site, or distal embolization [7]. Myocardial perfusion defects might depend on many other factors, such as residual and distal stenosis, microcirculation, and the amount of myocardial necrosis that has occurred before reperfusion. Ito et al. [8] demonstrated that restoration of normal epicardial blood flow is not sufficient to ensure adequate myocardial reperfusion; the latter requires perfusion at the level of the coronary microcirculation and myocytes. Myocardial perfusion in the distribution of the dilated artery was shown to improve progressively until 3 months [7].

Many authors have shown diagnostic and prognostic value of ST segment for myocardial perfusion and functional recovery [9]; however, other authors have shown that QRS complex and T waves are also informative [10]. In clinical practice, these criteria (taken simultaneously) are traditionally used for the determination of four ECG stages reflecting the development of myocardial injury after acute MI [11]. However, there are no studies dedicated to examine the informativeness of ECG stage changing velocity after reached post-PCI TIMI flow grade 3. In this study we compared the improvement in myocardial perfusion and function in cases of rapid and slow ECG stage dynamics between patients with TIMI-3 flow after primary angioplasty for acute MI.

2. Materials and methods

2.1. Study design

We divided the patients with TIMI flow grade 3 after PCI into group A (no rapid change of ECG stages) and group B (with a ≥2 ECG stages per 2 days change rate). We assessed the difference in changes of scintigraphic and echocardiographic data before discharge from a hospital and 3 months later between these two groups.

Treatment assignment was not randomized and patients were treated by the judgment of the attending cardiologist. As this center has a skilled PCI laboratory with experienced interventional cardiologists on duty 24 h a day, patients admitted to this hospital undergo primary PCI if coronary arteries are suitable, as recommended in standard guidelines [1]. All patients provided written informed consent. The segmental plaque load was assessed in 15 segments according to the classification of the American College of Cardiology/American Heart Association [12]. The antegrade radiocontrast flow of the IRA was determined after PCI by the operator with the use of TIMI criteria: grade 0 perfusion is no antegrade flow beyond the point of occlusion; grade 1 is minimal incomplete perfusion of contrast medium around the clot; grade 2 (partial perfusion) is complete but delayed perfusion of the distal coronary bed with contrast material; and grade 3 (complete perfusion) is antegrade flow to the entire distal bed at a normal rate [4].

2.2. Patient selection

This study was performed prospectively on consecutive patients who underwent primary angioplasty due to the first acute ST elevation MI diagnosed in the presence of typical chest pain greater than 30-min duration and ST segment elevation ≥1 mm (at the J point) in two or more contiguous leads on the 12-lead ECG. We included patients who agreed to undergo scintigraphic examination not only before discharge, but also in 3 months to get scintigraphic and echocardiographic examination repeated. Exclusion criteria were the following: acute MI without abnormal Q waves in 2 or more precordial leads in the first two days; stage III/IV MI on admission; concomitant valvular or myopathic heart disease; intraventricular conduction defects; previous MI, or coronary artery bypass graft surgery.

2.3. Electrocardiogram evaluation

Serial 12-lead ECGs recorded at admission, on the first and the second days after PCI were analyzed, and ECG stages of MI were assessed by the following criteria [11]: stage I, the ST segment elevation ≥0.1 mV, a positive T-wave, no abnormal Q-wave; stage II, the ST segment elevation ≥0.1 mV, abnormal Q-wave; stage III, the ST segment still elevated but a negative T-wave has started to form, and stage IV, the ST segment in isoelectric line with the negative T-wave. In accordance with the Selvester QRS scoring system [13], Q-wave was considered abnormal, if it was present in leads V1, V2, V3, or it was ≥20 ms in lead V4, or it was ≥30 ms in any other lead except III and aVR and the relevant leads for anterior infarcts were V1 to V4; for lateral, I, aVL, V5, and V6; for inferior, II and AVF; and for posterior, V1 and V2.

The resolution of two or more ECG stages during the first 48 h after IRA recanalization was considered as a rapid change, based on our previous studies [14,15]. All ECGs were assessed manually by the single observer who was unaware of the clinical status of the patients and their angiographic, scintigraphic and echocardiographic data.

2.4. Myocardial scintigraphy

Improvement in myocardial perfusion was estimated by the data of myocardial perfusion imaging with technetium (Tc)-99m-sestamibi (single-photon emission computed tomography). All myocardial perfusion studies were performed with a low-energy collimated dual-head Siemens gamma camera (E. Cam). Reconstruction and analysis of the tomographic data was performed by the observer who was unaware of the clinical status of the patients and their ECG, angiographic and echocardiographic data. Tomograms were divided into 20 segments, corresponding myocardial area: anterior (segments 1, 2, 3, 7, 12, 13, 18, 19), lateral (segments 5, 6, 10, 11, 16, 17), and inferior (segments 4, 8, 9, 14, 15, 20). The myocardial perfusion was scored using such scale. The myocardial segment with the maximum number of counts was considered as the normal reference region, and the tracer uptake in all other segments was then expressed as a percentage of the reference region activity: 0, normal perfusion; 1, slightly reduced perfusion (perfusion reduced to 60%–80% of the maximal myocardial perfusion); 2, moderately decreased tracer uptake (40%–60% of the maximal uptake); 3, markedly reduced perfusion (myocardium uptake lower than 40%); and 4, no perfusion (a myocardium uptake 10% and less). Myocardial wall thickness was scored using such scale: 0, normal thickness; 1, slightly reduced thickness; 2, moderately decreased thickness; and 3, markedly reduced wall thickness (akinesis). Myocardial wall movement was scored using the following scale: 0, normal movement; 1, a slightly reduced movement; 2, a moderately decreased movement; and 3, a markedly impaired wall movement (akinesis or dyskinesis). A modified Simpson's formula was used to determine the chamber volume at end-diastole and end-systole and LV ejection fraction was automatically computed.

2.5. Echocardiographic examination

Transthoracic echocardiography was performed by the physician who was unaware of the clinical status of the patients and their ECG, angiographic and scintigraphic data using the ultrasound system SONOS 7500 with a 2.4-MHz phased-array transducer. Echocardiographic abnormalities of LV function estimated in 16 segments by consensus of the American Society of Echocardiography's Guidelines and Standards Committee and the European Association of Echocardiography [16] were expressed as normal (1 point), hypokinesis (2 points), akinesis (3 points), dyskinesis (4 points), and aneurysm (5 points). The summarized score of global LV dysfunction was estimated by the sum of points for all regions and divided by the number of segments. Ejection fraction was measured by the biplane method of disks (modified Simpson's rule), which is currently recommended method of choice [16].

2.6. Statistical analysis

Values were expressed as the mean ± standard deviation. Statistical significance was accepted when the exact probability value was $P < 0.05$. Differences in continuous variables between the two groups were assessed using the Mann–Whitney *U*-test (two-sided). Differences in the same groups between the discharge data and in 3 months were assessed using the Wilcoxon Rank Sum test (one-sided).

3. Results

During the period of the study, there were 10 patients who met the inclusion criteria (Tables 1 and 2). Initial ECG stage was 1.8 in both groups. There were two cases of stenosis in S6 of the IRA with involvement of anterior LV wall into infarction process in both groups. Stenosis of the IRA was 99% in one case in both groups and 100% in all other cases. One patient had stenosis of 50% or greater in 3 segments in both groups.

Table 1 – Initial characteristics of patients' groups.

Parameter	Group A ($n = 5$)	Group B ($n = 5$)	P
Age, years	57.2 ± 8.9	60.2 ± 4.0	NS
Women/men, *n*	1/4	1/4	NS
Door-to-balloon time, min	83 ± 47.3	106 ± 117.6	NS
Residual stenosis, %	7 ± 8.4	16 ± 5.5	NS

Data presented are mean ± standard deviation unless otherwise stated. NS, not significant.
Group A, patients with TIMI-3 flow after primary angioplasty, no rapid change of electrocardiographic stages; group B, patients with TIMI-3 flow after primary angioplasty and with a ≥2 electrocardiographic stages per 2 days change rate.

Table 2 – Electrocardiographic and angiographic characteristics of patient groups.

Group A ($n = 5$)			Group B ($n = 5$)		
ECG infarct locations	Infarct-related segment	Residual stenosis, %	ECG infarct locations	Infarct-related segment	Residual stenosis, %
Anterior	S6	5	Lateral	S11	10
Inferior	S4	10	Inferior	S3	20
Anterior	S6	0	Inferior	S12	20
Inferior	S1	20	Anterolateral	S6	20
Inferoposterior	S13	0	Anterolateral	S6	10

Group A, patients with TIMI-3 flow after primary angioplasty, no rapid change of electrocardiographic stages, group B, patients with TIMI-3 flow after primary angioplasty and with a ≥2 electrocardiographic stages per 2 days change rate.

Table 3 – Changes in scintigraphic and echocardiographic data during 3 months after acute myocardial infarction in patient groups.

	Group A ($n = 5$)			Group B ($n = 5$)		
	At discharge	After 3 months	P	At discharge	After 3 months	P
Scintigraphic data						
Ejection fraction (%)	44.6 ± 9.3	42.0 ± 3.4	0.4	34.6 ± 3.9	52.0 ± 7.3	0.03
Perfusion deficit severity score	3.0 ± 0.7	2.3 ± 0.8	0.1	2.8 ± 0.6	1.5 ± 0.8	0.03
Wall thickness score	2.1 ± 0.7	2.0 ± 0.8	0.3	2.6 ± 0.5	1.4 ± 0.6	0.03
Wall movement score	2.0 ± 0.8	2.0 ± 0.8	0.5	2.2 ± 0.3	1.1 ± 0.4	0.03
Echocardiographic data						
Ejection fraction (%)	39.4 ± 5.6	42.6 ± 4.3	0.1	42.0 ± 6.6	50.6 ± 11.3	0.06
Dysfunction score	1.9 ± 0.2	1.6 ± 0.5	0.2	1.8 ± 0.2	1.4 ± 0.4	0.06

Values are mean ± standard deviation. Group A, patients with TIMI-3 flow after primary angioplasty, no rapid change of electrocardiographic stages; group B, patients with TIMI-3 flow after primary angioplasty and with a ≥2 electrocardiographic stages per 2 days change rate.

Stenosis in 2 segments was found in two cases in group A and in one case in group B. One patient had stenosis in 4 segments in group B. Other patients had stenosis only in one segment in both groups. In one case angioplasty was complicated by coronary artery dissection and followed by stent implantation in both groups.

Scintigraphic data improved and echocardiographic data tended to improve during 3 months only in group B (Table 3).

4. Discussion

In these studied cases, between patients with post-PCI TIMI flow grade 3 in the IRA improvement in myocardial perfusion and LV function in the future was not observed in a case of slow ECG changes following the first 2 days after the event.

It was discussed in Introduction that restoration of normal epicardial blood flow is not sufficient to ensure adequate myocardial reperfusion. Moreover, recent studies showed that post-PCI TIMI flow grade often was overestimated [3,17]. Re-examination of the ''gold standard'' in myocardial reperfusion assessment [9] showed that the ST segment resolution patterns were predictive for the combined outcome of mortality or heart failure, whereas TIMI flow grade was not. Tjandrawidjaja et al. found that the prognostic impact of ST depression resolution among patients with ST-segment elevation MI undergoing primary PCI was incremental to ST elevation resolution [18]. However, Terkelsen et al. showed that traditional 90-min ST-resolution analysis may have limited value in the era of primary PCI [19]. Whereas changes in ST segment dislocation amplitude have been extensively studied, the significance of QRS complex and T-wave changes during reperfusion and the first days is less clear, especially when changes in the QRS complex and T-wave may be complementary and additive to ST segment monitoring [10]. Recently, infarct size on contrast-enhanced cardiac magnetic resonance imaging was found higher than that by QRS score in the acute and subacute phases of infarction [20]. Thus, there is a discussion in the medical literature regarding which marker of reperfusion is believed to be better.

In our previous studies [14,15], we have shown the highly informative value of ST segment, T wave and QRS changes (taken simultaneously), expressed by the rate of ECG stage dynamics for quite an early (two days) prediction of follow-up improvement in myocardial perfusion and function. The sensitivity of the method was 87.5% for a decrease in size of perfusion defect on testing technetium-99m-sestamibi scan, and 100% for a decrease in the severity of perfusion defect; the specificity was 80% and 100%, respectively [14].

Dynamics of ECG stages reflects myocardial rather than epicardial flow; that explains why in cases of post-PCI TIMI-3 flow improvement in myocardial perfusion and function was not observed between the patients with slow post-PCI change of ECG stages. Myocardial perfusion improved and LV function tended to improve between the patients with rapid post-PCI change of ECG stages, but may be in larger patient groups LV function would be also significantly improved as myocardial perfusion. The sample size because of the scintigraphic study is too small to draw a definite conclusion. We suggest further future assessment of post-PCI myocardial perfusion and prognosis in larger patient groups by this ECG method since it is a readily accessible, simple method of ECG examination, which carries no risk to the patient.

5. Limitations

Our statistical analysis must be taken with caution due to a small number of patients. We recommend looking at our data as case series.

6. Conclusions

There was no any change in myocardial perfusion and LV function in a case of slow change of ECG stages after reached post-PCI TIMI flow grade 3, while myocardial perfusion improved and LV function tended to improve in a case of the rate at least two ECG stages in two days after primary angioplasty for acute MI.

Conflict of interest

The authors state no conflict of interest.

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