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Clinical and angiographic characteristics of patients with spontaneous reperfusion in ST-segment elevation myocardial infarction

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Abstract

This study aims to investigate the clinical and angiographic characteristics of patients with spontaneous reperfusion in ST-segment elevation myocardial infarction (STEMI).

A total of 519 patients with STEMI were enrolled in this study, who underwent primary percutaneous coronary intervention (PCI) treatments at Beijing Anzhen Hospital from January 2015 to December 2018. The patients were divided into 2 groups according to the TIMI flow grade before primary PCI, the non-spontaneous reperfusion group (TIMI flow grade 0–II) and the spontaneous reperfusion group (TIMI flow grade III). The incidence rate, the clinically relevant factors, and the features of the coronary angiographic lesions of spontaneous reperfusion from the 2 groups were recorded and analyzed.

There were significant differences between the 2 groups in age, CTnI peak value, high thrombus burden, and locations of lesions in the distant of left anterior descending artery (LAD) ($P = .000$, .000, .002, .000, and .003, respectively). However, there were no significant differences between the groups in other clinic aspects including gender, hypertension, diabetes mellitus, smoking history, hyperlipemia, angina pectoris history, culprit vessel distribution, lesion distribution in left circumflex artery (LCX) and right coronary artery (RCA), and collateral circulation ($P > .05$ for all).

Compared to the patients without spontaneous reperfusion, patients with spontaneous reperfusion were younger in age, lower in CTnI peak value, and higher in thrombosis burden, with culprit lesions mostly located in the distant of LAD.

Abbreviations: IRA = infarction related artery, LAD= left anterior descending artery, LCX = left circumflex artery, PCI = percutaneous coronary intervention, PPCI = primary percutaneous coronary intervention, QCA = quantitative coronary angiography, RCA = right coronary artery, STEMI = ST-segment elevation myocardial infarction, TVR = target vessel revascularization.

Keywords: primary percutaneous coronary intervention, spontaneous reperfusion, ST-segment elevation myocardial infarction

1. Introduction

As primary percutaneous coronary intervention (PPCI) has been widely used for patients with ST-segment elevation myocardium infarction (STEMI), cumulative coronary angiographic data[1–3] show that as high as 30% of the patients with acute STEMI have spontaneous reperfusion. It was shown that patients with spontaneous reperfusion had smaller myocardial infarction area and better clinical outcomes than those patients without spontaneous reperfusion.[1–3] Therefore, a better understanding of spontaneous reperfusion in patients with STEMI will be of great clinical significance. Here we carried out a retrospective study on patients with STEMI and provide detailed clinical and angiographic analyses on spontaneous reperfusion.

2. Methods

2.1. Study design and participants

All participants or their family members have been informed about the potential publication of their identities and images and all completed the consent forms. All procedures and protocols were approved by the ethics committee of Capital Medical University, and the experiments were conducted according to the Helsinki declaration (1975 and subsequent revisions).

From January 2015 to December 2018, 519 patients (361 males and 158 females) with acute STEMI who underwent PPCI treatment were enrolled in this retrospective study. All clinical

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We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality.

The authors have no conflicts of interest to disclose.

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data were collected from cache database of department of cardiology in Beijing Anzhen Hospital.

Their age ranged from 32 to 82 (61.2 ± 10.7). Inclusion criteria:

(1) AMI for <12 hours (i.e., evidence of ischemic chest pain lasting for >30 minutes, and new ST-segment elevation of ≥2 mm in 2 or more contiguous electrocardiographic (ECG) leads, a de novo lesion, single vessel treatment in a native vessel ≥2.5 mm in diameter and occluded, thrombus-containing, TIMI flow grade 0–3 culprit artery).
(2) No contraindications of anticoagulation or antiplatelet therapy.

The main exclusion criteria include following: previous percutaneous coronary intervention (PCI) in an infarction related artery (IRA) (n = 3), Killip class ≥3 (n = 3), left or right bundle branch block (n = 4), IRA with excessive proximal tortuosity or severe calcification (n = 5), left ventricular ejection fraction <35% (n = 5), lack of clinical and angiographic follow-up (n = 10), in-hospital death after PPCI (n = 4), myocardial infarction within 2 weeks of PPCI to exclude potential subacute stent thrombosis of the intervened arterial segment (n = 3), and repeated PCI of culprit coronary lesions for restenosis or progression (n = 17).

Coronary angiography was performed using the Judkins method, and coronary artery lesion classification was based on an ACC/AHA guideline.[3] Thrombus aspiration catheters (DIVER CE) were used for thrombotic burden lesions. Stents were implanted using a routine method, and the procedure succeeded with residual stenosis <20%, TIMI flow grade III, and no acute complication (death, myocardial infarction, emergency CABG), and no major adverse cardiac events [(cardiac death, myocardial infarction, target vessel revascularization (TVR)] in hospital.

According to no-reflow was defined as TIMI flow grade <2 and normal-reflow was defined as TIMI flow grade 3 in STEMI patients, we defined non-spontaneous reperfusion as TIMI flow grade ≤2 and defined spontaneous reperfusion as TIMI flow grade 3 in STEMI patients. All patients were divided into the non-spontaneous reperfusion group (TIMI flow grade 0–II) and the spontaneous reperfusion group (TIMI flow grade III) according to the TIMI flow grade before primary PCI (Fig. 1). The characteristics of the culprit vessels (location, numbers of the culprit vessels, thrombus burden) and the relevant factors (age, gender, hypertension, diabetes mellitus, smoking history, hyperlipemia, CTnI peak value, and angina pectoris history) were analyzed.

All patients underwent primary PCI for the culprit lesions. Quantitative coronary angiography (QCA) analyses were performed by 2 independent investigators who were blinded to the results. Lesions were classified according to the American College of Cardiology/American Heart Association classification, based on the morphological characteristics of lesions that cause significant stenosis of the coronary arteries. We then categorized the lesions accordingly into simple lesions (A or B1 lesions) and complex lesions (B2 or C).

2.2. Statistical analysis

The results for normally distributed continuous variables were expressed as the mean value ± standard deviation (SD), while categorical variables were expressed as percentages. Continuous variables were tested for normal distribution with the Kolmogorov–Smirnov test and for homogeneity of variances with Levene's test. The differences in the continuous variables were initially evaluated by one-way analysis of variance (ANOVA) or Student's *t* test, and then by Tukey's post hoc test where appropriate.

The categorical data were analyzed using Fisher's exact test or the chi-square test. Pearson's correlation coefficient was used to quantify the degree of stenosis of nonculprit artery lesions between clinical correlated factors. The differences were considered to be statistically significant if the null hypothesis could be rejected with >95% confidence. The SPSS 14.0 statistical software package (SPSS Inc, Chicago, IL) was used for all calculations.

3. Results

In this study, a total of 519 patients with STEMI (361 males and 158 females) underwent primary PCI. Among these patients, 134 people developed spontaneous reperfusion (92 males and 42 females) and were included in the spontaneous reperfusion

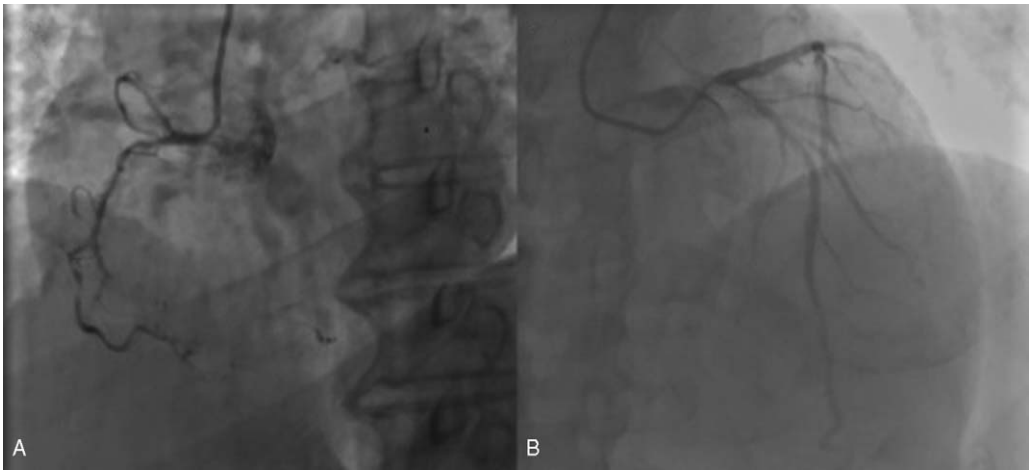

Figure 1. Angiographic data of the non-spontaneous reperfusion group and the spontaneous reperfusion group. A: the non-spontaneous reperfusion group; B: the spontaneous reperfusion group.

Table 1

Baseline characteristics between 2 groups.

N = 519	Spontaneous reperfusion group (N = 134)	Non-spontaneous reperfusion group (N = 385)	*P* value
Age	54 ± 13	59 ± 14	<.001
Male (n/%)	92/69%	269/70%	NS
Hypertension (n/%)	46/34%	139/36%	NS
Diabetes mellitus (n/%)	35/26%	96/25%	NS
Smoking history (n/%)	83/62%	234/61%	NS
Hyperlipemia (n/%)	61/46%	185/48%	NS
CTnI peak value (ng/ml)	18.13 ± 3.98	24 ± 4.21	<.001
Angina pectoris history (n/%)	61/46%	165/43%	NS
Time from attack to reperfusion (min)	372 ± 176	359 ± 169	NS
Aspirin (n/%)	134/100%	385/100%	NS
Clopidegrel (n/%)	134/100%	385/100%	NS
Unfractioned heparin (n/%)	134/100%	385/100%	NS

group. The rest of 385 STEMI patients had no spontaneous reperfusion (269 males and 116 females) were included in the non-spontaneous reperfusion group. The incidence of spontaneous reperfusion in patients with STEMI was 26%. The coronary angiographic data showed that there were significant differences between the 2 groups in patient age, CTnI peak value, high thrombus burden, degree of stenosis, and lesion location in distant left anterior descending artery (LAD) ($P < .001$, $P < .001$, $P < .01$, $P < .001$, and $P < .05$, respectively). However, there were no significant differences between the 2 groups in gender, hypertension, diabetes mellitus, smoking history, hyperlipemia, angina pectoris history, time from attack to reperfusion, antithrombotic drug, culprit vessel distribution, lesion distribution in left circumflex artery (LCX) and right coronary artery (RCA), and collateral circulation ($P > .05$ respectively) (Tables 1 and 2).

Baseline morphological characteristics of culprit lesions indicated that the complex lesion rate was higher in non-spontaneous reperfusion group than in the spontaneous reperfusion group ($P < .001$) (Table 3).

Table 2

Angiographic characteristics between 2 groups.

N = 519	Spontaneous reperfusion group (N = 134)	Non-spontaneous reperfusion group (N = 385)	*P* value
Culprit lesion: LAD	59 (44%)	181 (47%)	NS
Proximal	15 (25%)	142 (37%)	NS
Middle	13 (22%)	134 (35%)	NS
Distant	31 (53%)	109 (28%)	<.05
Culprit lesion: RCA	48 (36%)	146 (38%)	NS
Proximal	13 (27%)	52 (36%)	NS
Middle	12 (26%)	50 (34%)	NS
Distant	23 (47%)	44 (20%)	NS
Culprit lesion: LCX	27 (20%)	58 (15%)	NS
Proximal	7 (26%)	22 (38%)	NS
Middle	7 (26%)	18 (31%)	NS
Distant	13 (48%)	18 (31%)	NS
≥2 vessel lesion rate (n (%))	82 (61%)	177 (46%)	NS
Collateral circulation	43 (32%)	92 (24%)	NS
High thrombosis burden*	75 (56%)	135 (35%)	<.01
Degree of stenosis (%)	57 ± 18	73 ± 21	<.001

LAD = left anterior descending artery, LCX = left circumflex artery, RCA = right coronary artery.
* High burden thrombosis defined as the length of the thrombus is 3 times as the diameter of vessel.

Table 3

Baseline morphological characteristics of culprit lesions.

Type of lesion	Spontaneous reperfusion group (N = 134)	Non-spontaneous reperfusion group (N = 385)	*P*
A (n (%))	102 (76%)	124 (32%)	<.0001
B1 (n (%))	15 (11%)	131 (34%)	<.0001
B2 (n (%))	9 (7%)	65 (17%)	<.001
C (n (%))	8 (6%)	65 (17%)	<.001

4. Discussion

Previous studies have shown that the incidence of spontaneous reperfusion in STEMI patients could reach up to 30%. Most of the spontaneous reperfusions were not actually independent but as a result of antithrombotic drugs (such as aspirin, clopidogrel, low molecular weight heparin, unfractionated heparin, and platelet glycoprotein IIb/IIIa inhibitor) and vasodilator drugs treatment before primary PCI.[3–5]

As for the impact of Gp IIb/IIIa inhibitors on no reflow, a meta-analysis by De Rosa and colleagues provided evidence of a net clinical benefit for intracoronary versus intravenous abciximab administration, with the highest benefit observed in high-risk ACS patients, such as those with reduced baseline LVEF. This result showed that intracoronary Gp IIb/IIIa inhibitors administration may be a better therapeutic approach than intravenous GpIIb/IIIa inhibitors administration for reducing no reflow damage and it may be related to intracoronary administration results in a higher degree of GP IIb/IIIa receptor occupancy and a more pronounced platelet inhibition.[6]

As for the impact of adenosine administration and the specific route of administration on myocardial reperfusion and no reflow, a meta-analysis by Polimeni et al demonstrated a clinical benefit for IC adenosine in hard endpoints, such as adverse cardiovascular events, in patients undergoing primary PCI. This result indicated that intracoronary adenosine administration may improve no reflow, and this effect is at least in part related to an increased release of t-PA.[7]

De Rosa et al investigated the impact of thrombectomy (rheolytic thrombectomy and aspiration thrombectomy) on coronary reperfusion and no reflow, and the results indicated that both mechanical thrombectomy and manual thrombectomy may improve no reflow. This effect is related to reduced intracoronary thrombus burden.[8,9]

Previous research showed a better prognosis in STEMI patients with spontaneous reperfusion than in STEMI patients without spontaneous reperfusion.[10–13] However, lack of data on clinical and angiographic characteristics of those patients with spontaneous reperfusion greatly hindered our better understanding of the mechanism of the observation, and therefore further development of clinical treatment.

It was shown previously that there were no significant differences in age, risk factor, and lesion distribution between spontaneous reperfusion and non-spontaneous reperfusion groups.[4–6] But Lees' study indicated that preinfarction angina, heavy thrombi, good angiograthic collaterals were independent predictors of spontaneous reperfusion in patients with STEMI.[14] Our study also showed that clinical conditions such

as diabetes, smoking, hyperlipemia were not associated with non-spontaneous coronary reperfusion. It indicated that these clinical conditions may be not the critical factors for non-spontaneous reperfusion.

Our study showed that patients with spontaneous reperfusion were younger in age, lower in CTnI peak value, and higher in thrombosis burden, with culprit lesions mostly located in the distant LAD compared to the patients without spontaneous reperfusion. These data suggested that spontaneous reperfusion could more likely occur in younger patients, with high thrombosis burden and slight stenosis in culprit arteries. Our observation of the culprit lesions as mostly located in the distant LAD is consistent with the conclusions from Harjai and colleague.[15] In addition, it was reported that patients with spontaneous reperfusion had smaller myocardial infarction area.[12–14] In our study, we did not find significant differences between the 2 group of patients in gender, hypertension, diabetes mellitus, smoking history, hyperlipemia, angina pectoris history, culprit vessels distribution, lesions distribution in LCX and RCA, and collateral circulation ($P > .05$ respectively). Our data also showed that culprit lesions located more likely at the distant of RCA or LCX, and with more collateral circulations in STEMI patients with spontaneous reperfusion, when compared to STEMI patients without spontaneous reperfusion, albeit the differences were not significant. Baseline morphological characteristics of culprit lesions indicated that the complex lesion rate was higher in non-spontaneous reperfusion group than in spontaneous reperfusion group ($P < .001$), which suggested that spontaneous reperfusion occurs more likely in simple lesions.

In conclusion, this study suggested that, compared to the patients without spontaneous reperfusion, patients with spontaneous reperfusion are younger in age, lower in CTnI peak value, and higher in thrombosis burden, with simple culprit lesions mostly located in the distant of LAD.

5. Limitations of the study

This retrospective study was performed at 1 center, thus posing a risk for possible bias in data analysis. The number of patients enrolled in this study was low, it might have been underpowered in identifying other clinical conditions.

Author contributions

J.W. designed and coordinated the study, J.W. wrote the main manuscript text. S.-Y.H. collected samples. All authors reviewed the manuscript.
Conceptualization: Jian Wang.
Data curation: Jian Wang.
Formal analysis: Jian Wang.
Funding acquisition: Jian Wang.
Investigation: Jian Wang.
Methodology: Jian Wang.
Project administration: Jian Wang.
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Software: Jian Wang, Song-yuan He.
Supervision: Jian Wang.
Validation: Jian Wang.
Visualization: Jian Wang.
Writing – original draft: Jian Wang, Song-yuan He.
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