The effect of ticagrelor on myocardial microcirculation, cardiac function, and adverse cardiovascular events in STEMI patients after PCI

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Abstract. – **OBJECTIVE:** This study aimed to investigate the effects of ticagrelor on myocardial microcirculation, cardiac function, and adverse cardiovascular events in ST-segment elevation myocardial infarction (STEMI) patients after percutaneous coronary intervention (PCI).

PATIENTS AND METHODS: A total of 80 STEMI patients admitted to our hospital from February 2020 to March 2023 were selected and included in the retrospective study, all receiving PCI treatment. They were randomly and retrospectively divided into a control group (40 cases) and an observation group (40 cases), and treated with clopidogrel and ticagrelor, respectively. The clinical effects were compared.

RESULTS: The starting perfusion time of the contrast agent in the myocardial infarction area in the observation group was 2.22±0.27 s, and the peak perfusion time was 2.62±0.27 s, which was lower than those in the control group (2.51±0.29 s and 3.21±0.39 s, t=4.629, 7.867, p=0.000). The ratio of peak perfusion intensity between the two groups was significantly different (t=2.363, p=0.021). Left ventricular ejection fraction, stroke volume index, and cardiac index in the observation group were higher than those in the control group (55.03±6.03 *vs.* 52.33±5.13; 57.39±6.81 *vs.* 51.11±6.31 L/min·m^{-2}; 3.49±0.45 *vs.* 3.12±0.38 mL/m^2, t=2.157, 4.278, 3.973, p<0.05). The observation group had lower levels of brain natriuretic peptide and C-reactive protein compared to the control group (425.35±55.71 *vs.* 589.36±70.24 pg/mL; 15.13±1.03 *vs.* 21.64±2.74 mg/L; t=11.570, 14.066, p=0.000). There was no statistical significance in the incidence of adverse cardiovascular events between the two groups (2.50% *vs.* 7.50%, χ^2=1.920, p=0.166).

CONCLUSIONS: The use of ticagrelor can regulate myocardial microcirculation and improve cardiac function in STEMI patients undergoing PCI.

Introduction

ST-segment elevation myocardial infarction (STEMI) is the most common type of myocardial infarction. Patients often have ischemic chest pain, which lasts for more than 20 minutes. The electrocardiogram (ECG) examination showed ST segment elevation[1]. This disease has a high risk of morbidity, disability, and death, endangering the health and safety of patients. Percutaneous coronary intervention (PCI) is the preferred method for treating STEMI as it controls the disease[2]. It can open the blocked coronary vessels and save the ischemic myocardium. However, some patients with PCI have abnormal myocardial perfusion and slow blood flow after surgery[3], which will reduce left ventricular function and adversely affect prognosis. Relevant literature[4] has indicated that the main pathological basis of STEMI is coronary artery stenosis and occlusion, which requires early recovery of coronary blood flow in treatment. It has been pointed out in relevant literature[5] that antiplatelet drugs can inhibit platelet aggregation and have certain protective and repairing effects on blood vessels and myocardial muscle[6]. Ticagrelor and clopidogrel are both commonly used antiplatelet drugs, among which ticagrelor is a new inhibitor of platelet aggregation and can produce direct efficacy without liver metabolic activation[7]. This study focused on

the efficacy of ticagrelor therapy in patients with STEMI after PCI.

Patients and Methods

General Information

A total of 113 STEMI patients who underwent PCI in our hospital from April 2021 to November 2022 were selected for this retrospective study. Inclusion criteria: 1) consistent with the diagnosis and treatment guidelines for STEMI formulated by the Chinese Medical Association[8]; 2) first onset; 3) understand the content and sign the consent form. Exclusion criteria: 1) patients with cardiogenic shock; 2) patients with anticoagulant contraindications; 3) adverse reactions to the drugs used; 4) patients with immune diseases. Thirty-three patients were excluded according to the exclusion criteria. Therefore, 80 patients were finally included. They were randomly and retrospectively divided into a control group (40 cases) and an observation group (40 cases). This study complied with the relevant requirements of the Declaration of Helsinki of the World Medical Association and was approved by the Ethics Committee of our Hospital.

Methods

Control group

PCI was performed in both groups. The control group received load dose aspirin (manufacturer: Jinling Pharmaceutical Co., LTD. Nanjing Jinling Pharmaceutical Co., LTD., National drug approval code: H32023680, specification: 300 mg), the dose was 300 mg, and 600 mg load dose clopidogrel (manufacturer: Shenzhen Xinlitai Pharmaceutical Co., LTD., national drug approval code: H20203616, specification: 75 mg), 100 mg aspirin was taken once a day after surgery for a long time; 75 mg of clopidogrel was administered once a day for 1 year.

Observation group

Before PCI, the observation group received a 300-mg load dose of aspirin and a 180-mg load dose of ticagrelor (manufacturer: Shanghai Huilun Jiangsu Pharmaceutical Co., LTD., national drug approval number: H20205005, specification: 60 mg). The dosage of aspirin was 100 mg once a day after operation, and long-term administration was needed. Ticagrelor was given at 90 mg twice a day for 1 year. STEMI patients in the two groups were injected with 100 U/kg heparin intravenously during PCI. During the intervention period, activated coagulation time should be maintained at more than 250 s, and anti-coagulation with low molecular weight heparin was required after surgery, and measures such as blood pressure lowering and lipid regulation were implemented[9,10].

Index Observation

(1) Before and after PCI, myocardial microcirculation was evaluated from the perfusion time (AT), the peak perfusion time (APT), and the peak perfusion intensity (PI) of contrast media in the myocardial infarction area using myocardial contrast imaging. (2) The cardiac function parameters were recorded by ultrasound, including cardiac index, left ventricular ejection fraction (LVEF), and stroke output index (SVI). (3) Serum C-reactive protein (CRP) and brain natriuretic peptide (BNP) were detected. (4) Statistics of adverse cardiovascular events should be conducted during PCI treatment.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 27.0 (IBM Corp., Armonk, NY, USA) was used to analyze the data. Measurements were normally distributed, and Chi-square was described using mean ± standard deviation (SD), and comparisons between the two groups were made by independent samples t-test or paired t-test. Repeated-measure data were analyzed by ANOVA with a repeated-measures design, and an LSD t-test was used for comparisons between the two groups. Count data were described as [n(%)], χ^2 test or Fisher's exact probability method was used for the comparison of unordered data, and Z-test was used for the comparison of ordered data. $p<0.05$ was statistically significant.

Results

The General Clinical Characteristics

There were 25 males (62.50%) and 15 females (37.50%) in the control group, with an average age of 62.79±3.14 years. The longest course of coronary heart disease was 10 years, the shortest course was 4 years, and the average course was 7.18±1.24 years. In the observation group, there were 24 males (60.00%) and 16 females (40.00%), with an average age of 63.08±3.22 years old. The average course of coronary heart disease was 7.27±1.31 years. There was no difference in data
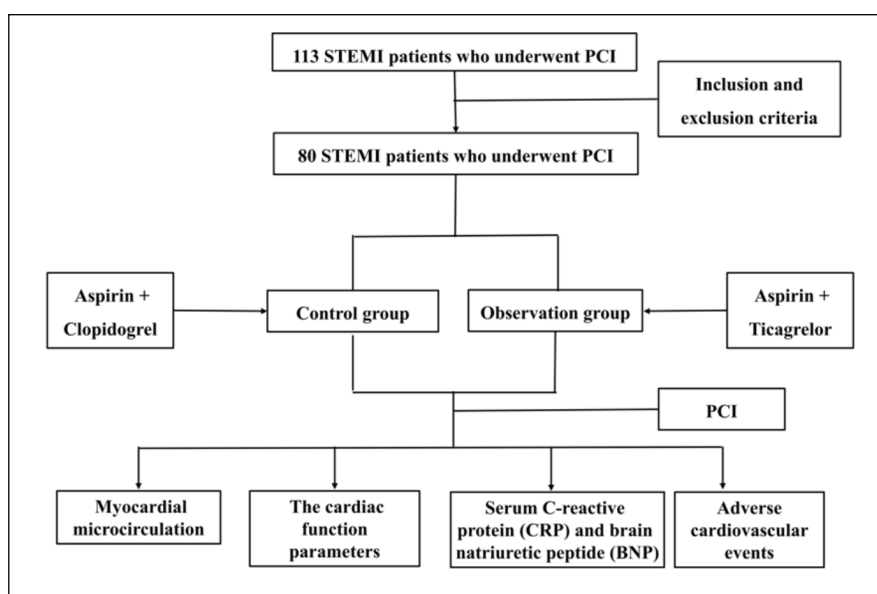
Figure 1. The flow chart of this study.

comparison between the two groups (*p*>0.05) (Figure 1).

Myocardial Microcirculation Parameters Were Compared Between the Two Groups

The beginning time of contrast agent perfusion in the myocardial infarction area (AT), the peak time of perfusion (APT), and the peak intensity of perfusion (PI) of the observation group were better (*p*<0.05) 1 week after PCI, as shown in Table I.

Comparison of Cardiac Function Between the Two Groups

Left ventricular ejection fraction (LVEF), heart index, and stroke output index (SVI) in the observation group improved after intervention (*p*<0.05), as shown in Table II.

Brain Natriuretic Peptide and Serum C-reactive Protein Were Compared Between the Two Groups

Brain natriuretic peptide (BNP) and C-reactive protein (CRP) in the observation group were lower than those in the control group (*p*<0.05), as shown in Table III.

Adverse Cardiovascular Events Were Compared Between the Two Groups

Cardiovascular adverse events in the observation group were less than those in the control group (*p*>0.05), as shown in Table IV.

Discussion

In this study, we evaluated the effect of ticagrelor on myocardial microcirculation, cardiac

Table I. Comparison of myocardial microcirculation before and after PCI.

	AT (s)		PI (dB)		APT (s)	
Groups	Before PCI	1 week after PCI	Before PCI	1 week after PCI	Before PCI	1 week after PCI
Control group	2.71±0.32	2.51±0.29	5.61±0.63	6.01±0.62	3.48±0.52	3.21±0.39
Observation group	2.72±0.34	2.22±0.27	5.42±0.54	6.31±0.51	3.50±0.53	2.62±0.27
t-value	0.135	4.629	1.448	2.363	0.170	7.867
p-value	0.893	0.000	0.152	0.021	0.865	0.000

PCI (percutaneous coronary intervention), AT (the beginning time of contrast agent perfusion in myocardial infarction area), APT (the peak time of perfusion), PI (the peak intensity of perfusion).

Table II. Comparison of cardiac function parameters.

Groups	LVEF (%)		Cardiac index (L·min⁻¹·m⁻²)		SVI/ (mL/m²)	
	Before PCI	1 week after PCI	Before PCI	1 week after PCI	Before PCI	1 week after PCI
Control group	45.37±6.10	52.33±5.13	2.47±0.31	3.12±0.38	46.11±5.87	51.11±6.31
Observation group	45.34±5.88	55.03±6.03	2.50±0.34	3.49±0.45	46.09±5.76	57.39±6.81
t	0.022	2.157	0.412	3.973	0.015	4.278
p	0.982	0.034	0.681	0.000	0.988	0.000

PCI (percutaneous coronary intervention), LVEF (left ventricular ejection fraction), SVI (stroke output index).

function, and adverse cardiovascular events in STEMI patients after PCI. Aspirin and ticagrelor were given in the observation group, and aspirin and clopidogrel were given in the control group. Our results showed that the application of ticagrelor and aspirin on top of PCI for STEMI can effectively increase the level of myocardial perfusion, protect cardiomyocytes, improve cardiac function, and reduce the risk of adverse events in patients.

STEMI patients typically exhibit elevated ST segments on electrocardiograms, and all have coronary artery blockage due to thrombus, leading to acute myocardial ischemia with potential necrosis[11]. Patients often experience pain in the heart, syncope, coma, dyspnea, and other symptoms, which may lead to sudden death in severe cases[12]. Currently, PCI is a crucial treatment for STEMI, as it effectively restores blood flow in the coro-

nary arteries[13]. However, patients often experience incomplete myocardial blood perfusion after treatment, and the occurrence of adverse events is the main reason for incomplete blood perfusion to the myocardium after treatment[14]. Survey results[15] show that about 5-25% of patients after PCI will have the problem of no coronary reflow, so it is very important to explore solutions.

Stent implantation, as well as balloon in PCI surgery, may prompt vascular plaque dislodgement, create blockage to microvessels, stimulate platelet aggregation, and then form more emboli, which ultimately triggers microcirculation dysfunction[16]. In addition, ischemia and reperfusion will damage the patient's blood vessels, and ischemic coronary arteries will cause damage to microvascular endothelial cells, and contractile dysfunction, which in turn triggers microvascular lumen narrowing, abnormal contraction, ab-

Table III. Comparison of BNP and serum CRP.

Groups	Cases	BNP before PCI (pg/mL)	BNP 1 week after PCI (pg/mL)	CRP before PCI (mg/L)	CRP 1 week after PCI (mg/L)
Control group	40	991.26±182.54	589.36±70.24	36.48±4.39	21.64±2.74
Observation group	40	987.69±180.31	425.35±55.71	36.52±4.42	15.13±1.03
t		0.088	11.570	0.041	14.066
p		0.930	0.000	0.968	0.000

PCI (percutaneous coronary intervention), LVEF (left ventricular ejection fraction), SVI (stroke output index).

Table IV. Comparative Adverse Cardiovascular events [n (%)].

Groups	Cases	Sudden cardiac death	Nonfatal acute cerebral infarction	Target vessel revascularization	Incidence rate
Control group	40	1	1	1	3 (7.50)
Observation group	40	1	0	0	1 (2.50)
χ^2					1.920
p					0.166

PCI (percutaneous coronary intervention), LVEF (left ventricular ejection fraction), SVI (stroke output index).

normal spasm, and myocardial ischemia is exacerbated[17]. Reperfusion injury also increases the release of intravascular reactive oxygen species, pro-inflammatory factors, platelets, and neutrophils, aggravating vascular inflammation, and all of the above factors will affect the recovery of cardiac function and myocardial perfusion[18]. Therefore, it is particularly important to choose the appropriate drug regimen to cooperate with the treatment after PCI.

Drugs are needed to improve the situation and to ensure that myocardial blood is fully perfused. The main reason for the incomplete perfusion of blood to the myocardium after treatment is the occurrence of adverse events. Clopidogrel is a platelet aggregation inhibitor that selectively inhibits the binding of platelets to adenosine diphosphate receptors. However, in the perioperative period, the use of this drug can increase the risk of bleeding. Ticagrelor is an adenosine diphosphate receptor antagonist, which can rapidly and effectively inhibit platelet aggregation[19,20] and effectively inhibit the uptake of adenosine into red blood cells. It takes effect quickly and does not require liver metabolism. In addition, it has anti-inflammatory effects and can reduce platelet activity[21,22].

In the TRITON-TIMI38 phase 3 trial[23], enhanced platelet inhibition by Prasugrel reduced major adverse cardiovascular events in STEMI patients treated with PCI. A foreign study[24] showed that ticagrelor provided prolonged platelet inhibition compared with clopidogrel in STEMI patients undergoing PCI. A clinical study[25] including 1,242 patients with STEMI demonstrated that the use of standard-dose ticagrelor infusion in addition to aspirin, high-dose Clopidogrel, and plain heparin before PCI therapy significantly improved myocardial reperfusion and adverse events in patients with STEMI without increasing the risk of major bleeding. However, it has also been shown that compared with ticagrelor combined with aspirin, ticagrelor monotherapy reduces clinically meaningful bleeding events in STEMI patients after PCI without increasing ischemic risk[26]. Our results showed that AT and APT in the observation group were lower than those in the control group, while PI was higher than that in the control group ($p<0.05$). It is suggested that ticagrelor can optimize myocardial blood perfusion and improve myocardial microcirculation. LVEF, heart index, and SVI in the observation group were higher than those in the control group at 1 week after PCI ($p<0.05$). It is speculated that ticagrelor can significantly improve left ventricular systolic function. BNP and CRP in the observation group were lower than those in the control group ($p<0.05$). There was no difference in the risk of sudden cardiac death, target vessel revascularization, and non-fatal acute reinfarction between the two groups ($p>0.05$). It may be related to time, number of cases, improvement of PCI technology, etc.

Limitations

This study still has some limitations. The sample size was limited and needs to be expanded in subsequent studies; in addition, long-term follow-up to observe myocardial function and the occurrence of adverse cardiovascular events was not performed.

Conclusions

In summary, ticagrelor can improve coronary microcirculation perfusion without increasing adverse events in patients with STEMI and PCI.

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Availability of Data and Materials

All data and materials can be obtained through the corresponding author via email.

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