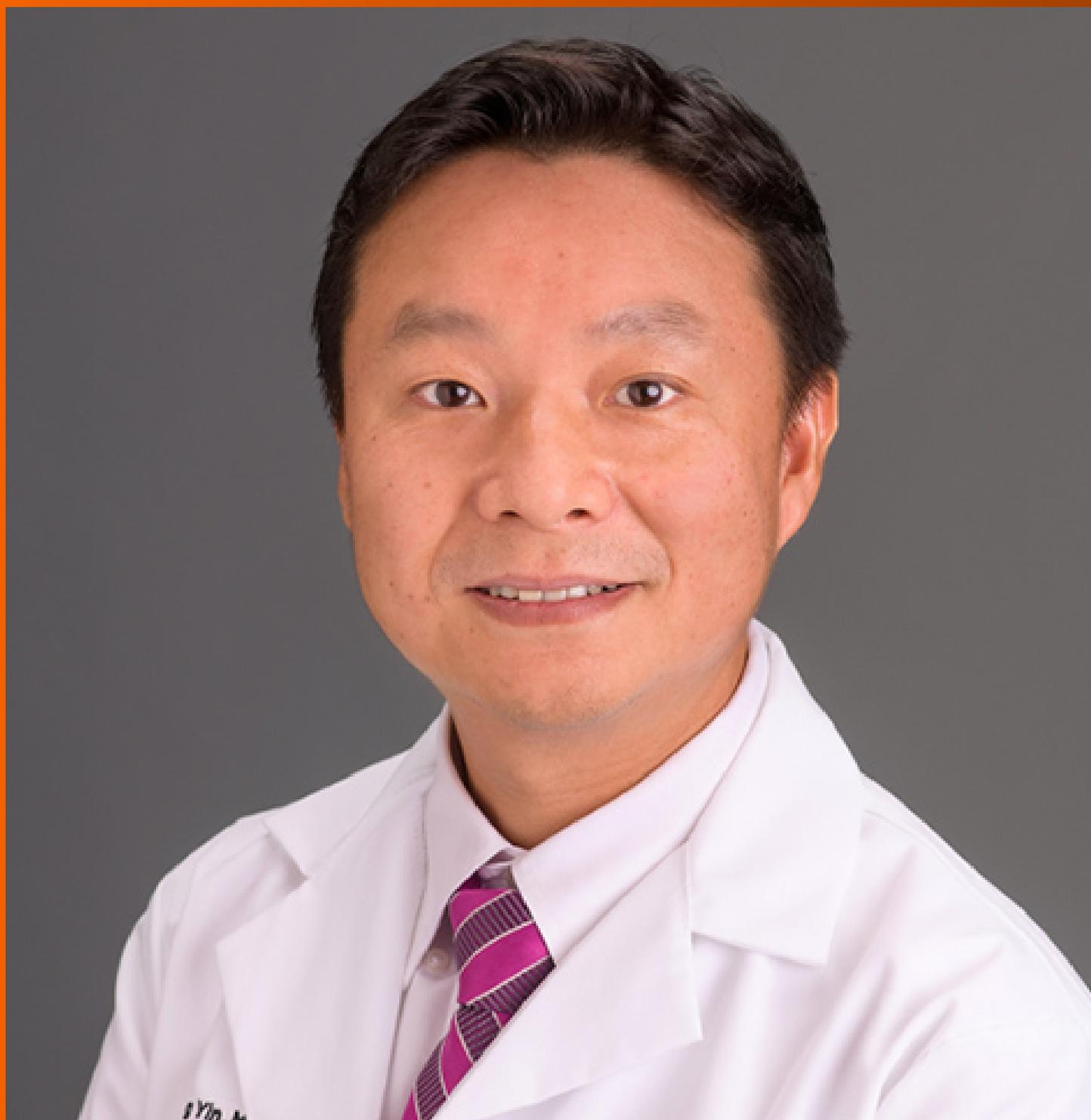


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## Retrospective Study

# Postoperative adverse cardiac events in acute myocardial infarction with high thrombus load and best time for stent implantation

Ming-Feng Zhuo, Ke-Lian Zhang, Xue-Bin Shen, Wen-Can Lin, Bin Hu, Hua-Peng Cai, Gang Huang

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## Abstract

### BACKGROUND

Myocardial infarction is one of the most common types of coronary heart disease. It is mainly caused by the rupture of coronary atherosclerotic plaque, which leads to platelet agglutination and thrombosis. The occlusion of coronary arteries and vessels leads to insufficient myocardial blood supply, subsequently causing cardiac interstitial fibrosis, gradual enlargement of ventricles, and heart failure, which affects the quality of life and safety of patients.

### AIM

To investigate the effects of emergency percutaneous interventional therapy (PCI) and delayed stenting in acute myocardial infarction with high thrombotic load and identify factors related to major adverse cardiovascular events (MACE).

### METHODS

A total of 164 patients with acute myocardial infarction and high thrombotic load who received PCI were included. Of them, 92 patients were treated with delayed stent implantation (delayed group) and 72 patients received emergency PCI (immediate group). Myocardial perfusion after stent implantation was compared between the two groups. Patients were followed up for 12 mo, and the occurrence of MACE was used as the endpoint. Univariate and multivariate models were used to analyze the factors affecting MACE occurrence.

### RESULTS

After stent implantation, 66 (71.74%) patients in the delayed group and 40

(55.56%) patients in the immediate group had thrombolysis in myocardial infarction (TIMI) flow grade 3 ( $P < 0.05$ ), while 61 (66.30%) patients in the delayed group and 39 (54.17%) patients in the immediate group reached TIMI myocardial perfusion grade 3 ( $P > 0.05$ ). MACE occurred in 29 patients. There were statistically significant differences between the MACE and non-MACE groups in diabetes rate, TIMI grading, stent implantation timing, intraoperative use of tirofiban, and the levels of white blood cells (WBC), neutrophils, red blood cell distribution width (RDW), and uric acid, and high-sensitivity C-reactive protein (hs-CRP) at admission ( $P < 0.05$ ). Logistic regression analysis showed that TIMI grade 3 and intraoperative use of tirofiban effectively reduced the risk of MACE ( $P < 0.05$ ), while immediate stent implantation, increased WBC, hs-CRP and RDW on admission increased the risk of MACE ( $P < 0.05$ ).

### CONCLUSION

Delayed stent implantation outweighs emergency PCI in improving postoperative myocardial perfusion in acute myocardial infarction with high thrombotic load, and effectively reduces MACE in these patients.

**Key Words:** Coronary thrombosis; Myocardial infarction; Emergency; Percutaneous coronary intervention; Treatment delay; Adverse cardiovascular events

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**Core Tip:** This study compared delayed stent implantation with emergency percutaneous intervention in terms of myocardial perfusion after stent implantation in 164 patients with acute myocardial infarction and high thrombotic load using univariate and multivariate models. Obtained results showed that delayed stent implantation is more beneficial than emergency percutaneous coronary intervention in improving postoperative myocardial perfusion in acute myocardial infarction with high thrombotic load, and effectively reduces major adverse cardiovascular events in these patients.

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## INTRODUCTION

Thrombosis is the main factor in the pathogenesis of all acute coronary syndromes[1]. An unstable plaque in the coronary artery causes platelet aggregation, activation, and aggregation, resulting in thrombosis, sharp reduction or even complete interruption of coronary blood flow, which in turn leads to myocardial necrosis and a series of complications[2]. A high coronary thrombotic load is positively correlated with the severity of vascular wall damage, the number of inflammatory cells, amount of collagen, and tissue factor production. Early opening of the occluded blood vessels reduces the incidence of cardiovascular adverse events and is very important to restore the myocardial reperfusion. Percutaneous coronary intervention (PCI) is currently the preferred strategy for the treatment of myocardial infarction, as it provides early and effective culprit artery opening, thus restoring myocardial reperfusion and saving the endangered damaged myocytes. However, other factors, such as smoking habit, male sex, and the inner diameter of the right coronary artery, may affect the prognosis of patients with acute myocardial infarction and high thrombotic load[3,4], and the best timing of PCI remains elusive in these patients[5,6]. The aim of this study was to analyze the effect of emergency PCI and direct stenting in comparison with delayed stenting in the treatment of patient with acute myocardial infarction and high thrombotic load, and to assess the related factors of adverse cardiovascular events after treatment in order to provide clinical guidance and basis.

## MATERIALS AND METHODS

### Data

A total of 164 patients with acute myocardial infarction with high thrombotic load who received PCI

from January 2018 to April 2020 were selected for clinical study. Of them, 92 patients were treated with delayed stent implantation based on standardized drug therapy (delayed group), and the other 72 patients were treated with emergency PCI after admission (immediate group).

Inclusion criteria: (1) Age between 18 and 75 years; (2) Acute ST-segment elevation myocardial infarction and admission within 12 h of onset; (3) Thrombus grading evaluated according to the results of coronary angiography during the operation (0: no thrombus; 1 point: blurred vessel lumen; 2 points: clear thrombus, length < 0.5 times the diameter of the vessel; 3 points: clear thrombus, length 0.5–2 times the diameter of blood vessel; 4 points: clear thrombus, length > 2 times the diameter of the vessel; and 5 points: clear thrombus, complete occlusion of the vessel); and (4) Medical ethics committee approval.

Exclusion criteria: (1) Ischemic stroke within 3 mo; (2) A history of intracranial hemorrhage; (3) Active bleeding or bleeding factors (gastrointestinal variceal bleeding); (4) Suspected aortic dissection; (5) Severe or uncontrolled hypertension ( $\geq 180/110$  mmHg); (6) Malignant tumors; (7) Severe trauma, major surgery, or blood vessel bleeding that cannot be compressed within 3 wk; (8) Severe liver and kidney disease; (9) Allergy or contraindications to thrombolytic agents and contrast agents; and (10) Coronary artery bypass grafting.

### **Basic drug therapy and PCI therapy**

Patients from the immediate group were treated with emergency PCI (GE Healthcare; USA) immediately after admission. Aspirin and ticagrelor or clopidogrel were administered before PCI, followed by intravenous heparin infusion. PCI was performed *via* the radial access and tirofiban was administered before the procedure; coronary anatomy, collateral circulation, and thrombosis were determined to decide the treatment plan. The criteria for successful PCI were residual stenosis  $\leq 20\%$  and distal infarct-related artery blood flow reaching thrombolysis in myocardial infarction (TIMI) grade 3.

Delayed group: Methods As with the immediate group, if complete coronary occlusion, occluded vessels were opened and delayed stent implantation restored the TIMI flow grade (the difference is only in stent and delayed implantation).

### **Myocardial perfusion index**

TIMI flow was graded as follows: Grade 0: complete vascular occlusion and distal vessels at occlusive sites do not fill with forward flow; Grade 1: a small amount of contrast agent can be observed to pass through the vascular occlusion site, a small part of distal vessels is opened, and vascular filling is incomplete; Grade 2: The contrast agent can completely fill the distal coronary artery, but the forward filling and emptying speed of contrast agent is significantly slower than that of normal coronary arteries; and Grade 3: Complete coronary refusion, complete filling or emptying of contrast within 3 cardiac cycles.

TIMI myocardial perfusion grading (TMPG) was as follows: Grade 0: no contrast agent enters the myocardium, no or only transient myocardial contrast agent staining; Grade 1: The contrast agent enters the myocardium slowly, the myocardial staining of the micro vessels does not disappear, and the contrast agent staining of the myocardium in the blood supply area persists in a sequence of angiography; Grade 2: The contrast agent enters the myocardial tissue and empties late, enters the myocardium like "ground-glass", or increases during blood supply and myocardial removal, and does not disappear for at least 3 cardiac cycles; Grade 3: The entry and emptying of contrast agents in myocardial tissue are normal.

ST segment drop was recorded 90 min after PCI. According to ST segment drop ( $\geq 50\%$  and  $< 50\%$  from baseline), patients were divided in the two groups (delayed and immediate groups).

A total of 3 mL of fasting venous blood was collected and centrifuged at 3000 r/min for 30 min. The concentrations of white blood cells (WBC), neutrophils (N), red blood cell distribution width (RDW) and uric acid (UA) were measured by an automatic biochemical analyzer (7600i; Hitachi, Tokyo, Japan). The high-sensitivity C-reactive protein (hs-CRP) concentration was measured using an enzyme-linked immunoadsorption test (Nanjing Jiancheng Biological Products Co., LTD, Nanjing, China).

### **Definition of major adverse cardiovascular events**

Patients from both groups were followed up for 12 mo after PCI for the occurrence of major adverse cardiovascular events (MACE), which was used as the primary endpoint. MACE was a composite of recurrent angina pectoris, recurrent acute myocardial infarction, sudden cardiac death, malignant arrhythmia, congestive heart failure, and other cardiovascular events[7,8].

### **Statistical analysis**

Normally distributed variables, such as age and body mass index (BMI), are expressed as mean  $\pm$  SD. Counting data are expressed as percentage, and  $\chi^2$  test was used for comparison. A logistic regression model was used for multivariate analysis, and SPSS 21.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The statistical significance was set at  $\alpha = 0.05$ .

## RESULTS

### **Comparison of TIMI flow grades between the two groups after stent implantation**

After stent implantation, 66 (71.74%) patients in the delayed group and 40 (55.56%) patients in the immediate group reached TIMI flow grade 3 ( $P < 0.05$ ) (Table 1). Simultaneously, 61 (66.30%) patients in the delayed group and 39 (54.17%) patients in the immediate group reached TMPG 3 ( $P > 0.05$ ).

### **Comparison of ST segment drop rate 90 min after PCI between the two groups after stent implantation**

At 90 min after stent implantation, the ST segment dropped  $\geq 50\%$  from baseline in 82.61% of patients from the delayed group and in 77.78% of patients from the immediate group ( $P > 0.05$ ) (Table 2).

### **Single factor analysis of MACE occurrence**

Among 164 patients with acute myocardial infarction and high thrombotic load treated with stenting, 29 had MACE events (11 with recurrent angina pectoris, 4 with recurrent acute myocardial infarction, 1 with sudden cardiac death, 1 with malignant arrhythmia, 5 with congestive heart failure, and 7 with other cardiovascular events) (Table 3). There were no statistically significant differences in age, BMI, heart rate, number of implanted stents, sex, combined hypertension, hyperlipidemia, smoking habits, infarct-related vascular distribution, Killip grading, use of angiotensin-converting enzyme inhibitors or  $\beta$ -blockers, and peak CK-MB between patients with MACE and those without MACE ( $P > 0.05$ ). However, there were statistically significant differences between them in the diabetes rate, TIMI grading, stent implantation timing, intraoperative use of tirofiban, and levels of WBC, N, RDW, UA and hs-CRP at admission ( $P < 0.05$ ).

### **Multiple factor analysis of MACE occurrence**

A logistic regression model was established, and statistically significant variables (diabetes rate, TIMI grading, stent implantation timing, intraoperative tirofiban, and WBC, N, RDW, UA and hs-CRP levels at admission) were used as dependent variables, whereas MACE were used as independent variables (Table 4). The results showed that TIMI grade 3 and intraoperative use of tirofiban were associated with reduced risk of MACE after stent implantation ( $P < 0.05$ ), while immediate stent implantation, increased WBC, hs-CRP and RDW on admission were associated with increased risk of MACE ( $P < 0.05$ ).

## DISCUSSION

This study showed that TIMI blood flow grading was better in the delayed group of stent implantation than in the immediate group of stent implantation, suggesting that delayed stent implantation was more beneficial in the improvement of postoperative myocardial perfusion than was emergency PCI in patients with acute myocardial infarction with high thrombus load. At the same time, logistic regression analysis showed that TIMI blood flow grade 3 and intraoperative use of tirofiban were protective factors in these patients due to effective reduction of the risk of MACE, while immediate implantation of stenting, increased levels of WBC, hs-CRP and RDW on admission increased the risk of MACE.

PCI can restore the blood flow of the infarct-related artery and ensure the integrity of the function of reperfusion myocardial cells, and the normal diastolic and systolic functions of the left ventricle. However, there are still some patients with left ventricular diastolic dysfunction after PCI, which affects their prognosis. Few studies have assessed the factors that determine this phenomenon to date[9]. In addition, there are potential risks associated with PCI, such as plaque rupture that induces debris formation, which leads to the distal coronary artery embolization, affecting the local microcirculation function and possibly causing irreversible reduction of perfusion volume[10]. On the other hand, the occurrence of capillary spasm in the human body is related to the formation of capillary dilate disorder caused by the interaction of neurohumoral factors. Various PCI maneuvers will lead to vascular endothelial structure damage, inhibition of nitric oxide production by endothelial cells, increased sympathetic nerve excitability, and vasoconstriction, which results in capillary spasm persistence[11]. In addition, previous studies have shown that there is a large number of WBC in the areas without reflow in the human body, blocking the capillary bed. After endothelial injury, activated platelets determine capillary constriction and aggravate the inflammatory response and cell edema. Meanwhile, the large amount of free radicals produced in the body will reduce the nitric oxide activity of endothelial cells, resulting in direct damage to cells. Therefore, no reflow phenomenon is related to the aggravation of the inflammatory response[12-14].

This study analyzed the risk factors of MACE after stent implantation in patients with acute myocardial infarction and high thrombus load. Patients with TIMI grade 3 had a reduced risk of MACE after PCI, suggesting a good improvement in microcirculation perfusion. Revascularization is the main objective of treatment in patients with acute myocardial infarction. However, this includes not only the vessel opening, but also the restoration of blood supply to the microcirculation of the myocardium, and

**Table 1 Comparison of thrombolysis in myocardial infarction flow grades and thrombolysis in myocardial infarction myocardial perfusion grade grading after stent implantation between the two groups, *n* (%)**

Group	Deferred group ( <i>n</i> = 92)	Immediate group ( <i>n</i> = 72)	Z	P value
TIMI flow grades			-2.302	0.021
0 degree	0 (0)	0 (0)		
1 degree	2 (2.17)	6 (8.33)		
2 degree	24 (26.09)	26 (36.11)		
3 degree	66 (71.74)	40 (55.56)		
TMPG grading			-1.836	0.066
0 degree	0 (0.00)	0 (0.00)		
1 degree	3 (3.26)	8 (11.11)		
2 degree	28 (30.43)	25 (34.72)		
3 degree	61 (66.30)	39 (54.17)		

TIMI: Thrombolysis in myocardial infarction; TMPG: TIMI myocardial perfusion grade.

**Table 2 Comparison of ST segment fall rate at 90 min after percutaneous coronary intervention, *n* (%)**

Group	<i>n</i>	≥ 50%	< 50%
Delayed Group	92	76 (82.61)	16 (17.39)
Immediate group	72	56 (77.78)	16 (22.22)
$\chi^2$		0.600	
P value		0.438	

the continuous and complete restoration of blood supply to the myocardium cells level. During ischemia and reperfusion, myocardial cell membrane sodium and potassium ATP are damaged, resulting in cell edema, further blocking the blood flow. The accumulation of WBC, especially N, caused by endothelial cell damage; blockage of capillary lumens, activation of platelets, and coagulation processes are also involved in this process. Intraoperative application of tirofiban can irreversibly bind to the corresponding receptor and inhibit platelet aggregation, both mechanisms being beneficial in this process[15-17]. The increase in the number of WBC at admission may be related to the large number of leukocytes infiltrating in the ischemic area after acute myocardial infarction. Due to their weak deformation ability, WBC pass slowly through capillaries, thus exacerbating the myocardial microcirculation disorder[18]. RDW reflects the degree of dispersion of RBC size in the peripheral blood, expressed as coefficient of variation of RBC volume. Currently, there are different theories about the correlation between its increase and the occurrence of clinical events in coronary heart disease, and it is considered to be mainly related to chronic inflammation, neuroendocrine activation, oxidative stress, impaired renal function, and malnutrition[19]. The hs-CRP is an acute protein secreted by the liver. Its secretion indicates the intensification of vascular inflammation and is, therefore, not beneficial to the stabilization of vascular plaques. When the blood is in a state of hypercoagulation, adverse cardiovascular events are likely to occur[20]. Immediate stent placement also increases the risk of MACE. Immediate PCI can cause damage to vascular endothelial structures. Nitric oxide formation in endothelial cells is inhibited and sympathetic nerve excitability is increased, resulting in vasoconstriction and the persistence of capillary spasm, which may be important reasons for increased MACE occurrence after immediate PCI treatment[9]. Therefore, high attention should be paid to patients with the above risk factors and patients' condition changes should be closely observed to reduce the occurrence of MACE.

This study analyzed the efficacy of immediate and delayed PCI, and the protective and risk factors for post-treatment MACE in patients with acute myocardial infarction with high load thrombus, covering almost all independent risk factors of MACE and providing a basis for clinical evaluation of the treatment effects and prevention of MACE. However, this was a single-center retrospective case analysis, which failed to further explore the pathogenesis of MACE at the cellular and molecular level. To explore effective prevention strategies and intervention methods for MACE occurrence and their internal mechanism of action, further studies with greater sample size and longer follow-up are necessary.

Table 3 Single factor analysis of major adverse cardiovascular events occurrence

Data	MACE group (n = 29)	Non-MACE group (n = 135)	t/ $\chi^2$	P value
Age (yr)	63.9 ± 7.7	65.0 ± 8.1	-0.669	0.504
BMI (kg/m <sup>2</sup> )	24.1 ± 2.0	23.8 ± 2.4	0.628	0.531
HR (times/min)	91.6 ± 8.2	93.0 ± 7.6	-0.888	0.376
Number of implanted stents	1.85 ± 0.45	1.98 ± 0.50	-1.292	0.198
Gender			1.002	0.317
Male	18 (62.07)	70 (51.85)		
Female	11 (37.93)	65 (48.15)		
Diabetes			4.314	0.038
Yes	9 (31.03)	20 (14.81)		
No	20 (68.97)	115 (85.19)		
Hypertension			3.758	0.053
Yes	13 (44.83)	36 (26.67)		
No	16 (55.17)	99 (73.33)		
Hyperlipidemia			1.851	0.174
Yes	18 (62.07)	65 (48.15)		
No	11 (37.93)	70 (51.85)		
Smoking			1.851	0.174
Yes	11 (37.93)	34 (25.19)		
No	18 (62.07)	101 (74.81)		
Infarct related blood vessel			5.729	0.126
Anterior descending branch	16 (55.17)	43 (31.85)		
Circumflex	4 (13.79)	29 (21.48)		
Left main stem	2 (6.9)	11 (8.15)		
Right coronary artery	7 (24.14)	52 (38.52)		
Killip rating			0.805	0.370
1-2 degree	22 (75.86)	112 (82.96)		
3-4 degree	7 (24.14)	23 (17.04)		
Use ACEI			1.277	0.258
Yes	18 (62.07)	98 (72.59)		
No	11 (37.93)	37 (27.41)		
Use beta blockers			0.818	0.366
Yes	21 (72.41)	108 (80.00)		
No	8 (27.59)	27 (20.00)		
TIMI grading			6.046	0.014
3 degree	13 (44.83)	93 (68.89)		
< 3 degree	16 (55.17)	42 (31.11)		
TMPG grading			3.861	0.049
3 degree	13 (44.83)	87 (64.44)		
< 3 degree	16 (55.17)	48 (35.56)		
Timing of stent implantation			6.683	0.010
Immediately	19 (65.52)	53 (39.26)		

Extension	10 (34.48)	82 (60.74)		
Intraoperative use of tirofiban			4.599	0.032
Yes	17 (58.62)	105 (77.78)		
No	12 (41.38)	30 (22.22)		
CK-MB peak (U/L)	226.4 ± 44.1	218.0 ± 40.8	0.992	0.323
WBC (10 <sup>9</sup> /L)	12.63 ± 2.01	11.18 ± 1.80	3.854	0.000
N (10 <sup>9</sup> /L)	9.80 ± 1.14	15.13 ± 0.63	-35.022	0.000
RDW	13.54 ± 2.08	12.61 ± 1.86	2.392	0.018
UA (μmol/L)	368.1 ± 42.2	340.7 ± 38.5	3.418	0.001
hs-CRP (mg/L)	10.58 ± 2.81	8.62 ± 2.51	3.734	0.000

MACE: Major adverse cardiovascular events; BMI: Body mass index; HR: Heart rate; ACEI: Angiotensin-converting enzyme inhibitor; TIMI: Thrombolysis in myocardial infarction; TMPG: TIMI myocardial perfusion grade; WBC: White blood cells; N: Neutrophils; RDW: Red blood cell distribution width; UA: Uric acid; hs-CRP: High-sensitivity C-reactive protein.

**Table 4 Logistic regression analysis of factors affecting major adverse cardiovascular events occurrence**

Factor	b	SE	Walds	P value	OR	95%CI	
Diabetes	0.471	0.288	2.675	0.166	1.602	0.911	2.816
TIMI rating	-0.552	0.24	5.290	0.033	0.576	0.360	0.922
TMPG rating	-0.464	0.317	2.142	0.247	0.629	0.338	1.170
Timing of stent implantation	0.758	0.336	5.089	0.036	2.134	1.105	4.123
Intraoperative use of tirofiban	-0.392	0.15	6.830	0.011	0.676	0.504	0.907
WBC	0.608	0.275	4.888	0.042	1.837	1.071	3.149
N	0.418	0.336	1.548	0.304	1.519	0.786	2.935
RDW	0.577	0.22	6.879	0.009	1.781	1.157	2.741
UA	0.718	0.484	2.201	0.243	2.050	0.794	5.294
hs-CRP	0.466	0.215	4.698	0.045	1.594	1.046	2.429

MACE: Major adverse cardiovascular events; TIMI: Thrombolysis in myocardial infarction; TMPG: TIMI myocardial perfusion grade; WBC: White blood cells; N: Neutrophils; RDW: Red blood cell distribution width; UA: Uric acid; hs-CRP: High-sensitivity C-reactive protein.

## CONCLUSION

Delayed stent implantation is more beneficial to improve postoperative myocardial perfusion than is direct stent implantation by emergency PCI in patients with acute myocardial infarction and high thrombus load. Furthermore, delayed stent implantation can effectively reduce the risk of MACE after coronary stent implantation in these patients.

## ARTICLE HIGHLIGHTS

### Research background

Myocardial infarction is one of the most common types of coronary heart disease. The occlusion of coronary arteries and blood vessels leads to insufficient blood supply to the myocardium, which in turn leads to cardiac interstitial fibrosis, gradual expansion of the ventricles, and heart failure, which affect the quality of life and safety of patients.

### Research motivation

This study explored the treatment of myocardial infarction.

**Research objectives**

This study aimed to investigate the effects of emergency percutaneous interventional therapy (PCI) and delayed stenting in acute myocardial infarction with high thrombotic load and identify factors related to major adverse cardiovascular events (MACE).

**Research methods**

A total of 164 patients with acute myocardial infarction and high thrombotic load who received PCI were included.

**Research results**

After stent placement, 66 patients in the delayed group and 40 patients in the immediate group were classified as thrombolysis in myocardial infarction (TIMI) blood flow grade 3, 61 patients and 39 patients in the delayed group. MACE occurred in 29 patients. The MACE group and the non-MACE group had statistically significant differences in the incidence of diabetes, TIMI classification, timing of stent placement, *etc.*

**Research conclusions**

Delayed stent implantation outweighs emergency PCI in improving postoperative myocardial perfusion in acute myocardial infarction with high thrombotic load, and effectively reduces MACE in these patients.

**Research perspectives**

It has certain reference significance for the treatment of acute myocardial infarction.

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**FOOTNOTES**

**Author contributions:** Zhuo MF and Zhang KL contributed equally to this article and should be regarded as co-first authors; Zhuo MF and Zhang KL designed the experiment; Shen XB drafted the work; Lin WC, Hu B, and Cai HP collected the data; Huang G and Zhuo MF analyzed and interpreted data; Zhang KL, Shen XB, and Lin WC wrote the manuscript.

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