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Article

Effect of Early Heparin Anticoagulation on Blood Flow and Cardiac Function in Patients with Acute ST Segment Elevation Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention

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Abstract

Objective: This study aimed to investigate the effect of early administration of heparin anticoagulation on blood flow and cardiac function in patients with acute ST segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PPCI). **Methods**: A retrospective analysis was conducted on 730 patients with STEMI who underwent PPCI at the Department of Cardiology of the Chengdu Fifth People's Hospital of Chengdu from December 2017 to May 2023. According to the timing of heparin administration. The patients were divided into two groups based on the timing of heparin administration: the early group (3000 U unfractionated heparin administered immediately after the diagnosis of STEMI) and the delayed group (Intravenous injection of ordinary heparin 3000 U after successful interventional catheterization following the diagnosis of STEMI). The study compared general clinical data, myocardial injury markers (initial troponin, peak troponin, and tmax troponin), interventional related indicators (preprocedural thrombolysis in myocardial infarction (TIMI) flow grade, postprocedural TIMI flow grade, stent length, and thrombus aspiration), and postoperative indexes ST segment resolution (STR), left ventricular ejection fraction (LVEF), n-terminal pro-brain natriuretic peptide (NT-proBNP), major adverse cardiovascular events (MACE), and bleeding events. **Results**: The early group had a lower proportion of TIMI 0–1 grade and a higher proportion of TIMI 2–3 grade compared to the delayed group ($p < 0.05$). The early group showed better ST segment resolution ($p < 0.05$). There was no significant difference in LVEF and NT-proBNP classification between the two groups ($p > 0.05$). Subgroup analysis suggested an interaction between early heparin anticoagulation and left anterior descending infarct-related artery (IRA) on cardiac function. There was no significant difference in the incidence of MACE and bleeding events between the two groups ($p > 0.05$). Logistic regression analysis revealed that early heparin anticoagulation was a predictor of immediate TIMI grade 2–3 flow, and TIMI grade 2–3 flow was negatively correlated with early heparin anticoagulation. **Conclusions**: Early heparin anticoagulation can improve the patency of the IRA and myocardial perfusion in patients with STEMI. Additionally, it can reduce myocardial injury and improve cardiac function without increasing the risk of in-hospital bleeding.

Keywords

acute ST-segment elevation myocardial infarction; primary percutaneous coronary intervention; unfractionated heparin; myocardial perfusion; cardiac function

Introduction

The most prevalent critical condition associated with coronary atherosclerotic heart disease is ST-segment elevation myocardial infarction (STEMI), which commonly arises from the rupture, erosion, or ulceration of coronary atherosclerotic plaques. These events result in intracoronary thrombosis and prompt reduction or cessation of blood flow within the coronary arteries [1]. STEMI patients have a very short treatment window [2], and the incidence of adverse cardiovascular events is gradually increasing with the extension of treatment time [3]. Early and timely reperfusion therapy is particularly important to improve the prognosis and reduce the mortality of STEMI patients [4]. Whether the prognosis of patients with STEMI is related to the size of the infarct size, the establishment of collateral circulation, and the re-opening of infarct-related artery (IRA) [5]. Primary percutaneous coronary intervention (PPCI) or thrombolytic therapy is the main method of reperfusion recommended by guidelines for STEMI. Since thrombolytic therapy is limited by many factors and angiography is required to determine the extent of IRA reperfusion [6], PPCI treatment as soon as possible is the most effective reperfusion method for STEMI patients [7–9]. Guidelines recommend that STEMI patients start anticoagulation therapy before PPCI, which can effectively block the coagulation cascade, reduce thrombosis, inhibit the further development of thrombosis, and even promote the dissolution of coronary thrombosis and the re-opening of IRA [10]. Yet the start timing for a PPCI preoperative anticoagulant ther-

apy study is less, and there is no clear early heparin anticoagulationization large clinical study of IRA recanalization. In addition, even in STEMI patients with fully opened IRA after PPCI, there are still coronary microcirculation disorders [11] and myocardial hypoperfusion [12]. Thrombolysis in myocardial infarction (TIMI) flow grade is the main evaluation method for the degree of reperfusion at the coronary artery level, and it is the most commonly used clinical index to judge the degree of IRA patency. which reflect the structure and function of coronary microvessels, while ST segment resolution (STR) of corresponding electrocardiogram (ECG) leads falls back can be used to evaluate reperfusion at the myocardial cell level [13], and the efficacy of reperfusion can be evaluated by TIMI blood flow grade of IRA combined with STR. The aim of this study is to explore the effects of early heparin anticoagulationization on IRA recanalization, myocardial perfusion, cardiac function and prognosis in patients with STEMI, and to provide a theoretical basis for the early and standardized use of unfractionated heparin in STEMI.

Materials and Methods

General Information

This study was granted exemption by the Ethics Committee of the Chengdu Fifth People's Hospital. A total of 730 patients with STEMI who underwent percutaneous coronary intervention (PPCI) in the Department of Cardiovascular Medicine of the Chengdu Fifth People's Hospital from December 2017 to May 2023 were retrospectively analyzed.

The inclusion criteria for this study were as follows: (1) Age between 18 and 80 years old; (2) Acute ST-segment elevation myocardial infarction (STEMI) with refractory chest pain, persistent ST-segment elevation, or new left bundle branch block within 12 to 24 hours; (3) Consent to undergo coronary angiography and percutaneous transluminal coronary angioplasty (PTCA) without any contraindications; (4) Prior to primary percutaneous coronary intervention (PPCI), all patients received a loading dose of dual antiplatelet therapy and intravenous unfractionated heparin anticoagulation as per the guidelines.

The exclusion criteria for this study include the following: (1) patients who had received thrombolytic therapy before PPCI or used anticoagulant drugs within 48 hours prior to onset; (2) patients with active bleeding or recent bleeding events or bleeding tendency, such as recent gastrointestinal bleeding (within the past 3 months), recent cerebral hemorrhage (within the past 6 months), and a history of cerebral infarction (within the past 3 months), should not undergo PPCI; (3) patients with severe renal dysfunction; (4) patients with hemoglobin levels less than 90 g/L and platelet count less than 100×10^9/L; (5) patients with acquired thrombocytopenia caused by heparin; (6) patients in cardiogenic shock or using circulatory assist device such as extra-corporeal membrane oxygenation (ECMO) or intra-aortic balloon pump (IABP); (7) other conditions that are not suitable for PPCI treatment or may interfere with the continuation of research.

Research Methods

Study Groups

Patients were divided into two groups based on the timing of unfractionated heparin administration.

Early group: Intravenous administration of 3000 U unfractionated heparin immediately after the diagnosis of STEMI.

Delayed group: Intravenous injection of ordinary heparin 3000 U after successful interventional catheterization following the diagnosis of STEMI.

Indicators of Observation

All patients in the emergency department of the Fifth People's Hospital in Chengdu were subjected to a history collection, physical examination, and a 12-lead electrocardiogram (ECG) within 10 minutes. Additionally, various tests were conducted, including troponin, blood pressure, heart rate, medical history (hypertension, diabetes, hyperlipidemia, smoking, cerebrovascular disease, obesity), high-sensitive C-reactive protein, blood routine (hemoglobin, red blood cell count, white blood cell count, platelet count), liver function (alanine aminotransferase, aspartate aminotransferase), blood lipids (triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein, total cholesterol), creatinine, uric acid, and potassium levels. Once STEMI was diagnosed, the patients were immediately administered an enteric-coated aspirin tablet (300 mg) (J20171021, Via Delle Groane, 126, 20024 Garbagnaye Milanese MI, Italy) and a ticagrelor tablet (180 mg) (H20171079, Gärtunavägen, SE-151 85 Södertalje, Sweden). Informed consent for interventional surgery was obtained from the patients. The right radial artery was used as the surgical approach for all patients. After successful puncture, the patient's body weight was considered to determine the amount of ordinary heparin to be supplemented. The activated clotting time (ACT) was monitored intraoperatively and maintained between 250–350 seconds. PPCI was performed in both groups using conventional methods. According to the specific blood flow conditions, such as the presence of no reflow or a large thrombus in the coronary artery, platelet glycoprotein IIb/IIIa receptor antagonists or thrombus aspiration were employed. After the procedure, the patients were admitted to the coronary care unit (CCU) ward. Within 24 hours, various tests including troponin, n-terminal pro-brain natriuretic peptide (NT-proBNP), blood routine, electrocardiogram (to assess ST-segment resolu-

tion), and echocardiography (to determine the lowest left ventricular ejection fraction (LVEF) during hospitalization) were conducted. Malignant cardiac events (such as heart failure, recurrent angina, recurrent myocardial infarction, and cardiac death), bleeding events, and the length of hospital stay were recorded. For secondary prevention, all patients received aspirin 100 mg qd, ticagrelor 90 mg bid, and statins. Additionally, ACEI/ARB and other medications were routinely administered to improve myocardial remodeling, reduce blood pressure and blood glucose levels, enhance circulation, control ventricular rate, and promote diuresis after myocardial infarction.

The PPCI was conducted by a skilled cardiovascular intervention team. The intraoperative procedures were determined based on the actual situation during the operation and the surgeon's expertise. The results of coronary angiography and TIMI flow grade were analyzed by two or more experienced physicians. The IRA was identified based on ST-segment elevation in the electrocardiogram, and echocardiography was performed by experienced cardiac sonographers.

Definition of Relevant Indicators

TIMI myocardial perfusion grading (TMPG): Grade 0 indicates no perfusion, Grade 1 indicates microperfusion, Grade 2 indicates partial perfusion, and Grade 3 indicates full perfusion.

In the electrocardiogram (ECG) of confirmed ST-elevation myocardial infarction (STEMI), the TP segment was used as the isopotential, and the highest amplitude of the ST segment after the J point was measured (the lead with the largest ST segment elevation was used as the criterion). The ECG was reexamined at 60 minutes and 120 minutes after PPCI, and STR was measured. STR greater than 50% was considered to have good resolution, while less than or equal to 50% was considered to have poor resolution.

Troponin peak time refers to the difference between the maximum troponin peak time monitored during hospitalization and the onset of chest pain symptoms.

Bleeding events were classified according to the Bleeding Academic Research Consortium (BARC) criteria. Type 0 represents no bleeding, type 1 indicates inactive bleeding, type 2 refers to any significant active bleeding, type 3a is characterized by marked bleeding with a decrease in hemoglobin of 3–5 g/dL, type 3b indicates marked bleeding with a decrease in hemoglobin $\geq$5 g/dL, type 3c represents intracranial hemorrhage, type 4 refers to bleeding related to coronary artery bypass grafting, and type 5 represents fatal bleeding.

Statistical Methods

SPSS 17.0 (IBM Corp., Armonk, NY, USA) statistical software was utilized for data analysis. The measurement data were presented as mean $\pm$ standard deviation. The comparison between groups was conducted using independent sample t-test for quantitative data that followed a normal distribution and had homogeneity of variance. Frequency and percentage were used to describe count data. Chi-square test was employed for group comparisons, with a significance level of $p < 0.05$. Non-normally distributed or non-homogeneous data were analyzed using Mann-Whitney U test. Binary logistic regression analysis was performed to assess the impact of early heparin anticoagulation on preprocedural TIMI flow grade 2–3. Additionally, two-way ANOVA was used to examine the effect of early heparin anticoagulation in combination with IRA on cardiac function.

Results

General Clinical Data

There were no significant differences between the two groups in age, gender, blood pressure, heart rate, past medical history, high-sensitivity C-reactive protein, blood routine, blood lipids, liver function, renal function, potassium, time from onset to visit, time from visit to guide wire passage and length of hospital stay ($p > 0.05$) (Table 1).

Infarct-Related Arteries

IRA distribution difference between two groups has no statistical significance ($p > 0.05$) (Table 2).

Markers of Myocardial Injury

There was no significant difference in the initial troponin and peak troponin levels between the early group and the delayed group ($p > 0.05$). However, the peak time of troponin in the early group was found to be earlier than that in the delayed group, and this difference was statistically significant ($p < 0.05$) (Table 3).

Myocardial Perfusion and Cardiac Function

Indicating significant differences in the proportion of preoperative TIMI flow grade 2–3 and the degree of ST segment resolution between the two groups ($p < 0.05$). However, there was no significant difference observed in thrombus aspiration, postoperative TIMI grade 3 flow rate, LVEF, and NT-proBNP between the two groups ($p > 0.05$) (Table 4).

In-Hospital MACE and Bleeding Events

There was no significant difference in major adverse cardiovascular events (MACE) and bleeding events between the two groups ($p > 0.05$) (Table 5).

Table 1. General clinical data.

	Early group (N = 170)	Delay group (N = 560)	*p*
Age (years)	71.39 ± 7.42	71.53 ± 7.33	0.832
Sex: Male [cases (%)]	129 (75.9%)	428 (76.4%)	0.883
Systolic blood pressure (mmHg)	131.39 ± 28.41	130.62 ± 25.98	0.740
Diastolic blood pressure (mmHg)	81.82 ± 21.17	80.98 ± 19.06	0.624
Heart rate (beats/min)	79.14 ± 17.33	78.54 ± 20.20	0.727
Smoking	96 (56.5%)	315 (56.3%)	0.738
Hypertension	88 (51.8%)	273 (48.8%)	0.597
Diabetes mellitus	64 (37.6%)	214 (38.2%)	0.894
Hyperlipidemia	18 (10.6%)	62 (11.1%)	0.724
Cerebrovascular disease	11 (6.5%)	40 (7.1%)	0.453
Coronary heart disease	13 (7.6%)	46 (8.2%)	0.548
Obesity	5 (2.9%)	20 (3.5%)	0.692
hs-CRP (mg/L)	5.57 (1.10, 8.50)	5.27 (1.10, 8.40)	0.819
RBC ($\times 10^9$/L)	4.17 ± 0.86	4.12 ± 0.89	0.466
Hb (g/L)	111.15 ± 14.75	114.77 ± 14.88	0.060
WBC ($\times 10^{12}$/L)	7.04 ± 6.95	6.68 ± 5.30	0.707
PLT ($\times 10^9$/L)	151.60 ± 48.25	156.95 ± 51.83	0.231
ALT (U/L)	27.86 (13.00, 32.00)	30.41 (17.00, 36.75)	0.162
AST (U/L)	39.70 (26.75, 47.00)	37.20 (27.00, 45.00)	0.278
UA (μmol/ L)	422.14 ± 193.14	395.28 ± 157.27	0.099
K (mmol/L)	4.04 ± 0.83	3.99 ± 0.78	0.417
TC (mmol/L)	4.78 ± 1.12	4.96 ± 1.23	0.074
TG (mmol/L)	1.54 (0.69, 1.63)	1.33 (0.72, 1.56)	0.188
HDL-C (mmol/L)	1.15 ± 0.30	1.17 ± 0.40	0.667
LDL-C (mmol/L)	2.82 (2.23, 3.39)	3.37 (2.22, 3.47)	0.369
Cr (μmol/L)	104.22 (63.95, 114.50)	92.40 (62.20, 106.33)	0.256
Length of hospitalization (days)	7.08 ± 1.64	7.24 ± 1.97	0.399
Time from onset to consultation (min)	182.40 (80.00, 230.00)	187.48 (80.00, 230.00)	0.739
Time from consultation to guidewire passage (min)	73.25 ± 11.84	74.32 ± 12.90	0.335

hs-CRP, high-sensitivity C-reactive protein; RBC, red blood cell count; Hb, hemoglobin; WBC, white blood cell count; PLT, blood platelet count; ALT, alanine amiotransferase; AST, aspartate aminotransferase; UA, uric acid; K, kalium; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; Cr, creatinine.

Table 2. Infarct-related arteries.

	Early group (N = 170)	Delay group (N = 560)	*p*
IRA Distribution			0.139
LAD	73 (42.9%)	282 (50.3%)	
LCX	28 (16.5%)	66 (11.8%)	
RCA	69 (40.6%)	212 (37.9%)	

IRA, infarct-related artery; LAD, left anterior descending artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

Multivariate Logistic Regression Analysis of Influence on Preoperative TIMI Grade 2–3 Blood Flow

In the multivariate regression analysis, several factors including early heparin anticoagulation, gender, heart rate, culprit vessel, low density lipoprotein, high density lipoprotein, total cholesterol, hemoglobin, and uric acid were considered. After adjusting for confounding factors, it was found that early heparin anticoagulation remained an independent influencing factor for TIMI 2–3 grade (odds ratio (OR) = 0.366, 95% confidence interval (CI) 0.228–0.588, $p < 0.05$) (Table 6).

Subgroup Analysis Affecting Cardiac Function

There were significant differences in troponin peak value and time to peak value, as well as in LVEF, between the two groups when the left anterior descending artery (LAD) was the IRA ($p < 0.05$). However, there was no significant difference in NT-proBNP between the two groups ($p > 0.05$) (Table 7).

Table 3. Myocardial injury markers.

	Early group (N = 170)	Delay group (N = 560)	*p*
Peak troponin (ng/mL)	25.91 (8.10, 50.00)	27.80 (8.33, 50.00)	0.292
Initial troponin (ng/mL)	6.91 (0.10, 15.08)	5.91 (0.10, 3.14)	0.231
Troponin peak time (h)	15.12 ± 2.52	17.29 ± 2.68	0.000

Table 4. Myocardial perfusion and cardiac function.

	Early group (N = 170)	Delay group (N = 560)	*p*
Preoperative TIMI grade 2–3	52 (30.6%)	98 (17.5%)	0.001
Aspiration of thrombus	23 (13.5%)	106 (18.9%)	0.106
Postoperative TIMI grade 3	167 (98.2%)	537 (95.9%)	0.278
ST segment falls back well	130 (76.5%)	369 (65.9%)	0.009
NT-proBNP (ng/mL)	1863.96 (438.53, 2008.66)	2391.90 (578.33, 2350.00)	0.113
LVEF (%)	54.29 ± 9.69	54.34 ± 9.68	0.956

LVEF, left ventricular ejection fraction; TIMI, thrombolysis in myocardial infarction; NTproBNP, n-terminal pro-brain natriuretic peptide.

Table 5. In-hospital MACE and bleeding events.

	Early group (N = 170)	Delay group (N = 560)	*p*
Cardiac death	3 (1.8%)	7 (1.3%)	0.613
Recurrent myocardial infarction	0 (0%)	0 (0%)	\
Recurrent angina	17 (10.0%)	41 (7.3%)	0.258
Heart failure	18 (10.6%)	68 (12.1%)	0.528
Bleeding events	6 (3.5%)	11 (2.0%)	0.236

MACE, major adverse cardiac events.

Table 6. Multivariate Logistic regression analysis of influencing TIMI grade 2–3 blood flow.

Risk factor	OR	95% CI	*p*
Early intervention	1.462	1.398–2.437	0.001
Distinguishing between the sexes	0.607	0.337–1.094	0.097
HR	1.007	0.996–1.018	0.237
IRA	1.552	0.917–2.527	0.105
HDL-C	0.581	0.256–1.272	0.174
LDL-C	0.834	0.475–1.465	0.528
TC	1.076	0.669–1.729	0.763
Hb	0.989	0.974–1.004	0.164
UA	1.000	0.999–1.002	0.450

OR, odds ratio; CI, confidence interval; HR, heart rate.

Discussion

The occurrence of STEMI is often caused by the rupture, erosion, or erosion of coronary atherosclerotic plaque. This leads to the formation of coronary artery thrombosis, rapid reduction or interruption of coronary blood flow, and acute myocardial ischemia and hypoxia. These conditions can result in various severe cardiac events, including malignant arrhythmia, cardiogenic shock, cardiac rupture, and sudden death. Early reperfusion therapy is crucial for improving the prognosis of STEMI patients and reducing mortality. Anticoagulant therapy plays an essential role in enhancing the effectiveness and prognosis of immediate reperfusion of the IRA in STEMI. Anticoagulant therapy plays a crucial role in enhancing the effectiveness of IRA reperfusion and the prognosis of STEMI. The timing of anticoagulation initiation is positively associated with patient prognosis [14,15]. Early heparin anticoagulation has been shown to significantly improve IRA recanalization, preoperative TIMI flow grade, and mortality [16]. Numerous studies have demonstrated a significant relationship between preoperative TIMI flow grade and the prognosis of STEMI [17–19]. Despite some studies suggesting that the timing of unfractionated heparin anticoagulation does not significantly affect TIMI flow before IRA in STEMI, it is important to consider that the experimental results may be limited by the start time of the catheterization laboratory and the level of medical expertise. Nonetheless, early heparin anticoagulation still holds stronger evidence. In this study, myocardial non-perfusion was defined as TIMI grade 0–1, while myocardial effective perfusion was defined as TIMI grade 2–3. The study revealed that the proportion of preoperative TIMI grade 2–3 blood flow in the early group was significantly higher than that in the delayed group, with a statistically significant difference ($p < 0.05$). Even after adjusting for confounding factors through multivariate regression analysis, early heparin anticoagulationization remained an independent predictor of preoperative

Table 7. Subgroup analysis of effects on cardiac function.

	Early group (N = 73)	Delay group (N = 282)	*p*
Peak troponin (ng/mL)	27.49	29.27	0.028
Peak time (h)	15.09	17.29	0.001
NT-proBNP (ng/mL)	1878.13	1910.57	0.051
LVEF (%)	57.12	55.65	0.000

TIMI grade 2–3 flow. These findings are consistent with recent conclusions from experts and scholars on the efficacy of early heparin anticoagulationization in improving the patency of IRA in STEMI. Therefore, this study reaffirms the necessity of early unfractionated heparin anticoagulation in STEMI and highlights the potential maximized benefit for patients through early heparin anticoagulationization.

The assessment of myocardial cell reperfusion after PPCI treatment has been a focal point of attention and discussion in the field of interventional therapy. Compared to other invasive evaluation methods, STR offers advantages such as non-invasiveness, affordability, and simplicity in determining myocardial reperfusion. Unfractionated heparin promotes the release of tissue plasminogen activator from vascular epithelial cells and autolysis of red thrombus of IRA, resulting in reperfusion of ischemic myocardium and subsequent ST-segment resolution in ECG. While TIMI blood flow classification focuses on evaluating reperfusion at the coronary microvascular level, STR serves as a straightforward and non-invasive index for evaluating reperfusion at the myocardial cell level post-operation [20]. STR also plays a crucial role in the prognosis evaluation of STEMI, as several randomized clinical controlled trials have confirmed its status as an independent predictor of MACE events [21]. Considering the stringent requirements of randomized clinical controlled trials regarding the study population and the difficulty in generalizing the results to the "real world", STR in the context of "real world studies" can genuinely, specifically, and comprehensively reflect the efficacy of anticoagulation in STEMI. In this study, 76.5% of the early group and 65.9% of the delayed group had a good STR. The difference between the two groups was statistically significant. The results of good STR in the early group were similar to those in Wu *et al.*'s study (good STR: 79.4%) [21]. It is considered that early heparin anticoagulation can improve myocardial perfusion at the level of cardiomyocytes. The proportion of good STR in the delayed group was relatively low, which may be related to the long time from the visit to the guide wire crossing and the late use of unfractionated heparin. It is important to note that STR interpretation in this study was measured by bedside 12-lead ECG and not from continuous ECG monitoring. Therefore, the optimal timing of STR measurement cannot be determined, and STR values are subject to measurement error. Studies have shown that 24 to 36% of STEMI patients with restored TIMI grade 2–3 flow after PPCI have poor ST-segment resolution, suggesting that some STEMI patients do not benefit from immediate IRA opening [22]. This study also found that only 65.9%–76.5% of patients had good STR after TIMI grade 3 blood flow recovery, and there was a difference in STR time, which may be related to the use of antiplatelet drugs during the perioperative period. STR can be used to evaluate the efficacy of reperfusion, guiding clinical anticoagulation and antiplatelet therapy. In conclusion, in this "real world study", we found that STEMI patients should be routinely evaluated for STR after PPCI regardless of the degree of TIMI flow recovery, and patients with poor STR should be actively treated with anticoagulant and antiplatelet therapy.

When STEMI occurs, the extent of myocardial injury is closely correlated with the duration of ischemia. The longer the reperfusion time, the greater the extent of myocardial necrosis and the more severe the cardiac function of the patient may be. NT-proBNP plays a crucial role not only in the diagnosis and evaluation of heart failure but also in determining the degree of myocardial injury in patients with STEMI [23]. A study on the correlation between NT-proBNP and the prognosis of STEMI revealed a significant decrease in the peak value of NT-proBNP in the experimental group. Additionally, there was a statistically significant difference in LVEF between the experimental group and the control group, suggesting that early heparin anticoagulation can improve the cardiac function of patients [24]. However, the effectiveness of early heparin anticoagulation in improving cardiac function is still a topic of debate [25]. In this study, objective indicators related to cardiac function were collected for both groups, including NT-proBNP, LVEF, and STR. The peak value of NT-proBNP showed a decreasing trend in the early group, although there was no significant difference between the two groups. It is important to note that NT-proBNP may be influenced by factors such as age and renal function, which were not stratified in this experiment, potentially introducing bias. The left ventricle is primarily supplied by the left anterior descending artery. In this study, subgroup analysis was conducted on patients with the left anterior descending artery as the IRA who received early heparin anticoagulation. It is believed that early heparin anticoagulation improves myocardial perfusion, reduces myocardial ischemia time, decreases the improvement of LVEF, and decreases the level of NT-proBNP. However, it should be noted that the assessment of cardiac function in this study is not comprehensive. Additional measures such as the 6-minute walk test, cardiac

rehabilitation exercise measurement, echocardiography before and during follow-up, and statistical analysis of LVEF changes should be included to provide more convincing evidence. Furthermore, there is a lack of studies investigating the long-term prognosis and changes in cardiac function of STEMI patients treated with early heparin anticoagulation.

To assess the impact of the timing of unfractionated heparin on the risk of MACE and bleeding in patients with STEMI, several studies have consistently demonstrated that early heparin anticoagulation does not raise the risk of bleeding during hospitalization [26] and is associated with good safety outcomes [27]. In this study, the occurrence of in-hospital myocardial infarction, heart failure, recurrent angina, and cardiac arrest was recorded for both patient groups, yielding results consistent with recent research findings. Specifically, early heparin anticoagulation in STEMI patients does not increase the incidence of in-hospital MACE [28] or bleeding events [29].

Conclusions

In summary, early heparin anticoagulationization after the onset of STEMI can improve the patency of IRA, improve myocardial perfusion, reduce myocardial injury, and improve cardiac function, and did not increase the risk of MACE and bleeding in hospital.

Availability of Data and Materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Author Contributions

ML designed the research study. XH and XJ performed the research. XW and MT collected data. XH and LD analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was granted exemption by the Ethics Committee of the Chengdu Fifth People's Hospital. All patients have signed informed consent forms.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Li SY, Zhou MG, Ye T, Cheng LC, Zhu F, Cui CY, *et al*. Frequency of ST-segment elevation myocardial infarction, non-ST-segment myocardial infarction, and unstable angina: results from a Southwest Chinese Registry. Reviews in Cardiovascular Medicine. 2021; 22: 239–245.

[2] Bhatt DL, Lopes RD, Harrington RA. Diagnosis and Treatment of Acute Coronary Syndromes: A Review. JAMA. 2022; 327: 662–675.

[3] Ouaddi NE, de Diego O, Labata C, Rueda F, Martínez MJ, Cámara ML, *et al*. Mechanical complications in STEMI: prevalence and mortality trends in the primary PCI era. The Ruti-STEMI registry. Revista Espanola De Cardiologia (English Ed.). 2023; 76: 427–433.

[4] Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, *et al*. 2023 ESC Guidelines for the management of acute coronary syndromes. European Heart Journal. 2023; 44: 3720–3826.

[5] Surve TA, Kazim MA, Sughra M, Mirza AMW, Murugan SK, Shebani KAM, *et al*. Revascularization Modalities in Acute Coronary Syndrome: A Review of the Current State of Evidence. Cureus. 2023; 15: e47207.

[6] Chacón-Diaz M, Custodio-Sánchez P, Rojas De la Cuba P, Yábar-Galindo G, Rodríguez-Olivares R, Miranda-Noé D, *et al*. Outcomes in ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention or pharmacoinvasive strategy in a Latin American country. BMC Cardiovascular Disorders. 2022; 22: 296.

[7] Dauerman HL, Ibanez B. The Edge of Time in Acute Myocardial Infarction. Journal of the American College of Cardiology. 2021; 77: 1871–1874.

[8] Kastrati A, Coughlan JJ, Ndrepepa G. Primary PCI, Late Presenting STEMI, and the Limits of Time. Journal of the American College of Cardiology. 2021; 78: 1306–1308.

[9] Tang N, Chen X, Li K, Li H, Qi C. Myocardial Perfusion in ST-Segment Elevation Myocardial Infarction Patients After Percutaneous Coronary Intervention: Influencing Factors and Intervention Strategies. Cureus. 2023; 15: e42841.

[10] Poston RN, Chughtai J, Ujkaj D, Louis H, Leake DS, Cooper D. Monocytic Cell Adhesion to Oxidised Ligands: Relevance to Cardiovascular Disease. Biomedicines. 2022; 10: 3083.

[11] Ranjbar A, Sohrabi B, Sadat-Ebrahimi SR, Ghaffari S, Kazemi B, Aslanabadi N, *et al*. The association between T wave inversion in leads with ST-elevation and patency of the infarct-related artery. BMC Cardiovascular Disorders. 2021; 21: 27.

[12] Dong Q, Wen X, Chang G, Xia R, Wang S, Yang Y, *et al*. ST-segment resolution as a marker for severe myocardial fibrosis in

ST-segment elevation myocardial infarction. BMC Cardiovascular Disorders. 2021; 21: 455.

[13] Wang Z, Peng J. The predictive value of the nomogram model of clinical risk factors for ischemia-reperfusion injury after primary percutaneous coronary intervention. Scientific Reports. 2023; 13: 5084.

[14] Giralt T, Ribas N, Freixa X, Sabaté M, Caldentey G, Tizón-Marcos H, *et al*. Impact of pre-angioplasty antithrombotic therapy administration on coronary reperfusion in ST-segment elevation myocardial infarction: Does time matter? International Journal of Cardiology. 2021; 325: 9–15.

[15] Giralt T, Carrillo X, Rodriguez-Leor O, Fernandez-Nofrerias E, Rueda F, Serra-Flores J, *et al*. Time-dependent effects of unfractionated heparin in patients with ST-elevation myocardial infarction transferred for primary angioplasty. International Journal of Cardiology. 2015; 198: 70–74.

[16] Maioli M, Zeymer U, van 't Hof AWJ, Gibson CM, Dudek D, Bellandi F, *et al*. Impact of preprocedural TIMI flow on myocardial perfusion, distal embolization and mortality in patients with ST-segment elevation myocardial infarction treated by primary angioplasty and glycoprotein IIb/IIIa inhibitors. The Journal of Invasive Cardiology. 2012; 24: 324–327.

[17] Collet JP, Zeitouni M. Heparin pretreatment in STEMI: is earlier always better? EuroIntervention: Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2022; 18: 697–699.

[18] Maruszak N, Pilch W, Januszek R, Malinowski KP, Surdacki A, Chyrchel M. Risk Factors of Suboptimal Coronary Blood Flow after a Percutaneous Coronary Intervention in Patients with Acute Anterior Wall Myocardial Infarction. Journal of Personalized Medicine. 2023; 13: 1217.

[19] Fakhr-Mousavi A, Cheshmkhorooshan S, Vakilpour A, Mousavi SM. The effect of heparin administration time on thrombolysis in myocardial infarction flow grade in patients with acute ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. ARYA Atherosclerosis. 2022; 18: 1–7.

[20] Galli M, Niccoli G, De Maria G, Brugaletta S, Montone RA, Vergallo R, *et al*. Coronary microvascular obstruction and dysfunction in patients with acute myocardial infarction. Nature Reviews. Cardiology. 2023. (online ahead of print)

[21] Wu C, Gao X, Li L, Jing Q, Li W, Xu H, *et al*. Role of ST-Segment Resolution Alone and in Combination With TIMI Flow After Primary Percutaneous Coronary Intervention for ST-Segment-Elevation Myocardial Infarction. Journal of the American Heart Association. 2023; 12: e029670.

[22] Kleinbongard P, Heusch G. A fresh look at coronary microembolization. Nature Reviews. Cardiology. 2022; 19: 265–280.

[23] Fabris E, Ten Berg JM, Hermanides RS, Ottervanger JP, Dambrink JHE, Gosselink AM, *et al*. NT-proBNP level before primary PCI and risk of poor myocardial reperfusion: Insight from the On-TIME II trial. American Heart Journal. 2021; 233: 78–85.

[24] Wang JL, Guo CY, Li HW, Zhao XQ, Zhao SM. Prognostic Value of NT-proBNP in Patients With Successful PCI for ACS and Normal Left Ventricular Ejection Fraction. The American Journal of the Medical Sciences. 2022; 363: 333–341.

[25] Albuquerque F, Gomes DA, Ferreira J, de Araújo Gonçalves P, Lopes PM, Presume J, *et al*. Upstream anticoagulation in patients with ST-segment elevation myocardial infarction: a systematic review and meta-analysis. Clinical Research in Cardiology. 2023; 112: 1322–1330.

[26] Emilsson OL, Bergman S, Mohammad MA, Olivecrona GK, Götberg M, Erlinge D, *et al*. Pretreatment with heparin in patients with ST-segment elevation myocardial infarction: a report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). EuroIntervention: Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2022; 18: 709–718.

[27] Albuquerque F, Gomes DA, Ferreira J, de Araújo Gonçalves P, Lopes PM, Presume J, *et al*. Upstream anticoagulation in patients with ST-segment elevation myocardial infarction: a systematic review and meta-analysis. Clinical Research in Cardiology: Official Journal of the German Cardiac Society. 2023; 112: 1322–1330.

[28] Kheifets M, Vaknin-Assa H, Greenberg G, Orvin K, Assali A, Kornowski R, *et al*. Trends in ST-elevation myocardial infarction. Coronary Artery Disease. 2022; 31: 1–8.

[29] Urban P, Gregson J, Owen R, Mehran R, Windecker S, Valgimigli M, *et al*. Assessing the Risks of Bleeding vs Thrombotic Events in Patients at High Bleeding Risk After Coronary Stent Implantation: The ARC-High Bleeding Risk Trade-off Model. JAMA Cardiology. 2021; 6: 410–419.