Late Percutaneous Coronary Intervention Prevents Left Ventricular Remodeling and Improves Clinical Outcomes in Patients With ST-Elevation Myocardial Infarction

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ABSTRACT

Background: The optimal strategy for treating late presenters of ST-elevation myocardial infarction (STEMI) remains uncertain.

Hypothesis: percutaneous coronary intervention (PCI) has a favorable effect on left ventricular (LV) remodeling and clinical outcomes in late presenters of STEMI.

Methods: Patients with STEMI who were hospitalized between 2009 and 2011 at 7 PCI-capable hospitals in China were selected. Cardiac characteristics were reassessed by echocardiography between August 2013 and January 2014. The clinical endpoints were evaluated during a median follow-up period of 36 months.

Results: 1090 patients who either underwent late PCI ($n = 786$) or received standard medical therapy alone ($n = 304$) was analyzed. Left ventricular remodeling was more pronounced in the conservative-treatment group. Logistic regression revealed that late PCI was independently and negatively correlated with LV remodeling (odds ratio: 0.356, 95% confidence interval [CI]: 0.251-0.505, $P < 0.001$). Kaplan-Meier analysis showed the lower risks of major adverse cardiovascular events (MACE), all-cause death, and rehospitalization for heart failure in the late-PCI group. Multivariate Cox regression revealed that late PCI was significantly associated with lower risks for MACE, all-cause death, and rehospitalization for heart failure both in all patients (hazard ratio [HR]: 0.507, 95% CI: 0.412-0.625, $P < 0.001$; HR: 0.419, 95% CI: 0.314-0.559, $P < 0.001$; and HR: 0.583, 95% CI: 0.379-0.896, $P = 0.014$, respectively) and in the matched patients (HR: 0.466, 95% CI: 0.358-0.607, $P < 0.001$; HR: 0.398, 95% CI: 0.277-0.571, $P < 0.001$; and HR: 0.498, 95% CI: 0.283-0.878, $P = 0.016$, respectively) by propensity-score analysis.

Conclusions: Late-PCI strategy prevents LV remodeling and improves clinical outcomes in STEMI patients compared with conservative strategies.

Introduction

Restoration of blood flow to an infarct-related artery (IRA) within the first 12 hours from onset of symptoms via an early invasive strategy is currently considered the best

approach to treating ST-elevation myocardial infarction (STEMI).^{1,2} However, a large proportion of patients with STEMI present beyond the initial 12-hour time limit. Due to their late presentation, up to one-third of STEMI patients do

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not receive any reperfusion therapy.³ The optimal strategy for treating late presenters of STEMI remains uncertain. For patients with ongoing ischemia between 12 and 24 hours after symptom onset, or 3 to 24 hours after thrombolysis regardless of the success of thrombolytic therapy, percutaneous coronary intervention (PCI) is a reasonable approach.^{1,2} However, for patients who present >24 hours after the initial event, the effectiveness of PCI remains controversial. Current treatment guidelines for patients with STEMI state that patients presenting between 3 and 28 days with persistent coronary artery occlusion without ongoing ischemia or inducible ischemia do not benefit from PCI,^{1,2} although the value of PCI for the majority of late presenters of STEMI is unclear. Recently, a few published studies have suggested that PCI could be beneficial to STEMI patients if performed just after 12 hours from onset of symptoms.^{4–7} However, there is currently not enough evidence supporting the application of PCI in STEMI patients who present >24 hours after symptom onset.

In the context of contemporary STEMI treatments, the purpose of our study was to determine the influence of late-PCI strategy applied >24 hours from onset of symptoms on left ventricular (LV) remodeling and clinical outcomes in the majority of late presenters of STEMI.

Methods

Study Protocol and Population

This study was a multicenter observational study involving 7 PCI-capable hospitals in China. Patients age >18 years with confirmed STEMI between January 2009 and December 2011 were included. Diagnosis of STEMI followed the 2007 American College of Cardiology Foundation/American Heart Association guidelines.⁸ The diagnostic criteria were as follows: ≥ 1 persistent symptoms of ischemia ≥ 30 minutes; ST-segment elevation ≥ 1 mm in ≥ 2 adjacent limb leads or ≥ 2 mm in ≥ 2 contiguous precordial leads, or the presence of a new or suspicious new left bundle branch block, or the development of pathological Q waves in the electrocardiography; and ≥ 1 episode of elevated serum biomarkers of myocardial necrosis (elevated creatine kinase and creatine kinase–myocardial band $>2\times$ the upper limit of normal, or elevated cardiac troponins). Patients were excluded if they had idiopathic cardiomyopathy, congenital heart disease, valvular heart disease, rheumatic or autoimmune disease, malignant tumors, severe liver or kidney dysfunction, or other uncontrollable systemic diseases; if their coronary anatomy was not amenable to PCI; or if they had an unsuccessful procedure. Echocardiography was reassessed at follow-up evaluations between August 2013 and January 2014. This study was approved by the local medical ethics committee, and informed consent was obtained from all participants. This study was performed in accordance with the guidelines of the Declaration of Helsinki.

Baseline Data Collection

All patient information, including demographic data, cardiovascular risk factors and history, clinical data, and cardiovascular medications, were collected using a standard case-report form. Coronary single-vessel disease

was defined as stenosis $>50\%$ in a major coronary artery (eg, left anterior descending coronary artery, left circumflex coronary artery, or right coronary artery) and in their main branches. Lesions observed in both major vessels and their main branches were still defined as single-vessel disease. Double-vessel disease and triple-vessel disease were defined as stenosis $>50\%$ in 2 and 3 major coronary arteries, respectively. Left-main coronary artery disease was defined as double-vessel disease.⁹ The severity of coronary artery stenosis was assessed using the Gensini score.¹⁰ Percutaneous coronary intervention was defined as late if the time from symptom onset to the initial balloon inflation to open the IRA was >24 hours.

Echocardiography Assessment

Comprehensive echocardiographic analysis of cardiac structure and function was performed by experienced physicians who were blinded to patients' information according to guidelines of the American Society of Echocardiography.¹¹ Left ventricular end-diastolic diameter, LV end-systolic diameter, LV fractional shortening, LV posterior wall thickness, and interventricular septum thickness were measured via the 2-dimensional guided M-mode. Left ventricular end-diastolic volume (LVEDV), LV end-systolic volume, and LV ejection fraction were measured according to the biplane Simpson method.¹² All measurements were averaged over 3 cardiac cycles. The indexes of LV end-diastolic diameter, LV end-systolic diameter, LVEDV, and LV end-systolic volume were normalized according to body surface area. Left ventricular mass was calculated using the formula recommended by the American Society of Echocardiography¹¹ and also expressed as the LV mass index. Regional wall motion was assessed using a 16-segment model of the LV¹² and a 4-point grade scale¹²: 1, normal contractility; 2, hypokinesia; 3, akinesia; and 4, dyskinesia. The wall-motion score index was calculated as the sum of the score of each segment divided by the number of segments scored. Thus, a higher wall-motion score index corresponds to worse wall motion.

Clinical Endpoints Definition

The clinical outcomes were obtained by reviewing hospital records and conducting face-to-face interviews. The major adverse cardiovascular events (MACE) included all-cause death, cardiovascular death, rehospitalization for heart failure (HF), rehospitalization for angina symptoms, recurrent nonfatal myocardial infarction (MI), repeated coronary revascularization, and stroke.

Statistical Analysis

Continuous variables are presented as mean $\pm$ SD or median and interquartile range, as appropriate. Categorical variables are presented as frequencies and percentages. Kolmogorov-Smirnov analysis was performed to assess the normality of data distribution. Independent-samples *t* test and Mann-Whitney *U* test, or 1-way analysis of variance and Kruskal-Wallis *H* test, were used to compare the differences between continuous variables. The Pearson χ^2 test or Fisher exact test were used to compare the differences between

categorical variables. Factors related to LV remodeling were investigated by logistic regression. Clinical endpoints were evaluated by the Kaplan-Meier method, and differences between groups were compared with the log-rank test. Cox proportional-hazard regression was performed to adjust for potential confounders. A propensity-score method⁷ was used to identify comparable patients. All statistical tests were 2-tailed, and a *P* value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows, version 18.0 (SPSS Inc., Chicago, IL).

Results

Clinical Characteristics of the Patients

A total of 1268 eligible STEMI patients were selected. Because 178 patients could not be contacted, data from the 1090 remaining patients were analyzed. These patients (81.7% men) were age 59.10 ± 11.53 years (range, 20–88 years). Of these patients, 786 patients had undergone the late-PCI approach (late-PCI group) and 304 patients had been treated with the standard medical therapeutic approach (nonrevascularization group). In the late-PCI group, the median time to open IRA from symptom onset was 10 days (range, 7–16 days). At least 1 stent was placed in 780 (99.2%) patients in the late-PCI group, all of whom received drug-eluting stents. Glycoprotein IIb/IIIa antagonists were administered to 461 (58.7%) patients in the late-PCI group. The clinical characteristics of the patients are presented in Table 1. Intergroup comparison showed that patients in the nonrevascularization group were older and more often female; had more history of MI, revascularization, and chronic HF; and had higher heart rate and Killip classification. Meanwhile, more history of smoking and hyperlipidemia were observed in the late-PCI group. Some differences were also observed in pharmacotherapy during hospitalization, with more patients in the late-PCI group receiving glycoprotein IIb/IIIa antagonists, clopidogrel, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers, and β -blockers, whereas more patients in the nonrevascularization group required nitrate, spironolactone, diuretics, and digoxin. However, there were no differences in the use of secondary prevention drugs recommended by the guidelines at the follow-up time point between the 2 groups. But nitrate, spironolactone, diuretics, and digoxin were still more frequently used in the nonrevascularization group at the follow-up time point, which may suggest more severe ischemic symptoms and HF in patients in the nonrevascularization group.

Comparison of Echocardiographic Parameters Between the Late-Percutaneous Coronary Intervention and Nonrevascularization Groups

Table 2 lists the key echocardiographic data of the late-PCI and nonrevascularization groups. The echocardiographic parameters did not differ at baseline between the 2 groups. However, a significant difference was observed at the follow-up evaluations: LV remodeling was more pronounced in the nonrevascularization group than in the late-PCI group. The patients in the nonrevascularization group had a greater LV diameter, volume, and mass, as well as more impaired

LV contractile function and wall motion. Moreover, the degree of these changes was also more serious in the nonrevascularization group than in the late-PCI group.

Analysis of Factors Related to Left Ventricular Remodeling

Left ventricular remodeling was defined as an increase in the LVEDV of $\geq 15\%$ from baseline to the follow-up evaluations.¹³ In our study population, 53.9% of the patients exhibited pronounced LV remodeling. After evaluation of all the clinical variables, univariate analysis identified 5 variables as potential contributors: late-PCI approach (odds ratio [OR]: 0.357, 95% confidence interval [CI]: 0.253–0.504, *P* < 0.001), ACEI/ARB use (OR: 0.594, 95% CI: 0.393–0.899, *P* = 0.014), and β -blocker use (OR: 0.638, 95% CI: 0.443–0.920, *P* = 0.016) during hospitalization were negatively correlated with LV remodeling; body surface area (OR: 5.378, 95% CI: 2.191–13.201, *P* < 0.001) and heart rate on admission (OR: 1.010, 95% CI: 1.001–1.019, *P* = 0.037) were positively correlated with LV remodeling. Multivariate analysis revealed that the late-PCI approach was independently negatively correlated with LV remodeling (OR: 0.356, 95% CI: 0.251–0.505, *P* < 0.001).

Reduced Risks for Major Adverse Cardiac Events With Late Percutaneous Coronary Intervention

During a median period of 36 months (range, 27–47 months), 389 patients had MACE (including 201 deaths). The Figure 1 shows that the lower relative risks of MACE (Figure 1A), all-cause death (Figure 1B), and rehospitalization for HF (Figure 1C) in the late-PCI group compared with the nonrevascularization group by the Kaplan-Meier curves, respectively. Table 3 summarizes the results of univariate and multivariate Cox proportional-hazard regression analysis. Univariate analysis showed that the late-PCI approach was associated with lower relative risks for MACE, all-cause death, and rehospitalization for HF. After adjusting for sex, age, body mass index, smoking, hypertension, diabetes mellitus, hyperlipidemia, prior MI, prior revascularization, prior chronic HF, anterior wall infarct location, heart rate, blood pressure, Killip classification, and ACEI/ARB and β -blocker use during hospitalization, multivariate analysis revealed that the late-PCI approach remained significantly associated with lower relative risks for MACE (hazard ratio [HR]: 0.507, 95% CI: 0.412–0.625, *P* < 0.001), all-cause death (HR: 0.419, 95% CI: 0.314–0.559, *P* < 0.001), and rehospitalization for HF (HR: 0.583, 95% CI: 0.379–0.896, *P* = 0.014).

Propensity-Score Analysis

To eliminate differences in baseline characteristics between the late-PCI and nonrevascularization groups, the comparable patients treated with invasive or conservative strategies were identified by the propensity-score method. The baseline characteristics of the matched patients are presented in Table 4. The lower relative risks of MACE (Figure 1D), all-cause death (Figure 1E), and rehospitalization for HF (Figure 1F) in the late-PCI group were still observed by the Kaplan-Meier curves in the matched patients. Multivariate Cox proportional-hazard regression further revealed

Table 1. Clinical Characteristics of the Patients

	Late-PCI Group (n = 786)	Nonrevascularization Group (n = 304)	P Value
Female sex	116 (14.8)	83 (27.3)	<0.001
Age, y	57.98 ± 11.13	62.02 ± 12.05	<0.001
BMI (kg/m ²)	23.97 ± 2.93	23.75 ± 2.09	0.226
HR on admission (bpm)	75.49 ± 14.88	78.77 ± 17.80	0.002
SBP on admission (mm Hg)	122.00 ± 20.23	123.27 ± 21.69	0.362
DBP on admission (mm Hg)	76.70 ± 12.98	76.13 ± 14.15	0.524
Smoking	521 (66.3)	168 (55.3)	0.001
Hypertension	328 (41.7)	132 (43.4)	0.612
DM	113 (14.4)	56 (18.4)	0.098
Hyperlipidemia	127 (16.2)	34 (11.2)	0.038
Prior angina	190 (24.2)	87 (28.6)	0.131
Prior MI	52 (6.6)	34 (11.2)	0.012
Prior revascularization	18 (2.3)	14 (4.6)	0.042
Prior chronic HF	5 (0.6)	7 (2.3)	0.045
Family history of CAD	57 (7.3)	23 (7.6)	0.859
Anterior wall infarct	459 (58.4)	191 (62.8)	0.181
Killip classification on admission			<0.001
I	469 (59.7)	166 (54.6)	
II	252 (32.1)	89 (29.3)	
III	50 (6.4)	24 (7.9)	
IV	5 (1.9)	25 (8.2)	
TC, mmol/L	4.07 ± 1.09	4.09 ± 1.15	0.816
LDL-C, mmol/L	2.32 ± 0.88	2.25 ± 0.76	0.236
eGFR, mL/min/1.73 m ²	110.55 ± 41.86	113.02 ± 63.43	0.454
Thrombolytic therapy during the first 24 h after onset of index STEMI	124 (15.8)	48 (15.8)	0.996
Glycoprotein IIb/IIIa antagonists	461 (58.7)	9 (3.0)	<0.001
Coronary angiography characteristics			
IRA			
RCA	278 (35.4)	—	
LAD	439 (55.9)	—	
LCX	62 (7.9)	—	
LM	7 (0.9)	—	
TIMI flow grade in IRA			
0–1	295 (37.5)	—	
2–3	491 (62.5)	—	

Table 1. continued

	Late-PCI Group (n = 786)	Nonrevascularization Group (n = 304)	P Value
No. of diseased vessels			
1	208 (26.5)	—	
2	271 (34.5)	—	
3	307 (39.1)	—	
Gensini score	55 (36, 82)	—	
Medication during hospitalization			
Aspirin	782 (99.5)	300 (98.7)	0.229
Clopidogrel	782 (99.5)	294 (96.7)	0.001
ACEI/ARB	689 (87.7)	244 (80.3)	0.002
β-Blocker	660 (84.0)	221 (72.7)	<0.001
Statin	753 (95.8)	284 (93.4)	0.101
CCB	77 (9.8)	26 (8.6)	0.529
Nitrate	155 (19.7)	95 (31.2)	<0.001
Spironolactone	100 (12.7)	71 (23.4)	<0.001
Diuretic	90 (11.5)	79 (26.0)	<0.001
Digoxin	16 (2.0)	19 (6.2)	<0.001
Medication at follow-up			
Aspirin	650 (94.3)	186 (93.0)	0.481
Clopidogrel	121 (17.6)	45 (22.5)	0.115
ACEI/ARB	445 (64.6)	142 (71.0)	0.092
β-Blocker	514 (74.6)	138 (69.0)	0.115
Statin	566 (82.1)	168 (84.0)	0.543
CCB	75 (10.9)	20 (10.0)	0.721
Nitrate	93 (13.5)	47 (23.5)	0.001
Spironolactone	36 (5.2)	31 (15.5)	<0.001
Diuretic	37 (5.4)	31 (15.5)	<0.001
Digoxin	11 (1.6)	17 (8.5)	<0.001
Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blocker; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, heart rate; IQR, interquartile range; IRA, infarct-related artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LDL-C, low-density lipoprotein cholesterol; LM, left main coronary artery; MDRD, Modification of Diet in Renal Disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; SBP, systolic blood pressure; SCr, serum creatinine; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction; TC, total cholesterol; TIMI, Thrombolysis In Myocardial Infarction. Data are presented as the mean ± SD, median (IQR), or n (%). eGFR was calculated according to the MDRD formula: eGFR (mL/min/1.73 m ² of body surface area) = 186 × (SCr) ^{−1.154} × (Age) ^{−0.203} (×0.742 for females). SCr is reported in mg/dL.			

that the late-PCI approach remained significantly associated with lower relative risks for MACE (HR: 0.466, 95% CI: 0.358-0.607, $P < 0.001$), all-cause death (HR: 0.398, 95% CI: 0.277-0.571, $P < 0.001$), and rehospitalization for HF (HR: 0.498, 95% CI: 0.283-0.878, $P = 0.016$) in the matched patients.

Discussion

The main finding of our study is that the late-PCI strategy prevents LV remodeling, protects LV function, and reduces risks of MACE, all-cause death, and rehospitalization for HF compared with conservative strategies in STEMI patients presenting >24 hours from onset of symptoms.

Table 2. Comparison of Echocardiographic Parameters Between the Late-PCI and Nonrevascularization Groups

	Late-PCI Group (n = 689)	Nonrevascularization Group (n = 200)	P Value
At Baseline			
LVEDDI, cm/m ²	2.99 ± 0.43	3.00 ± 0.40	0.698
LVESDI, cm/m ²	2.11 ± 0.46	2.17 ± 0.46	0.101
LVEDVI, mL/m ²	57.54 ± 14.56	58.73 ± 13.94	0.081
LVESVI, mL/m ²	30.15 ± 11.78	31.54 ± 11.97	0.051
LV mass index, g/m ²	92.09 ± 24.20	94.13 ± 27.74	0.310
LVEF, %	53.75 ± 10.69	52.34 ± 12.37	0.112
LVFS, %	29.09 ± 7.34	28.50 ± 8.98	0.347
WMSI	1.26 ± 0.20	1.28 ± 0.20	0.261
At Follow-up			
LVEDDI, cm/m ²	3.11 ± 0.43	3.28 ± 0.47	<0.001
LVESDI, cm/m ²	2.23 ± 0.50	2.45 ± 0.55	<0.001
LVEDVI, mL/m ²	66.58 ± 23.70	80.79 ± 24.41	<0.001
LVESVI, mL/m ²	33.68 ± 18.56	45.31 ± 19.66	<0.001
LV mass index, g/m ²	87.41 ± 21.38	103.24 ± 32.09	<0.001
LVEF, %	52.43 ± 11.61	45.35 ± 10.49	<0.001
LVFS, %	28.56 ± 8.86	25.20 ± 8.00	<0.001
WMSI	1.28 ± 0.24	1.39 ± 0.28	<0.001
Changes of Parameters			
ΔLVEDDI, cm/m ²	0.13 ± 0.37	0.27 ± 0.33	<0.001
ΔLVESDI, cm/m ²	0.12 ± 0.43	0.28 ± 0.45	<0.001
ΔLVEDVI, mL/m ²	9.04 ± 22.88	22.06 ± 21.40	<0.001
ΔLVESVI, mL/m ²	3.53 ± 16.35	13.77 ± 16.39	<0.001
ΔLV mass index, g/m ²	−4.67 ± 24.91	9.11 ± 26.10	<0.001
ΔLVEF, %	−1.33 ± 11.46	−6.99 ± 12.40	<0.001
ΔLVFS, %	−0.53 ± 9.13	−3.31 ± 9.27	<0.001
ΔWMSI	0.02 ± 0.25	0.11 ± 0.25	<0.001

Abbreviations: LVEDDI, left ventricular end-diastolic diameter index; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESDI, left ventricular end-systolic diameter index; LVESVI, left ventricular end-systolic volume index; LVFS, left ventricular fractional shortening; SD, standard deviation; WMSI, wall motion score index.

Data are presented as the mean ± SD.

Our findings indicate that late PCI has a favorable effect on LV remodeling and clinical outcomes in late presenters of STEMI.

Shortening the time from symptom onset to the first medical contact and implementing effective reperfusion via PCI early are critical in the treatment of STEMI.¹⁴ However, only a small proportion of STEMI patients receive timely and effective reperfusion therapy due to patient or treatment delay, and this proportion of patients is even lower in developing countries. Thus, there is a large proportion of late presenters of STEMI in the real world.

The open-artery hypothesis proposes that recanalization of a totally occluded IRA, even late in the course of an acute MI, has a favorable effect on LV remodeling and long-term outcomes, as potentially viable (hibernating and stunned) myocardium is thought to be salvaged through reperfusion.^{15,16} Recent clinical studies demonstrate that myocardium can be salvaged beyond the first 12-hour time limit, even when the IRA is totally occluded.^{4–6} It has been documented that late reperfusion can interrupt the ischemia-driven apoptosis cascade and its consequences¹⁷ and prevent the reduction of capillary density.¹⁸ In humans,

Figure 1. Kaplan-Meier survival curves for MACE (A, D), all-cause death (B, E), and rehospitalization for HF (C, F). (A–C: in all patients; D–F: in matched patients). Patients in the late-PCI group had lower relative risks of MACE, all-cause death, and rehospitalization for HF compared with the patients in the nonrevascularization group. Abbreviations: HF, heart failure; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention.

Table 3. Cox Proportional-Hazards Regression Analysis of Factors Related to Clinical Endpoints

	MACE			All-Cause Death			Rehospitalization for HF		
	HR	95% CI	P Value	HR	95% CI	P Value	HR	95% CI	P Value
No Adjustment									
Late-PCI approach	0.435	0.355–0.532	<0.001	0.311	0.236–0.410	<0.001	0.560	0.364–0.861	0.008
Multivariate Adjustment									
Late-PCI approach	0.507	0.412–0.625	<0.001	0.419	0.314–0.559	<0.001	0.583	0.379–0.896	0.014
Age	1.026	1.017–1.036	<0.001	1.038	1.024–1.052	<0.001	1.027	1.008–1.047	0.005
Heart rate	1.010	1.004–1.016	0.001	1.017	1.010–1.025	<0.001	—	—	—
Killip classification	1.356	1.204–1.528	<0.001	1.508	1.297–1.753	<0.001	—	—	—
β-Blocker	0.716	0.568–0.902	0.005	0.679	0.497–0.928	0.015	—	—	—
Anterior wall infarct	—	—	—	—	—	—	2.233	1.395–3.575	0.001

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; CI, confidence interval; DM, diabetes mellitus; HF, heart failure; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction. Multivariate Cox proportional hazard regression adjusted for sex, age, BMI, smoking, hypertension, DM, hyperlipidemia, prior MI, prior revascularization, prior chronic HF, anterior wall infarct location, heart rate, BP, Killip classification, and ACEI/ARB and β-blocker use during hospitalization.

the IRA may preserve residual anterograde blood flow and present spontaneous reopening.⁴ Moreover, repetitive myocardial ischemia results in preconditioning,¹⁹ which increases the resistance of myocardium to ischemia. Furthermore, ischemia itself stimulates the formation of collateral circulation.²⁰ These factors may potentially prolong the viability of the affected myocardium. In fact, the viability of myocardium has indeed been demonstrated days

to weeks after acute MI.^{21,22} Therefore, late presenters of STEMI are likely to benefit from reperfusion.²³

A few studies indicate that late PCI can improve LV function^{24,25} and remodeling^{26,27} and reduce the incidence of cardiovascular events.²⁸ Similarly, our results demonstrated that late PCI indeed prevented adverse LV remodeling and deterioration of contractile function and improved clinical outcomes in late presenters of STEMI. In contrast, the

Table 4. Baseline Characteristics of the Matched Patients by Propensity-Score Analysis

	Late-PCI Group (n = 293)	Nonrevascularization Group (n = 293)	P Value
Female sex	72 (24.6)	76 (25.9)	0.704
Age, y	60.69 ± 11.54	61.59 ± 11.93	0.357
BMI, kg/m ²	23.61 ± 2.83	23.73 ± 2.09	0.562
HR on admission, bpm	77.64 ± 16.05	78.32 ± 17.57	0.625
SBP on admission, mm Hg	123.29 ± 21.27	123.60 ± 21.69	0.860
DBP on admission, mm Hg	76.64 ± 13.43	76.22 ± 14.11	0.708
Smoking	169 (57.7)	167 (57.0)	0.867
Hypertension	121 (41.3)	129 (44.0)	0.504
DM	51 (17.4)	52 (17.7)	0.914
Hyperlipidemia	46 (15.7)	34 (11.6)	0.149
Prior angina	80 (27.3)	83 (28.3)	0.782
Prior MI	26 (8.9)	31 (10.6)	0.486
Prior revascularization	14 (4.8)	12 (4.1)	0.688
Prior chronic HF	2 (0.7)	4 (1.4)	0.686
Family history of CAD	20 (6.8)	23 (7.8)	0.635
Anterior wall infarct	173 (59.0)	183 (62.5)	0.398
Killip classification on admission			0.072
I	155 (52.9)	165 (56.3)	
II	104 (35.5)	87 (29.7)	
III	27 (9.2)	23 (7.8)	
IV	7 (2.4)	18 (6.1)	
Thrombolytic therapy during the first 24 h after onset of index STEMI	46 (15.7)	48 (16.4)	0.822
Glycoprotein IIb/IIIa antagonists	166 (56.7)	9 (3.1)	<0.001
Medication during hospitalization			
Aspirin	293 (100.0)	289 (98.6)	0.124
Clopidogrel	292 (99.7)	284 (96.9)	0.011
ACEI/ARB	245 (83.6)	240 (81.9)	0.584
β-Blocker	228 (77.8)	220 (75.1)	0.436
Statin	279 (95.2)	273 (93.2)	0.289
CCB	33 (11.3)	25 (8.5)	0.268
Nitrate	66 (22.5)	92 (31.4)	0.016
Spironolactone	39 (13.3)	67 (22.9)	0.003
Diuretic	43 (14.7)	75 (25.6)	0.001
Digoxin	8 (2.7)	16 (5.5)	0.095
Medication at follow-up			
Aspirin	236 (94.4)	184 (92.9)	0.523
Clopidogrel	39 (15.6)	45 (22.7)	0.055

Table 4. continued

	Late-PCI Group (n = 293)	Nonrevascularization Group (n = 293)	P Value
ACEI/ARB	158 (63.2)	141 (71.2)	0.074
β -Blocker	179 (71.6)	138 (69.7)	0.660
Statin	202 (80.8)	166 (83.8)	0.404
CCB	26 (10.4)	20 (10.1)	0.918
Nitrate	41 (16.4)	46 (23.2)	0.069
Spironolactone	15 (6.0)	30 (15.2)	0.001
Diuretic	15 (6.0)	30 (15.2)	0.001
Digoxin	4 (1.6)	16 (8.1)	0.001

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blocker; DBP, diastolic blood pressure; DM, diabetes mellitus; HF, heart failure; HR, heart rate; MI, myocardial infarction; SBP, systolic blood pressure; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction.
Data are presented as the mean $\pm$ SD or n (%).

Occluded Artery Trial (OAT),^{29,30} a largest randomized controlled trial, shows the similar rate of clinical endpoints between the late-PCI group and the conservative-treatment group. Notably, the OAT includes patients with IRAs of Thrombolysis in Myocardial Infarction (TIMI) grade 0 to 1 and without ongoing ischemia. Moreover, 50% of the IRAs are right coronary artery disease. So, the OAT includes a very small minority of STEMI patients, which cannot represent the true population of late presenters of STEMI in real-life clinical practice. In addition, the use rate of drug-eluting stents is only 8% in the OAT, which is far from the status of contemporary STEMI treatments. Due to the improvement in operating skill, intervention devices, and pharmacology, the treatment of STEMI has substantially evolved over the past decade.^{31,32} Waiting for the development of stable phase in late presenters of STEMI to apply PCI may not be appropriate.³³ Recent studies have shown that late PCI is safe and has a high rate of success.^{34,35} In the context of contemporary STEMI treatments, our results provided supporting evidence for the application of PCI in late presenters of STEMI.

Study Limitations

Our study had several potential weaknesses. First, because patients were selected at PCI-capable hospitals, the number of nonrevascularization cases was relatively low. Second, due to the lack of coronary angiographic characteristics for the nonrevascularization group, we could not report the details of the coronary artery lesions of nonrevascularization patients.

Conclusion

In comparison with conservative strategies, the late-PCI strategy prevents LV remodeling, protects LV function, and improves clinical outcomes in STEMI patients presenting >24 hours after symptom onset. Our study provides supporting evidence for late PCI and also underscores the need to further investigate the subpopulation of patients experiencing the best benefit from late PCI.

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