

Impact of the Magnitude of the Initial ST-Segment Elevation on Left Ventricular Function in Patients With Anterior Acute Myocardial Infarction

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Background In the percutaneous coronary intervention (PCI) era, the impact of initial ST-segment elevation magnitude on left ventricular (LV) function in patients with acute myocardial infarction (AMI) remains unclear. **Methods and Results** In the present study, 239 patients with total occlusion and 81 patients with spontaneous reperfusion within 12 h of their first anterior AMI were evaluated. The sum of ST-segment elevation (Σ ST) was measured in leads I, aVL and V₁₋₆ shortly before angiography. PredischARGE LV ejection fraction (LVEF) was obtained at 15 $\pm$ 5 days. In total occlusion, the predischARGE LVEF was significantly lower in patients with Σ ST $\geq$ 10 mm than in those with Σ ST <10 mm (51 $\pm$ 14% vs 57 $\pm$ 14%, p <0.01). However, in spontaneous reperfusion, there was no significant difference between patients with Σ ST $\geq$ 10 mm and those with Σ ST <10 mm (61 $\pm$ 13 vs 62 $\pm$ 14 %, p =NS). PredischARGE LVEF significantly correlated with Σ ST in total occlusion (r =–0.25, p <0.01), but not in spontaneous reperfusion (r =0.03, p =NS).

Conclusion The results suggest that initial Σ ST is an important predictor of LV function in patients with total occlusion, but not in those with spontaneous reperfusion. (Circ J 2004; 68: 903–908)

Key Words: Electrocardiogram; Myocardial infarction; Reperfusion; ST-segment; Ventricular function

The standard 12-lead electrocardiogram (ECG) is noninvasive and routinely performed at the time of admission in patients with chest pain, and its role in the diagnosis of acute myocardial infarction (AMI) is well established. Studies in either the prethrombolytic or thrombolytic era have assessed the size of the infarct on the basis of ST-segment measurements, such as the number of leads with ST-segment elevation or the magnitude of the elevation.^{1,2} More recently, percutaneous coronary intervention (PCI) is widely performed to restore coronary reflow to the jeopardized myocardium, and complete coronary reflow can be obtained in most patients with AMI.^{3,4} Although it has been shown that infarct size is determined by the size of the ischemic area at risk, the duration of ischemia, and the effectiveness of protective mechanisms such as residual antegrade flow, collateral circulation or ischemic preconditioning,^{5–8} the impact of the magnitude of the initial ST-segment elevation in the PCI era remains to be investigated. We therefore proposed to the impact of this factor on left ventricular function in patients with anterior AMI in the PCI era.

Methods

Study Patients

The study group consisted of 320 consecutive patients

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with a first anterior AMI in whom coronary angiography was performed within 12 h of the onset of chest pain, and in whom Thrombolysis in Myocardial Infarction (TIMI) 3 flow⁹ was obtained on the final angiogram. Anterior AMI was diagnosed by chest pain consistent with ongoing myocardial ischemia persisting for $\geq$ 30 min, elevation of serum creatine kinase (CK) to more than twice the normal upper limit and a culprit lesion of the proximal left anterior descending artery on angiography. Prodromal angina was defined as a typical chest pain episode persisting for <30 min either at rest or during effort $\leq$ 24 h before the onset of AMI. To assess infarct size, serum CK was measured every 3 h for at least 24 h and the peak CK value was obtained.

Cardiac Catheterization

Emergency cardiac catheterization was performed via the right femoral artery or left brachial artery after heparin administration. Contrast left ventriculography was performed in the 30° right anterior oblique projection before reperfusion therapy and approximately 2 weeks later. Left ventricular ejection fraction (LVEF) was calculated by means of the area–length method. Selective coronary angiography was performed in multiple projections before reperfusion therapy. Immediately after diagnostic angiography, reperfusion was performed with PCI or coronary thrombolysis, whichever was appropriate. The allocation of reperfusion therapy was not randomized and was based on the physician's decision.¹⁰

Angiographic Analysis

All coronary angiograms were reviewed by 2 cardiologists without knowledge of the clinical variables. Initial

Table 1 Baseline Characteristics of Patients With Total Occlusion and Those With Spontaneous Reperfusion

	Total occlusion (n=239)	Spontaneous reperfusion (n=81)	p value
Age (years)	60±11	64±10	<0.01
Male	193 (81%)	61 (75%)	NS
Diabetes mellitus	44 (18%)	19 (23%)	NS
Hypertension	83 (35%)	30 (37%)	NS
Prodromal angina	84 (35%)	34 (42%)	NS
Time to angiography (h)	3.5±2.4	4.2±3.1	<0.05
Site of culprit lesion			NS
Proximal to the first septal branch	147 (62%)	47 (58%)	
Distal to the first septal branch	92 (38%)	34 (42%)	
Collateral circulation	101 (42%)	9 (11%)	<0.01
Multivessel disease	67 (28%)	23 (28%)	NS
ΣST before angiography (mm)	15.6±10.9	10.7±10.1	<0.01
ΣST after angiography (mm)	11.5±9.5	6.5±4.0	<0.01
Reperfusion therapy			<0.01
Coronary intervention	232 (97%)	66 (82%)	
Thrombolysis	7 (3%)	10 (12%)	
Neither	0 (0%)	5 (6%)	

Table 2 Comparison Between Patients With ΣST ≥10 and Those With ΣST <10 in Total Occlusion

	Total occlusion		p value
	ΣST ≥10 (n=162)	ΣST <10 (n=77)	
Age (years)	60±11	60±12	NS
Male	132 (81%)	61 (79%)	NS
Diabetes mellitus	26 (16%)	18 (23%)	NS
Hypertension	65 (40%)	18 (23%)	NS
Prodromal angina	48 (30%)	36 (47%)	<0.01
Time to angiography (h)	3.3±2.1	4.0±2.8	<0.05
Site of culprit lesion			<0.05
Proximal to the first septal branch	91 (56%)	56 (73%)	
Distal to the first septal branch	71 (44%)	21 (27%)	
Initial TIMI flow grade			NS
0	146 (90%)	63 (82%)	
1	16 (10%)	14 (18%)	
Collateral circulation	56 (35%)	45 (58%)	<0.01
Multivessel disease	46 (28%)	21 (27%)	NS
ΣST before angiography (mm)	20.8±9.4	4.8±2.7	<0.01
ΣST after angiography (mm)	13.6±9.5	7.4±8.3	<0.01
Reperfusion therapy			NS
Coronary intervention	157 (97%)	75 (97%)	
Thrombolysis	5 (3%)	2 (3%)	
Neither	0 (0%)	0 (0%)	

TIMI flow grade was assessed before initiation of reperfusion therapy, and final TIMI flow grade was assessed on the final coronary angiogram. Total occlusion was defined as TIMI 0 or 1 flow, and spontaneous reperfusion was defined as TIMI 2 or 3 flow on the initial coronary angiogram. Multivessel coronary disease was defined as ≥75% stenosis remote from the infarct artery. Collateral circulation was considered present if partial or complete filling of the infarct artery distal to the infarct lesion was present.¹¹

ECG Analysis

Twelve-lead ECGs were obtained shortly before initiation of emergency angiography and on return to the coronary care unit. The sum of ST segment elevation (ΣST) was measured 20ms after the end of the QRS complex from leads I, aVL and V₁₋₆.¹² Patients with bundle branch block or persistent ventricular arrhythmia were excluded. In both those with total occlusion and spontaneous reperfusion, patients were divided into 2 groups according to the degree of initial ΣST: patients with ΣST ≥10mm and those

with ΣST <10mm.

Data Analysis

Statistical analysis was performed with the chi-square test for categorical variables. Analysis of variance was used for continuous variables. Relationships between variables were determined by linear regression analysis. Differences were considered significant if the p-value was <0.05. All data are expressed as mean±SD.

Results

Baseline Characteristics (Table 1)

There were 239 patients with total occlusion and 81 patients with spontaneous reperfusion. Patients with total occlusion were associated with shorter time to angiography, more collateral circulation and higher ΣST before or after angiography compared with those with spontaneous reperfusion. Reperfusion therapy was performed more frequently in patients with total occlusion.

Table 3 Comparison Between Patients With $\Sigma ST \geq 10$ and Those With $\Sigma ST < 10$ in Spontaneous Reperfusion

	Spontaneous reperfusion		p value
	$\Sigma ST \geq 10$ (n=37)	$\Sigma ST < 10$ (n=44)	
Age (years)	64±10	64±11	NS
Male	27 (73%)	34 (77%)	NS
Diabetes mellitus	8 (22%)	11 (25%)	NS
Hypertension	12 (32%)	18 (41%)	NS
Prodromal angina	12 (32%)	22 (50%)	NS
Time to angiography (h)	3.7±2.8	4.7±3.3	NS
Site of culprit lesion			NS
Proximal to the first septal branch	24 (65%)	23 (52%)	
Distal to the first septal branch	13 (35%)	21 (48%)	
Initial TIMI flow grade			NS
2	21 (57%)	20 (45%)	
3	16 (43%)	24 (55%)	
Collateral circulation	4 (11%)	5 (11%)	NS
Multivessel disease	11 (30%)	12 (27%)	NS
ΣST before angiography (mm)	18.4±10.5	4.3±2.7	<0.01
ΣST after angiography (mm)	7.9±3.9	5.3±3.8	<0.01
Reperfusion therapy			NS
Coronary intervention	29 (78%)	37 (84%)	
Thrombolysis	7 (19%)	3 (7%)	
Neither	1 (3%)	4 (9%)	

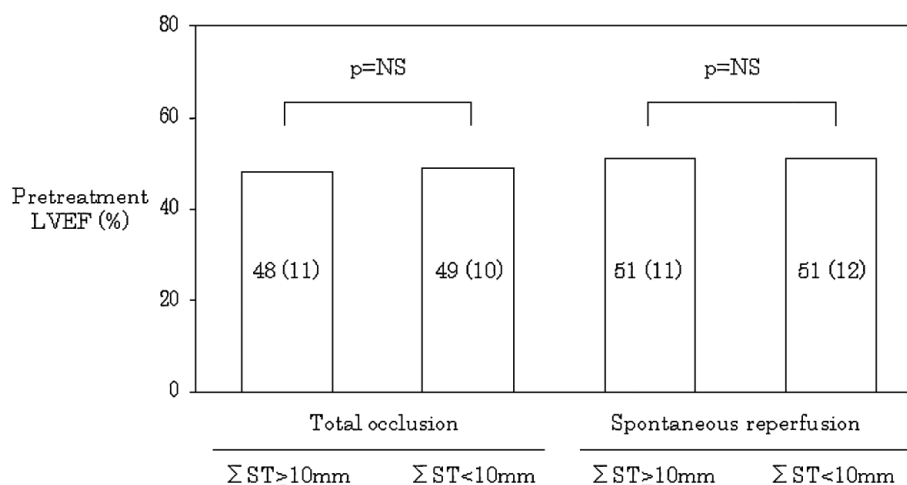


Fig 1. Pretreatment left ventricular ejection fraction (LVEF) tended to be lower in patients with acute myocardial infarction with total occlusion than in those with spontaneous reperfusion (48±11% vs 51±11%, p=NS). There was no significant difference in pretreatment LVEF between patients with $\Sigma ST \geq 10$ mm and those with $\Sigma ST < 10$ mm in both total occlusion (48±11 vs 49±10%, p=NS) and spontaneous reperfusion (51±11% vs 51±12%, p=NS). Data are mean (SD).

ΣST in Total Occlusion (Table 2)

Among the patients with total occlusion, there were 162 patients with $\Sigma ST \geq 10$ mm and 77 with $\Sigma ST < 10$ mm. There was no significant difference in baseline clinical and angiographic variables between the 2 groups except for less prodromal angina, shorter time to angiography, more culprit lesions distal to the first septal branch and less collateral circulation in patients with $\Sigma ST \geq 10$ mm. Reperfusion therapy significantly decreased ΣST in patients with $\Sigma ST \geq 10$ mm (20.8±9.4mm to 13.6±9.5mm, p<0.01), but increased ΣST in patients with $\Sigma ST < 10$ mm (4.8±2.7mm to 7.4±8.3mm, p<0.05).

ΣST in Spontaneous Reperfusion (Table 3)

Among the patients with spontaneous reperfusion, there were 37 patients with $\Sigma ST \geq 10$ mm and 44 with $\Sigma ST < 10$ mm. There was no significant difference in baseline

clinical and angiographic variables between the 2 groups. Reperfusion therapy significantly decreased ΣST in patients with $\Sigma ST \geq 10$ mm (18.4±10.5mm to 7.9±3.9mm, p<0.01), but did not change ΣST in patients with $\Sigma ST < 10$ mm (4.3±2.7mm to 5.3±3.8mm, p=NS).

Infarct Size

The peak CK value was significantly higher in patients with total occlusion than in those with spontaneous reperfusion (4,205±2,652 IU/L vs 2,139±1,815 IU/L; p<0.01). It was significantly higher in patients with $\Sigma ST \geq 10$ mm than in those with $\Sigma ST < 10$ mm in both total occlusion (4,642±2,702 IU/L vs 3,297±2,309 IU/L; p<0.01) and spontaneous reperfusion (2,900±2,092 IU/L vs 1,499±1,245 IU/L; p<0.01).

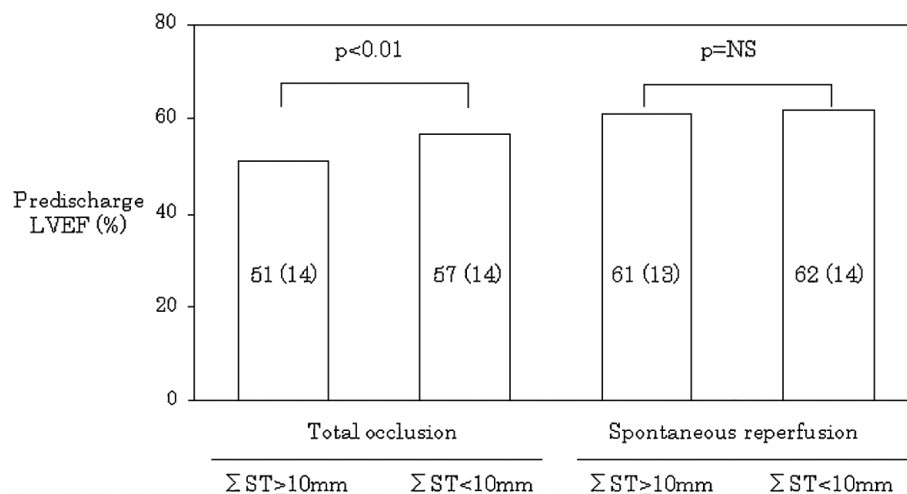


Fig 2. Predischarge left ventricular ejection fraction (LVEF) was significantly lower in patients with total occlusion than in those with spontaneous reperfusion ($53 \pm 14\%$ vs $61 \pm 14\%$, $p < 0.01$). In total occlusion, predischarge LVEF was significantly lower in patients with $\Sigma ST \geq 10$ mm than in those with $\Sigma ST < 10$ mm ($51 \pm 14\%$ vs $57 \pm 14\%$, $p < 0.01$). However, in spontaneous reperfusion, there was no significant difference in predischarge LVEF between patients with $\Sigma ST \geq 10$ mm and those with $\Sigma ST < 10$ mm ($61 \pm 13\%$ vs $62 \pm 14\%$, $p = \text{NS}$). Data are mean (SD).

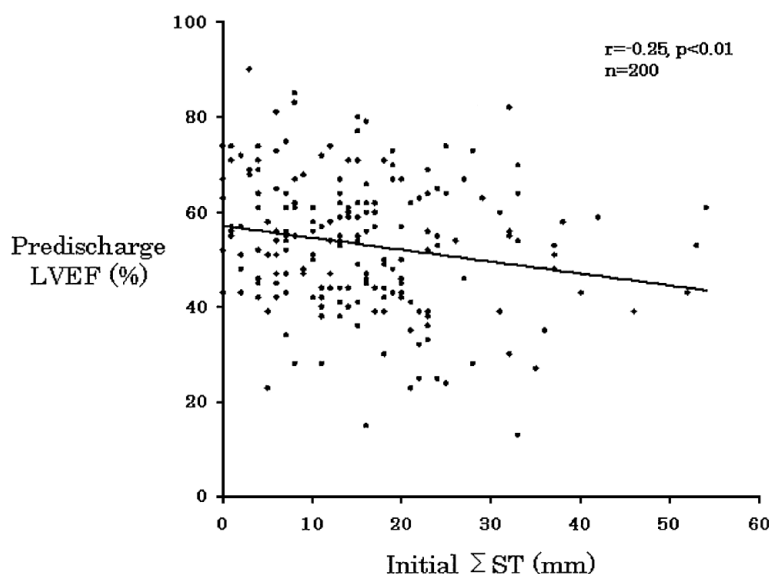


Fig 3. Scatterplots show the relationship between predischarge left ventricular ejection fraction (LVEF) and initial ΣST in total occlusion ($n = 200$).

Ventricular Function

Pretreatment LVEF, which was obtained in 273 patients (85%), tended to be lower in patients with total occlusion than in those with spontaneous reperfusion ($48 \pm 11\%$ vs $51 \pm 11\%$, $p = \text{NS}$). There was no significant difference in pretreatment LVEF between patients with $\Sigma ST \geq 10$ mm and those with $\Sigma ST < 10$ mm in both total occlusion ($48 \pm 11\%$ vs $49 \pm 10\%$, $p = \text{NS}$) and spontaneous reperfusion ($51 \pm 11\%$ vs $51 \pm 12\%$, $p = \text{NS}$) (Fig 1). Predischarge LVEF, which was obtained in 267 patients (83%) at 15 ± 5 days, was significantly lower in patients with total occlusion than in those with spontaneous reperfusion ($53 \pm 14\%$ vs $61 \pm 14\%$, $p < 0.01$). In total occlusion, predischarge LVEF was significantly lower in patients with $\Sigma ST \geq 10$ mm than in those with $\Sigma ST < 10$ mm ($51 \pm 14\%$ vs $57 \pm 14\%$, $p < 0.01$). However, in spontaneous reperfusion, there was no significant difference in predischarge LVEF between patients with $\Sigma ST \geq 10$ mm and those with $\Sigma ST < 10$ mm ($61 \pm 13\%$

vs $62 \pm 14\%$, $p = \text{NS}$) (Fig 2). Predischarge LVEF significantly correlated with SST in total occlusion ($r = -0.25$, $p < 0.01$, $n = 200$) (Fig 3), but did not in spontaneous reperfusion ($r = 0.03$, $p = \text{NS}$, $n = 67$). $\Sigma ST \geq 10$ mm predicted predischarge LVEF $< 40\%$ with 87% sensitivity and 35% specificity in total occlusion.

In-Hospital Outcomes

In-hospital death occurred in 5 patients (3.1%) with total occlusion and $\Sigma ST \geq 10$ mm. There was no significant difference in the rate of in-hospital death among the 4 groups.

Discussion

The present study demonstrated that, in the PCI era, the initial ST-segment elevation, as evidenced by $\Sigma ST \geq 10$ mm, was associated with depressed predischarge

LVEF in patients with anterior AMI and total occlusion, but not in those with spontaneous reperfusion. In addition, in spontaneous reperfusion, reperfusion therapy decreased Σ ST in patients with Σ ST ≥ 10 mm markedly, and resulted in a preserved predischARGE LVEF equivalent to that in those with Σ ST < 10 mm.

Previous Studies

Previous studies assessing whether the initial ECG can be used to predict myocardial infarct size have focused on the magnitude of the ST-segment elevation. Hackworthy et al reported that there was a close correlation between the sum of ST-segment elevation and myocardial infarct size at predischARGE in patients with anterior AMI.¹ On the other hand, Birnbaum et al reported no correlation between variables in patients with anterior AMI who did or did not undergo thrombolytic therapy.¹³ Those studies were performed either in the prethrombolytic era or the thrombolytic era, and did not assess acute angiographic findings such as the patency of the infarct artery or collateral circulation. Furthermore, even the most aggressive thrombolytic regimen (accelerated front-loaded tissue plasminogen activator) achieves TIMI 3 flow in only 50% of patients within 90 min of initiation of therapy.¹⁴ In addition, early reocclusion has been reported in 5–10% of patients and late reocclusion in 30% of patients.¹⁵ These may be reasons why the results have been conflicting.

Present Study

PCI is widely performed in patients with AMI to restore coronary reflow to the jeopardized myocardium, and TIMI 3 flow can be obtained in most patients.^{3,4} However, the impact of the magnitude of the initial ST-segment elevation on left ventricular function in patients with AMI has not been assessed in the PCI era and to evaluate this we selected only patients with a first anterior AMI in whom TIMI 3 flow was obtained on the final angiogram.

In total occlusion, initial ST-segment elevation as evidenced by Σ ST ≥ 10 mm was associated with depressed predischARGE LVEF. The degree of initial Σ ST is possibly dependent on ischemic preconditioning, time from the onset, or the establishment of collateral circulation after the onset of AMI. This study demonstrated that patients with Σ ST ≥ 10 mm had significantly less prodromal angina or collateral circulation than those with Σ ST < 10 mm, and these results agree with those of previous reports demonstrating cardioprotective effects of prodromal angina or collateral circulation. In the present study, time to angiography was shorter in patients with Σ ST ≥ 10 mm than in those with Σ ST < 10 mm. Because the peak CK value is significantly lower in patients with Σ ST < 10 mm than in those with Σ ST ≥ 10 mm, it cannot mean that Σ ST has passed its peak and is decreasing in patients with Σ ST < 10 mm. The more likely mechanism is that effects of prodromal angina or collateral circulation prevent ongoing myocardial ischemia or infarction, resulting in a lower initial Σ ST, even with longer time from the onset, in patients with Σ ST < 10 mm. In patients with Σ ST ≥ 10 mm, reperfusion therapy decreased Σ ST significantly, but the degree was less than that in spontaneous reperfusion. A possible mechanism of the incomplete ST-segment resolution is lack of myocardial perfusion, which can be detected by myocardial contrast echocardiography.¹⁶ This so-called ‘no-reflow phenomenon’ is explained mainly by increased microvascular impedance to flow, which is caused by

neutrophil plugging of capillaries, myocyte contracture and edema, distal microvascular spasm, and endothelial blistering,^{17,18} and is associated with large infarct size. Because we could not perform myocardial contrast echocardiography routinely, a precise correlation between initial ST-segment magnitude and the no-reflow phenomenon remains unclear. However, this study indicates the need for adjunctive pharmacological^{19–22} or mechanical therapy²³ to improve myocardial perfusion, especially in patients with total occlusion and Σ ST ≥ 10 mm. In addition, in patients with Σ ST < 10 mm, reperfusion therapy increased Σ ST slightly but significantly. Additional elevation of Σ ST after reperfusion is known to be associated with reperfusion injury, which causes large infarct size and poor left ventricular function.²⁴ Even if the initial Σ ST is less than 10 mm, adjunctive therapy might be required in patients with a high elevation of Σ ST after reperfusion.

In spontaneous reperfusion, there was no significant difference in predischARGE LVEF between patients with Σ ST ≥ 10 mm and those with Σ ST < 10 mm. Because there was no significant difference in baseline clinical and angiographic variables between these 2 groups, it was unclear what regulated the magnitude of the initial ST-segment elevation in spontaneous reperfusion. One possible regulating factor was the time from onset to spontaneous reperfusion, but we could not determine a precise time according to the patients’ symptoms. The other mechanism may be that the no-reflow phenomenon sometimes occurs after spontaneous reperfusion (spontaneous no-reflow phenomenon), because the peak CK value was significantly higher in patients with Σ ST ≥ 10 mm than in those with Σ ST < 10 mm even in spontaneous reperfusion. Whatever regulates the magnitude of the initial ST-segment elevation in spontaneous reperfusion, reperfusion therapy decreased Σ ST markedly in patients with Σ ST ≥ 10 mm, and resulted in preserved predischARGE LVEF. This favorable effect on left ventricular function in patients with Σ ST ≥ 10 mm was equivalent to that in patients with Σ ST < 10 mm, suggesting that aggressive reperfusion therapy using PCI or thrombolysis in spontaneous reperfusion may lead to myocardial reperfusion and microvascular integrity rather than only infarct artery patency.

Study Limitations

First, allocation to reperfusion therapy was based on the physician’s decision; however, there was no significant difference in the choice of reperfusion therapy and final TIMI 3 flow between patients with Σ ST ≥ 10 mm and those with Σ ST < 10 mm in both total occlusion and spontaneous reperfusion. Second, in total occlusion, patients with Σ ST ≥ 10 mm had more culprit lesion distal to the first septal branch than those with Σ ST < 10 mm. Although this baseline characteristic might result in a smaller area at risk in patients with Σ ST ≥ 10 mm, the predischARGE LVEF was significantly lower in patients with Σ ST ≥ 10 mm than in those with Σ ST < 10 mm. Thus, it was at least certain that Σ ST ≥ 10 mm was associated with a depressed predischARGE LVEF in total occlusion. Third, we do not have enough data about conservative therapy in patients with spontaneous reperfusion and Σ ST ≥ 10 mm, and could not compare reperfusion therapy to conservative therapy. Finally, the predischARGE LVEF was obtained in 267 patients (83%); however, the inclusion and exclusion criteria were strict, and these are enough data to clarify the impact of the magnitude of the initial ST-segment elevation on left

ventricular function in patients with anterior AMI in the PCI era.

Clinical Implications

Our data suggest that, compared with $\Sigma\text{ST} < 10\text{ mm}$, initial ST-segment elevation as evidenced by $\Sigma\text{ST} \geq 10\text{ mm}$ is associated with a depressed predischARGE LVEF in patients with AMI and total occlusion, but not in those with spontaneous reperfusion. In the case of total occlusion and $\Sigma\text{ST} \geq 10\text{ mm}$, reperfusion therapy decreases ΣST , but the degree is often incomplete, indicating the need for adjunctive pharmacological or mechanical therapy to improve myocardial perfusion in these patients. In spontaneous reperfusion and $\Sigma\text{ST} \geq 10\text{ mm}$, reperfusion therapy decreases ΣST markedly, and results in a preserved predischARGE LVEF, indicating the need for aggressive reperfusion therapy to obtain myocardial reperfusion and microvascular integrity rather than simply a patent infarct artery.

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