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Persistent ST-Segment Elevation after Primary Stenting for Acute Myocardial Infarction: Its Relation to Left Ventricular Recovery

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Summary

Background: Early restoration of coronary artery patency in acute myocardial infarction (AMI) has been linked to improvement in survival. However, early recanalization of an occluded epicardial coronary artery by either thrombolytic agents or percutaneous transluminal coronary angioplasty (PTCA) does not necessarily lead to left ventricular (LV) function recovery.

Hypothesis: The aim of this study was to evaluate the relation between persistent ST elevation shortly after primary stenting for acute myocardial infarction (AMI) and LV recovery.

Methods: Thirty-one patients with primary stenting for AMI were prospectively enrolled. To evaluate the extent of microvascular injury, serial ST-segment analysis on a 12-lead electrocardiogram recording just before and at the end of the coronary intervention was performed. Persistent ST-segment elevation (Persistent Group, n = 11) was defined as ≥ 50% of peak ST elevation and resolution (Resolution Group, n = 20) was defined as < 50% of peak ST elevation. Echocardiography was performed on Day 1 and 3 months after primary stenting.

Results: At 3 months, infarct zone wall-motion score index (WMSI, 2.1 ± 0.6 vs. 2.7 ± 0.3, $p < 0.05$) was smaller in the Resolution Group than in the Persistent Group, whereas wall motion recovery index (RI, 0.4 ± 0.3 vs. 0.1 ± 0.2, $p < 0.05$) and ejection fraction (58 ± 5 vs. 43 ± 10%, $p < 0.05$) were larger in the Resolution Group than in the Persistent Group. The extent of persistent ST elevation (% ST) shortly after successful recanalization of the infarct-related artery was significantly related to RI at 3 months ($r = -0.4$, $p < 0.05$). However, time to reperfusion was not related to RI at 3 months. There was also significant correlation between corrected TIMI frame count and %ST ($r = 0.4$, $p < 0.05$).

Conclusions: Persistent ST-segment elevation shortly after successful recanalization (≥ 50% of the peak value), as a marker of impaired microvascular reperfusion, predicts poor LV recovery 3 months after primary stenting for AMI.

Key words: electrocardiography, myocardial infarction, wall motion recovery

Introduction

Early restoration of coronary artery patency in acute myocardial infarction (AMI) has been linked to improvement in survival.[1, 2] However, early recanalization of an occluded epicardial coronary artery by either thrombolytic agents or percutaneous transluminal coronary angioplasty (PTCA) does not necessarily lead to left ventricular (LV) function recovery.[3–5] In fact, restoration of blood flow to ischemic myocardium causes impairment of flow at the level of microcirculation. This so-called "low or no-reflow" phenomenon was first described by Kloner *et al.* in an animal model.[6] Thereafter, this phenomenon has been evaluated by various methods, including myocardial contrast echocardiography (MCE),[7, 8] scintigraphy,[9, 10] and positron emission tomography (PET)[11] in patients with AMI. However, these techniques are costly and unavailable in routine clinical practice. Hence, there is a need for simple, noninvasive markers that identify the impairment of microcirculatory flow. Recently, myocardial reperfusion injury has been studied by serial ST-segment analysis during primary angioplasty.[12] Investigators reported that persistent ST-segment ele-

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vation shortly after successful infarct-related artery (IRA) recanalization reflects impairment of microvascular flow.[13–15]

We therefore hypothesized that the extent of ST-segment resolution can predict LV recovery after reperfused AMI. To test this hypothesis, we examined the relationship between persistent ST-segment elevation shortly after primary stenting for AMI and functional recovery of regional LV function.

Methods

Study Patients

From June 1999 to May 2000, 31 patients with AMI, in whom successful primary stenting for occluded IRA was performed at our institution, were prospectively enrolled. Criteria for inclusion were (1) initial episode of AMI, (2) chest pain lasting > 30 min and presentation 12 h after the onset of symptoms, (3) ST-segment elevation > 1 mm in at least two contiguous electrocardiographic (ECG) leads, (4) adequate two-dimensional (2-D) echocardiographic images, and (5) successful primary stenting (Thrombolysis in Myocardial Infarction [TIMI] flow grade 3 and postprocedural residual stenosis < 30%). Patients with concomitant severe disease, significant valvular heart disease, the culprit lesion in the left main trunk, left bundle-branch block, or poorly interpretable ST segments were excluded from the study. Informed consent was obtained from each patient.

Electrocardiogram

To assess the extent of microvascular reperfusion injury, serial ST-segment analysis on a 12-lead ECG was performed on admission to hospital (pre ECG) and at the end of coronary intervention (post ECG), according to the protocol. All ECGs were analyzed by one observer blinded to clinical data. The sum of ST-segment elevation was measured 20 ms after the end of the QRS complex in leads I, aVL, and V_1–V_6 for anterior and leads II, III, aVF, and V_5–V_6 for nonanterior infarction. The post ECGs were classified by comparison of the ST segments with those on the pre ECGs. The peak ST-segment level was defined as the highest ST-segment level measured on the pre ECG. Inadequate resolution of ST-segment elevation after successful recanalization was expressed as a percentage of the peak ST-segment elevation (%ST). Persistent ST-segment elevation ≥ 50% of the peak value (ST ≥ 50%) was defined as a marker of impaired microvascular reperfusion.

Angiographic Analysis

Stents were deployed using standard technique. Aspirin plus ticlopidine was used as an antithrombotic regimen. The IRA was identified based on ECG changes, angiographic appearance of the artery, and associated with regional wall motion abnormalities. Measurement of the minimal lumen diameter, reference diameter, and percent diameter stenosis was performed quantitatively in matched view using on-line quantitative coronary angiographic systems (Ancor version 2.0, Siemens, Erlangen, Germany). Angiographic measurements were made during diastole after intracoronary nitroglycerin administration. After stenting, the TIMI frame was obtained for the infarct-related artery using the technique described previously.[16] In brief, the TIMI frame count is the number of cine frames required for contrast to reach a standard distal landmark on cinefilms at 30 frames/s, and this raw number was corrected for normal differences in coronary artery length (corrected TIMI frame count).

Echocardiogram Analysis and Definitions

Two-dimensional echocardiography was performed on Day 1 and 3 months after primary stenting. Images were recorded on videotape by a S-VHS cassette recorder for analysis. Two investigators blinded to clinical and angiographic data analyzed the echocardiogram. The LV end-systolic and end-diastolic volumes were calculated by computer software according to a modified Simpson's rule. Three measurements of the technically best cardiac cycle were taken from each examination, and the average volumes were obtained. The LV ejection fraction was calculated as stroke volume/end-diastolic volume. The left ventricle was examined using standard views, and wall motion was scored for each of the 16 myocardial segments. Wall motion was graded for each segments as follows: 1 = normal, 2 = hypokinesia, 3 = akinesia, 4 = dyskinesia. In each patient, infarct-zone wall-motion score index (WMSI) was derived. Wall-motion recovery index (RI) was obtained by dividing the number of improved wall-motion segments (> grade 1) at follow-up by the number of abnormal wall-motion segments within the infarct-zone at baseline. The agreement was good for measurements of WMSI (interobserver variability: $r = 0.92$, $p < 0.01$; intraobserver variability: $r = 0.94$, $p < 0.01$).

Total ischemic time was measured as the time from the onset of symptoms until coronary reperfusion was established with balloon inflation. The impact of preinfarction angina on wall-motion recovery was evaluated based on the presence or absence of antecedent angina within 24 h before the onset of AMI. Cardiac enzyme (creatine kinase, creatine kinase-MB) was serially measured at 4-h intervals up to 24 h, and later at 8-h intervals up to 72 h after intervention, and the maximum level was used as an enzymatic marker of infarct size.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS, Inc., Chicago, Ill., USA) 7.5 for Windows. Data were expressed as mean ± standard deviation (SD) for continuous variables and frequency for the categorical variables. Continuous variables were compared by paired or unpaired Student's *t*-test and categorical variables by chi-square test. The comparisons between the two groups over time were done with a two-way repeated measures analysis of variance (ANOVA). Linear regression analysis was performed on all variables to identify determinants of wall-motion RI. A p value of < 0.05 was considered statistically significant.

TABLE I Baseline clinical characteristics

	Resolution (n = 20)	Persistent (n = 11)
Ages (years)	63 ± 10	58 ± 9
Male gender (%)	15 (75)	9 (82)
Risk factors		
Systemic hypertension (%)	9 (45)	6 (55)
Diabetes mellitus (%)	6 (30)	3 (27)
Total cholesterol (> 200 mg/dl) (%)	4 (20)	2 (18)
Current smoker (%)	12 (60)	9 (82)
Preinfarction angina (%)	7 (35)	5 (45)
Multivessel disease (%)	3 (15)	3 (27)
Previous myocardial infarction	0	0
Cardiogenic shock (%)	2 (10)	1 (9)
Reopro (%)	5 (25)	3 (27)
Reperfusion arrythmia (%)	10 (50)	5 (45)
Total ischemic time (min)	187 ± 119	220 ± 118
Peak CK, U/l	3741 ± 2750	5174 ± 4242
Systolic BP on admission (mmHg)	107 ± 32	114 ± 28
ST-segment elevation		
Peak ST, before, mm	13 ± 6	16 ± 9
after, mm [a]	4 ± 4	10 ± 5
%ST [a]	20 ± 11	64 ± 16

[a] $p < 0.05$.

Abbreviations: CK = creatine kinase, BP = blood pressure, %ST = percentage of the peak ST-segment elevation.

TABLE II Baseline angiographic characteristics

	Resolution (n = 20)	Persistent (n = 11)
Infarct-related coronary artery		
Left anterior descending	6	7
Left circumflex	3	0
Right	11	4
Reference vessel diameter (mm)	3.3 ± 0.4	3.4 ± 0.3
Minimal lumen diameter (mm)		
Pre	0	0
Post	3.1 ± 0.4	3.1 ± 0.3
Diameter stenosis (%)		
Pre	100	100
Post	7 ± 5	8 ± 6
Maximum inflation pressure (atm)	13.6 ± 3.6	12.1 ± 3.7

No statistical difference between the two groups.

Results

Baseline Characteristics

The mean patient age was 61 years, and 77.2% were male. The study population was divided into two groups: Persistent Group (ST ≥ 50%, n = 11) and Resolution Group (ST < 50%, n = 20). As shown in Tables I and II, baseline and angiographic characteristics were similar between the two groups. Patients in the Persistent Group had higher peak levels of creatine kinase (5,174 ± 4,242 vs. 3,741 ± 2,750 U/l, respectively) and longer total ischemic time (220 vs. 187 min, respectively) than did those in the Resolution Group, but this did not reach statistical significance. Cardiogenic shock was present in three patients (10%). Abciximab was used in eight patients (26%).

Changes in Global and Regional Left Ventricular Function

Figure 1 illustrates temporal changes of global and regional LV function. At baseline, LV ejection fraction (50 ± 8 vs. 53 ± 9%, respectively, p = NS) was similar between the Persistent and Resolution Groups. At 3-month follow-up, LV ejection fraction was significantly higher in the Resolution Group than in the Persistent Group (58 ± 5 vs. 44 ± 10%, respectively, $p < 0.05$). There was significant improvement in regional contractile function (WMSI and RI) within the infarct zone in the Resolution Group during follow-up. However, the improvement of regional contractile function was not observed in four patients of the Resolution Group. These data suggest that resolution of the ST segment shortly after successful recanalization does not necessarily indicate long-term improvement of regional contractile function.

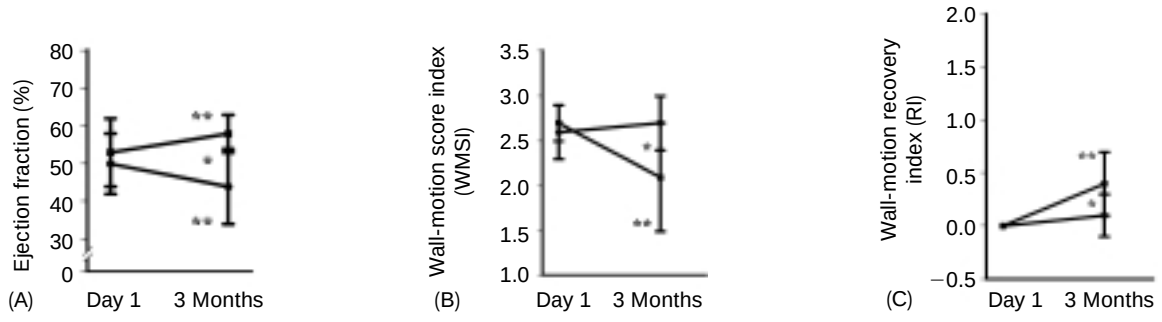

FIG. 1 Temporal changes of left ventricular ejection fraction (EF; A), infarct zone wall-motion score index (WMSI; B), and wall-motion recovery index (RI; C). *$p < 0.05$ between groups; **$p < 0.05$ within groups versus Day 1. Values are expressed as mean ± standard deviation. —■— = Persistent Group, —●— = Resolution Group.

TABLE III Univariate analysis predicting wall-motion recovery index at 3 months

	Continuous variables			Categorical variables		
	r Value	p Value		Present	Absent	p Value
%ST	−0.4	< 0.05	Use of abxicimab	0.29 ± 0.31	0.27 ± 0.41	NS
Age	0.3	NS	Reperfusion arrhythmia	0.26 ± 0.34	0.32 ± 0.34	NS
Peak ST elevation	−0.1	NS	Preinfarct angina	0.30 ± 0.36	0.28 ± 0.33	NS
Systolic BP, mmHg	0.16	NS				
Total ischemic time, min	−0.16	NS				

Abbreviation: NS = not significant. Other abbreviations as in Table I.

Predictors of Wall-Motion Recovery

As shown in Table III, clinical, hemodynamic, and angiographic variables were analyzed by regression analysis to evaluate the predictors of infarct zone RI at 3-month follow-up. Inverse correlation between RI and %ST was observed ($r = -0.4$, $p < 0.05$, Fig. 2). However, total ischemic time or peak ST elevation was not associated with RI at 3 months (Table III). There was also significant correlation between corrected TIMI frame count and %ST ($r = 0.4$, $p < 0.05$, Fig. 3).

Discussion

This study demonstrates that persistent ST-segment elevation shortly after successful recanalization (≥ 50% of the peak value) occurs in one-third of our patients with AMI and predicts poor LV recovery 3 months after primary stenting for AMI. These findings suggest that the extent of ST-segment elevation resolution may provide a reliable and simple marker for assessing microvascular reperfusion.

ST-Segment Resolution and Myocardial Perfusion

Impaired tissue reperfusion after successful recanalization of an epicardial coronary artery has been documented both in animals[6] and in patients[7–11] with AMI. Thus, the degree of functional recovery is related to the extent of microvascular damage. Ideally, a valid technique for identifying impaired microvascular flow should be simple, noninvasive, and easy to use in all patients. An assessment by ST-segment analysis criteria would fulfill all of these advantages. However, it remains uncertain whether the extent of ST-segment resolution would reflect differences in tissue perfusion. Recently, Santoro *et al.* found that the extent of ST-segment resolution is grossly related to the extent of microvascular integrity as assessed by MCE.[15] Others showed that ST-segment changes after reperfusion therapy reflect myocardial flow rather than epicardial flow because ST-segment change gives conflicting data about epicardial patency.[12, 13] The result of these studies may partially explain the relation between ST-segment resolution and myocardial reperfusion. Furthermore, we also demonstrated that %ST is related to the corrected TIMI frame count which may reflect microvascular flow in the absence of significant epicardial residual stenosis.

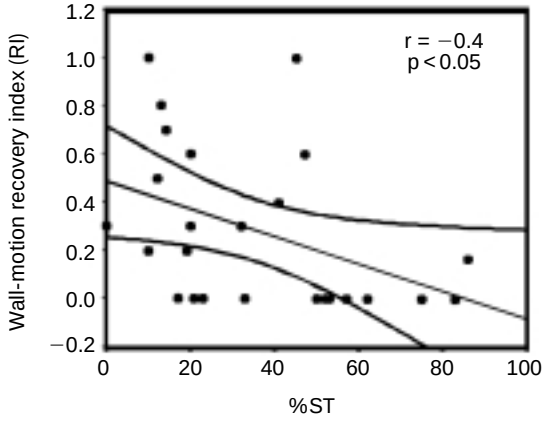

FIG. 2 Graph showing inverse correlation between %ST and wall-motion recovery index (RI).

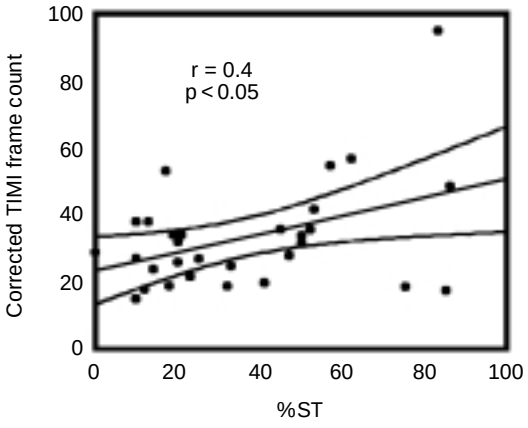

FIG. 3 Correlation between corrected TIMI frame count and %ST.

Relation between ST-Segment Resolution and Left Ventricular Recovery

The extent of ST-segment resolution, however, has modest correlation with regional LV recovery in this study. Various factors have been considered as influential in LV recovery. These factors include the perfusion status of the IRA and ischemic time. In addition, Asanuma *et al.* demonstrated that 25% of patients without contrast defect shortly after coronary reflow showed the late appearance of the contrast defect in MCE, and these patients had intramyocardial hemorrhage in MRI study.[17] They suggest that microvascular damage that leads to intramyocardial hemorrhage may progress for several days after coronary reflow and, consequently, contrast enhancement within the risk area does not necessarily indicate long-term LV recovery. Furthermore, the collateral circulation is an important source of blood supply to a jeopardized myocardium, favoring LV recovery after reperfusion therapy. Recently, Lee *et al.* demonstrated that LV recovery after reperfused AMI is primarily determined by pressure-derived fractional collateral flow.[18] They suggest that collateral circulation seems to be of major importance to LV recovery compared with total ischemic time. These observations may in part account for the modest correlation between %ST and RI.

Optimal Criteria for Reperfusion

In this study, the peak ST-segment level was used as the baseline for measuring changes reflecting reperfusion, in contrast to the initial ST-segment level that was used as the baseline in another study.[19] The reason for measurement from the peak ST-segment level is based on the observation that ST-segment fluctuations are unstable during the evolution of AMI and, therefore, the initial ST level is an unreliable baseline.

Determining the cutoff value of reperfusion on the basis of a ≥ 50% reduction in ST-segment level can be difficult. In fact, a substantial number of patients with successful reperfusion have ST-segment change around the 50% cutoff value. Several studies used different value (e.g., 30% or 70%) for reperfusion.[12, 19, 20] Recently, Claeys *et al.* demonstrated that the 50% cutoff value had a discriminative effect on progression of myocardial necrosis, as it was derived from the serial QRS score measurements and was associated with the highest differences in the extent of infarct necrosis among several cutoff values.[13] Therefore, the 50% cutoff value was used to stratify patients into impaired versus adequate microvascular flow in the present study.

Limitations

We call for caution in interpreting the results of our study because of the relatively small sample size. Furthermore, several potential limitations need to be addressed. First, exact measurement of the sum of ST-segment elevations would affect the simplicity of the model. However, in most cases exact measurements are not needed because they can be easily identified by visual comparison of the two ECGs. Second, ST-segment resolution was assessed by comparison of 12-lead ECGs. This approach might be less accurate than computer-derived ST-segment tracking; however, these systems are not generally available and less practical for clinical use. Third, our results showed no effect of reperfusion arrythmia or glycoprotein IIb-IIIa receptor blocker on LV recovery. However, the study population was relatively small, which may limit the statistical power to detect the relationship. Further studies are needed to investigate and evaluate the effect of these factors on LV recovery after reperfusion therapy. Finally, our findings are derived from a select population of patients with AMI who were successfully treated with primary stenting. Therefore, our results cannot be generalized to all patients receiving reperfusion therapy. Nevertheless, this study shows the importance of ST-segment resolution after reperfusion therapy.

Conclusion

Our study showed that persistent ST-segment elevation shortly after successful recanalization (≥ 50% of the peak value), as a marker of impaired microvascular reperfusion, predicts poor LV recovery 3 months after primary stenting for AMI. It reveals that the measurement of ST-segment elevation resolution, the simple clinical diagnostic tool to assess myocardial reperfusion, is therefore useful in early clinical decision making in treating patients with AMI.

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