Relation of Lateral ST-Segment Elevation Pattern to Myocardial Salvage in Patients with Recanalized Anterolateral Acute Myocardial Infarction

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Summary

Background: Although anterior acute myocardial infarction (AMI) with ST-segment elevation in lateral leads is associated with a poor prognosis, the significance of the pattern of lateral ST-segment elevation has not been examined.

Hypothesis: The aim of the study was to examine the relation of the pattern of lateral ST-segment elevation to myocardial reperfusion and infarct size in patients with AMI.

Methods: We studied 111 patients who had a first AMI presenting with anterolateral ST-segment elevation and Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow of the left anterior descending coronary artery within 6 h from symptom onset. Patients were classified into two groups according to the pattern of lateral ST-segment elevation on the admission electrocardiogram: Group 1, 42 patients with equivalent or greater ST-segment elevation in lead I than in lead aVL, and Group 2, 69 patients with lesser ST-segment elevation in lead I than in lead aVL. Left ventricular ejection fraction (LVEF) was measured by predischarge left ventriculography.

Results: There were no differences between the two groups in age, gender, time from onset to recanalization, culprit lesion, or collateral development. Group 1 patients had a higher probability of impaired myocardial reperfusion as indicated by a myocardial blush grade of 0 or 1 after recanalization, a higher peak creatine kinase level, and a lower LVEF than Group 2 patients ($p = 0.0001$, respectively).

Conclusions: We conclude that equivalent or greater ST-segment elevation in lead I than in lead aVL is associated with impaired myocardial reperfusion and less myocardial salvage in patients with recanalized AMI who present with anterolateral ST-segment elevation on the admission electrocardiogram.

Key words: acute myocardial infarction, ST-segment, reperfusion

Introduction

The clinical outcome of acute myocardial infarction (AMI) is determined mainly by infarct size, which is influenced by several factors, including the extent of area at risk, collateral circulation, preinfarction angina, and time from symptom onset to reperfusion.^{1–5} In patients with anterior AMI, the presence of ST-segment elevation in lateral leads is associated with a larger infarct size and a poorer short-term outcome, probably because of an extensive area at risk with anterolateral wall involvement.^{6,7} To our knowledge, however, the clinical significance of the pattern of lateral ST-segment elevation has not been examined.

Recent studies have suggested that even after successful recanalization of the infarct-related coronary artery, some patients do not have complete myocardial reperfusion and remain at risk for large infarcts and high mortality.^{8–12}

The aim of this study was to examine the relation of the pattern of lateral ST-segment elevation to the effectiveness of myocardial reperfusion and infarct size in patients with recanalized anterolateral AMI.

Methods

Patients

We studied 111 consecutive patients (91 men and 20 women, mean age 59 years, range 29–81) who were admitted to our coronary care with a first anterior AMI and fulfilled the

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following criteria: (1) admission within 6 h from symptom onset, (2) typical chest pain lasting ≥ 30 min, (3) persistent ST-segment elevation of ≥ 0.5 mm in lead I or aVL as well as ST-segment elevation of ≥ 2.0 mm in two or more contiguous precordial leads, (4) a subsequent increase in serum creatine kinase levels to more than two times the upper limit of normal, (5) no electrocardiographic evidence of left ventricular (LV) hypertrophy or bundle-branch block, (6) no findings of primary valvular or myocardial disease, (7) successful recanalization (Thrombolysis in Myocardial Infarction [TIMI] grade¹³ 3 flow) of the left anterior descending (LAD) coronary artery as confirmed by coronary angiography within 6 h from symptom onset, and (8) a patent LAD coronary artery as confirmed by predischarge coronary angiography.

Coronary Angiography

Coronary angiography was performed with the use of the Judkins technique immediately after admission and a mean of 14 days after AMI. The culprit lesion in the LAD was defined as the site with total occlusion, most severe stenosis, or a lesion with thrombus. The grade of collateral filling in the LAD was classified according to the criteria of Rentrop *et al.*¹⁴ Good collateral filling was defined as grade 2 or 3. Recanalization was defined as TIMI grade 3 flow and was established spontaneously in 8 patients, by thrombolysis in 35 patients, and by primary or rescue coronary angioplasty in 68 patients. The allocation of recanalization therapy was left to the doctor's discretion. Stenosis was considered significant if the lumen diameter was narrowed by $\geq 70\%$ in any projection. Myocardial blush was graded as follows on angiograms obtained immediately after recanalization by two observers who were blinded to all data apart from the coronary angiograms: 0, no myocardial blush or contrast density; 1, minimal myocardial blush or contrast density; 2, moderate myocardial blush or contrast density but less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery; and 3, normal myocardial blush or contrast density, comparable with that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery. When myocardial blush persisted, this finding was graded 0.⁹

Electrocardiographic Analysis

On admission, a 12-lead electrocardiogram (ECG) was recorded at a paper speed of 25 mm/s and an amplification of 10 mm/mV. ST-segment elevation above the baseline (as defined by the preceding TP segment) was measured to the nearest 0.5 mm 20 ms after the end of the QRS complex from each of the 12 standard leads. Measurements of three contiguous beats obtained by two independent observers blinded to all clinical and angiographic data were averaged for each lead. ST-segment deviation was considered clinically significant if it was ≥ 0.5 mm above the isoelectric line, and the number of leads with ST-segment elevation indicating the extent of area at risk was calculated.¹⁵ In addition to ST-segment measurement, the 32-point Selvester QRS score was calculated.^{16, 17}

Additional ST-segment elevation of at least 5 mm in leads V₁₋₆ shortly after recanalization was defined as ST-segment re-elevation.^{18, 19}

Left Ventriculography

Left ventricular function was evaluated on right anterior oblique views of left ventriculograms obtained a mean of 14 days after AMI. Left ventricular end-diastolic volume index, end-systolic volume index, and LV ejection fraction were determined by the area-length method described by Sandler and Dodge.²⁰ Regional wall motion in the territory of the LAD coronary artery was assessed by the centerline method²¹ and expressed as standard deviation (SD)/chord.

Cardiac Enzyme Study

Blood samples were obtained on admission and at 3-h intervals during the first 24 h, at 6-h intervals for the next 2 days, and then daily until discharge.

Statistical Analysis

Data are expressed as mean values $\pm$ SD for continuous variables and as percentages for categorical variables. Continuous variables were compared with the use of nonparametric tests (Mann-Whitney U test between groups). Chi-square analysis was used to compare categorical variables. Differences were considered significant at $p < 0.05$. Statistical analysis was performed using Stat View, version 5.0 (SAS Institute, Cary, N.C., USA).

Results

Patient Characteristics

Patients were divided into two groups according to the pattern of lateral ST-segment elevation on the admission ECG: Group 1, 42 patients with equivalent ($n = 11$) or greater ($n = 31$) ST-segment elevation in lead I than in lead aVL (Fig. 1A); and Group 2, 69 patients with lesser ST-segment elevation in lead I than in lead aVL (Fig. 1B). The baseline characteristics of the two groups are summarized in Table I. There were no differences in age, gender, hemodynamics on admission, or method of recanalization. Previous angina occurring within 48 h before the onset of infarction⁵ was less frequent in Group 1 than in Group 2. Time from symptom onset to recanalization was slightly longer in Group 1 than in Group 2, but the difference was not statistically significant.

Angiographic Findings on Admission (Table I)

On initial coronary angiography, the site of the culprit lesion, TIMI grade flow in the LAD coronary artery, collateral circulation, and the incidence of multivessel disease did not differ between the two groups.

FIG. 1 Representative electrocardiograms of the two groups. (A) Group 1: The magnitude of ST-segment elevation in lead I (1.5 mm) was greater than that in lead aVL (0.5 mm). Culprit lesion was seg. 6. Time from symptom onset to recanalization was 4.0 h. Left ventricular ejection fraction (LVEF) at discharge was 25%. (B) Group 2: The magnitude of ST-segment elevation in lead I (1.0 mm) was less than that in lead aVL (2.0 mm). Culprit lesion was seg. 6. Time from symptom onset to recanalization was 3.6 h. LVEF at discharge was 62%.

TABLE I Baseline characteristics

	ST I $\geq$ aVL n = 42 (Group 1)	ST I < aVL n = 69 (Group 2)	p Value
Age (years)	60 $\pm$ 11	58 $\pm$ 10	0.39
Sex (male) (%)	37 (76)	59 (86)	0.22
Previous angina within 48 h before the onset of infarction (%)	15 (36)	38 (55)	0.05
Systolic blood pressure on admission (mmHg)	140 $\pm$ 28	145 $\pm$ 28	0.45
Heart rate on admission (beats/min)	88 $\pm$ 15	83 $\pm$ 17	0.54
Time from symptom onset to recording ECG (h)	2.5 $\pm$ 1.8	2.2 $\pm$ 1.1	0.15
Findings on admission ECG			
Sum of ST-segment elevation in leads V ₁₋₆ (mm)	23 $\pm$ 10	18 $\pm$ 14	0.05
Sum of ST-segment elevation in leads I, aVL (mm)	2.3 $\pm$ 1.7	1.5 $\pm$ 1.8	0.13
QRS score	4.2 $\pm$ 2.0	3.2 $\pm$ 1.7	0.01
Number of leads with ST-segment elevation	7.0 $\pm$ 1.4	6.0 $\pm$ 1.8	0.01
ST re-evaluation immediately after recanalization (%)	28 (67)	33 (48)	0.05
Reperfusion therapy			
Spontaneous reperfusion (%)	2 (5)	6 (9)	
Thrombolysis (%)	14 (33)	21 (30)	0.73
Angioplasty (%)	26 (62)	42 (61)	
Time from symptom onset to recanalization (h) ^a	3.8 $\pm$ 1.5	3.4 $\pm$ 1.3	0.09
Initial angiographic findings			
Culprit lesion			
Proximal to first septal perforator (%)	25 (60)	46 (67)	0.45
Proximal to first diagonal branch (%)	26 (62)	41 (59)	0.80
TIMI grade flow			
0–1 (%)	39 (93)	59 (86)	0.24
2–3 (%)	3 (7)	10 (14)	
Rentrop 2–3 collaterals ^a (%)	11/39 (28)	24/59 (41)	0.21
Multivessel disease (%)	8 (19)	11 (16)	0.39

Values are expressed as means $\pm$ standard deviation or as percentages (%).

^a Only patients with totally occluded culprit lesions were studied.

Abbreviation: ECG = electrocardiogram.

Electrocardiographic Findings on Admission (Table I)

The sum of ST-segment elevation in lateral leads was slightly but not significantly higher in Group 1 than in Group 2. The sum of ST-segment elevation in precordial leads, QRS score, and number of leads with ST-segment elevation were greater in Group 1 than in Group 2. Additional ST-segment elevation after recanalization was more frequent in Group 1 than in Group 2.

Myocardial Reperfusion after Recanalization

Figure 2 shows the distribution of myocardial blush grade after recanalization. In Group 1, the majority (81%) of patients had impaired myocardial reperfusion as indicated by myocardial blush grade 0 or 1, and no patient had complete myocardial reperfusion as indicated by myocardial blush grade 3. In contrast, 33% of the patients in Group 2 had impaired myocardial reperfusion, whereas 23% had complete myocardial reperfusion.

Infarct Size and PredischARGE Left Ventricular Function (Table II)

Infarct size as estimated on the basis of peak creatine kinase level was larger in Group 1 than in Group 2. PredischARGE LV ejection fraction and regional wall motion were lower in Group 1 than in Group 2. PredischARGE LV end-systolic and end-diastolic volumes were larger in Group 1 than in Group 2.

In-Hospital Clinical Course (Table II)

During hospitalization, congestive heart failure and pericarditis occurred more frequently in Group 1 than in Group 2. Intra-aortic balloon pumping was needed to maintain hemodynamic stability more frequently in Group 1 than in Group 2.

Discussion

In patients with anterior AMI, greater ST-segment elevation in precordial leads and lateral leads on the admission ECG has been shown to be associated with a large infarct size and high in-hospital mortality.²² To our knowledge, however, no study has examined the relation between the pattern of lateral ST-segment elevation and infarct size in patients with anterior AMI. Our study demonstrated that in patients who had recanalized AMI presenting with anterolateral ST-segment elevation on the admission ECG, equivalent or greater ST-segment elevation in lead I than in lead aVL was associated with an extensive area at risk, impaired myocardial reperfusion, and subsequently less myocardial salvage as indicated by higher peak creatine kinase levels and poorer LV function.

FIG. 2 Distribution of myocardial blush grade after recanalization in the two groups. Impaired myocardial reperfusion as indicated by myocardial blush grade 0 or 1 was observed in the majority of Group 1 patients, but not in the majority of Group 2 patients. □ = Myocardial blush 0/1, ■ = myocardial blush grade 2, ■ = myocardial blush grade 3.

TABLE II Infarct size, predischARGE left ventricular function, and in-hospital clinical outcome

	ST I ≥ aVL n = 42 (Group 1)	ST I < aVL n = 69 (Group 2)	p Value
Peak creatine kinase (mU/ml)	6704 ± 2502	3993 ± 2434	0.0001
Time from onset to peak creatine kinase (h)	9.0 ± 2.4	10.6 ± 4.2	0.04
Left ventriculographic findings at discharge			
LVEF (%)	39 ± 10	51 ± 10	0.0001
SD/chords	-2.9 ± 0.6	-2.1 ± 1.1	0.0001
LVESVI (ml/m ²)	53 ± 20	39 ± 16	0.0001
LVEDVI (ml/m ²)	86 ± 25	78 ± 20	0.07
In-hospital clinical outcomes			
IABP (%)	10 (24)	5 (7)	0.013
Congestive heart failure (%)	10 (24)	1 (1)	0.0001
Pericarditis (%)	10 (24)	2 (3)	0.0006

Values are expressed as means ± standard deviation or as percentages (%).

Abbreviations: LVEF = left ventricular ejection fraction, LVESVI = left ventricular end-systolic volume index, LVEDVI = left ventricular end-diastolic volume index, IABP = intra-aortic balloon pumping.

Mechanisms of Greater ST Elevation in Lead I than in Lead aVL

ST-segment elevation in leads I and aVL probably reflects transmural ischemia in the basal anterolateral region supplied by the diagonal branch.²³ Because the location of the culprit lesion in relation to the first major septal perforator and the first major diagonal branch did not differ between the two groups in this study, the direction of the injury current produced by transmural ischemia in the basal area was considered similar. However, patients with equivalent or greater ST-segment elevation in lead I than in lead aVL had more leads with ST-segment elevation on the admission ECG, suggesting more extensive myocardial damage, than those with lesser ST-segment elevation in lead I than in lead aVL. Generally, in anterior AMI due to occlusion of the proximal LAD, the vector of injury current originating from the anterolateral region would be from -30° to -60° , which is more parallel to lead aVL than to lead I.²⁴ Therefore, the magnitude of ST-segment elevation in lead aVL is greater than that in lead I in most patients with anterolateral AMI. However, we speculated that in the presence of proximal LAD occlusion with severe myocardial ischemia extending to the inferolateral wall in addition to the anteroapical wall, indicating a larger jeopardized myocardial area, the injury current would be directed more to the left and downward. Such an injury current vector is more parallel to lead I than lead aVL and results in greater ST-segment elevation in the former lead than in the latter. During anterolateral AMI, greater ST-segment elevation in lead I might reflect more extensive myocardial damage (Fig. 3).

FIG. 3 In most patients with anterior acute myocardial infarction due to occlusion of the proximal left anterior descending coronary artery (LAD), the vector of injury current originating from the anterolateral region ranges from -30° to -60° (①). Such a vector is more parallel to lead aVL than to lead I, resulting in greater ST-segment elevation in the former than in the latter. When severe myocardial ischemia extends to the apical and inferolateral walls in the territory of the LAD, the injury current is directed more to the left and downward (②). Such a vector is more parallel to lead I than to lead aVL, resulting in greater ST-segment elevation in the former than in the latter lead.

Myocardial Reperfusion and Pattern of Lateral ST-Segment Elevation

Because of potential microvascular damage, the achievement of TIMI grade 3 flow in the infarct-related artery does not necessarily mean successful myocardial reperfusion.^{8–12} Myocardial contrast echocardiography has shown that the so-called “no-reflow” phenomenon, that is, impaired myocardial perfusion even after successful coronary recanalization as demonstrated by angiography, is associated with poor recovery of LV function.¹¹ In this study, we found that patients with equivalent or greater ST-segment elevation in lead I than in lead aVL had severe myocardial damage as indicated by higher QRS scores,¹⁷ as well as more frequent additional ST-segment elevation after recanalization, suggesting microcirculation reperfusion injury.^{18, 19} Such patients had impaired myocardial reperfusion, as indicated by a lower myocardial blush grade after recanalization, a larger infarct size, and poorer LV function associated with congestive heart failure or pericarditis during hospitalization. Recently, Iwakura *et al.*²⁵ reported that in patients with recanalized anterior AMI, the size of area at risk and the severity of myocardial damage before recanalization were closely related to the development of the no-reflow phenomenon. In patients with equivalent or greater ST-segment elevation in lead I than in lead aVL, microvascular injury might be caused primarily by rapid progression of myocardial necrosis in the extensive area at risk as indicated by this ECG finding before recanalization and also by reperfusion injury. In addition, these findings might be associated with a lower incidence of previous angina within 48 h before the onset of infarction, indicating less ischemic preconditioning.⁵

Clinical Implications and Conclusion

Patients with equivalent or greater ST-segment elevation in lead I than in lead aVL on the admission ECG may require additional pharmacologic interventions, such as antiplatelet therapy,²⁶ adenosine,²⁷ or nicorandil,²⁸ which have beneficial effects on the microvascular circulation. We believe that our results have important clinical implications for risk stratification in patients with anterolateral AMI.

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