Are Reciprocal Changes a Consequence of “Ischemia at a Distance” or Merely a Benign Electrical Phenomenon? A Pulsed-Wave Tissue Doppler Echocardiographic Study

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Objectives: The aim of the present study was to investigate whether ST segment depression in precordial leads at the time of acute inferior myocardial infarction represents a reciprocal change rather than concurrent anterior wall ischemia on the surface electrocardiography.

Background: The mechanism of reciprocal ST segment depression during acute myocardial infarction is controversial. “Ischemia at a distance” or a benign electrical phenomenon has been implicated in numerous reports. Pulsed-wave tissue Doppler (PWTD) echocardiography can be used to examine the regional diastolic motion of the left ventricular myocardial wall and may allow the detection of ischemic segments.

Methods: We evaluated regional myocardial ischemia using PWTD echocardiography in 48 patients with a first inferior wall myocardial infarction. The left ventricle was divided into 16 segments. PWTD echocardiographic velocities were obtained from each left ventricular segments.

Results: Reciprocal ST segment depression was present in 35 patients (Group 1) but not in the remaining 13 patients (Group 2). There were no significant differences between groups 1 and 2 with respect to systolic (S) (7.4 ± 1.1 vs 6.8 ± 0.9 cm/s; $P > 0.05$), early (E) (10.5 ± 2 vs 9.4 ± 1.2 cm/s; $P > 0.05$), and late (A) (9.5 ± 3.2 vs 8.5 ± 2.3 cm/s; $P > 0.05$) diastolic waves peak velocities, E/A ratio 1.1 ± 0.2 vs 1.1 ± 0.1 ; $P > 0.05$), Ewave deceleration time (DT) (92 ± 17 vs 101 ± 16 ms; $P > 0.05$) and regional relaxation time (RT) (82 ± 19 vs 93 ± 21 ms; $P > 0.05$) in anterior wall (basal levels), which correspond to reciprocal ST segment depression on electrocardiography. According to E/A ratio detected by PWTD echocardiography in anterior wall and anterior septum, patients with reciprocal ST segment depression were also divided into two groups: Group A, with E/A ratio > 1 ; Group B, with E/A ratio < 1 . Among the 35 patients with reciprocal ST segment depression, anterior wall ischemia was present in 10 patients and absent in 25 patients, whereas anterior septal ischemia was present in 12 patients and absent in 23 patients.

Conclusions: Reciprocal ST segment depression during the early phases of inferior infarction is an electrical reflection of primary ST segment elevation in the area of infarction.

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myocardial infarction; reciprocal ST segment depression; pulsed-wave tissue Doppler
echocardiography

In acute myocardial infarction (MI), ST segment depression in lead remote from those showing ST segment elevation has been attributed to several mechanisms. The mechanism of the reciprocal ST segment depression remains uncertain. Some investigators have suggested that it may be a benign electrical phenomenon.^{1–3} Others have suggested

that it is due to ischemia in another region distant from the infarct^{4–7} or that it is a finding of a large infarct.^{8,9}

Tissue Doppler imaging is a novel echocardiographic method that can be used to examine the regional diastolic motion of the left ventricular myocardial wall by modifying filter setting and

reducing velocity ranges of the standard Doppler signal.¹⁰ This method could be useful as a noninvasive test to detect ischemic myocardial left ventricular segments. Regional diastolic wall motion is impaired at the baseline in ischemic myocardial segments, even when systolic contraction is preserved.¹¹ The aim of the present study was to utilize this technique to test whether ST segment depression in precordial leads at the time of acute inferior myocardial infarction represents a reciprocal change rather than concurrent anterior wall ischemia on the surface electrocardiography (ECG).

METHODS

Patients

We studied 48 consecutive patients (mean age 59 ± 11 years; 40 men, 8 women) with an acute inferior wall MI. Acute inferior wall MI was diagnosed by: typical chest pain at least 30 minutes, ST-segment elevation of more than 0.1 mV in at least two leads representing the inferior wall (II, III, AVF), and an increase in cardiac enzymes to more than twice normal (5 U/L for creatine kinase-MB isoenzyme). The presence of right ventricular infarction was defined by an ST segment elevation ≥ 0.1 mV in lead V4R. R wave to S wave ratio >1 in V_1 and V_2 was defined as posterior MI. Exclusion criteria were (1) previous MI, (2) previous revascularization, (3) associated posterior or right ventricular MI, (4) intraventricular conduction disturbances, (5) valvular heart disease, (6) systemic hypertension, (7) hypertrophic, dilated, or restrictive cardiomyopathies, and (8) significant arrhythmias including atrial fibrillation, supra ventricular or ventricular tachycardia, and ventricular bigeminy. A standard 12-lead ECG was recorded immediately after arrival at the coronary care unit. Reciprocal changes in the ST segment were defined as ST depression of >1 mm in at least two out of four of the precordial leads V_1 – V_4 in patients with inferior infarction. The patients were divided into two groups according to the presence or absence of precordial ST segment depression.

Echocardiography

All echocardiographic examinations were performed within 1 hour after arrival to the coronary care unit. The equipment used was a Hewlett-Packard sonos 5500 phased array system equipped with Doppler tissue imaging technology (Aligent

Technology, Andover, MA). Left ventricular end-diastolic and end-systolic volumes and ejection fraction were determined from an apical two- and four-chamber view using the Simpson's biplane formula, according to the recommendations of the American Society of Echocardiography.¹² Tracing of endocardial borders in end-diastole and end-systole was performed in the technically best cardiac cycle. Segmental regional wall motion analysis was performed by using of a standard 16-segment model.¹² For each segment, wall motion was scored from 1 (normal) to 4 (dyskinetic). Left ventricular wall motion score index was defined as the sum of score of the individual segments divided by the total number of segments. Left ventricular diastolic filling patterns were determined by the mitral inflow pulsed-wave Doppler examination with a 2.5 MHz transducer. In the apical 4-chamber view, the Doppler sample volume was placed in the middle of the left ventricular inflow tract = 1 cm below the plane of mitral annulus between the mitral leaflet tips, where maximal flow velocity in early diastole was recorded.¹³ The following parameters were obtained: early diastolic filling peak velocity (E wave), late diastolic filling peak velocity (A wave), their ratio (E/A ratio), the isovolumetric relaxation time, and the deceleration time of the E velocity. The isovolumetric relaxation time, defined as the time from aortic valve closure to mitral valve opening, was assessed by simultaneously measuring the flow into the left ventricular outflow tract and mitral inflow by Doppler echocardiography.¹⁴

The pulsed-wave tissue Doppler (PWTD) echocardiography was performed using the same apparatus. A variable-frequency, phased-array transducer (2–4 MHz) was used. To display tissue velocities, the high pass filter was bypassed and lower gain amplification was used. The left ventricle was divided into 16 segments according to American Society of Echocardiology recommendations. In each subject, PWTD echocardiographic velocities were obtained from the apical echocardiographic window using 4-chamber, 2-chamber, and long-axis views. These three views provided visualization of six walls: posterior septum and lateral wall from 4-chamber, anterior and inferior walls from 2-chamber, and anterior septum and posterior wall from the long axis.¹² Each left ventricular wall was divided into three segments of equal length to obtain basal, mid, and apical segments. We did not analyze the apical segments because of suboptimal image quality. The Doppler

sample volume was placed equidistant between the endocardial and epicardial borders. A mean of five consecutive cycles was used for the calculations of all echocardiographic tissue Doppler parameters. Systolic (S), early (E), and late (A) diastolic waves were recorded from each left ventricular segment. The following parameters were obtained: S, E, and A peak velocities (cm/s) and peak velocity E/A ratio, E wave deceleration time (DT in ms) and regional relaxation time (RT in ms)—as the time interval occurring between the end of S and the onset of E.

Statistical Methods

Comparison of continuous variables was performed with the unpaired Student's *t* test or the Mann Whitney *U* test for continuous data when tests for normal distribution failed. Comparison of proportions was performed with the chi-square test and the Fisher's exact test. A *P* value of <0.05 was considered statistically significant.

RESULTS

Patient Characteristics (Table 1)

According to reciprocal ST segment changes study patients were assigned to the following two groups: group 1, with reciprocal depression (35 patients, 73%), group 2, without reciprocal depression (13 patients, 27%). In the comparison of patients with and those without reciprocal changes, there

were no significant differences in age, gender, and risk factors for atherosclerosis such as hypertension, smoking, and diabetes mellitus. Mean peak serum creatine kinase level was 2605 ± 995 IU/L in patients with reciprocal depression and 2194 ± 1128 IU/L in those without. This difference was not statistically significant (*P* = 0.08).

Patients with acute myocardial infarction received the following medication during hospitalization: β -blocker 35%, thrombolytic therapy 60%, aspirin 97%, angiotensin-converting enzyme inhibitor 65%, and digoxin 13%, respectively.

Standard Echocardiographic Analysis (Table 2)

There was no significant difference between groups 1 and 2 with regard to the echocardiographic parameters.

Pulse Wave Doppler Tissue Sampling (Table 3). S, E, and A peak velocities (cm/s) and E/A ratio, E wave deceleration time (DT in ms) and regional relaxation time (RT in ms) in the anterior wall and anterior septum, which correspond to the reciprocal ST segments depression, were similar in both groups. According to the E/A ratio detected by PWTD echocardiography in the anterior wall and anterior septum, patients with reciprocal ST segment depression were also divided into two groups: Group A, with E/A ratio >1; Group B, with E/A ratio <1. Among the 35 patients with reciprocal ST segment depression, anterior wall and anterior

Table 1. Baseline Patient Characteristics

	Reciprocal Change (n = 35)	No Reciprocal Change (n = 13)	P
Age (years)	56 $\pm$ 5	53 $\pm$ 6	0.13
Men	30 (87%)	10 (77%)	0.66
Systemic hypertension	6 (17%)	4 (31%)	0.42
Cigarette smoking	27 (77%)	11 (85%)	0.70
Diabetes mellitus	4 (11%)	2 (15%)	0.65
Systolic blood pressure (mmHg)	121 $\pm$ 40	138 $\pm$ 31	0.17
Diastolic blood pressure (mmHg)	72 $\pm$ 22	82 $\pm$ 16	0.14
Creatine kinase (U/L)	2605 $\pm$ 995	2194 $\pm$ 1128	0.08
Medications			
Thrombolytic	20 (57%)	9 (69%)	0.44
β Blocker	13 (37%)	4 (31%)	0.74
Digoxin	5 (14%)	1 (7%)	0.92
ACE inhibitors	21 (60%)	10 (77%)	0.33
Time from chest pain onset to thrombolysis (h)	4.3 $\pm$ 1.2	4.6 $\pm$ 1.7	0.54

ACE = Angiotensin-converting enzyme; values are mean $\pm$ standard deviation or percentages.

Table 2. Standard Echocardiographic Characteristic in Patients with and without Reciprocal ST Segment Changes

	Reciprocal Change (n = 35)	No Reciprocal Change (n = 13)	P
Ejection fraction (%)	45 ± 5	47 ± 5	0.21
Wall Motion Score Index	1.7 ± 0.25	1.6 ± 0.28	0.49
Deceleration time (ms)	159 ± 14	172 ± 28	0.18
Isovolumic relaxation time (ms)	98 ± 15	103 ± 11	0.17
Peak velocity of E wave (cm/s)	80 ± 14	71 ± 11	0.05
Peak velocity of A wave (cm/s)	68 ± 21	63 ± 24	0.49
E/A ratio	1.2 ± 0.4	1.1 ± 0.4	0.68

Values are mean ± standard deviation.

septum ischemia, which expressed E/A ratio <1, was detected in 10 (28%) and 12 (34%) patients and was absent in 25 (72%) and 23 (66%) patients, respectively.

Ten randomly selected and previously recorded studies were evaluated by a second investigator. The mean absolute difference between observations was calculated to assess interobserver variability. Interobserver mean absolute variability was 0.4 ± 0.1 cm/s for S, 0.2 ± 0.1 cm/s for E, and 0.1 ± 0.08 cm/s for A peak velocity.

DISCUSSION

The significance of reciprocal ST segment depression on the electrocardiogram during the early stages of myocardial infarction has interested many researchers and has been the subject of many debates regarding its mechanism. Opinion is divided

as to whether it is a sign of multivessel coronary disease and an adverse prognosis,⁴⁻⁹ or a benign electrical phenomenon.¹⁻³ Numerous imaging techniques have been used to investigate this issue including coronary angiography,^{2,15,16} echocardiography,⁵ gated radionuclide angiography,¹⁷ treadmill exercise testing,¹⁸ and position emission computed tomography.¹⁹ In the present study, we utilized PWTD echocardiography to detect noninvasively ischemic myocardial left ventricular segments in patients with acute inferior wall myocardial infarction. Among the 35 patients with reciprocal ST segment depression, anterior wall ischemia, which expressed E/A ratio <1 was detected in 10 patients (28%) and was absent in 25 (72%) patients. Thus, reciprocal ST segment depression during the early phases of inferior infarction may be an electrical reflection of primary ST segment elevation in the area of infarction. In our study,

Table 3. Basal and Midwall Pulsed-Wave Tissue Doppler Velocities in Patients with and without Reciprocal ST Segment Depression

	S (cm/s)	E (cm/s)	A (cm/s)	E/A Ratio	DT (ms)	RT (ms)
Basal anterior wall (1)	7.4 ± 1.1	10.5 ± 2	9.5 ± 3.2	1.1 ± 0.2	92 ± 17	82 ± 19
Basal anterior wall (2)	6.8 ± 0.9	9.4 ± 1.4	8.5 ± 2.3	1.1 ± 0.1	101 ± 16	93 ± 21
Mid-anterior wall (1)	6.5 ± 0.8	8.2 ± 1.3	7.9 ± 3.1	1.1 ± 0.3	84 ± 15	103 ± 19
Mid-anterior wall (2)	7 ± 1.3	7.6 ± 1.9	6.7 ± 1.2	1.1 ± 0.2	87 ± 11	113 ± 21
Basal anterior septum (1)	6.8 ± 1.3	9.4 ± 1.8	8.1 ± 2.1	1.2 ± 0.4	94 ± 19	97 ± 12
Basal anterior septum (2)	6.6 ± 0.3	8.2 ± 1.4	7.3 ± 1.1	1.1 ± 0.2	104 ± 15	103 ± 3
Mid-anterior septum (1)	6.1 ± 2.7	7.9 ± 1.3	6.6 ± 1.3	1.2 ± 0.3	92 ± 13	118 ± 26
Mid-anterior septum (2)	5.6 ± 0.5	6.9 ± 1.5	6.7 ± 1.9	1.1 ± 0.4	93 ± 14	116 ± 23
Basal inferior wall (1)	7.8 ± 1.3	9.9 ± 2.2*	9 ± 2.8	0.9 ± 0.3	110 ± 24*	78 ± 15
Basal inferior wall (2)	6.4 ± 0.3	7 ± 1.9	9 ± 0.8	0.8 ± 0.2	143 ± 20	82 ± 2
Mid-inferior wall (1)	5.7 ± 1.1*	6.6 ± 1.4*	7.9 ± 2.4	0.9 ± 0.3	99 ± 34	84 ± 15*
Mid-inferior wall (2)	4.4 ± 0.7	5.2 ± 1.4	6.3 ± 1	0.8 ± 0.3	112 ± 12	132 ± 31

1 = Group 1 (patients with reciprocal changes); 2 = Group 2 (patients without reciprocal changes); S = systolic velocity; E = Early diastolic velocity; A = late diastolic velocity; DT = E-wave deceleration time; RT = regional relaxation time. Values are expressed as mean ± standard deviation. *P < 0.05; 1 versus 2.

however, some patients with reciprocal ST segment depression had anterior wall ischemia detected by PWTD echocardiography. For this reason, in some cases reciprocal ST segment depression may represent distant ischemia.

PWTD Echocardiography

Ischemic heart disease involves the heart regionally. Myocardial diastolic function is impaired early in patients with ischemic heart disease, even when systolic contraction is preserved.¹¹ Although there are numerous imaging techniques that allow these functions to be evaluated, their methods are complex or require invasive interventions.^{20–21} Tissue Doppler imaging is a new echocardiographic method that assesses the velocity of myocardial structures instead of blood flow.¹⁰ PWTD echocardiography has been used in several heart diseases.^{10,22,23} In the present study, we used this echocardiographic method to assess ischemic myocardial wall segments in patients with acute inferior wall myocardial infarction.

Previous Studies

As mentioned above, some previous studies have suggested that reciprocal ST segment changes represent a benign electrical phenomenon; others have suggested that they represent ischemia in another region distant from the infarct. In contrast to our study, most of the previous investigations regarding this issue have been compromised by delayed assessment occurring days^{3,7} or months.^{15,18,24} Also, in most of these studies ischemia was not directly evaluated. A few studies directly evaluated ischemia as in our study: Billadello et al.¹⁹ used positron tomography to show that 67% of patients with reciprocal ST depression did not have anterior wall metabolic abnormalities during acute inferior wall infarction. Crawford et al.²⁵ used an animal model to demonstrate that inferior ST segment depression represents a reciprocal ECG change. The left anterior descending artery was ligated in 13 baboons, and all had inferior lead ST depression. Further evidence supporting a reciprocal phenomenon was provided by studies of controlled coronary occlusion during angioplasty, in which reciprocal change is no more common in patients with multivessel disease than in those with single vessel disease.²⁶ Previous studies reported that patients with reciprocal ST depression had higher peak

serum creatine kinase levels, lower ejection fractions, and more postinfarction complications.^{4,7,15} In the present study, patients with reciprocal depression had higher creatine kinase levels than those without reciprocal depression but this difference was not statistically significant.

Study Limitations

The first limitation is angle dependence of PWTD echocardiography, as in all Doppler-based methods. Accurate determination of myocardial velocities needs an adequate alignment between the ultrasound beam and the main vector direction of the left ventricular segmental wall motion. Second, we did not analyze PWTD in the apical segments because the apex is in the near field of the echo transducer, with consequent suboptimal image quality and it is virtually fixed with respect to longitudinal movement. Third, regional E/A velocity ratio is not a specific signal of myocardial ischemia and may be associated with other pathological conditions, such as old age, ventricular hypertrophy, intraventricular conduction disturbances, and others. However, we excluded such patients from this study. Finally, we did not perform coronary angiography. But, the correlation between the distribution of the coronary arterial anatomy and the echocardiographic myocardial wall segment location is not completely accurate and the presence of angiographic coronary arterial stenosis is not necessarily associated with ischemia.

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