Myocardial Viability in Patients with Thrombolized Myocardial Infarction: Is It Assessable by PredischARGE Exercise Electrocardiography Test?

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Summary

Background: Most studies concerning exercise electrocardiography (ECG) testing after acute myocardial infarction (AMI) were carried out in the prethrombolytic era. ST-segment elevation in the infarction area during exercise has usually been interpreted as indicating the presence of dyskinesia as a result of extensive left ventricle damage.

Hypothesis: This study was undertaken to evaluate the contributions of exercise-induced ST-segment elevation and T-wave pseudonormalization to the assessment of myocardial viability in patients with thrombolized myocardial infarction (MI), compared with low-dose dobutamine echocardiography.

Methods: The study comprised 52 consecutive patients with AMI treated with thrombolysis. All patients underwent low-dose dobutamine echocardiography and symptom-limited exercise testing before discharge.

Results: Nineteen patients showed ST-segment elevation (Group 1), 9 showed isolated T-wave pseudonormalization (Group 2), and 24 patients did not exhibit either of these ST-T segment changes (Group 3). Low-dose dobutamine echocardiography revealed evidence of viability in 16 patients (84%) in Group 1 ($p = 0.01$), 5 (56%) in Group 2 ($p = \text{NS}$), and 11 patients (46%) in Group 3 ($p = \text{NS}$).

Conclusion: Exercise-induced ST-segment elevation may contribute to the evaluation of myocardial viability in patients with AMI treated with thrombolysis. However, in the absence

of exercise-induced ST-segment elevation, further noninvasive studies might be indicated to assess myocardial viability.

Key words: acute myocardial infarction, dobutamine stress echocardiography, exercise electrocardiogram, myocardial viability

Introduction

Most studies concerning exercise electrocardiography (ECG) testing after acute myocardial infarction (AMI) were carried out in the prethrombolytic era. ST-segment elevation in the infarction area during exercise has usually been interpreted as indicating the presence of dyskinesia as a result of extensive left ventricle damage.^{1–4} However, the significance of exercise-induced ST-segment elevation and/or T-wave pseudonormalization in the infarction area in patients with AMI treated with thrombolysis remains unclear. Recently, Touboul *et al.*⁵ studied the risk stratification in the era of thrombolysis and found that it remains roughly unchanged; however, the roles of ST-segment elevation and T-wave pseudonormalization during exercise were not examined in their study. Some investigations of transient ST-segment elevation^{6,7} and pseudonormalization of the T wave⁸ during exercise after AMI have shown a relationship between the presence of viable myocardium and these ECG changes. We analyzed these exercise-induced ECG changes in patients with a recent thrombolitically treated myocardial infarction and compared them with echocardiographic signs of viability during low-dose dobutamine echocardiography (LDE).

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Methods

Subjects and Study Design

The patients in the study were prospectively recruited from the coronary care unit at Söder Hospital between November

1994 and November 1996, and between August and November 1998.

The inclusion criteria were (1) AMI treated with thrombolysis: a typical history of chest pain, ST elevation on the ECG, and a typical pattern of enzyme leakage supporting the diagnosis of AMI; (2) age >45 and <76 years; (3) for logistic reasons, only patients admitted to the coronary care unit on Sunday to Tuesday; (4) verbal informed consent.

The exclusion criteria were: (1) previous AMI treated with thrombolysis within the last 3 months; (2) indication for acute coronary angiography/intervention; (3) second- or third-degree atrioventricular block; (4) clinical signs of severe heart failure (Killip 3–4); (5) or other illness with a severe prognosis.

The study was approved by the local ethics committee.

Exercise Test

All patients performed a symptom-limited bicycle exercise test on Days 5–8 after admission. A 12-lead ECG was recorded and monitored before exercise, continuously during exercise, and for up to 10 min after completion of the exercise test. The initial workload was 30 W, with successive 10-W increments every min. The patients graded their level of exhaustion on the 0–20 Borg scale, and chest pain was graded on the 0–10 Borg scale. Endpoints for exercise were: exhaustion grade 16–17 out of 20 on the Borg Scale, moderate chest pain grade 4–5 on the Borg Scale, severe arrhythmia, > 10 mmHg drop in blood pressure, or ≥ 3 mm ST depression.

ST depression was defined as a ≥ 1 mm horizontal or downsloping ST segment (measured 60 ms after the J point) in at least two leads. Exercise-induced ST elevation was defined as ≥ 1.5 mm elevation in infarct-related leads, above the resting baseline level of the J point in the precordial leads, or > 1 mm in the limb leads. Pseudonormalization of the T wave was defined as a negative resting T wave becoming upright or isoelectric during exercise. The ECGs were interpreted off-line by two readers blinded to the echocardiographic data.

Echocardiographic Study

Two-dimensional echocardiography and LDE were performed 4 ± 2 days after admission in all patients. Scans were videotaped for off-line analysis. An intravenous infusion of dobutamine at a dosage of 5 µg · kg⁻¹ · min⁻¹ was started and continued for 5 min, and then the dosage was increased to 10 µg · kg⁻¹ · min⁻¹ for another 5 min. The left ventricle was divided into 16 segments as proposed by the American Society of Echocardiography.⁹ Wall motion was assessed visually regarding both endocardial motion and wall thickening. The following scoring system was used: 1 = normal: normal wall motion and thickening; 2 = hypokinesia: marked reduction in endocardial motion and systolic thickening; 3 = akinesia or dyskinesia: absence of inward motion and systolic thickening or paradoxical wall motion away from the center of the left ventricle in systole.¹⁰ The dysfunctional myocardium was considered to be viable when there was an enhancement of at

least one grade or more in at least two contiguous infarct zone segments at LDE in comparison with baseline. Dobutamine echocardiograms were interpreted off-line by two experienced readers blinded to the exercise test data. Discrepancies were resolved by consensus.

Statistical Analysis

Continuous variables and results are expressed as means ± standard deviation. The Student's two-tailed, unpaired *t*-test or the chi-square test was used. Probability levels of ≤ 0.05 were considered significant.

Results

Of the 52 subjects included in the study, only 1 patient had a previous AMI.

Electrocardiograms at Rest

Sixteen patients (31%) developed Q-wave anterior and 26 (50%) Q-wave inferior AMI. The remaining 10 patients (19%) had non-Q-wave infarction.

Reasons for Terminating the Exercise Test

Thirty-seven patients terminated the exercise test because of physical exhaustion, 7 because of chest pain, 2 because of hypotension, and 6 because of ST depression.

The patients were divided into three groups based on the exercise-induced ECG findings. The clinical characteristics of the three groups are presented in Table I.

Group 1

Exercise-induced ST-segment elevation in two or more infarct-related leads occurred in 19 patients (37%), 6 with and 13

TABLE I Clinical and laboratory characteristics of patients with exercise-induced ST-segment elevation (Group 1), isolated T-wave pseudonormalization (Group 2), and neither of these two ECG changes (Group 3)

	Group 1 n = 19	Group 2 n = 9	Group 3 n = 24
Age (years)	60 ± 8	67 ± 9	62 ± 10
Male (%)	16 (84)	3 (33)	21 (88)
Previous AMI (%)	1 (5)	0	0
Anterior Q-wave AMI (%)	13 (68)	0	3 (13)
Inferior Q-wave AMI (%)	6 (32)	6 (67)	14 (58)
Non-Q-wave infarction (%)	0	3 (33)	7 (29)
Ejection fraction (%)	45 ± 7	51 ± 8	47 ± 8
Troponin-T (µg/l)	12 ± 4	9 ± 4	8 ± 5

Abbreviation: AMI = acute myocardial infarction.

without T-wave pseudonormalization. Thirteen patients (68%) had an anterior and 6 (32%) an inferior Q-wave infarction.

Group 2

Isolated T-wave pseudonormalization occurred in nine patients (17%). Six patients had had an inferior Q-wave AMI, and three a non-Q-wave AMI.

Group 3

Twenty-four patients (46%) showed neither ST elevation nor T-wave pseudonormalization. Three patients had had an anterior Q-wave AMI, 14 patients an inferior Q-wave and 7 patients a non-Q-wave infarction.

The exercise testing data are presented in Table II.

Echocardiographic Results

Low-dose dobutamine echocardiography was performed in all patients according to the protocol. In the 52 patients, 774 segments of the total of 832 (93%) were successfully analyzed. Under resting conditions, 302 segments (39%) were hypokinetic or akinetic. During dobutamine stimulation, 139 dysfunctional segments (46%) showed improvement by at least one grade as defined above. Myocardial viability was found in 32 of the 52 patients. Table III shows the echocardiographic wall motion score index in the three groups at baseline and during LDE.

In Group 1, LDE showed signs of viability in 16 patients (84%) ($p = 0.01$), and all 7 patients with both ST-segment elevation and T-wave pseudonormalization displayed signs of viability at LDE. In Groups 2 and 3, LDE showed signs of viability in 5 of 9 (56%), and 11 of 24 patients (46%), respectively ($p = \text{NS}$) (Table IV).

Safety of the Tests

No major complications occurred during the exercise tests or LDE.

Discussion

The significance of ST-segment elevation during an exercise test following AMI has been evaluated and debated since the 1970s. In the prethrombolytic era, transient ST-segment elevation in the infarct zone during exercise testing was usually interpreted as abnormal left ventricular wall motion in the damaged myocardium,⁶ as a sign of a left ventricular aneurysm,^{1, 11, 12} or as a result of peri-infarction ischemia.⁷ These discrepancies still persist in the thrombolytic era.

Recent studies focusing on the significance of ST-segment elevation induced by dobutamine have yielded variable results. In several studies no correlation was found between dobutamine-induced ST-segment elevation and myocardial ischemia or myocardial viability,^{13, 14} while a few other studies

TABLE II Exercise test characteristics in patients with ST-segment elevation (Group 1), isolated T-wave pseudonormalization (Group 2), and neither of these two ECG changes (Group 3)

	Group 1 n = 19	Group 2 n = 9	Group 3 n = 24
Max. workload (W)	95 ± 23	80 ± 16	98 ± 27
Resting heart rate (min ⁻¹)	73 ± 9	73 ± 16	69 ± 15
Max. heart rate (min ⁻¹)	116 ± 12	113 ± 10	112 ± 12
ST-segment elevation	19	0	0
T-wave pseudonormalization	6	9	0
ST depression	4	2	8
Chest pain	2	1	4

No significant changes were found regarding workload, resting heart rate, and maximum heart rate among the three groups.

TABLE III Wall motion score index (WMSI) at rest and during low-dose dobutamine echocardiography (LDE). Patients with exercise-induced ST-segment elevation (Group 1), patients with isolated T-wave pseudonormalization (Group 2), and patients without these ECG changes (Group 3)

	Group 1	Group 2	Group 3
WMSI at rest	1.69 ± 0.29	1.45 ± 0.23	1.57 ± 0.33
WMSI during LDE	1.45 ± 0.26	1.28 ± 0.19	1.44 ± 0.25
Difference between WMSI at rest and during LDE	0.24	0.17	0.13

TABLE IV Concordance between evidence of viability at low-dose dobutamine echocardiography (LDE) and ST-T changes at predischarge exercise test

	Viability	
	+	-
Group 1 (n = 19) (%)	16 (84)	3
ST-segment elevation		
Group 2 (n = 9) (%)	5 (56)	4
T-wave pseudonormalization		
Group 3 (n = 24) (%)	11 (46)	13
No ST-T changes		

have shown that transient ST-segment elevation or T-wave pseudonormalization during dobutamine stress might be indicative of viability in the infarct-related area.^{15, 16} The results of these studies may not be applicable to exercise-induced ST-segment elevation. Dobutamine stress may induce less wall motion abnormalities than exercise, which may affect the ECG changes.^{17, 18}

Conflicting results have also been obtained regarding the importance of exercise-induced T-wave pseudonormalization, which has been associated with both ischemic¹⁹ and nonischemic mechanisms.²⁰

Few studies have focused on the relationship between exercise-induced ECG changes and myocardial viability in patients with AMI.

Margonato *et al.*⁸ found a reversible thallium perfusion defect at the infarction site in patients with exercise-induced ST-segment elevation. This observation occurred in 50% of the patients with pseudonormalization of the T wave. In another study by Margonato *et al.*,²¹ there was good correlation between exercise-induced ST-segment elevation and the presence of viability as evaluated by fluorodeoxy-glucose and positron emission tomography (PET). In these two studies, only 28 and 42% of the patients, respectively, were treated with thrombolysis. Thus, the results may not be applicable to patients post thrombolysis. Furthermore, in these studies the patients were enrolled 15–400 days after AMI.

Recently, Schneider *et al.* reported that exercise-induced ST-segment elevation and negative T-wave pseudonormalization predict improvement of left ventricular function after revascularization.²²

The present prospective study included patients post AMI treated with thrombolytic agents, and all investigations were performed before discharge. Low-dose dobutamine echocardiography was used to detect myocardial viability. In the literature, PET has been considered as the standard of reference for assessment of myocardial viability. However, the clinical application of PET has been restricted by its lack of general availability and its high cost. Stress echocardiography has been demonstrated as an available and accurate alternative to PET in detecting viability early after AMI treated with thrombolysis.^{23–26} Adding peak dose dobutamine to LDE probably would have given more information both about myocardial viability and residual myocardial ischemia in the present study. However, these studies were made 2–6 days after the infarction and we did not consider it safe to perform a high-dose dobutamine stress test that early.

Low-dose dobutamine echocardiography showed a higher proportion of viability in patients with Q-wave infarction, which may be related to the larger dyskinetic/akinetic areas in these patients. This finding has to be regarded with caution because of the limited number of patients in the present study. To our knowledge, the true frequency of viability in patients with non-Q-wave versus Q-wave infarction is not settled enough in the literature, and this issue needs to be investigated further in future studies.

ST-segment elevation or isolated T-wave pseudonormalization during a predischARGE exercise test in the present study was frequent, with a prevalence of 37 and 17%, respectively. ST-segment elevation was observed only in patients with Q-wave infarction, predominantly with an anterior location. The finding of transient exercise-induced ST-segment elevation in infarct-related ECG leads was associated with the presence of LDE signs of myocardial viability in 84% of the cases ($p = 0.01$). In addition, the coexistence of both ST-segment elevation and T-wave pseudonormalization indicated myocardial viability in all cases. However, myocardial viability was noted in about half of the patients without ST-segment elevation and in half of those with isolated pseudonormalization of the T

wave in infarct-related ECG leads. The specificity of exercise-induced ST-segment elevation in assessing myocardial viability was 85%; however, the sensitivity was low, 50%. Despite the low sensitivity, our results suggests that exercise-induced ST-segment elevation can be a marker of myocardial viability, although larger studies are needed to clarify the issue fully.

Conclusion

In patients with acute myocardial infarction treated with thrombolysis, exercise-induced ST-segment elevation in the infarct area seems to be associated with myocardial viability. Absence of ST elevation does not, however, exclude viability. To assess the myocardial viability in patients without exercise-induced ST-segment elevation, further noninvasive studies might be indicated.

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