Time-domain analysis of exercise-induced ST-segment elevation in Q-wave myocardial infarction: a useful tool for the screening of myocardial viability

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Key words:
**Exercise test;
Myocardial infarction;
Myocardial ischemia;
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Viable myocardium.**

Background. **Exercise-induced ST-segment elevation in Q-wave leads has been traditionally associated with passive stretching of the infarct wall, perinecrotic ischemia and, according to recent scintigraphic studies, with myocardial viability. At present, however, no definitive conclusions are available. We evaluated the potential role of a time-domain analysis of exercise-induced ST-segment elevation for the identification of viable myocardium and residual ischemia in patients with previous Q-wave myocardial infarction.**

Methods. **Sixty patients with a previous Q-wave myocardial infarction underwent a bicycle exercise stress test, dobutamine stress echocardiography, coronary arteriography and left ventriculography.**

Results. **Patients with exercise-induced ST-segment elevation in Q-wave leads (n = 36) showed more severe impairment of resting left ventricular function, when evaluated in terms of wall motion score index at echocardiography (1.62 ± 0.33 vs 1.41 ± 0.22, p < 0.01) and in terms of wall motion score at ventriculography (5.9 ± 1.6 vs 4.1 ± 1.5, p < 0.03), compared to patients without ST-segment shift (n = 24). No differences between the two groups were seen in the severity and extension of coronary artery disease. The two groups of patients did not differ in the overall incidence of viability (50% in patients with vs 62% in those without ST-segment elevation, p = NS) and homozonal ischemia (39 vs 26%, p = NS), when evaluated with dobutamine echocardiography. However, a time-domain analysis of the ST-segment changes during exercise showed that the duration of exercise up to 0.1 mV ST-segment elevation was significantly lower in patients with viability (6.2 ± 3.3 min) than in those without (10.2 ± 2.2 min) (p < 0.001). Accordingly, ST-segment elevation occurred within 3 and 6 min of exercise in 7/18 and in 12/18 patients with viability respectively, but in only 0/18 (p < 0.01) and in 1/18 (p < 0.01) patients without viability. Thus, ST-segment elevation occurring within the first two stages of the exercise test was, respectively, 39 and 67% sensitive and 100 and 94% specific for viability. Early onset ST-segment elevation (within 3 and 6 min) was also more frequent in patients with high-dose dobutamine-induced homozonal ischemia than in those without (sensitivity for ischemia 50 and 67%; specificity 95 and 74%, respectively).**

Conclusions. **After myocardial infarction, ST-segment elevation in Q-wave leads at the peak of exercise is associated with severe resting left ventricular dysfunction but fails to identify patients with a viable myocardium or residual ischemia. Instead, ST-segment elevation occurring in the early phases of exercise is a highly specific, although not very sensitive marker of dobutamine-assessed viability in the infarct area and may be indicative of residual ischemia.**

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Introduction

In patients with a previous myocardial infarction, transient ST-segment depression during exercise is considered to be a reliable marker of residual ischemia[1]. Instead, exercise-induced ST-segment elevation in leads with pathologic Q waves represents a less specific and often disregarded finding, the pathogenesis of which is still controversial. This electrocardiographic finding has been traditionally attributed to passive stretching of the infarct wall during exercise[2-5], severe ischemia arising from the perinecrotic myocardium[6,7] or both[8]. More recently, effort-induced ST-segment elevation in Q-wave leads has also been associated with reversible defects at thallium-201 myocardial perfusion scintigraphy[9] and with persisting metabolic activity in the infarct area at fluorodeoxyglu-

cose positron emission tomography[10], consistent with the presence of a viable myocardium. In all previous studies ST-segment elevation has been evaluated at the peak of exercise. Thus, it was not possible to obtain the additional information which may be derived from continuous analysis of ST-segment shift throughout the exercise. Actually, ST-segment elevation may occur at different intensities of cardiac work (thus at different stages of exercise), probably depending on the passive stretching of the infarct wall, perinecrotic ischemia or the viability in the infarct area.

Dobutamine stress echocardiography is an accurate and cost-effective technique for the detection of both myocardial ischemia and viability in patients with previous infarction[11-14].

The aim of this study was to obtain further information about the significance of exercise-induced ST-segment elevation after myocardial infarction. In particular, our aim was to assess the hypothesis that ST-segment elevation occurring in Q-wave leads during different phases of exercise could have a different pathophysiological significance. For this purpose, we performed a time-domain analysis of the ST-segment shift during exercise in order to precisely identify the onset of ST elevation and we correlated electrocardiographic findings with wall motion changes during dobutamine echocardiography.

Methods

Study patients. Sixty consecutive patients (55 males, 5 females; mean age 59 ± 10 years) with a previous Q-wave myocardial infarction and echocardiographic dyssynergy in the region corresponding to the abnormal Q-waves were enrolled in the study. All patients underwent a bicycle exercise stress test, dobutamine stress echocardiography and angiographic examination (coronary arteriography and left ventriculography).

The diagnosis of a Q-wave infarction was made when the following three criteria were fulfilled: a) chest pain lasting > 30 min; b) an increase in serum enzymes ≥ 2 times the normal values; c) the development of new Q-waves > 0.04 s in duration and with an amplitude > 25% of the subsequent R-wave in at least two contiguous electrocardiographic leads.

Patients were excluded from the study if they had: a recent myocardial infarction (within 1 month); infarction in multiple sites; unstable angina; overt heart failure; previous revascularization procedures (coronary angioplasty and/or coronary artery bypass graft); left ventricular hypertrophy, significant valvular heart disease, left and right bundle branch block and other conditions known to affect the interpretation of ST-segment changes; a true left ventricular aneurysm (diastolic distortion of the left ventricular shape, thinning of the wall, regional systolic expansion)[15]; ST-segment elevation in Q-wave leads at rest > 0.2 mV; exercise-induced ST-segment depression of 0.1 mV. All patients gave their informed consent before entering the study.

Exercise stress test. All patients were submitted to a symptom-limited, multistage bicycle exercise test performed using a computer-assisted exercise system (X Scribe, Mortara Rangoni, Bologna, Italy). The exercise tests were performed in the morning, after an appropriate therapeutic wash-out. To this end, digitalis compounds were withdrawn at least 1 week before the test and beta-blockers, calcium antagonists and long-acting nitrates were withdrawn at least 3 days previously. Only short-acting nitrates were allowed to control symptoms, when needed. In this case, the tests were always performed at least 4 hours after drug administration.

Starting from 25 W, the workload was increased by 25 W every 3 min. Three on-line electrocardiographic leads (II, V_1, V_5) were continuously monitored during the test. Moreover, 12 computer-averaged leads were shown and the level of ST-segment in each one was calculated throughout the test by the system. A 12-lead electrocardiogram and cuff-sphygmomanometer blood pressure were recorded at rest, at 0.1 mV ST-segment shift, at peak exercise and every minute during exercise and recovery. Exercise was stopped when any of the following events occurred: severe angina and/or dyspnea, a drop in systolic blood pressure (SBP) > 20 mmHg, life-threatening arrhythmias, an ST-segment shift > 0.2 mV, achievement of the maximal age-related heart rate (HR), muscular exhaustion.

Exercise-induced ST-segment elevation was considered to be significant in case of an upper shift of 0.1 mV (when compared with the resting electrocardiogram) at the J point and lasting 0.08 s thereafter, in at least two contiguous Q-wave leads.

Two experienced cardiologists, unaware of the echocardiographic and angiographic results, reviewed the exercise test tracings in order to identify the patients presenting with significant ST-segment elevation at the end of exercise. In these patients the duration of exercise (min) at the onset of the 0.1 mV ST-segment elevation and the corresponding values of HR, SBP and rate-pressure product (RPP) were also noted. The increments in HR, SBP and RPP at 0.1 mV ST-segment elevation, with respect to resting values, and the achieved percentage of the maximal age-related HR were then calculated.

Dobutamine stress echocardiography. Patients underwent dobutamine stress echocardiography in the morning after an over night fasting state and in pharmacological wash-out. The dobutamine test was always performed within 1 week of the exercise test. Dobutamine was infused intravenously in graded, increasing doses. Starting from 5 μg/kg body weight per minute for 5 min, the infusion rate was initially increased to 10 μg/kg/min for 3 min and then was increased by 10 μg/kg/min every 3 min up to a maximal dose of 40

μg/kg/min. In the analysis of results, the first two doses (5 and 10 μg/kg/min) were defined as "low dobutamine dose".

Patients underwent two-dimensional echocardiography in left lateral decubitus. Commercially available equipment (Toshiba Sonolayer SSH-160A, Japan; 2.5-MHz transducer) was used. The parasternal long- and short-axis and the apical 4- and 2-chamber images were continuously monitored throughout the test and intermittently recorded on a VHS videotape. Continuous electrocardiographic monitoring (II, V_4, V_5, V_6) was performed during the infusion and recovery periods. A 12-lead electrocardiogram and cuff-sphygmomanometer blood pressure were recorded at baseline, at the end of each stage and every 3 min during the recovery period.

Dobutamine infusion was interrupted if any of the following events occurred: severe hypertension (blood pressure > 220/130 mmHg) or hypotension (a fall in SBP > 20 mmHg); achievement of the maximal age-related HR; life-threatening arrhythmias; severe angina and/or dyspnea; unbearable side effects; ST-segment depression of 0.2 mV; new-onset or worsening of resting wall motion abnormalities. To reverse the clinical, electrocardiographic or echocardiographic signs of ischemia, patients received intravenous propranolol and/or sublingual nitrates.

Analysis of dobutamine data. Videotape recordings of dobutamine tests were independently reviewed by two experienced echocardiographers, blinded to the clinical, angiographic and exercise test results. Disagreements were settled by a third senior investigator who evaluated the videotape recordings. The left ventricular wall motion was qualitatively analyzed in resting conditions, during dobutamine infusion and during the recovery period. To assess wall motion, both systolic thickening and inward motion were considered. In accordance with the American Society of Echocardiography guidelines[16], the left ventricle was divided into 16 segments. In each segment the wall motion was quantitatively scored as follows: 1 = normal or hyperkinetic; 2 = hypokinetic; 3 = akinetic; 4 = dyskinetic. A semiquantitative scoring index was used to evaluate the severity and extension of left ventricular dyssynergies. The wall motion score index was derived by dividing the sum of each segment score by the number of the segments scored[16]. Improvement (i.e., a dyskinetic or akinetic segment becoming hypokinetic) or normalization of the wall motion in at least two dyssynergic segments was considered to be evidence of a viable myocardium. Dobutamine-induced ischemia was defined as the development of a new dyssynergy in a segment with normal function at rest or worsening of the wall motion in a dyssynergic segment (i.e., a hypokinetic segment becoming akinetic or dyskinetic). Homozonal ischemia was considered as worsening or extension of the resting infarct-related dyssynergy. Remote ischemia was considered as the onset of a new dyssynergy in myocardial segments not supplied by the infarct-related vessel.

Coronary arteriography and left ventriculography. Left and right selective coronary arteriography was performed according to the Judkins technique and filmed in multiple views. A narrowing 50% of the internal luminal diameter was judged to be hemodynamically significant. Left ventriculography was performed in the 30° right and 45° left anterior oblique projections. For the evaluation of regional wall motion abnormalities, the left ventricular silhouette was divided into 7 segments[17]. In each segment the contractility was judged as normal, hypokinetic, akinetic or dyskinetic and scored as 0, 1, 2 and 3 respectively. A semiquantitative index of global left ventricular dysfunction was then calculated in terms of wall motion score by summing the scores of each segment.

Statistical analysis. Data are presented as mean values ± SD. Discrete variables were compared using the χ^2 test and Fisher's exact test, when appropriate. Differences between continuous variables were assessed using the two-tailed Student's t-test. A p value < 0.05 was considered statistically significant.

Results

Clinical and exercise findings. Of 60 patients included in the study, 47 had had an anterior and 13 an inferior infarction. Twenty-six patients (43%) underwent intravenous thrombolysis within 6 hours of the onset of symptoms. The interval between infarction and enrollment in the study was 95 ± 131 days (range 30-500 days).

On the basis of ST-segment changes during exercise, patients were divided into two groups as follows. Group A comprised 36 patients with exercise-induced ST-segment elevation in Q-wave leads; group B comprised 24 patients without significant changes in the ST-segment during effort.

Eight patients (13%) experienced postinfarction angina. In accordance with the exclusion criteria, no patient showed ST-segment depression during effort. Only 6 patients (10%) experienced exercise-induced angina. No patient had an abnormal blood pressure response (no increase or a decrease in SBP) during exercise.

No differences were seen between groups A and B and between patients with/without viability and dobutamine-induced ischemia regarding gender, mean age, site of infarction, number of patients treated with thrombolysis, time interval between infarction and enrollment, postinfarction and exercise-induced angina, exercise test duration and maximal RPP (Table I).

Dobutamine stress echocardiography and comparison with exercise test findings. Of the 60 study patients, 54 underwent a maximal dobutamine echocardiography test. Three patients with a severely impaired left ven-

Table I. Clinical and exercise data of patients with and without exercise-induced ST-segment elevation in Q-wave leads.

	ST elevation (n=36)	No ST elevation (n=24)	p
Male sex	33 (92)	22 (92)	NS
Age (years)	59 ± 10	58 ± 9	NS
Site of infarction			
Anterior	30 (83)	17 (71)	NS
Inferior	6 (17)	7 (29)	NS
Thrombolysis	16 (44)	10 (42)	NS
Time AMI enrollment (days)	91 ± 126	102 ± 145	NS
Postinfarction angina	5 (14)	3 (13)	NS
Exercise-induced angina	4 (11)	2 (8)	NS
Exercise duration (min)	11.1 ± 3.1	11.8 ± 4.6	NS
Peak RPP (b/min*mmHg)	22 568 ± 4701	21 709 ± 5591	NS

Data are expressed as mean ± SD or number (%) of patients. AMI = acute myocardial infarction; RPP = rate-pressure product.

tricular function (ejection fraction < 30%) received only a low dose of dobutamine for myocardial viability evaluation; in another 3 patients, dobutamine infusion was interrupted at 10 μg/kg/min (1 patient) and 20 μg/kg/min (2 patients) due to the occurrence of complex ventricular arrhythmias. Nine patients experienced angina during dobutamine echocardiography, without significant differences between groups A and B and between patients with/without viability and dobutamine-induced ischemia. The results of dobutamine stress echocardiography in groups A and B are reported in table II.

Baseline. Left ventricular function at rest, estimated as the wall motion score index, showed significantly greater impairment in patients with exercise-induced ST-segment elevation than in those without (1.62 ± 0.33 vs 1.41 ± 0.22, p = 0.008).

Low dobutamine dose. An improvement or a normalization of the wall motion in the infarct area, consistent with the presence of viable myocardium, was detected in 33/60 patients (55%) at a mean dobutamine dose of 9.1 ± 1.3 μg/kg/min. No significant difference in this finding was found between the two groups [18 patients (50%) in group A and 15 patients (62%) in group B, p = NS]. Moreover, no significant difference between groups A and B was found in the mean dose of dobutamine at which wall motion changes were documented nor in the change of the wall motion score index from baseline (Table II). No patient developed ischemic changes at low doses of dobutamine.

High dobutamine dose. Of 54 patients who underwent both low and high-dose dobutamine echocardiography, 24 (44%) showed a worsening in the regional contractile performance at high dose, consistent with a dobutamine-induced ischemia (homozonal in 18 patients, remote in 6 patients). Homozonal ischemia was observed in 15 (48%) of 31 patients with and in 3 (13%) of 23 patients without evidence of viability (p = 0.006). No differences in the incidence of ischemia were seen between patients with and without exercise-induced ST-segment elevation [15/31 patients (48%) vs 9/23 patients (39%), respectively, p = NS], as well as in the mean dose of dobutamine at ischemia and in wall motion score index variations from baseline. Similar results were obtained when only homozonal ischemia was considered (39 vs 26%, p = NS, Table II).

Table II. Dobutamine stress echocardiography in patients with and without exercise-induced ST-segment elevation in Q-wave leads.

	ST elevation (n=36)	No ST elevation (n=24)	p
Baseline WMSI	1.62 ± 0.33	1.41 ± 0.22	0.008
Viability	18 (50)	15 (62)	NS
Homozonal ischemia	12/31 (39)	6/23 (26)	NS
Viability and/or homozonal ischemia	21 (58)	16 (67)	NS
Viability dose (μg/kg/min)	8.6 ± 2.6	9.3 ± 1.3	NS
Ischemia dose (μg/kg/min)	23.5 ± 4.3	26.3 ± 3.6	NS
Changes of WMSI			
At viability	-0.16 ± 0.09	-0.15 ± 0.11	NS
At ischemia	0.14 ± 0.09	0.12 ± 0.06	NS
Chest pain during the test	6 (17)	3 (13)	NS

Data are expressed as mean ± SD or number (%) of patients. WMSI = wall motion score index.

When only anterior infarctions (n = 47) were analyzed in the two groups, again no differences were found in the incidence of viability (group A: 15/30 patients; group B: 11/17 patients; p = NS) and of ischemia (group A: 13/26 patients; group B: 8/17 patients; p = NS).

Time-domain analysis of exercise-induced ST-segment elevation. To assess whether an early occurrence of ST-segment elevation during exercise could be predictive of myocardial viability and ischemia, we separately analyzed the exercise data of group A patients with or without viability/ischemia at dobutamine echocardiography.

Myocardial viability. There were 18 patients with and 18 patients without myocardial viability at dobutamine echocardiography among group A patients. There were no differences between these two subgroups in HR, SBP and RPP both at rest and at peak exercise (Table III). The duration of exercise was also similar in the two subgroups. However, the duration of exercise at 0.1 mV ST-segment elevation was significantly lower in group A patients with viability, compared to those without viability (6.2 ± 3.3 vs 10.2 ± 2.2 min, p = 0.0009). Similarly, HR, SBP and RPP at 0.1 mV ST-segment elevation were significantly lower in patients with evidence of a viable myocardium than in those without.

The sensitivity and specificity for myocardial viability of ST-segment elevation occurring at different exercise stages and at different values of HR, SBP and RPP are reported in table IV. A very early-onset ST-segment elevation (within 3 min of the beginning of exercise, i.e., 25 W) was observed in 7/18 patients with, but in 0/18 without viability (p = 0.003). Thus, the sensitivity for myocardial viability was low (39%) but the specificity was 100%. When considering the occurrence of ST-segment elevation within 6 min of exercise (i.e., within 50 W), the sensitivity and specificity for viability were 67 and 94%, respectively. On the contrary, ST-segment elevation occurring after 6 min of exercise was more frequent in patients without (17/18 patients, 94%), than in those with viability (6/18 patients, 33%, p = 0.0001). According to these results, patients with early ST-segment elevation had a significantly higher prevalence of myocardial viability, when compared to those with late ST-segment elevation, as well as to patients with no ST-segment shift during exercise (Fig. 1).

Since, by definition, ischemic myocardium is viable, although potentially insensitive to low dose dobutamine, the analysis has been extended to viable and/or ischemic segments considered as a whole and included 3 patients with homozonal ischemia, but without evidence of viability (Table V). Actually, these patients had ST-segment elevation within 6 min of exercise, thus slightly increasing the sensitivity of an early-onset ST-segment elevation for viability, without significantly altering the specificity.

Myocardial ischemia. There were 12 patients with and 19 patients without dobutamine-induced ischemia among group A patients (Table VI). The exercise duration at the onset of 0.1 mV ST-segment elevation was significantly lower in patients with, than in those without ischemia (6.6 ± 3.3 vs 10.1 ± 2.6, p = 0.015). No significant differences in the other exercise findings were observed between the two groups, although there was a trend towards an earlier occurrence of ST-segment elevation during exercise in patients with ischemia.

A very early-onset ST-segment elevation (within 3 min of the beginning of exercise) was observed in 6/12

Table III. Exercise test results and myocardial viability in patients with exercise-induced ST-segment elevation.

	Viability (n=18)	No viability (n=18)	p
Resting HR	72 ± 13	73 ± 18	NS
Resting SBP	125 ± 16	129 ± 20	NS
Resting RPP	9025 ± 2201	9450 ± 2421	NS
Maximal HR	127 ± 20	128 ± 19	NS
Maximal SBP	174 ± 22	178 ± 20	NS
Maximal RPP	22 501 ± 4881	22 690 ± 4801	NS
Exercise duration (min)	11.4 ± 4.1	11.2 ± 3.0	NS
Exercise time at 0.1 mV ST elevation (min)	6.2 ± 3.3	10.2 ± 2.2	0.0009
HR at 0.1 mV ST elevation	101 ± 18	124 ± 17	0.002
SBP at 0.1 mV ST elevation	154 ± 17	177 ± 24	0.010
RPP at 0.1 mV ST elevation	15 714 ± 3600	21 983 ± 4344	0.0005
Percent of maximal age-related HR at 0.1 mV ST elevation	62 ± 9	78 ± 10	0.0001
Increment of HR at 0.1 mV ST elevation	27 ± 13	48 ± 12	0.0001
Increment of SBP at 0.1 mV ST elevation	27 ± 13	46 ± 21	0.008
Increment of RPP at 0.1 mV ST elevation	6450 ± 2761	12 296 ± 3583	0.0001

Data are expressed as mean ± SD. HR = heart rate (b/min); RPP = rate-pressure product (b/min*mmHg); SBP = systolic blood pressure (mmHg).

Table IV. Sensitivity and specificity of early-onset ST-segment elevation for myocardial viability assessed by dobutamine echocardiography.

ST elevation occurring:	Patients with ST elevation		p	Sensitivity (%)	Specificity (%)
	Viability (n=18)	No viability (n=18)			
Within 3 min exercise (25 W)	7	0	0.003	39	100
Within 6 min exercise (50 W)	12	1	0.0001	67	94
≤ 100 HR	10	1	0.0011	56	97
≤ 120 HR	15	6	0.002	83	67
≤ 160 SBP	12	5	0.019	67	72
≤ 18 000 RPP	12	3	0.0023	67	83
≤ 20 000 RPP	15	6	0.0023	83	67
≤ 70% of maximal age-related HR	15	4	0.0002	83	78
≤ 30 increment HR from resting values	14	1	0.001	78	94
≤ 30 increment SBP from resting values	14	5	0.0027	78	72
≤ 8000 increment RPP from resting values	14	2	0.0001	78	89

Abbreviations as in table III.

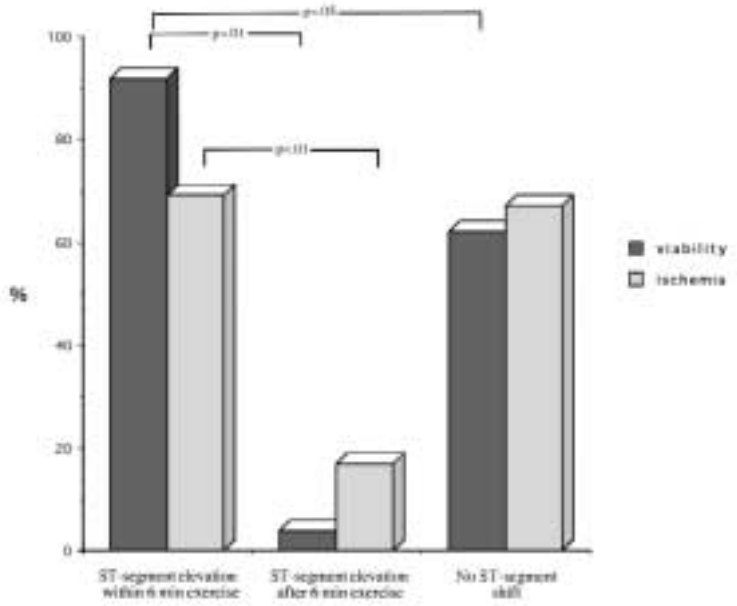

Figure 1. *Viability* (dark columns) *and ischemia* (light columns) *assessed using dobutamine echocardiography, in patients with early (within 6 min of exercise, i.e., 50 W), late (after 6 min of exercise) and no exercise-induced ST-segment elevation.*

Table V. Early-onset ST-segment elevation: sensitivity and specificity for myocardial viability and/or homozonal ischemia.

ST elevation occurring:	Patients with ST elevation		Sensitivity (%)	Specificity (%)
	Viability/ischemia (n=21)	No viability/ischemia (n=15)		
Within 3 min exercise	8	0	38	100
Within 6 min exercise	15	1	71	93
≤ 120 HR	18	6	86	60
≤ 20 000 RPP	18	6	86	60
≤ 30 increment HR from resting values	17	1	81	93

Abbreviations as in table III.

Table VI. Exercise test results and dobutamine-induced ischemia in patients with exercise-induced ST-segment elevation.

	Homozonal ischemia (n=12)	No ischemia (n=19)	p
Resting HR	78 ± 21	74 ± 16	NS
Resting SBP	123 ± 15	132 ± 20	NS
Resting RPP	9521 ± 2502	9467 ± 2320	NS
Maximal HR	124 ± 21	123 ± 20	NS
Maximal SBP	170 ± 20	175 ± 21	NS
Maximal RPP	21 180 ± 5003	21 702 ± 5050	NS
Exercise duration (min)	10.8 ± 3.5	12.1 ± 3.2	NS
Exercise time at 0.1 mV ST elevation (min)	6.6 ± 3.3	10.1 ± 2.6	0.015
HR at 0.1 mV ST elevation	108 ± 30	117 ± 13	NS
SBP at 0.1 mV ST elevation	158 ± 16	172 ± 28	NS
RPP at 0.1 mV ST elevation	17 030 ± 5481	20 390 ± 4502	NS
Percent of maximal age-related HR at 0.1 mV ST elevation	65 ± 15	75 ± 10	NS
Increment of HR at 0.1 mV ST elevation	32 ± 13	45 ± 16	NS
Increment of SBP at 0.1 mV ST elevation	33 ± 18	41 ± 24	NS
Increment of RPP at 0.1 mV ST elevation	7501 ± 3780	11 204 ± 4711	NS

Data are expressed as mean ± SD. Abbreviations as in table III.

patients with and in 1/19 patients without homozonal ischemia (p = 0.0037, sensitivity 50%, specificity 95%). ST-segment elevation occurred within 6 min of the beginning of exercise in 8/12 patients with and in 5/19 patients without homozonal ischemia (p = 0.0266, sensitivity 67%, specificity 74%). Accordingly, patients with early ST-segment elevation had a significantly higher incidence of dobutamine-induced ischemia when compared to patients with late ST-segment elevation (Fig. 1).

Of 36 patients with exercise-induced ST-segment elevation, 21 showed evidence of viability and/or homozonal ischemia during dobutamine testing while 15 patients had neither viability nor homozonal ischemia. In 13 of these 15 patients, ST-segment elevation invariably occurred after 6 min of exercise.

Coronary arteriography and left ventriculography. The angiographic data are shown in table VII. When compared to patients with no ST-segment shift, patients with exercise-induced ST-segment elevation had a significantly higher wall motion score (5.9 ± 1.6 vs 4.1 ± 1.5, p = 0.018) and a slightly lower left ventricular ejection fraction (42.9 ± 7.8 vs 48.2 ± 9.7%, p = NS). All but one study patient had significant stenosis of at least one major coronary branch. The number of diseased vessels among group A and group B patients was similar. The infarct-related artery was totally occluded in 20 patients (56%) in group A and in 13 patients (54%) in group B (p = NS). In all 20 patients of group A and in 11/13 patients of group B, collateral filling of the distal vessel was angiographically evident (p = NS). Patients with evidence of myocardial viability did not show significant differences in the frequency of occlusion of the infarct-related artery when compared to patients without viability (19/33 vs 14/27 patients, respectively; p = NS). All patients with viability and an occluded infarct-related artery had a collateral flow for the distal vessel; this finding was angiographically evident in 12/14 patients without viability (p = NS).

Table VII. Angiographic findings in patients with and without exercise-induced ST-segment elevation.

	ST elevation (n=36)	No ST elevation (n=24)	p
Wall motion score	5.9 ± 1.6	4.1 ± 1.5	0.018
Left ventricular ejection fraction (%)	42.9 ± 7.8	48.2 ± 9.7	NS
No significant stenoses	0	1 (4)	NS
One-vessel disease	20 (56)	13 (54)	NS
Two-vessel disease	11 (30)	7 (29)	NS
Three-vessel disease	5 (14)	3 (13)	NS
Occlusion of the IRA	20 (56)	13 (54)	NS
Mean stenosis of the non-occluded IRA (%)	66 ± 19	73 ± 17	NS

Data are expressed as mean ± SD or number (%) of patients. IRA = infarct-related artery.

Discussion

In accordance with those of previous reports[5,18], data from the present study, demonstrate that patients with previous myocardial infarction and exercise-induced ST-segment elevation in Q-wave leads have a severely impaired resting left ventricular function. This electrocardiographic finding, however, is not associated with a more severe or extensive coronary artery disease nor with a higher probability of occlusion of the infarct-related artery. In patients with exercise-induced ST elevation, the evaluation of the ST-segment shift at the end of exercise fails to identify viable myocardium and residual ischemia. In fact, ST-segment elevation at the peak of exercise had a similar incidence in patients with and without myocardial viability and ischemia, when assessed at dobutamine echocardiography. However, when a time-domain analysis of the ST-segment shift during exercise is performed, it is possible, by observing the duration of exercise up to the onset of ST-segment elevation, to distinguish patients with viable or ischemic myocardium from those with passive stretching of non-viable tissue. This original result, reported for the first time in the present study, implies that ST-segment elevation is a reliable marker of viability and of homozonal ischemia only when it occurs in the early phases of exercise, whereas late ST-segment elevation is a rather non-specific finding. In fact, despite a relatively low sensitivity (ranging from 39 to 67%), an early-onset ST-segment elevation showed a very high specificity (94-100%) for viability in the infarct area. On the contrary, no relation between ST-segment elevation occurring late during exercise and myocardial viability/ischemia has been found. Instead, in the present study a late ST-segment elevation has been frequently observed in the absence of both ischemia and of viable myocardium. The inotropic and chronotropic stimulation associated with strenuous effort may induce passive stretching of the infarct wall, perinecrotic ischemia or ischemia in a remote region. Therefore, ST-segment elevation occurring during the later stages of exercise could most probably be due to either abnormal motion of the infarct wall, or to homozonal or remote ischemia or to a combination of both. Finally, ST-segment elevation present at peak exercise may result from both an early ST-segment elevation persisting throughout the test or from a late ST-segment elevation. Therefore, evaluation of the ST-segment shift only at the end of exercise is an unreliable tool for the distinction between viability, wall stretching and ischemia. On the contrary, ST-segment elevation occurring during the early stages of exercise, when the sympathetic and hemodynamic responses to the effort are poorly activated, is likely to be mostly linked to the contractile reserve of the infarcted myocardium, thus representing a marker of viability.

The higher prevalence of viability/ischemia in patients with early, compared to those with late ST-segment elevation, is shown in figure 1. The figure also shows the high prevalence of viability and ischemia among patients without ST-segment elevation during exercise. This is even superior to that of patients with late ST-segment elevation. Considering the low sensitivity for viability/ischemia of exercise-induced ST-segment elevation, this finding is not so surprising. Indeed, after myocardial infarction the absence of this exercise finding does not allow one to rule out the persistence of viable myocardium and of residual ischemia.

Non-invasive imaging techniques have been extensively employed in the past decade for the assessment of myocardial viability in clinical practice: positron emission tomography (to evaluate myocardial perfusion and metabolic activity), thallium-201 scintigraphy (to evaluate myocardial perfusion and the integrity of the cell membrane), and dobutamine stress echocardiography (to evaluate the contractile reserve)[19]. Despite an overall high accuracy in the detection of viability, several important limitations still remain, particularly with regards to the availability of nuclear techniques. Dobutamine echo testing, on the contrary, can be easily implemented in most clinical laboratories, although its diagnostic accuracy strictly depends on the echocardiographic image quality and on operator experience[20]. In the present study we demonstrated that a simple electrocardiographic finding, easily available at exercise testing, could represent a useful tool for the assessment of viability in patients with a previous myocardial infarction.

Comparison with previous studies. Data from the present study, showing a worse resting wall motion score and a low ejection fraction in patients with effort-induced ST-segment elevation, are in agreement with several previous observations, according to which this finding is associated with severe impairment of the left ventricular function[2,5,18,21].

The pathogenesis of exercise-induced ST-segment elevation in leads exploring an infarct area has been traditionally attributed to abnormal ventricular wall motion during the effort[2-5], to reversible ischemia arising from perinecrotic myocardium[6,7] or to both[8]. In more recent years, an increasing number of reports referred this electrocardiographic finding to the persistence of viable myocardium in the infarct area[9,10,22-24].

In two different studies, Margonato et al.[9,10] showed that exercise-induced ST-segment elevation in Q-wave leads has an excellent diagnostic accuracy for the detection of viability, being almost invariably associated with reversible defects at thallium-201 myocardial perfusion scintigraphy[9] and with residual tissue viability at fluorodeoxyglucose positron emission tomography[10]. In the latter study in particular, exercise-induced ST-segment elevation was 67% sensitive and 100% specific for viability assessment. Using dobutamine echocardiography for the detection of viability, we found that an early-onset ST-segment elevation has a similar specificity but a lower sensitivity. It is also of great importance,

however, that no relationship between ST-segment elevation and myocardial viability was found in our study, when the ST-segment shift was analyzed at the end of exercise. This was not so in the studies by Margonato et al. Two possible explanations for these conflicting results are the different techniques used for evaluating viability and the different characteristics of the enrolled populations. In fact, the lower sensitivity of dobutamine echocardiography, as compared with nuclear techniques, for the detection of viable myocardium is well known[14]. Therefore, it is possible that radioisotopic methods would have revealed viability and/or ischemia in some patients with a negative dobutamine test. Furthermore, it is likely that the prevalence of viability and ischemia could differ among the two study populations. This, since we enrolled only patients with isolated ST-segment elevation, while in the study of Margonato et al.[10] about one third of patients had ST-segment depression in non-infarct-related leads. Finally, in the work of Margonato et al.[10], the group of patients with exercise-induced ST-segment elevation seems to be a very selected population (higher incidence of anterior infarctions and angina during effort and more recent infarctions). Therefore the probability that residual ischemia and viability be present is higher than in patients without ST-segment elevation.

Yamagishi et al.[22], using positron emission tomography, also found a higher incidence of fluorine-18-fluorodeoxyglucose uptake in the infarct territory in patients with exercise-induced ST-segment elevation compared to that observed in patients without an ST-segment shift. However, the diagnostic sensitivity and accuracy of exercise-induced ST-segment elevation for the detection of viable myocardium were relatively low in the Yamagishi series (54 and 62%, respectively). These figures are intermediate between those of our study and those reported in the work by Margonato et al.[10]. It is noteworthy that Yamagishi et al. enrolled patients in an earlier phase after myocardial infarction (on average 24 days after the acute event vs 95 days in our study). This probably increased the likelihood of viability persistence.

In a study by Schneider et al.[23], although based on a limited number of patients, exercise-induced ST-segment elevation predicted the improvement in left ventricular function after revascularization of the infarct-related artery, thus indirectly confirming the diagnostic value of this finding as a marker of viable myocardium.

Recently, Nakano et al.[24] reported that exercise-induced ST-segment elevation in Q-wave leads is invariably associated with tissue viability (as assessed at positron emission tomography) only when occurring along with ST-segment depression in the non-infarct area. Actually, the study population was highly selected (only patients with single-vessel disease were included), so that these findings cannot be directly applied to the general population of patients with infarcts.

Unlike previously reported studies, Bodì et al.[25] found that exercise-induced ST-segment elevation after a Q-wave infarction is related to a lesser contractile reserve. This original finding, inconsistent with both our and previous data, can be explained by methodological limitations and patient selection. In fact, in this study, in order to analyze the myocardial contractile reserve, only left ventriculography at low-dose dobutamine was used. Using this approach, instead of echocardiography, continuous monitoring of the wall motion and thickening throughout the stress cannot be performed, thus leading to a reduction in the sensitivity for viability assessment. Moreover, most of the study patients (71%) had significant ST-segment elevation at rest. Interestingly, the patients with ST-segment elevation during exercise, but not at rest, were those who showed the greatest improvement at dobutamine testing.

To our knowledge, in only one report by Lombardo et al.[26], has a time-domain analysis of the ST-segment changes occurring in Q-wave leads during a stress test been performed. In this study the authors demonstrate that ST-segment elevation is predictive of the contractile reserve only when it develops at a low dobutamine dose, while at a high dose it may be also associated with either ischemia or mechanical wall stretching. Our results, obtained using the same method for viability assessment, confirm the predictive value of an early-onset stress-induced ST-segment elevation and extend the findings to ST-segment changes induced by exercise.

Clinical implications. After an acute Q-wave myocardial infarction, the exercise stress test provides not only important information for the assessment of residual ischemia (ST-segment depression)[1] and for prognostic stratification[27], but may also represent a useful tool for the first-line screening of myocardial viability. Considering the relatively low sensitivity and very high specificity of an early-onset ST elevation, the following diagnostic strategy may be proposed. If a patient exhibits ST-segment elevation during the early phases of exercise, the presence of viable myocardium in the infarct area is almost certain; in this case further complex imaging tests could be avoided. Conversely, in patients with no or late ST-segment elevation, underlying viability cannot be ruled out and must be sought by dobutamine echocardiography or nuclear techniques.

Conclusions. ST-segment elevation occurring in electrocardiographic leads exploring an infarct area is a highly specific marker for reversible contractile dysfunction only when it appears in the early stages of exercise. After Q-wave myocardial infarction, the exercise stress test represents a simple, cost-effective and useful tool for the first-line screening of myocardial viability. Further investigations are needed to assess the accuracy of an early-onset ST-segment elevation in predicting spontaneous or post-revascularization recovery of left ventricular function.

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