Scintigraphic results in asymptomatic myocardial infarction patients with exercise-induced ST segment elevation

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Background. **The mechanism responsible for exercise-induced ST segment elevation is debated, but heterogeneous patients were likely included in previous studies. This study was specifically aimed at investigating the clinical meaning of isolated exercise-induced ST segment elevation in asymptomatic patients with a recent acute myocardial infarction (MI).**

Methods. **We studied 30 patients (28 males, 2 females, mean age 62 ± 9 years) with a recent MI who developed ST segment elevation in leads with a Q/QS wave pattern, and who did not develop angina or ST segment depression during exercise testing and did not have any history of post-infarction angina. Patients underwent bicycle 99m-Tc-sestamibi (MIBI) myocardial scintigraphy for the assessment of myocardial perfusion and of left ventricular function.**

Results. **Only 7 patients (23.3%) showed reversible perfusion defects on stress MIBI myocardial scintigraphy, which were mild and of limited extension in all. There were no statistically significant differences in the main exercise variables between groups with or without stress-related perfusion defects. Signs of exercise-related left ventricular dysfunction were detected in 6 patients (20%), 3 of whom also showed reversible perfusion defects. Again, no significant differences in the main exercise variables were found between patients with or without stress-induced scintigraphic abnormalities.**

Conclusions. **In asymptomatic MI patients, isolated exercise-induced ST segment elevation in leads with a Q/QS wave pattern is unlikely to represent clinically relevant residual myocardial ischemia during exercise, thus suggesting that further diagnostic investigations are not necessary in these patients.**

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In patients with a history of transmural myocardial infarction (MI) ST segment elevation is often induced by exercise or pharmacological stress tests in the electrocardiographic (ECG) leads with signs of myocardial necrosis (i.e., a Q or QS wave pattern). Despite numerous studies, in this clinical context the mechanism responsible for ST segment elevation during exercise (or alternative stress tests) remains controversial. Some authors suggested it is caused by transient myocardial ischemia[1-5] and/or by the presence of still viable but jeopardized myocardium in the infarcted area[4,6-9], whereas others denied any relationship with myocardial ischemia[8-18] and/or viability[5,16-18] and suggested that stress-induced ST segment elevation is more strictly correlated to left ventricular dysfunction[10-18]. However, neurovegetative changes, heart rate-related changes, or also a simple shift in the ST axis during exercise cannot be excluded as a mechanism contributing to ST segment elevation.

Previous studies on stress-induced ST segment elevation in MI patients included heterogeneous groups of patients with different pre-test and/or post-test probability for the presence of residual myocardial ischemia[19]. From a clinical point of view, however, the maximal importance in establishing whether exercise-induced ST segment elevation is actually caused by transient ischemia and/or viability is in MI patients who do not have any other apparent typical symptoms or signs of myocardial ischemia.

Methods

Patient selection. We enrolled in the study patients fulfilling the following inclusion criteria: 1) recent (< 3 months) acute transmural MI; 2) absence of any history of post-infarction angina (defined as angina occurring after 48 hours from MI onset); 3) ST segment elevation on ECG leads with a

Q/QS wave pattern during symptom/sign-limited treadmill exercise testing; 4) no ST segment depression or angina during the exercise test. Patients with left or right bundle branch block or any other ECG alterations which could interfere with ST segment analysis were also excluded.

Study protocol. Within 2 weeks of treadmill exercise test, all patients underwent a stress/rest myocardial scintigraphy. Patients performed a bicycle symptom/sign-limited exercise, starting with a workload of 25 W, with increments of 25 W every 2 min until an endpoint was approximated. Twelve-lead ECG and blood pressure were recorded at rest, in the last minute of each exercise stage, at peak, and at 1-min intervals into recovery. Furthermore, leads II, V_2 and V_5 were continuously monitored during the test. The test was terminated in case of fatigue or relevant clinical events (e.g., dyspnea, hypotension, complex ventricular arrhythmias). ST segment elevation in MI-related leads was not considered a reason for exercise termination. ST segment elevation was considered significant when the J point was elevated by ≥ 1 mm compared to pre-exercise and ST segment persisted elevated at 0.06 s after the J point.

At peak exercise, a 370 MBq dose of 99m-Tc-sestamibi was injected intravenously and the patient was encouraged to exercise for two additional minutes. A single-photon emission computed tomography (SPECT) acquisition was recorded 30 to 60 min from the termination of the exercise by means of a wide-field-of-view single head gamma camera (Philips Gamma-Diagnostics, Eindhoven, The Netherlands) equipped with a low-energy high-resolution collimator. The camera was rotated over a 180° arc in a circular orbit about the patient's thorax at 6° increments for 60 s each. The acquisition matrix was 64 × 64; zoom factor 1.25×. The rest SPECT acquisition was recorded 3 to 4 hours later, following the injection at rest of 1110 MBq of the same tracer. Image processing was accomplished by a Pegasys workstation (ADAC, Milpitas, CA, USA). After filtered back-projection using a Butterworth filter (cut-off frequency 0.5 cycles/pixel, order 5), a series of stress and rest short-axis, vertical long-axis and horizontal long-axis slices was generated.

The images were interpreted by two independent observers for the presence or absence of perfusion defects. According to the Cedars Sinai model the left ventricle was divided into 20 segments[20,21]. The observers independently attributed a score to each segment according to the following grading: 0 = normal perfusion, 1 = mild defect, 2 = moderate defect, 3 = severe defect, 4 = absence of perfusion. In case of disagreement the score was assigned by consensus. The sum of the stress scores and the sum of the rest scores were recorded (minimum total value = 0, maximum total value = 80) and the difference between the global stress and the global rest scores was calculated. Transient ischemia was considered to be present when this difference was > 0.

The dimensions of the left ventricular cavity were also qualitatively evaluated at rest by expert observers and classified as normal, or mildly, moderately or severely increased. The occurrence of reversible left ventricular dilation and/or increase in tracer lung uptake during exercise stress test were considered as signs of exercise-induced left ventricular dysfunction and both parameters were qualitatively classified by the observers as absent, mild-moderate or severe.

Statistical analysis. Comparisons of continuous variables were carried out by either two-tailed Student's t-test or Mann-Whitney U-test, as indicated. Differences were considered statistically significant for $p < 0.05$. Data are reported as mean ± SD.

Results

Thirty patients fulfilling the inclusion criteria were enrolled into the study. There were 28 males and 2 females, and mean age was 62 ± 9 years. The site of MI was anterior in 25 and inferior in 5. Two-dimensional left ventricular ejection fraction was 0.44 ± 0.09 (range 0.22 to 0.63).

All patients showed ST segment elevation during bicycle exercise stress test. No patient developed any symptoms and rate-pressure product at peak exercise was 22 319 ± 5544 b/min·mmHg.

Overall, abnormal findings on stress MIBI myocardial scintigraphy were detected in 10 patients (33%). Exercise-related perfusion defects of any extension were found in 7 patients (23.3%), but they were very mild in most (ischemia MIBI score = 8 in 1 patient, 4 in 3 patients, 3 in 2 patients, and 2 in 1 patient). There were no significant differences in most exercise variables between patients with and those without perfusion defects. Heart rate at 1 mm ST elevation on exercise test tended to be lower in patients with ischemia but there was no difference in rate-pressure product at 1 mm ST elevation; moreover, exercise duration was greater and maximal ST elevation lower in patients with than in those without signs of myocardial ischemia on stress MIBI scan (Table I).

Signs of exercise-related left ventricular dysfunction, on the other hand, were detected in 6 patients (20%), 3 of whom (10% of the total sample) also had some evidence of mild myocardial ischemia. Left ventricular dilation at rest was detected on radionuclide images in 13 patients without (54.2%) and in 5 patients with (83.3%) exercise-induced left ventricular dysfunction, a not statistically significant difference ($p = 0.38$). However, severe rest left ventricular dilation was present in only 1 patient without (4.2%) but in 4 patients with (66.7%) exercise-induced left ventricular dysfunction ($p = 0.003$). Two-dimensional left ventricular ejection fraction tended to be lower in patients with left ventricular dysfunction (0.40 ± 12 vs 0.45 ± 8), but the difference was not statistically significant ($p = 0.21$).

Table I. Main exercise results in patients with or without perfusion defects of any extension on exercise 99m-Tc-sestamibi scintigraphic study.

	No perfusion defects (n=23)	Perfusion defects (n=7)	p
Pre-exercise			
Heart rate (b/min)	79 ± 16	78 ± 17	0.84
Systolic blood pressure (mmHg)	130 ± 24	132 ± 30	0.86
Diastolic blood pressure (mmHg)	82 ± 11	83 ± 11	0.89
Rate-pressure product (b/min·mmHg)	10 204 ± 2298	10 369 ± 3605	0.88
1 mm ST segment elevation			
Heart rate (b/min)	116 ± 14	105 ± 16	0.08
Systolic blood pressure (mmHg)	150 ± 29	156 ± 31	0.68
Diastolic blood pressure (mmHg)	86 ± 13	87 ± 17	0.89
Rate-pressure product (b/min·mmHg)	17 525 ± 4032	16 412 ± 4637	0.54
Exercise time (s)	254 ± 143	333 ± 131	0.17
Peak exercise			
Heart rate (b/min)	137 ± 17	132 ± 25	0.52
Systolic blood pressure (mmHg)	162 ± 28	166 ± 30	0.76
Diastolic blood pressure (mmHg)	89 ± 15	86 ± 15	0.63
Rate-pressure product (b/min·mmHg)	22 324 ± 4948	22 304 ± 7666	0.99
Exercise duration (s)	466 ± 153	621 ± 68	0.007
Maximal ST segment elevation (mm)	2.7 ± 0.9	2.1 ± 0.7	0.09

The main exercise results of patients with or without stress-induced left ventricular dysfunction are shown in table II. There were no significant differences between the two groups in the main analyzed variables, although some differences did not likely reach statistical significance because of the low number of patients with scintigraphic left ventricular dysfunction. In particular, in the two groups, peak rate-pressure product was 22 625 ± 5064 vs 20 735 ± 7792 b/min·mmHg, and exercise duration was 494 ± 134 vs 497 ± 201 s in patients without and with left ventricular dysfunction, respectively.

Discussion

The mechanisms responsible for ST segment elevation induced by exercise or pharmacological (in particular, dobutamine) stress tests in ECG leads with Q/QS waves in patients with MI are controversial and very debated. For several years two major possible alternatives have been put forward: stress-induced left ventricular wall motion abnormalities[10-18] and transient myocardial ischemia[1-5]. More recently, with the development of the concepts of stunning[22] and hibernation[23]

Table II. Main exercise results in patients with or without exercise-related left ventricular (LV) dysfunction on exercise 99m-Tc-sestamibi scintigraphic study.

	No LV dysfunction (n=24)	LV dysfunction (n=6)	p
Pre-exercise			
Heart rate (b/min)	76 ± 17	87 ± 8	0.16
Systolic blood pressure (mmHg)	132 ± 23	126 ± 33	0.55
Diastolic blood pressure (mmHg)	83 ± 11	80 ± 13	0.50
Rate-pressure product (b/min·mmHg)	10 107 ± 2550	11 002 ± 3009	0.47
1 mm ST segment elevation			
Heart rate (b/min)	114 ± 15	111 ± 17	0.66
Systolic blood pressure (mmHg)	156 ± 28	138 ± 29	0.19
Diastolic blood pressure (mmHg)	88 ± 13	82 ± 16	0.37
Rate-pressure product (b/min·mmHg)	17 839 ± 4158	15 345 ± 4011	0.20
Exercise time (s)	280 ± 137	202 ± 119	0.16
Peak exercise			
Heart rate (b/min)	136 ± 18	131 ± 24.7	0.58
Systolic blood pressure (mmHg)	165 ± 26	155 ± 38.8	0.45
Diastolic blood pressure (mmHg)	90 ± 14	82 ± 17.2	0.22
Rate-pressure product (b/min·mmHg)	22 625 ± 5064	20 735 ± 7792	0.47
Exercise duration (s)	494 ± 134	497 ± 201	0.71
Maximal ST segment elevation (mm)	2.6 ± 0.9	2.3 ± 0.6	0.44

and the diffusion of imaging stress tests, there has been the tendency to look also at stress-induced ST segment elevation as a sign of myocardial viability[4,6-10].

The extremely variable and conflicting results reported in the numerous previous studies[11-18], in fact, are the most striking proof that it is likely wrong to state that ST segment elevation can simply be caused by only one among the different proposed mechanisms.

Moreover, the assessment in previous studies of the clinical and pathophysiological meaning of exercise-induced ST segment elevation in itself may have been biased by the inclusion of patients with a high pre-test probability of developing myocardial ischemia during the test, such as those with a history of post-infarction angina and those with ST segment depression and/or anginal pain induced during the stress test. Indeed, in these conditions, it is more likely to find some relationship between ST segment elevation and myocardial ischemia and/or viability, since a cause-effect relationship may be assumed also when ST segment elevation is actually caused by some other different mechanisms.

In fact, it is in asymptomatic patients that the assessment of whether ST segment elevation is or not ischemic in origin is mostly useful, being in this case the only sign possibly suggesting the need for revascularization procedures.

For this reason, the present study was conducted in a carefully selected group of consecutive patients with a recent MI who developed ST segment elevation in leads with a Q/QS wave pattern during fatigue-limited exercise testing, but who were free from angina or any other symptoms. Moreover, all patients had no clinical suspect for post-infarction angina and did not have any other apparent ECG evidence of myocardial ischemia during the test.

Our data show that, in this specific clinical setting, ST segment elevation by itself is unlikely to represent, and then can hardly be taken as a proof of, myocardial ischemia. Indeed, significant reversible perfusion defects on stress myocardial MIBI-radionuclide scan were detected in less than a quarter of patients. Moreover, when present, perfusion defects were mild and/or of limited extension, suggesting that it could not totally account for stress ST segment elevation, which was usually severe and/or extensive. Furthermore, maximal ST segment elevation tended to be higher in patients without than in those with any evidence of myocardial ischemia on stress MIBI scan.

Although we cannot totally exclude that ST segment elevation represented myocardial viability in some of our patients, as no specific test was performed to directly assess this possibility, we believe that it is very unlikely that myocardial viability was responsible for ST segment elevation in our patients. Indeed, most patients with evidence of myocardial viability at low stress stimuli (e.g., low-dose dobutamine), inevitably develop ischemia with the increase of the stimulus (e.g., high-dose dobutamine)[4,7]. All our patients performed fatigue-limited exercise test, achieving an average heart rate of 86.5 ± 13% of the maximal predicted heart rate, including 16 with a heart rate ≥ 85% and 25 with a heart rate ≥ 70% of the maximal predicted value. Thus a significant number of ischemic responses would have been expected if significant areas of viable myocardium were actually present.

Of note, our data cannot also confirm the hypothesis that exercise-induced ST segment elevation may usually represent exercise-induced left ventricular dysfunction, as only 20% of our patients had evidence of such an abnormality on stress radionuclide study. However, some limitations of the method used to assess left ventricular function in our study need to be recognized. First, the evaluation of signs of left ventricular dysfunction was obtained 30 to 60 min after the end of exercise; this may have allowed to identify patients with more severe and persistent left ventricular abnormalities, but those with milder alterations, which had recovered before scintigraphic evaluation, may have been missed, resulting in an underestimation of patients with stress-induced left ventricular abnormalities. Second, left ventricular function was only assessed using a qualitative method, which may also have reduced the detection of minor degrees of left ventricular dysfunction. Furthermore, we cannot exclude, on the basis of our data, that regional left wall motion abnormalities may contribute to exercise-induced ST segment elevation. Therefore, further studies are needed to clarify the possible relationship between exercise-induced abnormalities in left ventricular function and ST segment elevation.

Finally, our data do not allow us to clarify the mechanism of ST segment elevation in our patients. Speculative hypotheses, however, may include increased spatial heterogeneity in refractory periods of normal and peri-infarct myocardial cells caused by simple heart rate-related and adrenergic-driven changes, or even simple changes in ST vector caused by the absence of active myocardial cells in the necrotic areas.

In conclusion, our study shows that asymptomatic, isolated exercise-induced ST segment elevation in ECG leads with a Q/QS wave pattern is unlikely to represent, by itself, clinically relevant residual myocardial ischemia and viability, thus indicating that further diagnostic investigations, aimed at assessing "residual ischemia", are unlikely to be helpful in this specific, well-characterized group of patients.

References

1. Margonato A, Ballarotto C, Bonetti F, et al. Assessment of residual tissue viability by exercise testing in recent myocardial infarction: comparison of electrocardiogram and myocardial perfusion scintigraphy. J Am Coll Cardiol 1992; 19: 948-52.
2. Lekakis JP, Prassopoulos V, Kostamis P, et al. Dobutamine-induced ST-segment elevation in patients with healed my-

ocardial infarction. A marker of myocardial viability. J Electrocardiol 1995; 28: 91-7.
3. Candell-Riera J, Santana-Boado C, Armandans-Gil L, et al. Comparison of patients with anterior wall healed myocardial infarction with and without exercise-induced ST-segment elevation. Am J Cardiol 1998; 81: 12-6.
4. Piérard LA, Lancellotti P, Kulbertus HE. ST-segment elevation during dobutamine stress testing predicts functional recovery after acute myocardial infarction. Am Heart J 1999; 137: 500-11.
5. Mezilis NE, Parthenakis FI, Kanakaraki MK, et al. Dobutamine- vs exercise-induced ST segment elevation early after Q wave myocardial infarction. Prediction of functional recovery after revascularization. Eur Heart J 2000; 21: 814-22.
6. Margonato A, Chierchia SL, Xuereb RG, et al. Specificity and sensitivity of exercise-induced ST elevation for detection of residual viability: comparison with fluorodeoxyglucose and positron emission tomography. J Am Coll Cardiol 1995; 25: 1032-8.
7. Lombardo A, Loperfido F, Pennestrì F, et al. Significance of transient ST-T segment changes during dobutamine testing in Q wave myocardial infarction. J Am Coll Cardiol 1996; 27: 599-605.
8. Elhendy A, Cornel JH, Roelandt JRTC, et al. Relation between ST segment elevation during dobutamine stress test and myocardial viability after a recent myocardial infarction. Heart 1997; 77: 115-21.
9. Yamagishi H, Akioka K, Takagi M, et al. Exercise four hour redistribution thallium-201 single photon emission computed tomography and exercise induced ST segment elevation in detecting the viable myocardium in patients with acute myocardial infarction. Heart 1999; 81: 17-24.
10. Lahiri A, Balasubramanian V, Craig MWM, et al. Exercise-induced ST segment elevation. Electrocardiographic, angiographic and scintigraphic evaluation. Br Heart J 1980; 43: 582-8.
11. Stiles GL, Rosati RA, Wallace AG. Clinical relevance of exercise-induced ST-segment elevation. Am J Cardiol 1980; 46: 931-6.
12. Gewirtz H, Sullivan M, O'Reilly G, et al. Role of myocardial ischemia in the genesis of stress-induced S-T segment elevation in previous anterior myocardial infarction. Am J Cardiol 1983; 51: 1289-93.
13. Haines DE, Beller GA, Watson DD, et al. Exercise-induced ST segment elevation 2 weeks after uncomplicated myocardial infarction: contributing factors and prognostic significance. J Am Coll Cardiol 1987; 9: 996-1003.
14. Coma-Canella I, Gomez MV, Terol I, et al. Radionuclide studies in patients with stress-induced ST-segment elevation after acute myocardial infarction. Am Heart J 1994; 128: 549-65.
15. Elhendy A, Geleijnse ML, Roelandt JRTC, et al. Evaluation by quantitative 99m-technetium MIBI SPECT and echocardiography of myocardial perfusion and wall motion abnormalities in patients with dobutamine-induced ST-segment elevation. Am J Cardiol 1995; 76: 441-8.
16. Lanzarini L, Fetiveau R, Poli A, et al. Significance of ST-segment elevation during dobutamine-stress echocardiography in patients with acute myocardial infarction treated with thrombolysis. Eur Heart J 1996; 17: 1008-14.
17. Ricci R, Bigi R, Galati A, et al. Dobutamine-induced ST-segment elevation in patients with acute myocardial infarction and the role of myocardial ischemia, viability, and ventricular dyssynergy. Am J Cardiol 1997; 79: 733-7.
18. Ho YL, Lin LC, Yen RF, et al. Significance of dobutamine-induced ST-segment evaluation and T-wave pseudonormalization in patients with Q-wave myocardial infarction: simultaneous evaluation by dobutamine stress echocardiography and thallium-201 SPECT. Am J Cardiol 1999; 84: 125-9.
19. Elhendy A, Fioretti PM. Stress-induced ST-segment elevation after a recent myocardial infarction: myocardial necrosis, viability or both? Eur Heart J 1996; 17: 975-7.
20. Berman DS, Hachamovitch R, Kiat H, et al. Incremental value of prognostic testing in patients with known or suspected ischemic heart disease: a basis for optimal utilization of exercise technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography. J Am Coll Cardiol 1995; 26: 639-47.
21. Hachamovitch R, Berman DS, Kiat H, et al. Effective risk stratification using exercise myocardial perfusion SPECT in women: gender-related differences in prognostic nuclear testing. J Am Coll Cardiol 1996; 28: 34-44.
22. Braunwald E, Kloner RA. The stunned myocardium: prolonged, post-ischemic ventricular dysfunction. Circulation 1982; 66: 1146-9.
23. Rahimtoola SH. The hibernating myocardium. Am Heart J 1989; 117: 211-21.