Exercise-Induced ST-Segment Elevation in Patients with a Recent Acute Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention

Fabio Infusino, M.D., Gaetano A. Lanza, M.D., Claudio Larosa, M.D., Gregory A. Sgueglia, M.D., Leonardo Marinaccio, M.D., Priscilla Lamendola, M.D., Luca Mariani, M.D., Pasquale Santangeli, M.D., Alfonso Sestito, M.D., and Filippo Crea, M.D.

Istituto di Cardiologia, Università Cattolica del Sacro Cuore, Rome, Italy

Objectives: To get insight in the mechanism of exercise-induced ST-segment elevation (STE) in patients with Q/QS waves at the electrocardiogram (ECG).

Methods: We performed exercise stress test in 13 patients with anterior acute myocardial infarction treated by successful primary percutaneous coronary intervention (PCI).

Results: Compared to rest, an additional STE ≥ 1 mm in one or more precordial ECG leads during exercise occurred in nine patients (69%), in the absence of symptoms.

Conclusions: In acute myocardial infarction (MI) patients, treated by primary PCI and showing optimal coronary blood flow restoration at angiography, STE can still be induced by exercise in Q/QS wave ECG leads. This finding lends further support to the theory that exercise-induced STE in this clinical context is unlikely to represent by itself transient myocardial ischemia or viability.

A.N.E. 2007;12(4):349–353

ST-segment elevation; exercise stress test; primary angioplasty

In patients with a recent transmural myocardial infarction (MI), the mechanism responsible for ST-segment elevation in ECG leads with a Q/QS wave pattern during exercise or pharmacological stress tests remains controversial. Some studies, indeed,⁵ have reported that ST-segment elevation was associated with transient myocardial ischemia^{1–6} and/or with the presence of still viable but jeopardized myocardium in the infarcted area,^{7–11} also showing a positive relationship between stress-induced ST-segment elevation in ECG leads with evidence of necrosis and functional recovery following coronary revascularization. Others, instead, have concluded that stress-induced ST-segment elevation is not a specific sign of regional myocardial ischemia in this context, but it is more significantly correlated with wider myocardial necrosis and regional wall motion abnormalities, in particular in the anteroapical and apical re-

gions, and an increased prevalence of ventricular aneurysm.^{12–20}

The use of primary percutaneous coronary intervention (PCI) to treat acute MI usually restores coronary blood flow in the occluded vessel responsible for the infarction. Thus, effective primary PCI of the culprit vessel would be expected to avoid the persistence of residual myocardial ischemia related to incomplete revascularization or impaired coronary flow reserve in peri-infarction areas, suggesting, therefore, that it should prevent ischemia-related ST-segment elevation in Q/QS wave leads induced during exercise stress test, whereas it could not have any significant influence on non ischemic ST-segment elevation.

The effect of successful primary PCI on exercise-induced ST-segment elevation in Q/QS wave ECG leads in patients with acute MI is still unknown.

Address for reprints: Gaetano A. Lanza, Istituto di Cardiologia, Università Cattolica del Sacro Cuore, Largo A. Gemelli, 8, 00168 – Roma, Italy. Fax: +039 06 3055 535; E-mail: g.a.lanza@inwind.it

METHODS

Patient Selection

We have studied consecutive patients admitted to our coronary care unit (CCU) for acute MI who satisfied all the following inclusion criteria: (1) prolonged typical retrosternal chest pain (>30 minutes); (2) ST-segment elevation ≥ 2 mm in ≥ 1 precordial ECG leads on admission and subsequent development of a QS wave pattern in ≥ 2 anterior ECG leads (V_1 – V_5 , transmural anterior MI); (3) typical increase of blood markers of myocardial necrosis (i.e., troponin T [TnT] and creatine-kinase MB [CK-MB]); (4) no history of previous angina episodes or previous MI; (5) primary PCI, with implantation of ≥ 1 stents, performed within 6 hours of symptom onset; (6) successful dilatation and recanalization of the culprit vessel (left anterior descending coronary artery), as indicated by a residual stenosis $<20\%$; (7) absence of significant ($>50\%$) stenosis in other epicardial coronary artery vessels.

Patients with ECG abnormalities (e.g., left or right bundle branch block), which could interfere ST-segment analysis in anterior leads were excluded from the study.

Echocardiographic examination was performed prior to discharge in all patients to assess left ventricular dimensions, regional wall motion abnormalities and left ventricular ejection fraction (by Simpson method).

Exercise Stress Test

Patients underwent a treadmill exercise test 5–7 days after acute MI, using a standard Bruce protocol. Leads II, V_2 and V_5 were continuously monitored during the test. Twelve-lead ECG and blood pressure were recorded at rest, in the last minute of each exercise stage, at peak exercise, when clinically indicated, and at 1-minute intervals in the recovery phase. The test was stopped when one or more of following clinical signs/symptoms occurred: (1) physical exhaustion; (2) severe angina (Borg scale ≥ 6); (3) ST-segment depression >2 mm; (4) clinically relevant events, including dyspnoea, hypotension (a systolic blood pressure decrease >20 mmHg compared to previous measurements), hypertension (systolic blood pressure ≥ 240 mmHg and/or diastolic blood pressure ≥ 140 mmHg), ventricular arrhythmias (frequent or repetitive premature ventricular beats).

ST-segment elevation was considered significant when the *J*-point was elevated by ≥ 1 mm, compared to the pre-exercise level, at 0.06 second after the *J*-point (Fig. 1). The ST-segment elevation in MI-related leads was not considered a criterion for exercise termination.

Statistical Analysis

Comparisons of continuous variables were carried out by *t*-test. Differences were considered statistically significant for $P < 0.05$. Data are reported as mean $\pm$ standard deviation.

RESULTS

Of 64 consecutive patients with acute MI treated by primary PCI screened for the study, 13 patients (20.3%) fulfilled the inclusion criteria for enrolment. The main clinical characteristics of these patients are summarized in Table 1. The group included 12 males and had a mean age of 56 ± 9 years. A TIMI flow grade 3 in the LAD vessel was achieved by primary PCI in 12 patients, whereas one patient showed a TIMI flow grade 2 after successful PCI. Two-dimensional echocardiographic left ventricular ejection fraction was $47 \pm 9\%$. Twelve patients had ST-segment elevation in one or more anterior precordial leads at basal ECG (1–2.5 mm, average 1.5 ± 0.7 mm).

The results of treadmill exercise stress test are summarized in Table 2. The mean duration of the test was 6 ± 4 minutes and the rate-pressure product at peak exercise 16966 ± 4054 bpm*mmHg. During exercise heart rate increased from 74 ± 10 to 113 ± 16 bpm ($P < 0.001$), and systolic blood pressure from 120 ± 17 to 149 ± 22 mmHg ($P = 0.001$). Compared to rest, an additional ST elevation ≥ 1 mm during exercise occurred in nine patients (69%). ST-segment elevation at peak exercise was 2.5 ± 1.0 mm ($P = 0.001$), for an average increase of 1.0 ± 0.8 mm, compared to rest. No patient developed angina or ST-segment depression in any leads during the test.

Dyskinetic segments of the left ventricle at two-dimensional echocardiography were detectable in six patients (Table 3).

DISCUSSION

Our study is the first one assessing exercise-induced ST-segment changes in anterior ECG leads

Figure 1. (A) Precordial leads showing Q/QS wave at rest; (B) Exercise-induced ST-segment elevation.

with Q/QS waves in patients with acute MI treated by primary PCI.

Our findings show that also these patients, as those in the pre-PCI era,^{21,22} present a high preva-

lence of exercise-induced ST-segment elevation (i.e., about 70%), despite successful coronary artery recanalization by PCI and an excellent TIMI coronary blood flow.

These results lend further support to the hypothesis that, in the clinical context of the recovery phase from a recent acute MI, exercise-induced ST-segment elevation in ECG leads with Q/QS waves does not represent a reliable sign of acute myocardial ischemia or viability.

Previous Studies

The mechanism responsible for ST-segment elevation induced by exercise or pharmacological stress tests in ECG leads with a Q/QS wave pattern in patients with MI is still debated.

Candell-Riera² showed that, when occurring in more than three ECG leads and presenting a biphasic response during dobutamine infusion, it may accurately predict functional recovery following revascularization. Accordingly, Lombardo et al. showed an association between ST-segment elevation and improvement of myocardial contractility

Table 1. Main Clinical Features of Patients

Age (years)	56 ± 9
Sex (M/F)	12/1
Cardiovascular risk factors	
Hypertension	8 (62%)
Diabetes	2 (15%)
History of coronary artery disease	2 (15%)
Hypercholesteremia	7 (54%)
Smoking	8 (62%)
Symptom onset (hour)	2.8 ± 2.0
Creatine kinase peak (mU/mL)	3169.6 ± 1579.0
Creatine kinase-MB peak (mU/mL)	295.7 ± 188.8
Troponin-T peak (ng/mL)	11.7 ± 7.0
Post-PTCA TIMI flow grade 3	12 (92%)
No coronary reflow	3 (23%)
Number of leads with Q/QS leads	4 ± 1
Basal STE in anterior precordial leads	12 (92%)
Exercise peak STE in precordial leads	9 (69%)

Table 2. Main Treadmill Exercise Stress Test Results

	Basal	Exercise peak	P
Test duration (minute)	–	6 ± 4	–
ST segment elevation (mm)	1.5 ± 0.7	2.5 ± 1.0	0.001
Heart rate (bpm)	74 ± 10	113 ± 16	<0.001
Systolic BP (mmHg)	120 ± 17	149 ± 22	0.001
Diastolic BP (mmHg)	74 ± 10	84 ± 11	0.013
Rate pressure product (bpm*mmHg)	8884 ± 1697	16966 ± 4054	<0.001

BP = blood pressure.

in akinetic myocardial segments with low dose dobutamine (myocardial viability), followed by impairment of contractility at high doses of the drug (myocardial ischemia).²³ Furthermore, Margonato et al.^{3,8} showed that exercise-induced ST-segment elevation was associated with reversible perfusion defects on stress thallium-201 myocardial scintigraphy and with significant uptake of ¹⁸F-deoxyglucose in hypoperfused myocardial regions on positron emission tomography (PET).

Thus, these studies strongly suggested that exercise/stress-induced ST-segment elevation often represents a marker of myocardial ischemia/viability.

Other authors, however, showed that, after MI, ST-segment elevation in Q/QS-wave leads at peak exercise is associated with a more significant impairment of left ventricular function, more extensive regional wall motion abnormalities and with the presence of akinetic/dyskinetic myocardial areas at rest.⁷⁻¹⁹ Recently, using symptom-limited exercise stress myocardial scintigraphy with 99m-Tc-sestamibi (MIBI), we showed that, in asymptomatic MI patients, exercise-induced ST-segment elevation in leads with a Q/QS wave pattern was unlikely to represent by itself clinically relevant residual myocardial ischemia, also suggesting an unlikely correlation with the presence of myocardial viability.¹²

In the present study, we assessed the prevalence of exercise-induced ST-segment elevation, early after admission, in a small but highly selected group of patients with Q-wave anterior acute MI treated

by primary PCI. Our data show that a high proportion of these patients presented exercise-induced ST-segment elevation in Q/QS wave ECG leads, despite all had an optimal coronary blood flow restoration and almost all (12 out of 13) also had optimal TIMI coronary blood flow grade. According to selection criteria, no patients developed angina or any other ECG abnormality suggesting myocardial ischemia during the symptom-limited exercise stress test.

Thus, these findings lend further support to the theory that exercise-induced ST-segment elevation in this clinical context is unlikely to represent, by itself, myocardial ischemia or myocardial viability. As known, possible mechanisms of exercise-induced ST-segment elevation in this context include left ventricular wall motion abnormalities and mere heart rate/autonomic related changes.

However, the possibility that myocardial ischemia related to coronary microvascular abnormalities was involved in some of our patients cannot be completely excluded from our data, as we did not attempt to demonstrate the possible presence of myocardial ischemia by diagnostic imaging stress tests in this group. However, although this point deserves appropriate investigation in future studies, this possibility seems unlikely due to the excellent TIMI coronary flow grade in our patients, suggesting optimal coronary reperfusion also at the microvascular level.

REFERENCES

1. Mezilis NE, Parthenakis FI, Kanakarakis 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;21:814-822.

2. Candell-Riera J, Santana-Boado C, Armadans-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;81:12-16.

Table 3. Main Echocardiographic Results

Ejection fraction (%)	47 ± 9
End-diastolic volume (ml)	97 ± 28
End-systolic volume (ml)	51 ± 16
Wall motion score index	16 ± 4
Left ventricular dyscinesia	6 (46%)

3. 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;19:948-952.
4. Lekakis JP, Prassopoulos V, Kostamis P, et al. Dobutamine-induced ST-segment elevation in patients with healed myocardial infarction. A marker of myocardial viability. *J Electrocardiol* 1995;28:91-97.
5. Fox KM, Jonathan A, Selwyn AP. Significance of exercise-induced ST segment elevation in patients with previous myocardial infarction. *Br Heart J* 1983;49:15-19.
6. Dunn RF, Bailey IK, Uren R, et al. Exercise-induced ST-segment elevation. Correlation of thallium-201 myocardial perfusion scanning and coronary arteriography. *Circulation* 1980;61:989-995.
7. Pierard LA, Lancellotti P, Kulbertus HE. ST-segment elevation during dobutamine stress testing predicts functional recovery after acute myocardial infarction. *Am Heart J* 1999;137:500-511.
8. Margonato A, Chierchia SL, Xuereb RG, et al. Specificity and sensitivity of exercise-induced ST segment elevation for detection of residual viability: Comparison with fluorodeoxyglucose and positron emission tomography. *J Am Coll Cardiol* 1995;25:1032-1038.
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. Orsini E, Lattanzi F, Reichenhofer B, Tartarini G. Time-domain analysis of exercise-induced ST-segment elevation in Q-wave myocardial infarction: a useful tool for the screening of myocardial viability. *Ital Heart J* 2001;2:529-538.
11. Bodi V, Sanchis J, Chorro FJ, et al. ST-segment elevation on Q-leads during exercise in patients with ST-segment elevation at rest after myocardial infarction. *Int J Cardiol* 2001;78:41-49.
12. Lanza GA, Sestito A, Giordano A, et al. Scintigraphic results in asymptomatic myocardial infarction patients with exercise-induced ST segment elevation. *Ital Heart J* 2002;3:330-334.
13. Elhendy A, Cornel JH, Roelandt JRTC, et al. Relationship between ST-segment elevation during dobutamine stress test and myocardial viability after a recent myocardial infarction. *Heart* 1997;77:115-121.
14. 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;79:733-737.
15. Elhendy A, Geleijnse ML, Roelandt JR, 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;76:441-448.
16. Hahalis G, Stathopoulos C, Apostolopoulos D, et al. Contribution of the ST elevation/T-wave normalization in Q-wave leads during routine, pre-discharge treadmill exercise test to patient management and risk stratification after acute myocardial infarction. A 2.5-year follow-up study. *J Am Coll Cardiol* 2002;40:62-70.
17. Gorlin R, Klein MD, Sullivan J. Prospective correlative study of ventricular aneurysm. *Am J Med* 1967;42:512-516.
18. Bruce RA, Fisher LD, Pettinger M, et al. ST segment elevation with exercise: a marker for poor ventricular function and poor prognosis. Coronary Artery Surgery Study (CASS) confirmation of Seattle Heart Watch results. *Circulation* 1988;77:897-905.
19. Stiles GL, Rosati RA, Wallace AG. Clinical relevance of exercise-induced ST segment elevation. *Am J Cardiol* 1980;46:931-936.
20. Gewirtz H, Sullivan M, O'Reilly G, et al. Role of myocardial ischemia in the genesis of stress induced ST segment elevation in previous anterior myocardial infarction. *Am J Cardiol* 1983;51:1289-1293.
21. Lahiri A, Balasubramanian V, Millar Craig MW, et al. Exercise-induced ST segment elevation. Electrocardiographic, angiographic, and scintigraphic evaluation. *Br Heart J* 1980;43:582-588.
22. Arora R, Ioachim L, Matza D, et al. The role of ischemia and ventricular asynergy in the genesis of exercise-induced ST elevation. *Clin Cardiol* 1988;11:127-131.
23. Lombardo A, Loperfido F, Pennestri 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.