Timing of Stress Testing in an Asymptomatic Survivor of Inferior Myocardial Infarction

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SUMMARY

Exercise electrocardiography with or without thallium-201 scintigraphy was performed (pre-hospital discharge) in 66 asymptomatic survivors of a first inferior myocardial infarction (IMI). Although coronary angiography revealed an 82% incidence of multivessel coronary artery disease (MV-CAD) in the total cohort, the sensitivity of exercise ECG for MV-CAD in the group with absent anterior ST-depression in the acute phase was low (11%). In contrast the presence of acute phase anterior ST-segment depression improved the yield for MV-CAD to 55%.

Forty-six patients agreed to a symptom-limited exercise ECG plus / minus thallium imaging at 8–10 weeks post IMI. The sensitivity of detecting MV-CAD improved by 15% in patients with no acute phase anterior ST-segment depression and 16% in patients with acute phase anterior ST-segment depression. At each exercise protocol, thallium improved the sensitivity of exercise in detecting ischemia in the noninfarct zone.

It is concluded that following IMI, a high percentage of asymptomatic patients whose acute phase ECG showed anterior ST-segment depression will have MV-CAD detected by heart-rate limited and, more so, by symptom-limited exercise ECG. The detection rate will double in patients with no anterior ST-segment depression if exercise testing is delayed until 8–10 weeks post IMI.

Additional Indexing Words:

Exercise electrocardiography Inferior myocardial infarction Anterior ST depression Timing

EVER since the safety of a limited exercise protocol in the early post-infarction period has been demonstrated,[1),2)] most patients routinely undergo stress testing prior to discharge. Beyond its safety, exercise testing

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Supported by Kuwait University Grant No. MM009.

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Received for publication February 18, 1989.

Accepted April 21, 1989.

in the early post MI period is an excellent prognosticator of future cardiac events in high risk patients.[1)-5)] Patients with inferior MI have a smaller infarct size compared to those with an anterior infarction. However, the strong association of inferior infarction with additional left anterior descending artery (LAD) stenosis[6),7)] will confer additional risk to the survivors. The "reciprocal" anterior ST-segment depression in some inferior infarct patients has been the subject of speculation as to whether it means larger infarct sizes or denotes additional disease in the LAD.[8)-10)] In this study we analyzed the yield of different exercise protocols in detecting ischemia in areas remote from the infarct in 66 asymptomatic survivors of first inferior MI predischarge and at 8–10 weeks post infarction. Additionally, the exercise results are displayed against the presence or absence of acute phase anterior ST-segment depression. Finally, angiographic results are correlated with the results of exercise testing and acute phase ST depression.

Methods

Study patients:

Seventy consecutive male patients admitted to the cardiac care units of 3 general hospitals in Kuwait with the diagnosis of a first inferior wall myocardial infarction were studied prospectively. They ranged in age between 27–60 years. The diagnosis of acute inferior myocardial infarction was accepted if all the following criteria were present:

1. Chest pain lasting 30 min or longer;
2. ST-segment elevation of at least 1 mm and new abnormal Q waves (0.04 sec duration) developing in at least 2 of the inferior leads (II, III, aV_F) within 48 hours, and
3. at least a two-fold elevation of serum creatine kinase with a positive MB fraction.

Patients were excluded for any of the following reasons:

1. An interval between the onset of symptoms and first electrocardiogram of more than 24 hours;
2. history of electrocardiographic evidence of previous myocardial infarction;
3. non-Q myocardial infarction;
4. evidence of new anterior infarction on the electrocardiogram; or
5. presence of left ventricular hypertrophy and strain or left bundle branch block.

Patients were categorized according to the Killip classification.[11)] Their peak serum creatine phosphokinase (CPK) was determined from 3 consecutive

samples collected on admission and on the next 2 days.

Electrocardiography:

Standard 12-lead electrocardiograms were recorded (25 mm/sec, 1 cm= 1 mv) at the time of presentation on the emergency floor, on admission to the coronary care unit and once daily thereafter. Significant anterior ST-segment depression was defined as 0.1 mv or greater occurring 0.08 sec after the J point in two or more of the precordial leads, V_1—V_4.

Exercise electrocardiography:

Patients were exercised on a treadmill according to the Naughton protocol[12] on days 10–12 after the onset of infarction. Patients already on β-blockers had their medication stopped 2 days before the test. Patients were exercised to 70% of their maximal heart rate (range 120–135 beats/min). The exercise was terminated if patients developed symptoms (angina pectoris, dyspnea, dizziness) had frequent (more than 10/min) multifocal or paired extrasystoles; ST-segment depression of 2 mm remote from the infarction zone or a fall in systolic blood pressure of 10 mmHg below peak value at the beginning of exercise. Resting 12-lead ECG was done for all patients in supine and standing positions at the beginning, after each 2 min of exercise and at 3, 6 and 9 min in the recovery period. All patients had continuous ECG monitoring of leads I, II, aV_F, V_1 and V_6 during exercise. The physician supervising the exercise electrocardiography was blinded to the results of the ECG's taken in the acute phase of myocardial infarction.

Eleven patients refusing revascularization procedure after early positive test and cardiac catheterization results, and 35 patients with negative early exercise tests underwent a second stress test at 8–10 weeks after infarction. There was no change in the patients' symptomatology between the 2 exercise tests. The Bruce protocol was used in the later test. Earlier precautions for test termination were followed as described above. Horizontal or downsloping depression of the ST segment of >0.1 mv persisting for 0.08 sec beyond the J points in leads other than those reflecting the infarct was considered abnormal.

Thallium-201 scintigraphy:

At peak exercise heart rate, the patient was injected with 2 mci thallium-201 chloride through a previously placed intravenous cannula. The exercise was continued for one further minute. Imaging was started within 5 min post injection using a GE 400 Gamma Camera, interfaced with a STAR computer. Three views were obtained; anterior, 45° and 70° left anterior

oblique (LAO) using an LEHR collimator, a triple pulse height of 80, 135 and 167 KeV, a 20% window and hardware zoom of 1.6. Acquisition took 400 sec per view. The same positions were repeated 3 hours later observing the same parameters. All data were stored on magnetic disc with a 128 $\times$128 matrix size. Quantitative analysis was carried out according to the General Electric STAR protocol. In brief, the anterior, 45° and 70° LAO images were divided into 9 myocardial segments, and each segment was evaluated separately. Criteria for classifying a scan segment as abnormal were based on the relative quantitative evaluation of both the initial images (5 min after exercise) and delayed images (3 hrs after exercise).

A normal scintigram was defined as one which showed uniform thallium uptake during the initial and post exercise phases. An abnormal myocardial segment was defined as one with uptake reduced by 25% on the initial images which subsequently normalized. Each thallium study was reviewed by 2 independent observers without prior knowledge of the clinical and ECG data. In cases of discordant interpretations a consensus reading with a third observer present was used.

Left ventriculography and coronary arteriography:

Left ventriculography and selective coronary arteriography were done in multiple projections using the Judkins technique at 4–6 weeks from the infarct day. Informed consent was obtained from all patients. Four patients refused and were excluded from further analysis. Each study was interpreted by 2 observers independently and differences were resolved by conference. Left ventricular ejection fraction was calculated by the single plane method in the right anterior oblique projection. Significant stenosis was defined as 50% luminal diameter narrowing. Stenosis of a major diagonal branch was considered left anterior descending artery disease. Similarly stenosis of a major obtuse marginal branch was considered to be stenosis of the left circumflex artery.

Statistical analysis:

The results are given as mean$\pm$standard deviation. Comparison is made between patients divided into 2 groups on the basis of presence or absence of significant anterior ST-segment depression on admission. Means were compared with Student's t-test. A probablity value of <0.05 was considered to be significant. Comparisons of different frequencies were analyzed with the chi-square method or Fisher's test.

RESULTS

Patients characteristics:

Of the 66 patients catheterized, 37 had no acute phase anterior ST-segment depression (group A). Group B comprised 29 patients with anterior ST-segment depression. Three of the 4 patients refusing catheterization were in group B. The levels of CPK were higher for group B patients. There was a proportionately higher percentage of patients in Killip class II in group B (31%) vs group A (14%) (Table I).

Angiographic results:

The left ventricular ejection fraction was higher for group A patients (Table II). The percentage of multivessel coronary artery disease (MV-CAD) for the full cohort was 82% but in group B, MV-CAD was found in 90% of patients. Luminal narrowing of 70% or more was present in at least 2 coronary arteries in all but 3 patients with MV-CAD. These 3 had narrowing of >70% in one-vessel and 50–70% in other vessel(s). There were 3 patients, all in group A and with ages of 27, 27 and 30 years, who

Table I. Clinical Characteristics of Inferior Myocardial Infarction Patients

	Inferior MI		
	Absence of anterior ST-segment depression (Group A)	Presence of anterior ST-segment depression (Group B)	Level of significance
No. of patients	37	29	
Age	45.5(8.9)	45.3(9.8)	N.S.
Killip class I	32	20	
II	5	9	
Peak CPK	921(341)	1479(416)	$p<0.05$

CPK=serum creatine phosphokinase, values in parenthesis equal standard deviation of the mean; N.S.=not significant.

Table II. Left Ventricular Ejection Fraction and Coronary Artery Anatomy in Inferior Myocardial Infarction Subgroups

Parameters		Group A	Group B	Level of significance
LVEF		55.6(7.5)	49.4(8.0)	$p<0.05$
	SVD	9	3	
Coronary artery disease	MVD	28(76%)	26(90%)	N.S.

LVEF=left ventricular ejection fraction; SVD=single vessel coronary artery disease; MVD=multivessel coronary artery disease.

had insignificant (<30% stenosis) disease of the right coronary artery only.

Exercise electrocardiography:

A. Early protocol. All patients underwent early (70% of expected maximal heart rate) exercise ECG testing. Thallium scintigraphy was performed in the same setting for 36 (18 in each group). There were only 4/37 patients (11%) who developed ischemia with exercise in the noninfarct zone in group A. Only 2 of these patients developed ST-segment depression in the anterior leads. However all showed reversible defects in the thallium study. In contrast 16/29 (55%) of group B showed noninfarct zone reversible ischemia ($p<0.05$). In group B, 12 had exercise induced ischemia by ECG and thallium. The remaining 4 patients had only a reversible thallium defect in the noninfarct zone with exercise.

B. Late exercise protocol. Twenty-seven patients in group A and 19 in group B underwent late (Bruce protocol) exercise ECG. Thallium-201 scintigraphy was performed in 15 of the 46 (9 in group A and 6 in group B) patients. The exercise-induced ischemia was demonstrated only by thallium scintigraphy in 1 patient in group A. In all others the ECG and thallium results were concordant. Table III displays the results of early and late exercise in the 2 groups. While in the majority of cases in both groups the early and late exercise results matched, there was a pick up of 7 additional cases (15% of patients) of ischemia at HR's 155–160/min which were not picked up earlier with the heart-rate limited protocol. These patients were fairly evenly divided between the 2 groups. Finally, the symptom-limited exercise protocol detected 22% (6/27) MV-CAD in group A and 63% (12/19) in group B patients.

Table III. Results of Early and Late Exercise Electrocardiography in Inferior Myocardial Infarction Patients

	Group A			Group B		
	Early exercise		Late exercise	Early exercise		Late exercise
Test results	No. of patients			No. of patients		
Concordance of early and late test	−	(21)	−	−	(7)	−
	+	(2)	+	+	(9)	+
Discordance of early and late test	−	(4)	+	−	(3)	+
Total	27			19		

(−) Result means no ST-segment depression and/or no decreased thallium uptake with exercise in noninfarcted zone.

(+) Result means ST-segment depression (≥1 mm) and/or reversible thallium defect with exercise.

Discussion

The prognosis of asymptomatic survivors of myocardial infarction is rather good.[13),14)] Since the extent of myocardial damage is the main prognostic factor, the inferior myocardial infarction survivor will do particularly well. In this group the LVEF is usually minimally depressed if at all. However the LVEF is more depressed in the subgroup of inferior infarction patients with anterior ST-segment depression in the acute phase (Table II). It is fair to state that this subgroup has larger infarct sizes as judged by higher CPK (Table I). Several echocardiographic and radionuclide angiographic studies attest to the same conclusion.[3),8)-10),15)-17)]

The other prognostic determinant in the post infarction patient is significant coronary artery disease in the noninfarcted myocardium.[3),4),14),18)] Exercise electrocardiography with or without thallium-201 scintigraphy has had a good track record in predicting future cardiac events in patients showing ischemia with stress.[1)-3),14),15)]

Early (predischarge) exercise electrocardiographic results have been utilized to predict future cardiac events and assess the patient for cardiac rehabilitation. Early testing is especially favored since most cardiac events occur early after the first infarction and usually within the first 6 months.[18)]

Inferior infarct patients with absent ST-segment depression in the acute phase give a low yield for exercise-induced ischemia in the noninfarcted zone. In group A only 4/37 patients showed ischemia in early (rate-limited) exercise. Although all 4 were true positives for MV-CAD, the exercise protocol failed to uncover the large percentage of patients with MV-CAD, which in this group amounted to 76%. On the other hand the patients with acute phase ST-segment depression showed a greater percentage of ischemia in the noninfarct zone (55%) with predischarge-exercise testing. Of interest is that 25% of patients showing ischemia by thallium did not have electrocardiographic changes. Thallium-201 scintigraphy has been shown to improve the yield for stress-induced ischemia by 10–15%.[3),19)] Although the percentage of patients with MV-CAD for this subgroup borders on 90%, this cannot explain the better yield for exercise-induced ischemia in these patients. It may be that the larger infarct size diminishes the threshold for stress-induced ischemia in the noninfarcted zone.

Following catheterization 46 patients agreed to symptom-limited exercise ECG testing with or without thallium scintigraphy. Of these patients, 11 had previously shown ischemia on their predischarge exercise testing. These patients had refused revascularization procedures. The second round of exercise testing was preconditioned on stability of the patients symptom-

atology. The patients showing ischemia in both subgroups again developed ischemic manifestations at similar, or insignificantly higher, heart rates. However, 7 additional patients were shown to develop ischemia (i.e. ischemic changes in the zone remote from infarction) at higher heart rates. These 7 patients were evenly divided with respect to acute phase anterior ST-segment depression or its absence. The overall percentage of MV-CAD for patients undergoing late exercise testing was 85%.

We conclude that there is a high incidence (82%) of MV-CAD in asymptomatic survivors of a first inferior infarction. This association has been observed previously.[6),7)] Secondly, exercise electrocardiography (especially when combined with thallium scintigraphy) unveils ischemia of the noninfarcted myocardium best in the patient with acute phase anterior ST-segment depression. Symptom-limited exercise testing at 8–10 weeks improves the sensitivity of stress-induced ischemia as a marker for MV-CAD in both subgroups. This is accomplished without increasing the risk of untoward effects in the interim, at least for patients in this study. Despite the better sensitivity of late exercise testing (especially when combined with thallium imaging) a sizeable proportion of patients with MV-CAD do not demonstrate ischemia with our testing modalities.

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