Negative and positive predictive values of routine exercise testing in stable, medically-treated patients several years following a Q-wave myocardial infarction

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Key words:
Coronary artery disease; Exercise test; Myocardial infarction; Prognosis.

Background. **Exercise testing (ET) is the preferred initial strategy for risk stratification after acute myocardial infarction (MI) in patients who are able to exercise and have an interpretable electrocardiogram (ECG). Although the current guidelines do not recommend annual follow-up ET of symptom-free patients years after MI, this is still common practice worldwide. Thus, this study was undertaken to explore the value of ET in the prediction of cardiac events in stable, medically-treated patients with a remote history of Q-wave MI.**

Methods. **Seven hundred sixty-six consecutive patients (male gender 89%, mean age 57 ± 8.6 years) with a remote history of Q-wave MI (mean time from MI 2.8 ± 0.75 years), who underwent Bruce treadmill ET and whose data were prospectively entered into our institutional database, were enrolled. Patients were followed up for an average of 7 ± 0.6 years. The endpoints were: 1) primary (cardiac death or non-fatal reinfarction), 2) secondary (cardiac death, non-fatal reinfarction or unstable angina), and 3) all-cause mortality.**

Results. **Two hundred and eighty-two recurrent ischemic events occurred [cardiac death (n = 67), non-fatal infarction (n = 54), and unstable angina (n = 161)] and an additional 103 patients underwent revascularization procedures. Multivariate risk predictors for the primary endpoints were: older age relative risk-RR 1.04 (95% confidence interval-CI 1.01-1.06 per year), baseline heart rate ≥ 90 b/min RR 2.34 (95% CI 1.37-4.0), and ST segment depression at rest ECG RR 1.91 (95% CI 1.22-2.98). For the secondary endpoints the predictors were: older age RR 1.02 (95% CI 1.01-1.04 per year), baseline heart rate ≥ 90 b/min RR 1.61 (95% CI 1.06-2.45), ST segment depression at rest ECG RR 1.8 (95% CI 1.33-2.44), exercise angina RR 1.94 (95% CI 1.4-2.69), and exercise time stage ≤ II RR 1.56 (95% CI 1.16-2.1). The addition of exercise variables improved the predictive power of the multivariate model only for secondary and all-cause mortality endpoints. Furthermore, clinical stratification alone had a predictive value comparable to that of ET results.**

Conclusions. **Although the identification of patients at risk for recurrent cardiac events is still the main goal of re-stratification in stable, asymptomatic patients with previous MI, the value of ET in these cases is negligible. Markers of exercise ischemia or ventricular dysfunction would be weak at best. The poor predictive performance of ET severely limits its usefulness as a screening measure for identifying patients likely to benefit from cardiac catheterization and revascularization. Therefore, cost-benefit considerations would suggest that risk stratification by means of ET in stable, asymptomatic patients with a remote history of Q-wave MI is inappropriate.**

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Introduction

Coronary risk stratification is in all respects of primary importance in the examination and management of patients with documented coronary artery disease and it is a stepwise process including data from the patient's history, clinical evaluation and several other laboratory tests[1]. However, the value of any further test used must always be considered in the light of what is added to what is already known about the patient's risk status. Because of its simplicity and widespread familiarity, exercise testing (ET) is usually the preferred initial strategy for risk stratification in patients who are able to exercise and have an interpretable electrocardiogram (ECG)[2]. The role of pre-discharge ET after myocardial infarction (MI) is well defined[2,3], while the utility of annual follow-up ET for the detection of silent coronary artery disease activity and progression,

is less clear[4]. Despite the fact that current American College of Cardiology/American Heart Association clinical guidelines discourage routine ET for asymptomatic individuals[2] with a remote history of Q-wave MI, this is quite a widespread habit and, given the very large number of patients with such a history, has serious public-health implications. Thus, this study was planned to assess the ability of annual follow-up ET to predict the prognosis in stable, asymptomatic medically-treated patients several years after a Q-wave MI.

Methods

Patient selection. Among more than 10 000 ETs performed between May 1988 and January 1991 at our Institution, we retrospectively identified 766 consecutive, stable, asymptomatic patients who underwent treadmill ET at least 1 year after the first Q-wave MI. All subjects were referred to our Institution by their general practitioners or by our outpatients' clinic, and ET was part of the annual follow-up evaluation at that time. The diagnosis of MI required Q-wave confirmation at resting ECG and a medical history suggestive of this event (hospitalization for prolonged chest pain with typical ECG and enzyme changes) in all patients. Due to the different natural histories of Q-wave and non-Q-wave MI[5], patients with non-Q-wave MI were not included. Abnormal baseline ST/T changes were not considered an exclusion criteria for further study because, in the clinical setting, this is a common finding in patients with previous MI and does not significantly alter ET analysis[2,6].

Exercise test. All patients underwent a symptom-limited treadmill ET (Bruce protocol) with continuous 12-lead ECG monitoring under fasting conditions. Drug therapy was suspended at least 24 hours before the test. The blood pressure was measured at rest and every 3 min during exercise and recovery. Exercise was terminated when the target heart rate (220 b/min minus age in years) was reached or when the patient presented with the usual symptoms (severe chest pain, severe fatigue, hypotension or ventricular tachycardia). The ET was considered positive for exercise-induced ischemia if there was at least a 0.1 mV (or 0.2 mV when ascending) horizontal or downsloping ST segment depression 80 ms after the J-point, without chest pain or with typical angina, or if there was at least an additional 0.1 mV ST segment depression. The ST segment/heart rate index was calculated by dividing the maximal, additional ST segment depression at the end of exercise, corrected for any rest ST segment depression in that lead on the supine pre-exercise control ECG, by the exercise-induced change in heart rate. A positive ST segment/heart rate index was defined as ≥ 160 μV/beat/min[7].

At the time of ET, a short clinical history and the main exercise parameters and symptoms at rest, during exercise and recovery were recorded for every single patient and all data stored prospectively in the database of the Division of Cardiology, as previously described[8].

Follow-up. Patients entered into the database were then followed continuously in our outpatients' clinic or by their private physicians. Medical therapy was not standardized and was left to the discretion of the patient's personal physician. The decision to recommend revascularization procedures was made by the clinician providing care for the patient and was usually based on increasing symptom severity refractory to medical therapy, or angiographic findings suggestive of left main coronary disease or three-vessel disease with a left ventricular ejection fraction < 40%. Follow-up data were updated yearly by checking hospital records or the databases of the Local Registry Office or by phone interviews.

Pre-specified and *post-hoc* endpoints. The pre-specified combined endpoints of the study were: 1) cardiac death or non-fatal reinfarction, whichever occurred first (primary endpoint), 2) cardiac death, non-fatal reinfarction or unstable angina, whichever occurred first (secondary endpoint), and 3) all-cause mortality as a single endpoint.

In order to avoid bias, physician-determined revascularization procedures (coronary artery bypass graft and coronary angioplasty) were excluded as endpoints. However, after carrying out the planned analyses, data were re-analyzed using the secondary cardiac events (cardiac death, non-fatal reinfarction or unstable angina) plus revascularization procedures, whichever occurred first, as endpoints (composite endpoint). Furthermore, to better understand the value of pre-test risk stratification for each patient, a clinical risk score was calculated as the simple arithmetic sum of single clinical factors (age > 65 years, rest ST segment depression and rest heart rate ≥ 90 b/min), based on the univariate-adjusted risk relationship. The risk score ranged from 0 to 3 and, after a best-fitted analysis, a cut-off value of 2 was set to discriminate between low (< 2 points) and high (≥ 2 points) risk.

The criteria for reinfarction were the same as those used for defining the first MI. Reinfarction was considered fatal when it was followed by cardiac death within 4 days of the recurrence. Patients who, following reinfarction, had survived the period of hospitalization were categorized as having had a non-fatal reinfarction. Unstable angina required hospital admission for an increase in the frequency or severity of typical angina symptoms, with either ischemic ST segment or T-wave changes. The occurrence of interventions (coronary angiography, coronary artery bypass graft or coronary angioplasty) was confirmed by hospital records

or physician's office records. Sudden, unobserved cardiac death occurring out of hospital was not considered to be associated with infarction. During follow-up, only the first reinfarction, first hospitalization for unstable angina or first revascularization were considered.

Statistical analysis. Data are expressed as mean ± SD. A χ^2 test was used to compare categorical variables. A two-sided p value < 0.05 was regarded as statistically significant. Univariate analysis for each of the endpoints was performed using all clinical and ET variables. Cumulative endpoint rates for all variables measured are initially reported as raw event rates with the relative risk (RR) of a positive test and its 95% confidence intervals (CI)[9]. The sensitivity, specificity and positive and negative predictive values of ET for predicting 6-year event rates were calculated according to standard definitions. Multivariate analysis was performed using the Cox proportional hazards regression model[10] for each of the endpoints. An initial model was constructed using the clinical variables of potential significance identified at univariate analysis. Exercise variables were then added to the model using a sequential forward selection procedure. The entry significance threshold into the model was $p < 0.05$ whereas a p value ≥ 0.10 was used for removing a variable; the maximum number of interactions was 20. The cumulative primary and secondary endpoints or mortality rates over time were described by Kaplan-Meier curves[11] and differences between curves were assessed by the log-rank statistics[12]. Patients who died of non-cardiac causes were censored at the time of death. Subjects who underwent revascularization procedures (coronary artery bypass graft or coronary angioplasty) during follow-up were censored from the analysis at the time of the procedures. The reported analyses used the database released on September 15, 1996.

Results

Study patients and clinical parameters. The clinical characteristics of the study population are shown in table I. All patients were stable and asymptomatic at the time of the ET which was performed at a mean of 2.8 ± 0.75 years after their first Q-wave MI. The average age of the study population was 57 ± 8.6 years (range 26-84 years) and 89% of the patients were male. The location of the MI was anterior in one third of the patients. Nearly 85% of the patients were taking antiplatelet agents (mainly aspirin) and 28% were on beta-blockers. The mean ejection fraction as measured at echocardiography or angiography was 56 ± 12%. It was available for 475 out of 766 patients (62%). After enrollment, coronary angiography was performed in 223 (29%) patients (42 with one-vessel disease, 75 with two-vessel disease, and 106 with three-vessel disease). Follow-up data concerning 32 (4%) patients were missing. The average length of follow-up for the study population was 7 ± 0.6 years (range 0.04-8.5 years). Two hundred and eighty-two recurrent ischemic events occurred during follow-up. Seventy-six patients died (9 of non-cardiac causes: 7 neoplasms, 1 stroke, and 1 acute renal failure respectively), 62 had a reinfarction (fatal in 8 patients), 161 developed unstable angina, and 103 underwent revascularization procedures. Only 11 patients (10%) underwent coronary angioplasty or coronary artery bypass graft before a first recurrent cardiac event. Thus, 229 patients had at least one recurrent ischemic event (death 20%, non-fatal reinfarction 21%, and unstable angina 59%) (Table II).

Table I. Main clinical features of the study population.

Characteristics	Population (n=766)
Clinical features	
Age (years)	57 ± 8.6
Male gender	89%
Anterior MI	32%
Inferior MI	47%
Posterior/lateral MI	21%
Aspirin	85%
Beta-blockers	28%
Ejection fraction (%)	56 ± 12
ST depression at rest ECG	63%
Exercise features	
Exercise duration (s)	506 ± 164
Stage ≤ II	21%
Peak HR < 85% of target HR	58%
ST depression ≥ 1.0 mm	38%
ST depression stage ≤ II	9%
Angina	14%
Abnormal ST segment/HR index	39%

HR = heart rate; MI = myocardial infarction.

Univariate analysis of clinical and exercise test variables. At univariate analysis, several clinical and ET variables were related to the endpoints. However, although exercise-induced ST segment depression or angina occurred more often in patients with recurrent events, the association was statistically significant only when the secondary or composite endpoint was considered or when it was related to work capacity. Reduced exercise capacity (ET time stage ≤ II) as well as a reduced blood pressure increase with exercise carried an increased risk for secondary endpoints or all-cause mortality. The risk curves for primary endpoints occurring within 6 years of follow-up according to exercise ST segment depression and workload are shown in figure 1.

Multivariate predictors of risk. Multivariate proportional hazards models are presented in table III. The most useful independent predictors for all of the endpoints

Table II. Frequency of endpoint events.

Event	No. patients	Event rate*	
		1-year %	6-year %
Specific events			
All-cause death	76	2.5	9.9
Cardiac death	67	2.5	8.9
Non-fatal reinfarction	54	1.2	7.6
Unstable angina	161	8.5	23
PTCA or CABG	103	5.9	15
Coronary angiograms	223	17	30
First recurrent event**			
Cardiac death, non-fatal reinfarction	106	3.1	15
Cardiac death, non-fatal reinfarction, unstable angina	229	10	32
Cardiac death, non-fatal reinfarction, unstable angina, revascularization procedures	275	12	38

CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angioplasty. * from Kaplan-Meier cumulative-event curves; ** one event per patient, whichever occurred first.

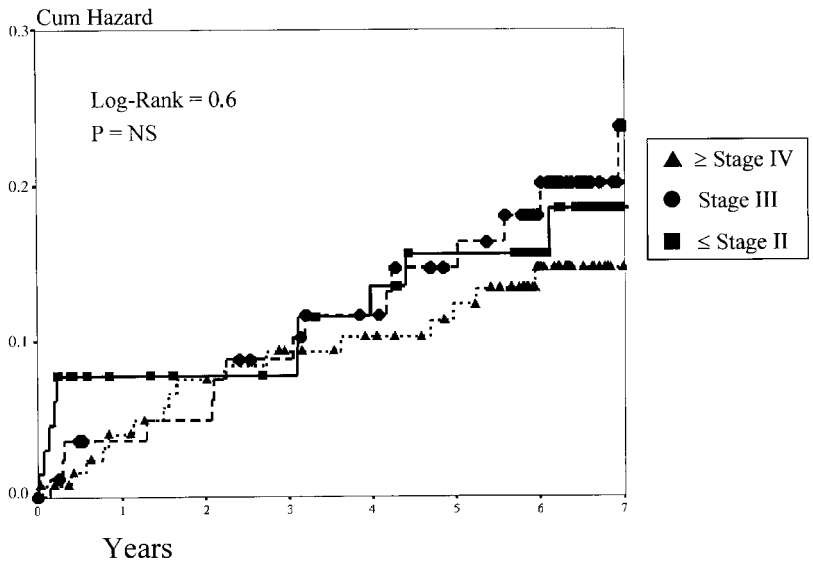

Figure 1. *Kaplan-Meier analysis for the time to the primary endpoint according to exercise ST segment depression and workload.*

were: older age and a baseline heart rate ≥ 90 b/min, both markers of increased risk. The addition of ET variables to clinical parameters improved the predictive power of the model only for secondary (χ^2 36.752, degrees of freedom-df 2, $p < 0.001$), composite (χ^2 96.59, df 2, $p < 0.001$), and all-cause mortality endpoints (χ^2 5.09, $p < 0.05$). Furthermore, variables reflecting reduced exercise ability (older age, exercise time stage ≤ II) or global cardiac dysfunction (anterior MI, baseline heart rate ≥ 90 b/min, ST segment depression at rest ECG) were more powerful predictors than variables reflecting ischemia as such.

Predictive accuracy of clinical and exercise test variables. The sensitivity, specificity and predictive accuracy of these variables were evaluated using the 6-year event rates (Table IV). For the group as a whole, the positive predictive value according to any clinical or exercise variable ranged from 13 to 24% for either a non-fatal reinfarction or cardiac death and from 29 to 52% for non-fatal reinfarction, unstable angina or death. The negative predictive accuracy for the same endpoints ranged from 74 to 87% and from 66 to 74% respectively. Furthermore, the limited clinical value of individual ET results becomes evident when event rates and absolute numbers are analyzed in a flow diagram (Fig. 2) relating the clinical risk profile and ET results. For example, among patients with a high clinical risk score and a positive ET (4% of the study population, n = 34), 26% (n = 9) developed the primary and 41% (n = 14)

Table III. Multivariate analysis by Cox proportional hazards model for each of the endpoints.

Variable	χ^2	RR (95% CI)	p
*Primary endpoint**			
Clinical			
Older age (per year)	10.27	1.04 (1.01-1.06)	0.0014
Baseline HR ≥ 90 b/min	9.83	2.34 (1.37-4.0)	0.0017
ST depression at rest ECG	8.2	1.91 (1.22-2.98)	0.0042
Secondary endpoint			
Clinical only			
Older age (per year)	10.4	1.02 (1.01-1.04)	0.0013
Baseline HR ≥ 90 b/min	5.1	1.61 (1.06-2.45)	0.023
ST depression at rest ECG	18.8	1.93 (1.43-2.61)	< 0.0001
Clinical and exercise			
Older age (per year)	6.38	1.02 (1.0-1.03)	0.011
Baseline HR ≥ 90 b/min	5.04	1.61 (1.06-2.44)	0.024
ST depression at rest ECG	14.85	1.8 (1.33-2.44)	0.0001
Exercise angina	16.27	1.94 (1.4-2.69)	0.0001
Exercise time stage ≤ II	9.0	1.56 (1.16-2.1)	0.0027
Composite endpoint			
Clinical only			
Older age (per year)	7.5	1.02 (1.0-1.05)	0.005
ST depression at rest ECG	26.8	2.07 (1.57-2.73)	< 0.0001
Clinical and exercise			
ST depression at rest ECG	21.39	1.9 (1.45-2.53)	0.0001
Exercise angina	23.26	2.11 (1.55-2.85)	0.0001
Exercise time stage ≤ II	25.77	1.95 (1.5-2.53)	0.0001
Abnormal ST segment/HR index	10.87	1.53 (1.18-1.97)	0.001

The addition of exercise variables improved the predictive power of the model for secondary (χ^2 36.752, df 2, $p < 0.001$) and composite (χ^2 96.59, df 2, $p < 0.001$) endpoints. CI = confidence interval; df = degrees of freedom; HR = heart rate; RR = relative risk. * no exercise variable was independently significant.

Table IV. Sensitivity, specificity and predictive values of exercise features for the 6-year endpoints.

Variables	No. patients	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Primary endpoint					
Exercise time stage ≤ II	163 (21%)	28	80	18	87
Exercise angina	105 (14%)	17	87	17	87
Exercise ST depression > 2 mm	206 (27%)	26	73	13	86
Positive ST/HR index	302 (39%)	43	61	15	87
ST depression stage ≤ II	69 (9%)	10	91	16	86
Secondary endpoint					
Exercise time stage ≤ II	163 (21%)	29	82	41	73
Exercise angina	105 (14%)	22	90	48	73
Exercise ST depression > 2 mm	206 (27%)	32	75	36	72
Positive ST/HR index	302 (39%)	48	64	36	74
ST depression stage ≤ II	69 (9%)	15	94	52	72

HR = heart rate; NPV = negative predictive value; PPV = positive predictive value.

the secondary endpoint respectively. However, 25% of the remaining 84 patients (n = 21) with a high clinical risk score and a negative or non-diagnostic ET developed the primary and 41% (n = 35) the secondary endpoint respectively. Again, among patients with a low clinical risk score and a positive ET (26% of the study population, n = 198), 10% (n = 20) developed the primary and 30% (n = 60) the secondary endpoint respectively. However, 12% of the remaining 450 patients (n = 56) with a low clinical risk score and a negative or non-diagnostic ET developed the primary and 26% (n = 120) the secondary endpoint respectively. Thus, the majority of patients who subsequently had an event had a negative or non-diagnostic ET at enrollment. In addition, as graphically shown in figure 3, ET results only minimally improve clinical risk stratification alone.

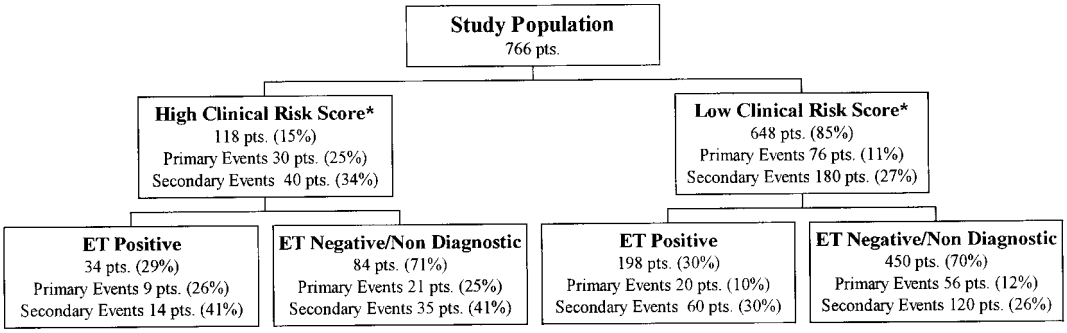

Figure 2. *Flow diagram showing the relationship between the clinical risk profile and exercise test (ET) results. * high clinical risk score defined as at least two of the following: age ≥ 65 years, rest ST segment depression, rest heart rate ≥ 90 b/min; low clinical risk score defined as less than two of the previous parameters.*

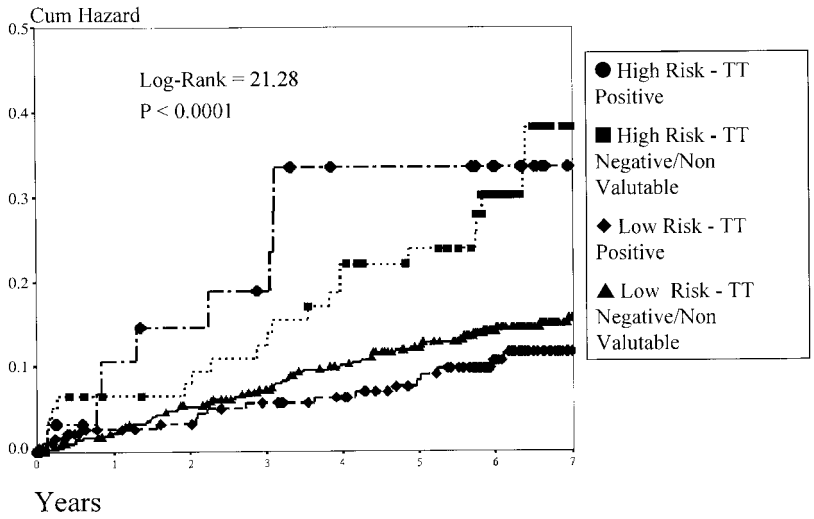

Figure 3. *Kaplan-Meier analysis for the time to the primary endpoint according to the clinical risk profile and exercise test results.*

Discussion

Interpretation of these results requires a clear understanding of the patient population that we studied. Our patients were definitively a low-risk population because all of them were stable and asymptomatic and able to exercise several years after a Q-wave MI. For all of them the ET was part of the annual follow-up evaluation performed in our Institution at that time. Thus, our main purpose was to assess if there is still a role for this policy in such a low-risk population. Our observations reveal that ET does not allow the identification of patients at risk of recurrence. Even the evaluation of indirect indexes of left ventricular dysfunction would be disappointing at best. Furthermore, the poor predictive accuracy limits the role of ET in clinical practice, when the test is used to screen patients likely to benefit from cardiac catheterization and revascularization. On the other hand, clinical risk stratification alone would have comparable results in such a low-risk population.

Failure of exercise-induced ischemia to predict recurrent ischemic events. ET, although commonly considered of pivotal importance for risk assessment in the early phases following MI[2,4], has not been a good predictor of coronary events when employed in the late phases[13-15] or when assessing hard events such as nonfatal reinfarction or death[16-18]. In fact, several studies[14,19] concerning very low-risk populations similar to the present one, detected only a borderline association between markers of exercise ischemia and future cardiac events. This finding is consistent with the notion that it is plaque composition and vulnerability, rather than plaque size, that matters in provoking coronary occlusion[20]. Hemodynamically significant lesions, although likely to result in a positive ET or, if advanced, in symptomatic angina, may not necessarily result in MI or sudden coronary death. The mechanism of MI or death involves mainly the sudden worsening of a mild stenosis due to plaque rupture and thrombosis[21].

"Hemodynamic" variables as predictors of coronary events. The finding that the most predictive ET variables were measures of exercise ability, which possibly operate as surrogates of left ventricular dysfunc-

tion, is not surprising. Several other studies emphasized the utility of exercise variables related to left ventricular dysfunction, such as limited exercise capacity[13,14,19,22,23], failure to increase systolic blood pressure[13-15,19] or inability to reach the target heart rate[13-15], in the formulation of a prognosis. Furthermore, most of the strongest predictors detected in our study, such as anterior MI, a baseline heart rate ≥ 90 b/min and ST segment depression at the rest ECG, are indirect indexes of left ventricular dysfunction or of permanent myocardial damage as well as of reversible ischemia[13].

Risk stratification in stable patients several years after myocardial infarction: is exercise test valuable or worthless? The results of this study suggest that despite a significant relation between exercise-induced ischemia at low workloads or limited exercise capacity and recurrent cardiac events, the poor predictive accuracy limits the role of ET in clinical practice. In fact, implicit in the process of risk stratification is the recognition that myocardial revascularization may improve outcome in patients identified as being at high risk during medical therapy[24]. On the other hand, myocardial revascularization will have little effect on the excellent prognosis of very low-risk subgroups. Thus, the survival benefits of revascularization depend mainly on the baseline level of medical risk. In this study, patients < 65 years old (more than two thirds of the population) had a 6-year survival rate of 91% (average annual mortality 1.5%). Since the risk of coronary artery bypass graft is of the order of 2-4%, their mortality in the next year would be higher with surgery than with medical therapy. Moreover, in our study exercise angina or short exercise duration were mainly predictive of unstable angina, which is an event that allows time for therapy in most cases, as opposed to the endpoints of death or MI, which do not permit therapeutic interventions. Therefore, the poor predictive accuracy of ET would have led to many unnecessary invasive investigations as well as to several inappropriate revascularization procedures on the basis of a positive result.

In addition, it is noteworthy that most of our best predictors could have been easily detected during clinical evaluation alone while ET added minimal information to what we already knew. Thus, such a low-risk population has an excellent prognosis and may be safely managed by careful observation and symptomatic medical therapy without further testing.

Study limitations. This study is an observational one and therefore pre-test referrals may be biased. However, in our Institution it was current practice, at the time of the study, to perform annual follow-up ET for risk restratification in asymptomatic patients several years after MI. Thus, it is quite reasonable that almost all low-risk, asymptomatic patients with a previous MI referred to our clinic were enrolled. That 14% of the patients had angina while on the treadmill would not be surprising, because many apparently symptom-free patients may actually manifest angina if stressed enough. Furthermore, medical therapy was withheld for 24 hours before ET. Discontinuation of these drugs might have enhanced the sensitivity of ET although the percentage of subjects on beta-blockers was low (28%). Moreover, ET has an acceptable power in the risk stratification of patients at low or high risk while it performs poorly in the intermediate-risk setting[2]. In the latter case radionuclide imaging or stress echocardiography, which are more powerful indicators of coronary anatomy and prognosis[25-27], are more useful for further risk stratification. In addition, our conclusions cannot be extended to other settings (prior to major surgery or when counseling patients and their families about daily activities). Data on risk factors (smoking, diabetes, hypercholesterolemia, etc.) were not available and it is well known how predictive they could be[28].

Our data refer primarily to a pre-thrombolytic mid '80s population with less than 10% of subjects submitted to thrombolysis during the acute phase of MI. Nowadays, this point could render the real meaning of our conclusions doubtful. However, although thrombolysis has proved to have prolonged benefits and in spite of the growing number of treated patients[3], this treatment is still underused in different settings in which very large populations are treated ("real world", rural or community hospitals, outside the United States)[29]. Thus, we believe that our population is still representative of several conservative medical contexts.

One of the major limitations of our study was the fact that medical and surgical management after enrollment were not controlled. The decision for revascularization is influenced by multiple, uncontrollable patient and physician personal biases. In fact, in our study, when secondary endpoints and revascularization were combined, several ischemic ET variables were associated with an increased rate of events (Table III). The significance of these findings is difficult to interpret since the ischemic test results were probably used in reaching the decision to perform the surgical procedures. Thus, since revascularization is an elective procedure rather than a potentially preventable ischemic event, it may not be appropriate to include it as an endpoint in survival analysis. In addition, the choice to censor the patients at the time of revascularization is a common practice and would not alter the natural history of the disease when the rate of interventions is low[30] (over a follow-up period of 6 years, it was about 15% on average in our study). In this context, even assuming that revascularization procedures would improve outcome in such patients, it is evident that the impact achieved by their use could not be other than negligible in the modification of the "natural" history of the disease. In fact, it is unlikely that the altered course of the 11 patients (10% of the revascularized group, but 1.4% of the overall population)

who underwent revascularization procedures before a first recurrent cardiac event, exerted a major impact on the prognostic significance of any ET variable. Similarly, medical therapy could not be standardized, although most patients were routinely treated with antiplatelet agents and beta-blockers.

Clinical implications. Although the identification of those patients at risk of recurrence is still the main objective of risk re-stratification in stable, asymptomatic subjects with a remote history of Q-wave MI, the value of ET in these cases is negligible. In fact, it is unlikely that an annual follow-up ET, performed to detect silent progression of the atherosclerotic disease, would aid prognostication or alter the patient's management. The poor predictive value limits the role of ET in clinical practice, when it is used to screen patients likely to benefit from coronary angiograms and revascularization procedures. In fact, compared to medical management, revascularization procedures exposed most of the patients selected for cardiac catheterization in our study to a higher risk. Thus, cost-benefit considerations would suggest that, in these stable patients, ET is inappropriate. This concept should allow substantial financial savings by reducing the utilization of ET in these low-risk subjects and shifting resources to more cost-effective strategies (aggressive and tailored modification of risk factors and symptomatic medical therapy).

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