Usefulness of Early Exercise Testing and Clinical Risk Score for Prognostic Evaluation in Chest Pain Units Without Preexisting Evidence of Myocardial Ischemia

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We investigated whether the result of early exercise testing yields prognostic information in addition to that afforded by a clinical risk score in patients who present with chest pain in the emergency department. The study group consisted of 340 patients without preexisting evidence of myocardial ischemia. A clinical risk score was calculated. Primary (mortality or myocardial infarction) and secondary (mortality, myocardial infarction, or rehospitalization due to unstable angina) end points at 1 year were defined. Patients with a positive exercise test result underwent invasive management. Frequencies of primary (7.4% vs 2.1%, p = 0.06) and secondary (9.3% vs 2.8%, p = 0.04) end points and risk score (1.6 ± 1.0 vs 1.0 ± 0.9 points, p = 0.0001) were higher in patients with a positive exercise test result. However, in multivariate analysis, clinical risk score was the only independent predictor for the primary (hazard ratio 2.0, 95% confidence interval 1.2 to 3.2, p = 0.004) and secondary (hazard ratio 1.9, 95% confidence interval 1.2 to 2.9, p = 0.003) end points. In conclusion, if a policy of invasive management is implemented for patients with positive exercise test results, the clinical risk score constitutes the main prognostic predictor of 1-year outcome. © 2006 Elsevier Inc. All rights reserved. (Am J Cardiol 2006;97:633–635)

The present study involved a series of patients with acute chest pain, a non–ST-segment deviation electrocardiogram, normal troponin concentrations, ability to exercise, and without preexisting evidence of myocardial ischemia. We investigated whether the result of early exercise testing provides prognostic information in addition to that afforded by the clinical risk score.

The study group consisted of 340 consecutive patients (from January 15, 2001 to September 1, 2004) who presented to the emergency department with acute chest pain of possible coronary origin. For inclusion in the study, patients were required to meet the following conditions: (1) absence of ST-segment deviation (≥1 mm) or confounding repolarization changes on electrocardiogram (left bundle branch block, paced rhythm, left ventricular hypertrophy, and preexcitation or treatment with antiarrhythmic drugs), (2) normal troponin levels after serial determination (on arrival and 8 and 12 hours after pain onset), (3) ability to exercise, and (4) absence of previous significant coronary stenosis, myocardial infarction, and coronary angioplasty or bypass surgery. Patients were evaluated by a chest pain unit protocol that was implemented in our institution that included analysis of clinical history and early (<24 hours) exercise testing.1–6 Clinical characteristics of chest pain at presentation by using a pain score7 and risk factors were documented. A previously validated risk score for predicting all-cause mortality or acute myocardial infarction at 1 year was calculated.4 Variables included in this score were age ≥67 years (1 point), pain score ≥10 points (1 point), ≥2 pain episodes in the previous 24 hours (1 point), and insulin-dependent diabetes mellitus (2 points).

A symptom-limited Bruce’s protocol was used. The result was considered positive in the case of ischemia induction (indicated by 1-mm horizontal or downsloping depression of the ST-segment at 80 ms after the J point or 1-mm ST elevation). A negative test was defined as at least submaximal testing without ST-segment changes. An inconclusive test was defined as an inability to achieve submaximal heart rate (85% of theoretical age-predicted heart rate) without ischemia. After exercise, all 231 patients (68%) with a negative result were discharged, whereas all 54 patients (16%) with a positive result were hospitalized. In the remaining 55 patients (16%) with inconclusive results, the final decision was left to the discretion of the supervising
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Patients were followed for 1 year. Complete follow-up was obtained in 97% of patients. The primary end point was a composite of all-cause mortality or acute myocardial infarction. The secondary end points comprised a composite of all-cause mortality, acute myocardial infarction, or rehospitalization due to unstable angina. Acute myocardial infarction was defined as a new episode of chest pain with increased troponin levels. Acute myocardial infarction was also considered if creatine kinase-MB mass increased to ≥3 times the upper limit of normal after percutaneous transluminal coronary angioplasty or to ≥5 times the upper limit of normal after coronary bypass surgery. Rehospitalization due to unstable angina was defined as a new episode of chest pain that required hospitalization with concomitant electrocardiographic changes indicating acute ischemia or a coronary angiogram showing a significant coronary stenosis without increases in troponin.

Continuous variables were expressed as mean ± SD and compared by unpaired t test. Categorical variables were expressed as percentages and compared by chi-square test. Cox’s regression model was used to identify predictors of the primary and secondary end points at 1 year. Hazard ratios (HRs) and their 95% confidence intervals (CIs) were calculated. Logistic regression analysis was used to calculate predictors of the secondary end point at 30 days. Odds ratio and their 95% CIs were also determined.

Table 1 presents characteristics of the patient population. Seventy-eight patients (74%) underwent cardiac catheterization during index hospitalization. An invasive study was recommended in patients with a positive exercise test result. Of the 54 patients with a positive result, 52 (96%) were catheterized and 26 (48%) revascularized.

During follow-up, 7 patients (2.1%) died, 3 from cardiac death, and the remaining 4 deaths were attributed to neoplasm in 3 and to brain hemorrhage in 1. Mortality rates were 3.7% in the positive subgroup and 2.2% in the negative subgroup. When considering only cardiac death, frequencies were 1.9% and 0.9%, respectively. At 1 year, the primary end point occurred in 10 patients (2.9%) and the secondary end point occurred in 13 (3.8%). After hospital discharge, 10 patients were revascularized, 6 with positive results, 1 with inconclusive results, and 3 with negative results.

Patients with a positive exercise test result showed a greater incidence of the primary (7.4% vs 2.1%, p = 0.06) and secondary (9.3% vs 2.8%, p = 0.04) end points at 1 year. Likewise, the risk score was higher in patients with a positive test result (1.6 ± 1.0 vs 1.0 ± 0.9 points, p = 0.0001).

The risk score allowed stratification of the global population into 4 risk categories according to number of points, namely 0 (n = 100), 1 (n = 134), 2 (n = 80), and ≥3 (n = 26). Frequency of events increased with risk category for the primary (0%, 3.7%, 2.5%, and 11.5%, p = 0.02) and secondary (0%, 4.5%, 5.0%, and 11.5%, p = 0.03) end points. Figure 1 displays the percentage of positive and negative exercise test results in each risk score category. As risk score increased, the percentage of patients with a positive exercise test result also increased significantly (0 points, 7%; 1 point, 13%; 2 points, 28%; and ≥3 points, 31%; p = 0.0001), whereas the percentage of patients with a negative result decreased (0 points, 81%; 1 point 70%; 2 points, 60%; and ≥3 points, 31%; p = 0.0001).

Cox regression analysis was performed, including the model clinical risk score and a positive early exercise test result. Risk score was the only variable independently related to the primary (HR 2.0, 95% CI 1.2 to 3.2, p = 0.004) and secondary (HR 1.9, 95% CI 1.2 to 2.9, p = 0.003) end points at 1 year. When considering the secondary end point at 30 days, a positive exercise test result was the only related variable (odds ratio 4.1, 95% CI 0.95 to 19.1, p = 0.06).

The findings of the present study indicate that early exercise testing is a useful tool for deciding hospitalization in patients who present to the emergency department with acute chest pain, a non–ST-segment deviation electrocardiogram,
and normal troponin levels. A positive exercise test result identified a subset of patients with a high probability of significant coronary stenosis that would prompt in-hospital revascularization and with a risk of short-term events. However, the 1-year outcome was better predicted by the clinical risk score.

Different proportions of positive and negative results of early exercise testing have been observed in studies carried out in chest pain units.\(^8\)\(^-\)\(^7\)\(^\) The definition of pain for inclusion in the chest pain unit protocol differed. This fact produces differences in the risk of included patients that would explain differences in the results of exercise testing. Accordingly, the following definitions have been used as inclusion criteria: atypical chest pain,\(^9\) low-risk unstable angina,\(^9\) nontraumatic chest pain,\(^13\)\(^15\) chest pain of possible coronary origin,\(^8\)\(^17\) or patients with <7% probability of acute myocardial infarction according to Goldman’s algorithm.\(^14\) However, some studies excluded patients with antecedents of ischemic heart disease.\(^19\) The reported percentages vary from 23%\(^8\) to 3%\(^13\) for positive tests and from 38%\(^8\) to 79%\(^16\) for negative tests. Our results, which comprised 16% positive results and 68% negative results, are in concordance with these previous reports.

By adopting a policy of hospitalization in the case of a positive exercise test result and of early discharge in the case of a negative result, a very low rate of cardiac events has been observed during follow-up in these patients.\(^8\)\(^,\)\(^14\)\(^,\)\(^15\)\(^,\)\(^17\) However, some studies have described a worse prognosis in patients with a positive test result.\(^11\)\(^,\)\(^13\)\(^,\)\(^16\) The following data should be taken into account in these studies: (1) routine invasive management was not performed after a positive exercise test result; (2) revascularization was defined as an end point instead of the form of management; and (3) the prognostic value of the exercise test was not adjusted for a clinical risk score.

In patients with a high clinical risk score (\(\geq 3\) points), the frequency of a negative exercise test was only 31%. If the main goal of a chest pain unit protocol is to identify the subgroup of patients with a negative exercise test result for early discharge, this protocol seems to be less beneficial in patients with such a high pretest clinical risk score. As a consequence, a policy of routine hospitalization could be advocated. In this sense, a recent study demonstrated that, in patients who were not suitable for exercise testing, stress imaging added little clinical information to guide admission decisions and was slightly more costly than routine admission alone.\(^20\)