

Prognostic Value of Normal Myocardial Radionuclide Scan in Patients with Positive Treadmill Test

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The purpose of this study was to determine the prognostic value of a normal ²⁰¹Tl scan in patients with a positive treadmill exercise stress test. We analyzed retrospectively 85 consecutive patients with a positive treadmill exercise test and normal ²⁰¹Tl scan who were studied for the diagnosis of coronary artery disease from January 1996 to December 2000. The pretest probability of coronary artery disease was intermediate or high in all patients. Seventy-eight patients (89%) were followed up for 2.03 years. Forty patients (51%) were men. Age was 56 years. The cardiac events considered were angina, revascularization, nonfatal myocardial infarction, and cardiac death. During the follow-up period, none of the patients suffered a major cardiac event. Eight patients had episodes of chest pain and one had angor that required revascularization. Patients with an intermediate probability of coronary artery disease before the test and normal myocardial radionuclide scan had a very good prognosis even with a positive treadmill exercise test.

Key words: Nuclear medicine. Stress. Follow-up studies.

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INTRODUCTION

The prognostic value of myocardial radionuclide scans with ²⁰¹Tl has been evaluated in studies carried out in a large number of patients under a wide variety of clinical conditions.¹⁻³ The main objective of noninvasive studies, whether in patients with chest pain or in those who have known coronary artery disease, is to be able to identify patients at risk of future infarction or cardiac death, in order to adopt the op-

Valor pronóstico de los estudios de perfusión miocárdica con ²⁰¹Tl normal en pacientes con ergometría positiva

El objetivo de este trabajo ha sido determinar el valor pronóstico a medio plazo de los estudios de perfusión miocárdica con ²⁰¹Tl normal en los pacientes con ergometría positiva. Se seleccionaron 85 pacientes consecutivos que desde enero de 1996 a diciembre de 2000 habían presentado gammagrafías normales con ergometrías eléctricamente positivas. La probabilidad pretest de enfermedad coronaria era intermedia o alta. Se efectuó seguimiento a 78 pacientes (89%) durante una media de 2,03 años. Un total de 40 pacientes (51%) eran varones. La edad media fue de 56 años. Se analizaron las siguientes variables: angina, revascularización, infarto no mortal y muerte cardíaca. Durante el período de seguimiento no se produjeron acontecimientos coronarios mayores; sólo 8 enfermos refirieron episodios de dolor anginoso y uno de ellos angina inestable que requirió revascularización. En pacientes con probabilidad pretest de enfermedad coronaria intermedia que presentan una gammagrafía de perfusión miocárdica normal, el pronóstico a medio plazo es excelente, aunque la ergometría haya sido eléctricamente positiva.

Palabras clave: Medicina nuclear. Estrés. Estudio de seguimiento.

portunity measures. It has been reported that the most useful variables for predicting future events are the existence of a defect of more than 20% of the size of the ventricle, defects in more than one territory suggesting multivessel disease, reversible defects in multiple myocardial segments, reversible or persistent dilatation of the left ventricle, increased pulmonary radiodrug uptake, or resting left ventricular ejection fraction of less than 40%.⁴ Nevertheless, one of the main characteristics of the treadmill test with a myocardial perfusion radionuclide scan is the excellent negative predictive value of normal results. It has been reported that patients with normal studies have a combined rate of cardiac mortality and non-mortal infarction of less than 1% in a year,⁵ which is why they generally do not require other invasive diagnostic tests.⁶ The present study was undertaken to determine the

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ABBREVIATIONS

SPECT: single-photon emission computed tomography.
Tl-201: thallium-201.

prognostic value of normal Tl-201 radionuclide scans in patients in whom the treadmill test has been electrically positive.

PATIENTS AND METHOD

Patients

From January 1996 to December 2000, treadmill exercise stress tests with Tl-201 were performed in 2845 patients in our laboratory. A retrospective selection was made of 85 patients who had been studied for the diagnosis of ischemic heart disease (n=73) or the evaluation of coronary bypass (n=11) and presented normal radionuclide scans with an electrically positive treadmill exercise stress test. A clinical follow-up and telephone survey were carried out in 78 patients (89% of the initial population), who constituted the study sample whose data are presented here.

None of the patients had a previous infarction or was in treatment with digitalis. A total of 40 patients were men (51%). The mean age of men was 54 ± 14 years and women, 59 ± 10 years. Ten (26%) women were premenopausal. The pre-test probability of coronary artery disease was low in 8 patients (a 22-year-old man, 4 premenopausal women with atypical chest pain, and 3 postmenopausal women with non-anginal chest pain), intermediate in 63, and high in 14.⁷ The

study was requested for angina, atypical chest pain, non-anginal chest pain, baseline repolarization disturbances, or previous positive exercise stress tests. The baseline electrocardiograms were normal in 52 patients and showed repolarization disorders in 18 patients. Four patients had signs of left ventricular hypertrophy. Patients with LBBB, atrial fibrillation, and pacemakers were excluded, and the following variables were considered: angina, revascularization, non-mortal infarction, and cardiac death. The mean follow-up time was 2.03 years (range, 0.4-4.8 years). The initial clinical characteristics of the patients studied are shown in Table 1.

Exercise stress test

The exercise stress tests were carried out on a treadmill, with a maximum stress test limited by symptoms. The exercise stress test was interpreted as electrically positive when an ST-segment horizontal deviation or depression of more than 0.1 mV appeared, measured 60-80 ms from the J point, during effort or in the recovery phase.^{8,9} Exercise stress tests with ST-segment elevation in the absence of a Q wave were also considered positive, which occurred in 4 patients, as well as those in which ST-segment depression appeared exclusively on the inferior face, a finding that appeared in 5 patients.

Tl-201 radionuclide scan

SPECT was performed following the routine protocol used in all patients. Minutes before finalizing the treadmill exercise test, 85 MBq of Tl-201 was injected intravenously. After 3-4 h the resting images were acquired after reinjecting another 37 MBq of Tl-201. Thirty-two images, 20 s each, were acquired over an arc of 180°. The tomographic studies were reconstructed and short-axis, horizontal-axis, and vertical-axis images were obtained. The images were analyzed qualitatively, but 46 patients also had a quantified study from polar images.^{10,11} The size of the perfusion defect was determined by comparing the findings with data from a reference bank of images obtained from normal individuals, and it was expressed as a percentage.

A simultaneous functional perfusion study was made (gated SPECT) in 16 patients.

Statistical analysis

The quantitative data are expressed as mean $\pm$ SD. Frequencies are expressed as percentages.

RESULTS

In agreement with the above criteria, exercise testing was electrically positive in all the patients and cli-

TABLE 1. Initial characteristics

Patients	(n = 78)
Sex	
Men	40 (51%)
Women 38 (49%)	
Age	56 ± 12
Men	54 ± 14
Women 59 ± 10	
Initial symptoms	
Asymptomatic or non-anginal chest pain	20 (25%)
Atypical chest pain	39 (50%)
Angina	19 (25%)
Risk factors	
Diabetes	5/78
AHT	29/78
Hypercholesterolemia	25/78
Smoking	5/78
Menopause	28/38
Clinically positive treadmill stress test	18 (22%)

nically positive in 18 (22%). The treadmill exercise test was weakly positive clinically in 12 of these patients, moderately positive in 4, and strongly positive in 2.

The study of myocardial perfusion with Tl-201 was normal in all the selected patients. In the patients who had a quantified study, quantitative analysis did not demonstrate a perfusion defect exceeding 9% in any of them. On the other hand, the study of ventricular function (gated SPECT) in 16 patients disclosed no disturbances in any of them.

During the follow-up period, none of the patients died and no non-mortal infarctions occurred. The only events recorded were several episodes of anginal pain in 8 patients and unstable angina that required revascularization in another patient. Six of these 9 patients presented chest pain in the course of the exercise stress test (Table 2).

DISCUSSION

The mean sensitivity of conventional exercise testing was 65%, with values ranging from 40% for single-vessel disease to 90% for 3-vessel disease. The specificity was 85%, the positive predictive value about 80%, and the negative predictive value 30%.¹² Nevertheless, these values depended on the prevalence of coronary artery disease in the population in which the test is made. The group of patients in whom diagnostic exercise stress testing is most valuable are patients with an intermediate pre-test probability – based on sex, age, and symptoms – of coronary artery disease.^{7,13-15} Several published studies reveal a broad variation in the sensitivity and specificity of exercise stress tests for the diagnosis of ischemic heart disease. A meta-analysis of 58 studies consecutively published has revealed a mean overall sensitivity of 67% and a specificity of 72%. Sensitivity decreased and specificity increased in the studies in which coronary angiography was performed on all patients, thus avoiding the bias of performing invasive tests only in patients with positive exercise stress test results.¹⁰ It has been affirmed that the true diagnostic value of exercise stress tests resides in their relatively high specificity,^{16,17} except for patients with baseline electrocardiographic abnormalities or left ventricular hypertrophy.¹⁸

The prognostic value of the exercise stress test depends on two types of markers, some related to exerci-

se capacity, such as the duration of maximum exercise and the MET or heart rate reached, and others dependent on exercise-induced ischemia, that is to say, ST-segment depression and angina.¹⁹ Nevertheless, it has been reported that the myocardial perfusion radionuclide scan adds short-term and intermediate-term prognostic value to the exercise stress tests.¹⁻³ In the long term, the radionuclide scan increases the prognostic value of the stress test for cardiac death. In addition, an abnormal study disclosing a large number of poorly perfused segments is related to the future appearance of myocardial infarction, whereas a positive exercise stress test does not predict the appearance of non-mortal infarction.²⁰

The findings of this study are similar to those reported in other studies in which myocardial perfusion radionuclide scans have been performed with technetium compounds.^{21,22} None of the patients studied presented a major coronary event during mid-term follow-up, showing that a normal Tl-201 perfusion radionuclide scan in patients with an intermediate pre-test probability of coronary artery disease indicates an excellent prognosis, even if the exercise stress test has been electrically positive. Given the lack of specificity and limited intermediate-term prognostic value of conventional exercise stress tests, we believe that myocardial perfusion radionuclide scans with Tl-201 should be performed in patients with positive exercise test results before undertaking more invasive studies.

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TABLE 2. Adverse events

Angina	8 (10%)
Bypass procedures	1 (1.2%)
Non-mortal infarction	–
Cardiac death	–
Total	9 (11.5%)

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