Negative exercise stress test Does it mean anything?

Hassan A. Mohamed
Department of Medicine, Division of Cardiology, Coronary Care Unit, Regina General Hospital, Regina, SK, Canada.

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Introduction

Despite its low sensitivity and specificity (67% and 72%, respectively), exercise testing has remained one of the most widely used noninvasive tests to determine the prognosis in patients with suspected or established coronary disease.

As a screening test for coronary artery disease, the exercise stress test is useful in that it is relatively simple and inexpensive. It has been considered particularly helpful in patients with chest pain syndromes who have moderate probability for coronary artery disease, and in whom the resting electrocardiogram (ECG) is normal. The following case presentation and discussion will question the predictive value of a negative stress testing in patients with moderate probability for coronary artery disease.

Case presentation

On October 02, 2006, a 56 year-old smoker male presented to our emergency room (ER) with a prolonged episode of epigastric and lower sternal discomfort. His discomfort was relieved with multiple doses of sublingual nitroglycerine and 2 doses of oral antacids. His physical examination, electrocardiogram (ECG),and cardiac markers (including creatine phosphokinase and Troponin I) were unremarkable. His past medical history is significant for mild hyperlipidemia and hypertension. He had a strong family history of premature coronary artery disease; his brother died of myocardial infarction at age 52 years.

Although his chest discomfort was atypical, he was considered as an intermediate-risk patient, based on his multiple cardiac risks. A symptom-limited exercise stress test was carried out. He exercised for 12 minutes on the standard Bruce protocol, achieving a peak heart rate of 144 per minute and a total workload equivalent to 12.1 METS. He reported no chest pain during this test. The exercise ECG revealed no significant ST-segment depression (Figure 1). Therefore, this test was considered as a low-risk negative test, predicting an annual mortality rate of less than 1%.

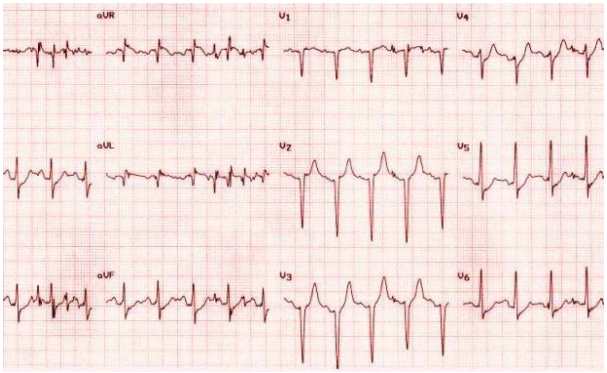

Figure 1: A twelve-lead exercise stress electrocardiogram (ECG) recorded within the first minute of recovery, showing no significant ST-segment depression in response to exercise.

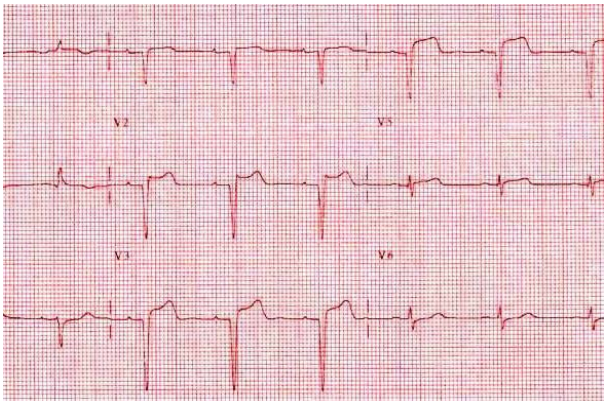

Figure 2: A twelve-lead electrocardiogram (ECG), recorded on admission to Cardiac Care Unit, showing recent extensive anterior wall myocardial infarction.

Coronary angiography revealed total occlusion of the proximal segment of left anterior descending artery, and severe disease involving the proximal segment of the obtuse marginal branch (Figure 3). He was treated with direct Percutaneous Coronary Intervention (PCI).

Discussion

Exercise stress testing has traditionally served as a noninvasive tool in the diagnosis of coronary artery disease. It complements the medical history and physical examination, and it remains the second most commonly performed cardiologic procedure next to the routine ECG.

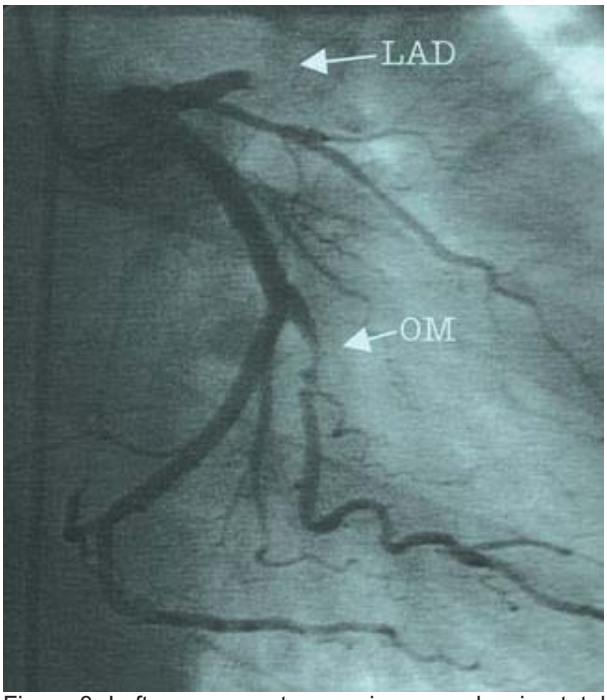

Figure 3: Left coronary artery angiograms showing total occlusion of the left anterior descending artery (LAD) and subtotal occlusion of the obtuse marginal (OM) branch of the left circumflex coronary artery.

Our patient (described above) is also considered an intermediate-risk patient. Atypical chest pain in a 56-year-old man is associated with a 50% probability of CAD. Diagnostic stress testing is most valuable in this intermediate pretest probability category, because the test result has the largest potential effect on diagnostic outcome.

The type of patient being tested and the results of the exercise stress test must be considered together when determining the likelihood of subsequent cardiac event [1].

The estimation of pretest probability of obstructive CAD is based on the patient's history (including age, gender, and chest pain characteristics), physical examination, and initial testing.

Typical or definite angina (table 1) makes the pretest probability of obstructive CAD so high that the test result does not dramatically change the probability.

Exercise-induced typical anginal chest pain can be a valuable indicator of the presences of coronary artery disease. The presence of diagnostic ST-segment depression in association with exercise-induced chest pain is highly predictive of significant coronary artery disease [2] (table 2).

Major non-electrocardiographic observations that carry prognostic importance include the maximum work capacity, the peak systolic blood pressure achieved, the presence or absence of angina, and ventricular tachycardia [3].

Table 1 Characteristics of anginal pain

A- Typical or definite angina can be defined as a substernal chest pain or discomfort that is provoked by exertion or emotional stress and relieved by rest and/or nitroglycerine.
B- Atypical or probable angina can be defined as chest pain or discomfort that lacks one of the three characteristics of typical angina.

Table 2 High-risk exercise electrocardiographic variables

1- ST segment depression ≥ 2.0 mm
2- ST segment depression in stage I ≥ 1.0 mm
3- ST segment depression in multiple leads
4- ST segment depression persists for greater than 5 min during recovery period
5- Achievement of a workload of less than 4 METS or a low exercise maximal heart rate
6- Abnormal blood pressure response

Exercise capacity has also been considered of prognostic value in patients with coronary artery disease. An exercise capacity of more than 12 METS (Bruce protocol stage 4) is indicative of a good prognosis in patients with coronary artery disease regardless of other responses or whether medical or surgical therapy is selected for management [1,4].

Our patient, described above, was able to exercise for 12 minutes; a workload equivalent to 12.1 METS, without any chest pain or ischemic ST-segment depression. Therefore, his stress test was considered a low-risk test, predictive of an annual mortality rate of less than 1%. Nevertheless, he presented in less than 2 months with an extensive anterior wall myocardial infarction.

The rupture of plaques is now considered to be the common pathophysiological substrate of the acute coronary syndromes. During the natural evolution of the atherosclerotic plaques, an abrupt and catastrophic transition may occur, characterized by plaque rupture and exposure of substances that promote platelets activation and thrombin generation [5].

These changes may lead to the conversion of previously stable and non-obstructive plaques to unstable and occlusive ones. This transition, from an asymptomatic or a minimally symptomatic chronic stable state to acute unstable coronary heart disease, may take place in few hours.

This means that, coronary artery disease that has not resulted in sufficient luminal occlusion to

cause ischemia during stress testing can still lead to ischemic events through spasm, plaque rupture, and thrombosis. These non-obstructive lesions explain some of the events that may occur after a negative exercise stress test. This dynamic process of plaque rupture may evolve to a completely occlusive thrombus, typically producing ST elevation on the ECG.

Therefore, we should not be surprised if an asymptomatic patient with underlying insignificant coronary disease, who had a negative stress test just few weeks ago, develops an acute coronary syndrome as result of this dynamic process of plaque rupture.

A negative exercise or even pharmacological radionuclide stress may not mean very much if we consider the dynamic nature of this disease. Therefore, a negative result should not exclude the diagnosis of significant coronary artery disease.

The above-described clinical case provides an example to this view.

More recently, other noninvasive modalities, including coronary CT-angiography and whole-heart coronary magnetic resonance angiography, showed moderate sensitivity and high specificity in detecting coronary artery disease [6-8]. These noninvasive imaging modalities are able to detect the location of the coronary atherosclerotic plaque and to estimate the degree of lumen reduction. It is likely that these relatively new imaging modalities will replace stress testing, as a screening test for coronary artery disease, in future.

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