Acute Myocardial Infarction Following Recovery from a Normal Treadmill Exercise Test

John Passalaris, MD,* Massimiliano Szulc, PhD,* Jay Dubowsky, MD,* Rory Hachamovitch, MD†

*Weill Medical College of Cornell University and the New York Presbyterian Hospital, New York
†St Francis Hospital, Roslyn, NY

Cardiologists today rely on stress testing to provide valuable diagnostic information about their patients. How and why can it cross the line to become a trigger for acute coronary events? Is patient selection important to avoid complications? Follow this patient through his stress test. [Rev Cardiovasc Med. *2000;2(1):48-57, 60*]

The patient is a 46-year-old man referred for a dual isotope (thallium-201 [^{201}Tl] and technetium Tc 99m sestamibi [^{99m}Tc sestamibi]) exercise stress single-photon emission CT (SPECT) study for the evaluation of recurrent chest pain. The patient described episodes of substernal chest pressure radiating to the right shoulder and right arm during the previous 2 months. All episodes were associated with minimal exertion, climbing 2 flights of stairs, or walking 2 to 3 blocks. Symptoms would resolve within 5 minutes of rest. He denied any shortness of breath, diaphoresis, or nausea. The severity of his chest discomfort during the 3 days before his hospital admission prompted him to present to the emergency room for further evaluation.

His medical history for the previous 5 years was significant for mild hypercholesterolemia and hypertension. He had no previous history of myocardial infarction (MI) but had undergone percutaneous transluminal coronary angioplasty (PTCA) with stent implantation in the proximal right coronary artery 1 year before for class IV unstable angina. His outpatient medications include extended-release metoprolol, 100 mg/d; simvastatin, 20 mg/d; and 1 aspirin daily. He admitted to noncompliance with his medication regimen during the previous 2 to 3 months. He denied allergies to any medications.

His family history was significant for coronary artery disease (CAD). His mother died secondary to complications from an MI at age 72, and his father sustained an MI in his 70s. The patient smoked nearly 3 packs of cigarettes per day and had been
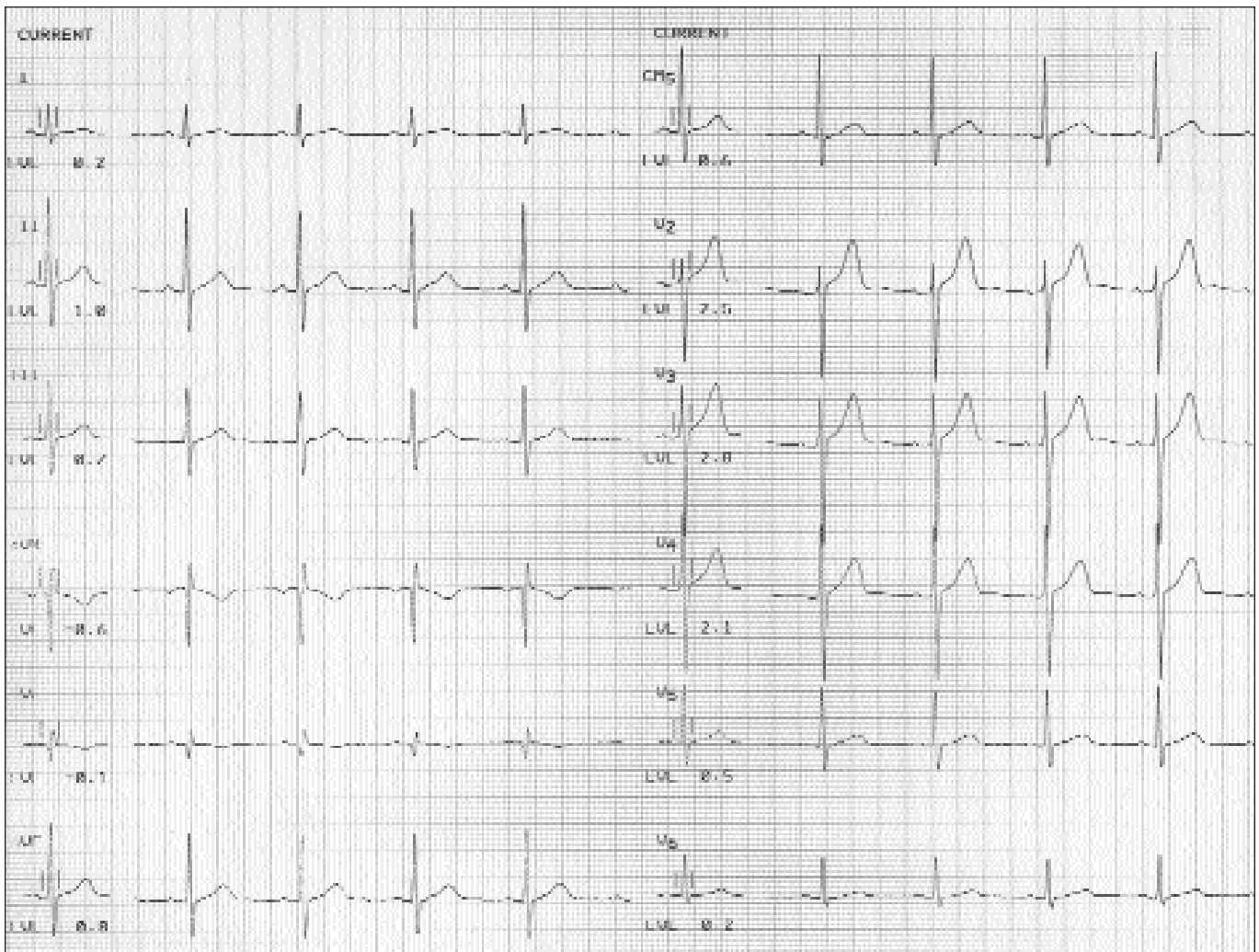
Figure 1. Resting ECG. Patient has normal sinus rhythm with a nonspecific repolarization abnormality.

doing so for 30 years. He reported rare alcohol intake, had a relatively sedentary lifestyle, and did not exercise regularly. He noted increased occupational stressors and concluded that his episodes of chest discomfort were secondary to anxiety and stress.

During the physical examination on presentation at the hospital and before the exercise portion of his stress test, the patient was free of pain and in no acute distress. His heart rate was 72 beats per minute (bpm), and his blood pressure was 160/90 mm Hg. He weighed 103 kg (227 lb); his height was 175 cm (5 ft 7 in). His neck was supple,

with normal jugular venous pulsations. Carotid upstrokes were normal. His cardiac examination revealed a regular rate and rhythm, with normal S_1 and S_2 sounds without audible murmurs, rubs, or gallops. Lungs were clear to auscultation, abdomen was benign without hepatosplenomegaly or masses, and the extremities revealed no cyanosis, clubbing, or edema. Dorsalis pedis and posterior tibial pulses, however, were diminished bilaterally.

His resting ECG showed normal sinus rhythm at 72 bpm with a nonspecific repolarization abnormality (Figure 1). His laboratory data on admis-

sion to the hospital (2 days before his stress test) were unremarkable, except for a mildly elevated white blood cell count at 12.3×10^9/L. Three creatine kinase levels taken during the 24 hours after admission were 181, 133, and 124 U/L, and a troponin I level was less than 0.3 mg/mL.

Before exercise, the dual-isotope protocol was initiated by obtaining ^{201}Tl resting SPECT images, which revealed mild to moderate defects in the basal inferoseptal, inferior, and inferolateral walls (Figure 2). A portion of these perfusion defects may be attributable to diaphragmatic attenuation.
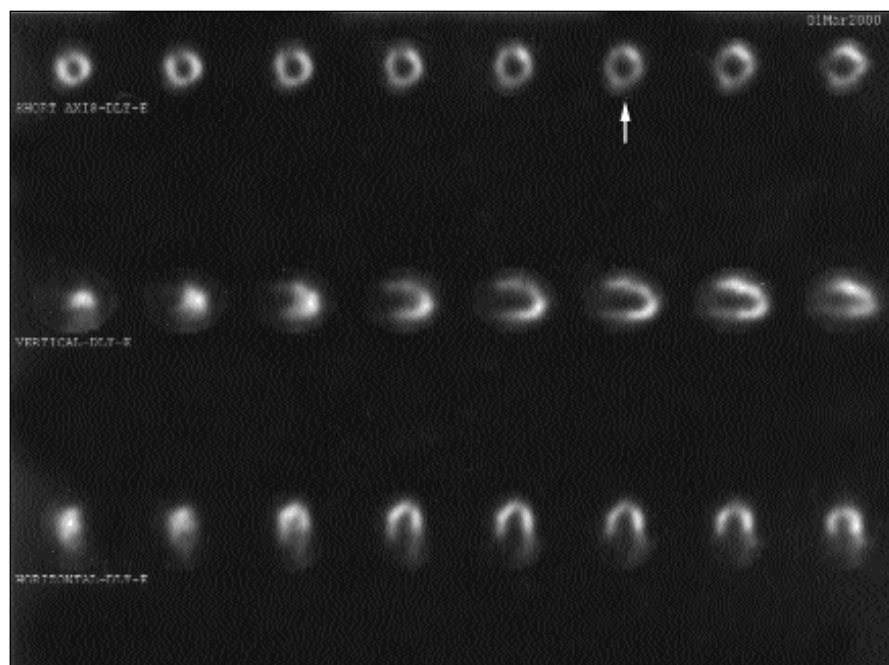
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Figure 2. Thallium-201 single-photon emission CT images at rest. Images acquired prior to exercise reveal mild to moderate defects in the inferolateral, inferior, and inferoseptal walls at the base (arrow).

Following acquisition of the resting images, the patient exercised to 9 minutes of a Bruce protocol. With stress, the heart rate increased from 71 bpm at rest to a peak heart rate of 141 bpm (82% of predicted maximum heart rate). Blood pressure increased from 162/94 mm Hg at rest to 214/100 mm Hg at peak exercise. A 35-mCi dose of ^{99m}Tc sestamibi was injected intravenously at the time of peak exercise. Exercise was terminated because of leg fatigue. The clinical response to exercise was nonischemic, and the ECG response to exercise was without significant changes (Figure 3).

Ten minutes after completion of the exercise portion of the stress test, while waiting to undergo poststress SPECT imaging, the patient reported severe crushing substernal chest discomfort with diaphoresis, nausea, and
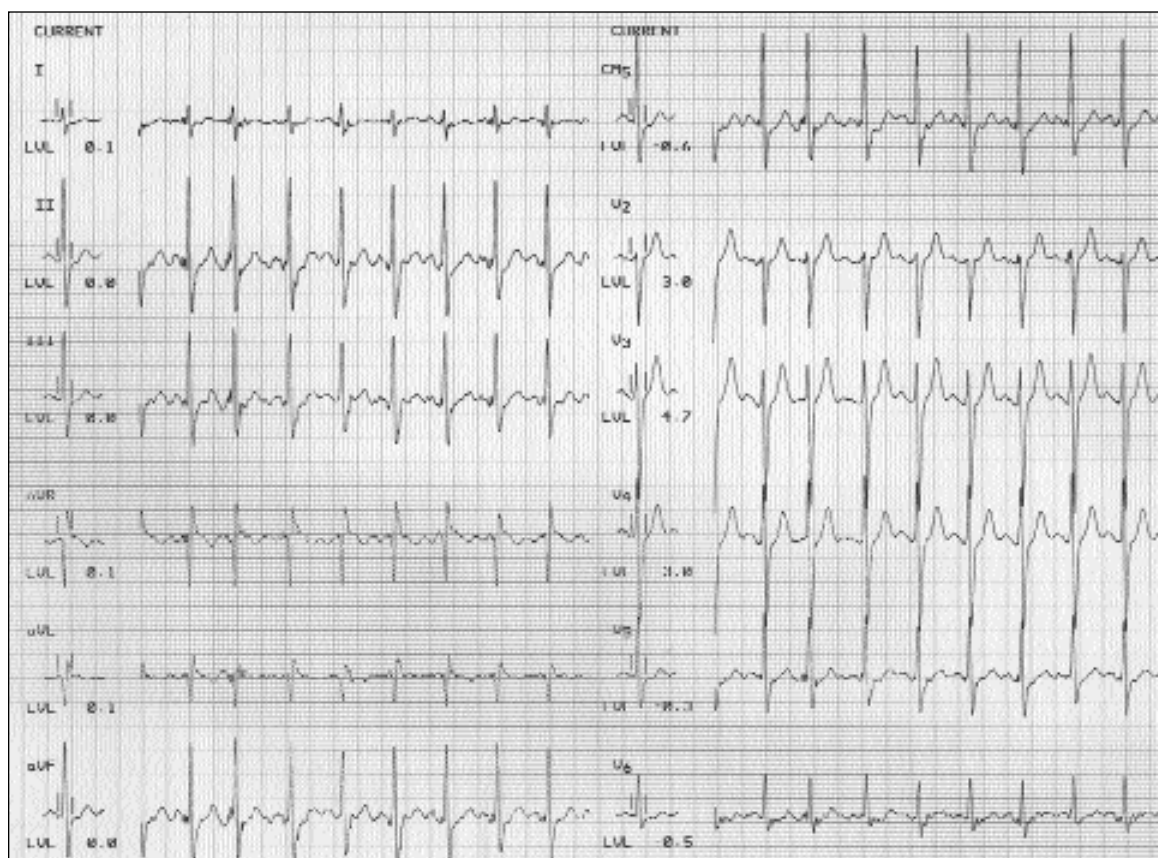

Figure 3. ECG at peak exercise. Patient has sinus tachycardia with an atrial premature complex. The ECG illustrates a negative response to symptom-limited exercise.

shortness of breath. He showed evidence of bradycardia (heart rate in the 50- to 55-bpm range) and hypotension (systolic blood pressure of 70 mm Hg). An ECG revealed sinus bradycardia with complete heart block and a narrow complex junctional escape at 50 bpm. There were also ST-segment elevations in the inferior leads, with reciprocal depressions in the anterior leads consistent with an inferior wall MI (Figure 4). Right-sided precordial lead findings were consistent with a right ventricular infarction. The patient was given an aspirin and received aggressive fluid resuscitation as well as pressor support with intravenous dopamine. He was also given atropine, but it had no effect on his bradyarrhythmia. The patient was emergently taken to the catheterization laboratory for primary angioplasty for an expected acute thrombosis of a proximal right coronary artery.

Angiography revealed 3-vessel CAD with an acute total occlusion within the previously placed stent in the proximal right coronary artery (Figure 5). There was also a chronic total occlusion of a proximal left circumflex artery and a first diagonal branch of the left anterior descending artery with a 60% stenosis. There were grade 3 collaterals from the distal left anterior descending artery to the distal left circumflex artery. The left ventriculogram revealed a moderately reduced left ventricular ejection fraction at 40% with an akinetic midinferior wall. The patient underwent a successful primary angioplasty with stent placement (proximal to the previous stent site) in the occluded proximal right coronary artery and restoration of Thrombolysis in Myocardial Infarction (TIMI) III blood flow. An intra-aortic balloon pump was placed for hemodynamic support at the beginning of the angioplasty; dopamine and phenylephrine were required transiently for pressure support, but they were stopped eventually. Although a transvenous pacemaker was placed prophylactically during catheterization, sinus rhythm was restored once angioplasty was successful.

Planar images were acquired at bedside within a 6-hour period from injection time of ^{99m}Tc sestamibi, using a portable gamma camera. Those images revealed lateral and inferoapical reduced perfusion, compared with the resting SPECT image using ^{201}Tl. The gated, planar ^{99m}Tc sestamibi images revealed apical hypokinesis. The right ventricle was hypokinetic as well (Figure 6). The patient had an
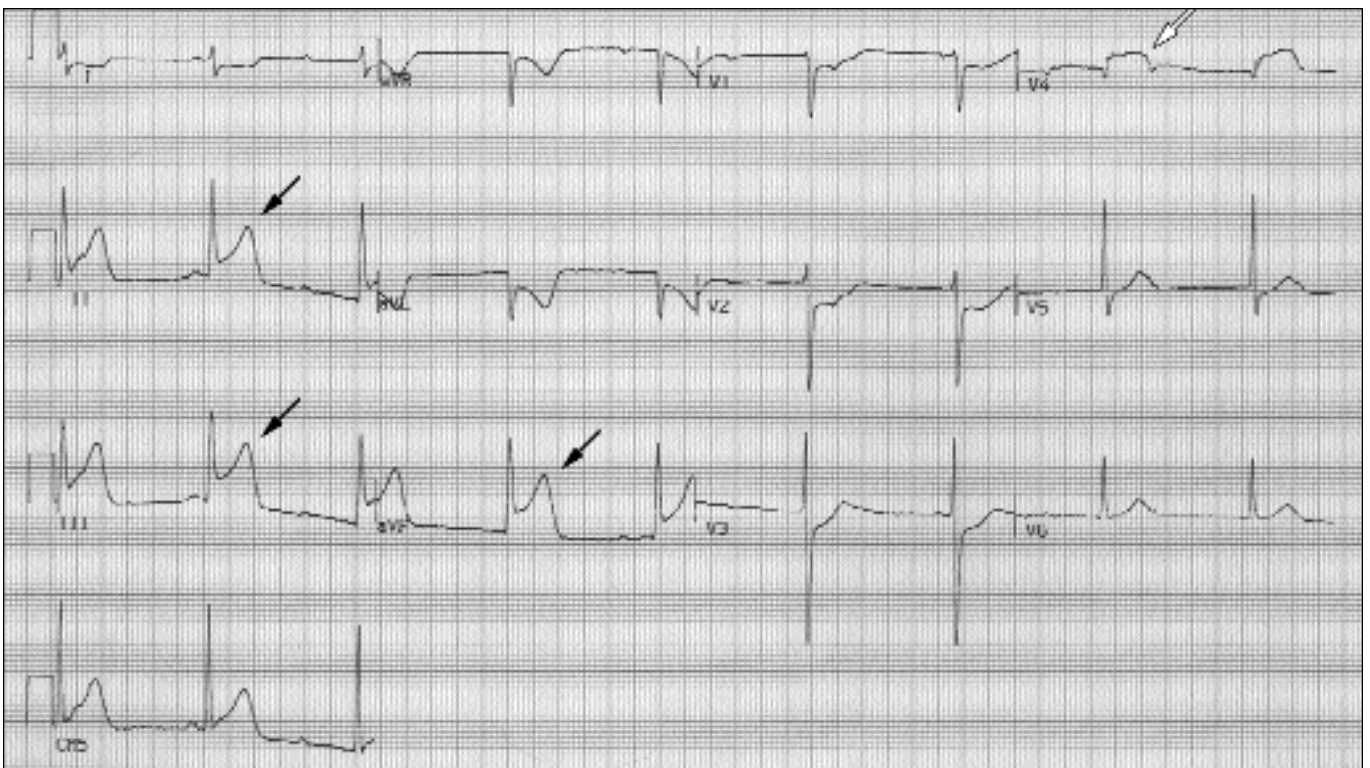

Figure 4. ECG 10 minutes after stress testing. The patient has sinus bradycardia with complete heart block. ST elevations in leads II, III, and aVF (black arrows) with reciprocal ST depressions in the V_1 and V_2 leads indicate an inferior wall myocardial infarction. Lead V_4 is a right precordial lead. The ST elevation in V_4R (white arrow) suggests a right ventricular infarct.

uncomplicated post-MI course and was discharged from the hospital after 5 days.

Discussion

This case illustrates that the significant physical exertion associated with stress testing may trigger unstable coronary syndromes and acute MIs (AMIs). It is a well-recognized phenomenon that heavy exertion sometimes immediately precedes and, indeed, appears to trigger the onset of AMI. While the precise incidence of AMI after stress testing is not known, observational studies[1,2] have estimated that approximately 5% of patients with an AMI have a preceding episode of heavy exertion, usually within 1 hour of symptom onset. The Determinants of Myocardial Infarction Onset Study Investigators[3] validated this observation in a case control study citing that 4.4% of patients reported heavy exertion within 1 hour before the onset of AMI. This translated to an estimated relative risk of AMI of 5.9 in the hour after heavy exertion, as compared with less strenuous physical exertion or no exertion. In subgroup analysis, the relative risk of AMI after heavy exertion was significantly greater (107) in patients who were habitually sedentary.

Data from the Framingham Heart Study indicate that the absolute risk that a 50-year-old nonsmoking, nondiabetic man will have an AMI during any given 1-hour period is about 1 in a million.[4] If the relative risk of a ha-
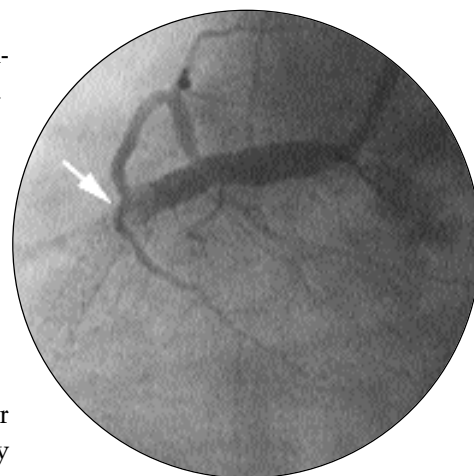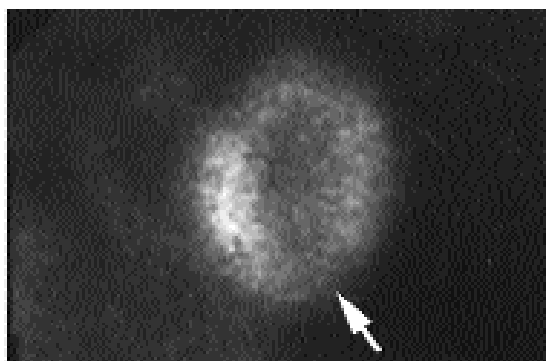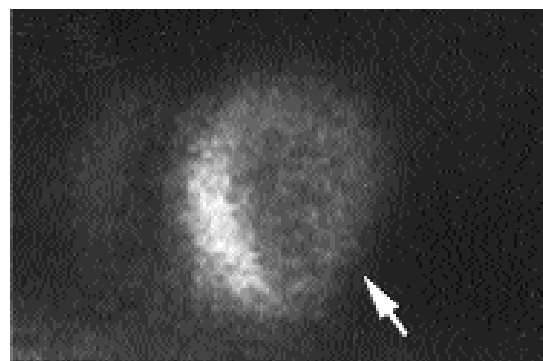

Figure 5. Coronary angiogram. Left anterior oblique projection of the right coronary artery reveals a total occlusion with thrombus of the proximal right coronary artery at the proximal end of the prior stent site.
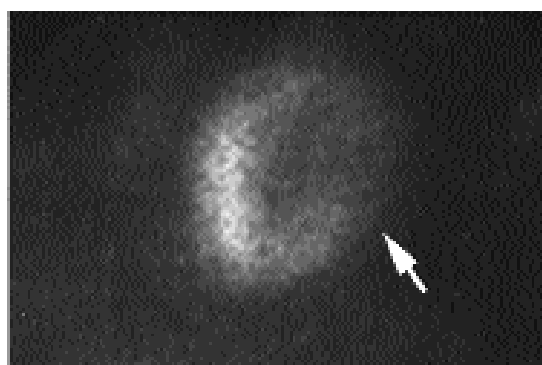
bitually sedentary man having an AMI after the heavy physical exertion of

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Figure 6. Technetium Tc 99m sestamibi planar images. Images acquired 6 hours after injection show reduced perfusion in the lateral and inferoapical walls (arrows).

Main Points

- The significant physical exertion associated with stress testing may trigger unstable coronary syndromes and acute myocardial infarctions (AMIs).

- Of patients with an AMI, about 5% have experienced an episode of heavy exertion, usually within 1 hour of symptom onset.

- It is not known whether exercise precipitates an AMI only in those predisposed to such an event.

- Stress testing can be considered in patients post-MI if they have been hemodynamically stable and pain-free without enzyme spill, ECG changes, or other high-risk markers for 48 hours; a vasodilator such as adenosine is the preferred stress agent.

stress testing, as in this case, were 107, then this would translate to an absolute risk of approximately 1 in 10,000. Although this represents a small risk, an understanding of the precipitants may lead to the ability to prevent occurrences.

In this case, it is presumed the patient had a nonobstructive but vulnerable plaque that ruptured postexercise, resulting in an occlusive intracoronary thrombus. How exercise testing can precipitate plaque rupture is not known but, theoretically, alterations in hemodynamic factors, precipitated by increased levels of circulating catecholamines postexercise, can induce coronary vasospasm.[5] Hemostatic forces postexercise (including increased blood viscosity secondary to an increase in fibrinogen levels) have also been theorized to cause endothelial cell injury and precipitate plaque rupture.[6]

Although epidemiologic and physiologic data suggest that exercise may precipitate an AMI, it is not known whether this is only the case in patients predisposed to such events. Retrospective analysis of data from the Northridge (Calif) earthquake revealed an increase in the number of sudden cardiac deaths in Los Angeles County on the day of the earthquake (24), compared with the average expected number of 4.6. In the 6 days after the earthquake, the average daily number of cases of sudden cardiac death dropped below baseline (to 2.7), suggesting that the emotional stress from the disaster initiated cardiac events in patients already predisposed to such events.[7] Further study of the triggers of acute coronary events may lead to new insights into the mechanisms involved and even to therapeutic strategies to prevent AMI.

This case also illustrates an important aspect of the dual isotope protocol. Since its first description in 1993, this protocol has become popular predominantly because of the dramatic reduction in the time a patient spends in the laboratory. In a well-organized laboratory, a patient should be able to have a dual isotope exercise stress protocol completed in 90 minutes. There are many other advantages to this protocol. Since the resting ^{201}Tl image is obtained prior to the stress test, patients with high-risk CAD can often be identified before undergoing the stress sestamibi portion of the examination. In many laboratories, a patient found to have severe, extensive defects on the resting ^{201}Tl image will undergo 4-hour and/or 24-hour redistribution imaging rather than the stress portion of the examination, thus defining whether the large, severe resting defects are scar or hibernating myocardium. In some patients, such as those presenting without a history of prior CAD, such a finding on the initial images may indicate a need for catheterization and may obviate performing the stress portion of the examination.

In all of these examples, this resting image clearly defines the patient as being at higher risk for adverse outcomes on both follow-up and exercise testing. Many experts advocate that if such a patient is going to undergo stress testing (not an inappropriate decision, since defining stress-induced ischemia is an aid to guiding revascularization), it should be performed with an ultra-short-acting agent. Currently, adenosine is probably the first-choice stress agent for such a patient.

Finally, we must ask whether this patient could have been identified as one who was at risk for an adverse outcome with stress testing. Whenever a patient who has been admitted with suspected unstable syndromes within 24 to 48 hours is referred for stress testing, the first question that must be asked—before testing—is whether this patient is stable.

Evidence of obvious Q wave AMI, particularly with hemodynamic embarrassment, identifies patients who should probably be referred for catheterization rather than for noninvasive testing. Growing evidence indicates that vasodilator stress is a safe procedure to risk-stratify such patients 48 to 72 hours after uncomplicated, non–Q wave MI. In patients presenting with unstable syndromes, recurring chest pain, dynamic ECG changes, evidence of cardiac enzyme spill, or significant

ectopy identify those at higher risk who probably need further medical therapy ("cooling off") if noninvasive testing (rather than catheterization) is the preferred next step in a testing algorithm.

In our laboratory, patients post-MI will be accepted as candidates for stress testing if they have been hemodynamically stable and pain-free without enzyme spill, ECG changes, or other high-risk markers for 48 hours. We will often request that these patients undergo testing with adenosine rather than exercise stress. Indeed, our laboratory and many others opt for this protocol, rather than the traditional post-MI "sub max exercise" protocol, because of perceived superior risk stratification and safety.

Given this, should the patient we presented have been treated differently? To the best of our knowledge, this patient had had no further symptoms since admission, no significant ECG changes or cardiac enzyme abnormalities, and no evidence of hemodynamic instability. The resting ^{201}Tl images demonstrated mild defects that may have been caused, in part, by attenuation but clearly did not represent significant myocardial damage. Since MI had been ruled out and the patient had been stable for 48 hours, we were comfortable with an exercise stress protocol. By all indications, this patient was low-risk with respect to adverse outcomes during the stress test. Yet, despite all precautions, an MI was triggered by the exertion. ∎

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