Family Practice Grand Rounds

Exercise Testing and Coronary Artery Disease

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DR. WILLIAM MOORE *(First-year family practice resident)*: Today's presentation is about G.M., a 69-year-old professor at the University of Florida, who has been followed by Dr. Curry for several years. He lives with his wife and has two grown children. Since suffering an uncomplicated myocardial infarction in 1972, G.M. has had remarkably stable angina pectoris, occurring only a few times a month and always relieved by nitroglycerine. He walks a mile a day. His risk profile is remarkable for a positive family history of coronary artery disease (a brother died of a myocardial infarction at 61 years of age), and hypertension that has been controlled on hydrochlorothiazide. He is not overweight, does not smoke or drink alcohol, and does not have diabetes mellitus or hypercholesterolemia. Physical examination has been unremarkable except for prostatic enlargement. An electrocardiogram has shown evidence of a previous inferior myocardial infarction and some minor nonspecific ST segment abnormalities, but no acute changes.

The patient has undergone treadmill testing on three occasions since 1977. Development of a progressively more abnormal response to exercise suggestive of three-vessel or left main coronary artery disease precipitated his admission for cardiac catheterization and consideration for possible coronary artery bypass surgery.

DR. KEN GRAUER *(Assistant Professor in Family Medicine)*: We chose this particular case because it illustrates a number of points to consider in the evaluation and management of patients with coronary artery disease. Before discussing G.M.'s serial exercise treadmill tests, I would like to review some of the basic principles of exercise testing. Dr. Curry will then address the issue of coronary artery disease and the treatment course we elected to follow.

Stress testing is a noninvasive means of determining how well the coronary circulation can respond to the increased demands of exercise. Despite over 40 years of use, this procedure retains a number of important clinical applications. The best known and most commonly used of these is the evaluation of patients with chest pain; a normal treadmill test may prove to be as valuable to the clinician for ruling out coronary artery disease

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as an abnormal response is in suggesting disease.

In patients with premature ventricular contractions, a stress test is complementary to the Holter monitor and allows physicians to see what happens to ventricular ectopy during exercise. In general, when otherwise healthy individuals exercise on a treadmill, premature ventricular contractions tend to decrease and often disappear, whereas ventricular ectopy may be exacerbated by exercise in patients who have underlying heart disease.

Treadmill testing may also be used to assess the functional capacity of healthy subjects, especially in the previously sedentary individual who is about to engage in an exercise program.

DR. LARRY KRAVITZ *(Third-year family practice resident)*: What is the role of exercise testing in the patient who has had a recent myocardial infarction?

DR. GRAUER: Exercise testing may give us important prognostic information in the immediate postinfarction period. Patients who develop ventricular arrhythmias, ST segment changes, or chest pain on minimal exertion cause particular concern, and they should be considered for early catheterization if they are surgical candidates. Stress testing may help in exercise prescription. Equally important in the postinfarction period is the psychological benefit to be derived by the patient who may be wondering whether his heart will stand up to the rigors of daily living when he leaves the hospital. The ability to complete a low level exercise test without the development of chest pain or electrocardiographic abnormalities is about the strongest vote of confidence we can give.[1-4]

DR. MOORE: When is the optimal time to do a treadmill test following a myocardial infarction? Is it safe?

DR. GRAUER: It is still controversial whether an exercise test should be performed within two to three weeks of an infarct, prior to discharge from the hospital or at six weeks after the infarct.[1] We only exercise the patient to a low level of activity, a level comparable with what he will be doing when he gets home. It has been said that by not performing a predischarge stress test under monitored conditions, we allow the patient to perform his own unmonitored exercise test as soon as he gets home.

Returning to the interpretation of stress tests in patients presenting with chest pain, what is the likelihood that a patient with an abnormal test will have coronary artery disease?

The answer resides in Bayes' theorem, which states that the probability of a given patient's having disease depends on the prevalence of that disease in the population being tested. For example, the prevalence of coronary artery disease in 20-year-old women is virtually zero. Nevertheless, over 10 percent of women in this age group will demonstrate an abnormal ST segment in response to exercise. Since the pretest likelihood of coronary artery disease in this population is exceedingly small, the overwhelming majority of these responses will be false positives.

On the other hand, symptomatic middle-aged men with multiple risk factors have a pretest likelihood of coronary artery disease that approaches 90 percent, and almost any abnormal response will be indicative of a true-positive result. Most patients fall in between these two extremes, presenting with atypical chest pain that gives them a 30 to 50 percent pretest likelihood of disease. Whereas an abnormal response in this group of patients lends support to the diagnosis, a normal treadmill suggests another etiology for the patient's chest pain.

DR. KRAVITZ: I might add that a normal exercise test does not completely rule out coronary artery disease in the group of patients with a high pretest likelihood of disease.

Are there any factors that might help assess the pretest likelihood of disease more accurately?

DR. GRAUER: The prevalence of coronary artery disease in a population has been found to increase if one or more of the following conventional risk factors are present: smoking, hypertension, hypercholesterolemia, or a positive family history.[5]

In the test itself there are four basic ST segment responses (Figure 1). Usually, some depression of the J point (ie, the junction between the end of the QRS complex and the beginning of the ST segment) occurs with exercise, rapidly returning to the baseline. This ST segment depression has a rapid upslope and is a normal response (Figure 1A). The two clearly abnormal responses to exercise are horizontal (ie, flat) (Figure 1C) and downsloping ST segment depression of at least 1 mm (Figure 1D). Each of these responses is associated with a high incidence of coronary artery disease,

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and multivessel disease is commonly seen with the latter.[6]

ST segment depression with a slow upslope represents an intermediate response (Figure 1B). We define an ST segment as having a slow upslope if it has not yet returned to the baseline at .08 seconds following the J point. Some patients manifesting this response will have heart disease, whereas others will have normal coronaries, so that the physician must interpret this response in the context of other findings. For example, the earlier during the test that ST changes occur and the longer they persist, the more it is likely that the patient has disease.[6] There is also a rough correlation between the degree of ST segment depression and the severity of disease. A patient having 3 mm or more of horizontal or downsloping ST segment depression that persists into recovery has a high chance of having multivessel or left main coronary artery disease, whereas the transient appearance of only 1 to 2 mm of slowly upsloping ST segment depression is probably not significant.[6]

Application of these principles to G.M.'s serial exercise test explains the reason for our concern. In the first treadmill performed in 1977, slowly upsloping ST segment depression developed during exercise, becoming horizontal during recovery, and persisting as 0.5 mm of flat ST segment depression for at least six minutes after exercise was stopped (Figure 2). This result is compatible with the diagnosis of a previous myocardial infarction in this patient.

DR. KRAVITZ: How many patients with a previous myocardial infarction have an abnormal treadmill test?

DR. GRAUER: The overwhelming majority, since by definition a previous myocardial infarction implies the presence of coronary artery disease.

Two years later we can see a significant change in the patient's response (Figure 3). Although G.M. was now able to exercise longer on the treadmill as a result of his daily walking, the degree of ST segment change is more impressive than in 1977. During peak exercise at the end of stage 2, we see 3 mm of slowly upsloping ST segment depression that becomes persistently downsloping throughout recovery.

G.M.'s most recent treadmill shows even more

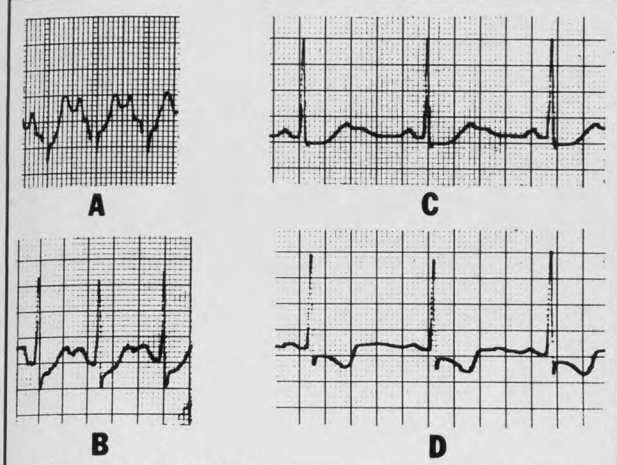

Figure 1. ST segment responses to exercise. (A) Rapid upslope—normal response, (B) Slow upslope—borderline response, (C) Horizontal ST segment—abnormal response, (D) Downsloping ST segment—abnormal response

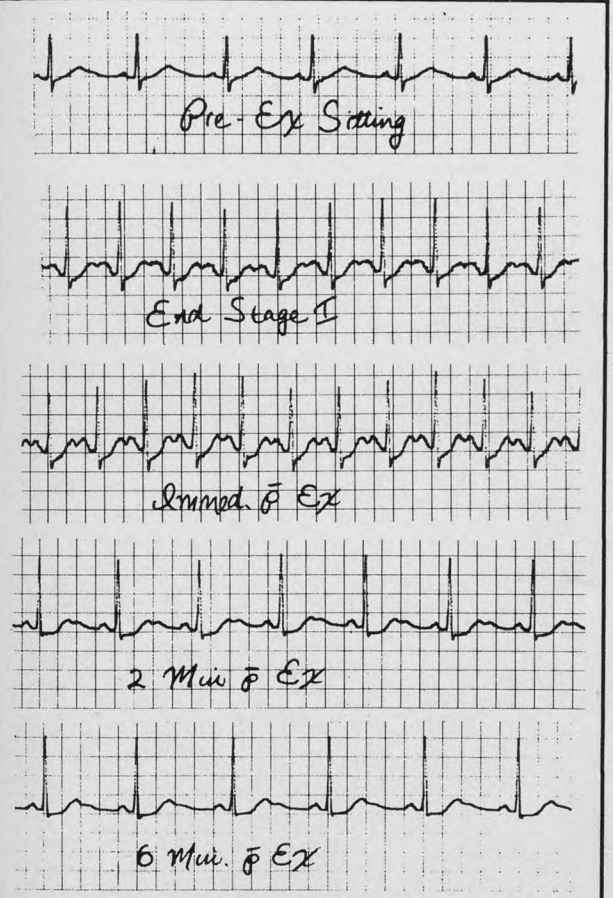

Figure 2. First exercise test performed in 1977. A 1.5-mm slowly upsloping ST segment depression is evident at peak exercise, becoming horizontal during recovery. A 0.5 mm ST segment depression is still seen 6 minutes into recovery

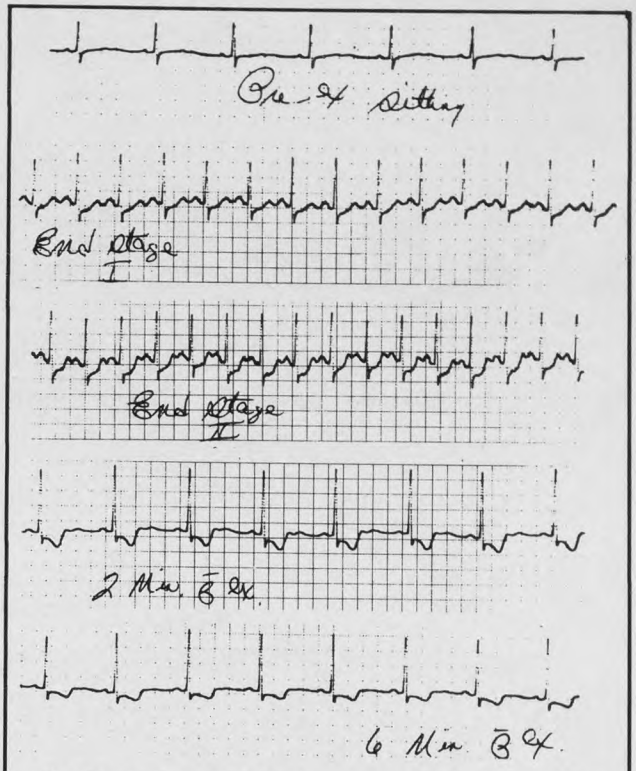

Figure 3. Exercise test performed in 1979. ST segment depression begins early, attains 3 mm with a slow upslope at peak exercise, and becomes persistently downsloping throughout recovery

profound ST segment changes (Figure 4). A 5-mm slowly upsloping ST segment depression occurs within the first two minutes of exercise, at which point the test was stopped. Downsloping ST segment depression is seen in recovery. This result strongly suggests multivessel or left main coronary artery disease.

DR. KRAVITZ: When should you stop the test?

DR. GRAUER: There are a number of reasons for terminating an exercise test. Development of a significant ventricular arrhythmia, a drop in systolic blood pressure, marked ischemic ST segment changes, or chest pain of an intensity that would normally stop the patient in his daily activities are all legitimate end points that suggest coronary ar-

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tery disease. It may be more difficult to decide on a cardiac etiology with other end points, such as dyspnea, fatigue, or claudication, which may end the test at a lower activity level than that needed to provoke angina. In the absence of any of these symptom-limiting end points, we terminate the test once the patient has achieved 85 percent of his maximal predicted heart rate.

G.M. did not develop chest pain during any of his tests. Exercise was stopped in the first two treadmills because of fatigue and because of marked ST segment changes in the third test.

Dr. Curry, would you discuss the catheterization findings?

DR. WHIT CURRY *(Director, Family Practice Residency Program)*: As Dr. Grauer mentioned, it was the progression of ischemic ST changes on serial exercise testing despite minimal symptoms that prompted us to strongly advise cardiac catheterization.

G.M.'s ventriculogram showed mild inferior hypokinesis that is due to his previous inferior myocardial infarction, but an otherwise well-functioning left ventricle. Coronary angiography revealed total occlusion of the distal right coronary artery and a high-grade stenosis of the circumflex artery. The left anterior descending coronary artery, totally occluded near its origin, is collateralized by a small anterolateral branch, but this branch also has a high-grade narrowing.

In summary, we have a 69-year-old gentleman with a previous myocardial infarction, documented three-vessel disease, normal left ventricular function, symptoms of stable angina pectoris, and a markedly abnormal stress test.

Several studies address the issue of prognosis associated with specific subgroups of patients with coronary artery disease. The Framingham Study indicated the overall risk of death following myocardial infarction to be about 5 percent to 7 percent per year.[7] In patients with angina pectoris, a 1980 European study demonstrated a five-year survival of 85 percent with medical treatment and 95 percent with surgical treatment in patients with three-vessel disease and good left ventricular function.[8] A review by Rahimtoola[9] indicated a surprisingly low annual mortality of 3.6 percent in patients with stable angina, good left ventricular

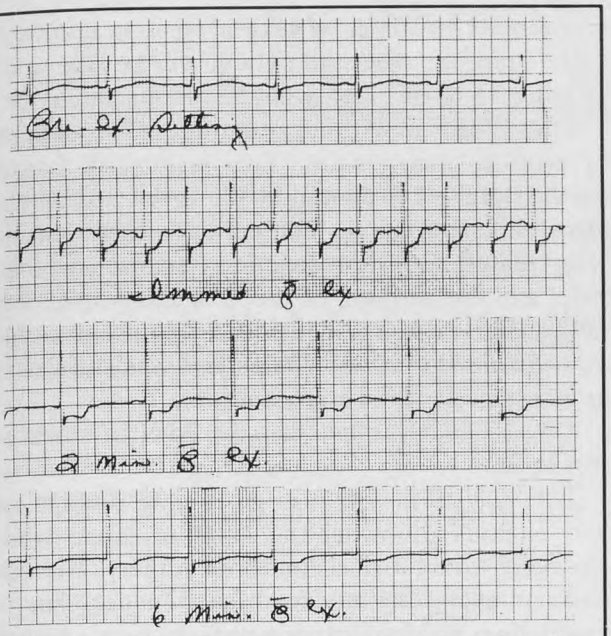

Figure 4. Exercise test performed in 1981. A 5-mm slowly upsloping ST segment depression occurs during the first stage of exercise and becomes downsloping in recovery

function, and three-vessel disease. The same review, however, associated an early positive treadmill test with a much higher annual mortality rate of 15 percent. More recently, Podrid et al[10] have questioned the belief that a markedly positive exercise test denotes such an ominous prognosis. In a study of 142 patients with stable angina pectoris and marked ST segment depression on exercise testing, these investigators found an annual mortality of only 1.4 percent on medical treatment during an average follow-up period of five years. An additional 1.3 percent of patients had bypass surgery. Although the methodology of this study has raised some questions because only a minority (12 percent) of the patients had been catheterized, the diagnosis of coronary artery disease seemed secure by virtue of a classic history of angina in all patients as well as documented myocardial infarction in 66 percent.

Thus, the annual mortality figures quoted in the literature for patients with coronary artery disease are in conflict with recent studies that indicate a lower mortality than that found in the older studies.

DR. KRAVITZ: This made us wonder whether the prospects of medical management for G.M. were not as dismal as we had initially perceived.

DR. GRAUER: With continued improvement in surgical technique, the overall mortality for coronary artery bypass surgery in centers that regularly perform this operation has dropped below 2 percent. Similarly, refinements in nonoperative management during recent years have greatly improved survival in medically treated patients, making it difficult at times to choose the most appropriate course of treatment.

DR. CURRY: There are four main factors to consider in evaluating patients for possible coronary artery bypass surgery: the coronary anatomy, the symptoms of the patient, objective evidence of ischemia, and left ventricular function.

It is generally agreed that surgery improves survival in patients with left main coronary artery disease. The National Institutes of Health Consensus-Development Conference Statement reached the agreement that in patients with three-vessel disease and good left ventricular function (G.M.'s subgroup), additional studies are needed before a firm conclusion can be reached on the question of improved survival with surgery.[11]

Another important indication for bypass surgery is angina refractory to medical treatment. Although everyone has his own idea about what is meant by the term *refractory,* symptoms improve in 90 percent of surgically treated patients compared with only 50 percent symptomatic improvement in patients treated medically. Clearly, G.M. did not have refractory symptoms.

As to evidence of ischemia, we are trying to determine how much myocardium is in jeopardy. A patient with adequate collateralization may be well compensated despite multivessel disease, whereas a patient with a significant lesion of the left main coronary artery is in danger of infarcting the entire left ventricle if the occlusion becomes complete. Here the exercise test or a thallium perfusion scan may provide objective evidence of ischemia.

Finally, the status of the left ventricle becomes a pivotal factor in determining survival of both medically and surgically treated patients. Once severe impairment of left ventricular function has occurred, damage is irreversible, and prognosis will no longer be improved by coronary artery bypass surgery.

DR. GRAUER: G.M.'s case was presented and his catheterization films reviewed at a conference attended by a number of cardiologists and cardiovascular surgeons. Although there was a difference of opinion, a majority recommended surgery.

SHAE KOSCH, Ph.D. *(Director, Behavioral Science Curriculum)*: What were the patient's feelings on the issue?

DR. CURRY: The patient was very much against having surgery if it could possibly be avoided. When asked my opinion, I told him I agreed with the majority of consultants who advised surgery but saw my primary role as providing sufficient information for *him* to make a fully informed decision. I arranged conferences between G.M. and his family with the cardiologist and later with the cardiac surgeon, at which time the catheterization films were reviewed and the case was further discussed. G.M. consulted with me alone on several additional occasions, and finally opted for medical treatment.

DR. KRAVITZ: Did you agree with that decision?

DR. CURRY: I saw my responsibility as G.M.'s family physician to support his decision regardless of my opinion once I was assured that he was fully informed of his options and their implications.

DR. WILLIAM STEWART *(Chairman, Department of Community Health and Family Medicine)*: An important point in this presentation is allowing the patient to decide which therapy is best for him and then supporting him in that decision regardless of whether it coincides with your own decision. I think that all too often we try to impose on the patient our own perceptions of what we think is best.

DR. KOSCH: Dr. Curry not only put the burden of decision making back into the patient's hands, but he also brought in several significant others, allowing the family as a group to arrive at a decision with which they felt comfortable.

Significant others can help to reduce the anxiety and depression that often accompany the threat of myocardial infarction or the anticipation of bypass surgery. These psychological symptoms are often a result of the patient's perceived loss of important activities such as job loss, reduced earning capacity, and the pleasurable activities of smoking, eating certain foods, sexual intercourse, and exercise. Therapeutically, it is best for the physician and family members to take a positive approach and emphasize what the patient will be able to do rather than to dwell on what he or she cannot do.

DR. CURRY: We began an intensive program of medical management. Two major risk factors we did not have to contend with were smoking and hypercholesterolemia. The patient's hypertension was treated by salt restriction, hydrochlorothiazide, and the addition of propranolol. Angina was infrequent and easily controlled by nitroglycerine on an as-needed basis. The patient was enrolled in an organized exercise program.

DR. KOSCH: What was his level of stress at this time?

DR. CURRY: He was extremely ambivalent and anxious following the catheterization while struggling with the decision about surgery. His wife had had a mastectomy for breast cancer about a year before and had just completed a year's course of chemotherapy. As a professor at the university, he was still involved in teaching. Overall then, he was under a moderate amount of stress.

DR. KOSCH: One of the most important things a family physician can do in managing such patients is to assess their level of social support and to encourage reliance on others for emotional support. Medalie and Goldbourt[12] have found that the incidence of angina is higher in men who have family problems. Cobb[13] reported that the cholesterol and uric acid levels in patients with inadequate social support become more elevated during periods of life stress than they do in patients with good support systems. In addition to drug regimens and dietary protocols, the family physician should be attuned to the patient's support system.

Attention to the marital and sexual relationship is an often neglected component of a cardiac rehabilitation program. The physician should inquire about the patient's previous sexual activities and then make specific suggestions on what may be undertaken after diagnosis of the disease. Once the patient is able to exercise into stage 2 of the treadmill test, climb two flights of stairs, or walk five blocks without undue changes, he or she has surpassed the work requirement of sexual activity.[14] It is important to discuss the resumption of sexual relations in the presence of the spouse. If either partner is still anxious about such activities,

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