editorial essay

Strategy for the Detection and Management of Coronary Artery Disease* “Physiology before Anatomy”

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A strategy for the diagnosis of ischemic heart disease should be based on knowledge of the prevalence of the disease in population subgroups. Asymptomatic patients should not be routinely screened. Asymptomatic patients or patients with nonanginal chest pain should have both a positive exercise electrocardiogram and stress nuclear scan before a diagnosis of ischemic heart disease is justified or arteriography is recommended. Patients with atypical angina should be evaluated with exercise radionuclide ventriculography. Coronary arteriography is rarely needed for diagnosis and is most properly used as a preoperative evaluation of a patient who has symptoms uncontrolled by medical management, or in whom a significant amount of myocardium is at risk as determined by physiologic testing with exercise electrocardiography or stress nuclear techniques.

The clinician is inundated with volumes of research data, often apparently conflicting, producing multiple and rapidly changing opinions about how best to evaluate and manage the patient with chronic coronary artery disease. Despite this apparent morass, however, we believe that when certain fundamental facts are analyzed and placed into proper perspective, one can formulate a clear strategy for the management of this common disorder.

Prevalence of Coronary Disease in Various Population Subgroups

Selection of appropriate tests to detect the presence of ischemic heart disease depends strongly upon the population subgroups studied. If one takes an unselected population of asymptomatic middle-aged males, coronary artery disease of potential clinical importance will approximate 5 percent. Inclusion only of individuals with nonanginal chest pain will yield an incidence of about 10 percent. Inclusion of individuals only with typical angina pectoris will yield an incidence of over 90 percent with important coronary obstruction(s). Certain individuals have features of both anginal and nonanginal pain, a syndrome which might be called atypical angina. This group generally has been found to yield approximately 50 percent with coronary disease.1-7

Risk of Mortality from Coronary Disease

The vast majority of data supports the fact that mortality correlates closely with the severity of resting left ventricular dysfunction, as measured by both invasive and noninvasive methods.6,10 Moreover, subsequent death rates correlate well with the total amount of myocardium rendered ischemic during increased oxygen requirement (i.e., with exercise) as measured by various stress tests, particularly radionuclide ventriculography. This correlation is better than that relating mortality to the number of obstructed coronary arteries demonstrated angiographically. Although there is a rough relationship between the number of diseased coronary arteries and the amount of myocardial tissue rendered ischemic by these lesions, the latter feature is the more important in determining risk of death. Thus, a given individual with disease of all three coronary vessels but with good resting and exercise myocardial performance enjoys a much better prognosis than does another patient with fewer vessels involved but significant impairment of large areas of the myocardium, especially when occurring at low levels of stress.11-13

Detection of Individuals with High Risk of Mortality

Since mortality depends primarily upon physiologic
impairment of blood supply to sizable portions of the ventricle (physiology) rather than simple demonstration of the number of diseased vessels (anatomy), tests which are designed to detect myocardial performance prove to be most useful clinically in the effort to stratify individuals into risk categories. This has been demonstrated through the use of both electrocardiographic and radionuclide stress testing. Attempts to modify mortality would appear to be most appropriately applied to the higher risk groups, especially if the therapeutic interventions entail significant mortality. Therefore, it generally serves little purpose to perform coronary angiography on individuals who demonstrate little or no physiologic impairment during testing. This is how we arrived at the caveat, "physiology before anatomy."

**Practical Approach to the Various Populations**

**Asymptomatic Individuals**

A question commonly asked is, "Should exercise electrocardiography be used in routine screening of asymptomatic individuals?" We do not recommend such testing, for the prevalence of disease in asymptomatic middle-aged men is only about 5 percent. In a population with such a low prevalence of disease, the predictive value of a positive test is low because the likelihood of a positive test being falsely positive is high. In fact, in this instance the predictive value of a positive test is estimated at about 24 percent, which means that the tests of three out of every four positively reacting individuals would actually be found to have false positives by subsequent testing. Screening in this group would, therefore, result in many individuals being subjected to undue mental stress, anxiety, expense, inconvenience, or risk of additional testing, particularly of the invasive variety. Although controversial, screening of population subgroups with a higher incidence of disease, such as middle-aged men with multiple risk factors, would result in a higher incidence of true positive tests and, therefore, are more easily justified. The screening of asymptomatic individuals may be justifiable in certain occupation groups or in individuals undertaking a more strenuous level of physical activity. A negative test in this population subgroup virtually excludes coronary artery disease. A positive exercise electrocardiogram per se in this subgroup is insufficient to make a diagnosis of coronary artery disease or to recommend coronary arteriography. Before such action is considered, an exercise nuclear scan should be done. If this latter test is negative in the presence of a positive electrocardiogram in this population group, one can virtually exclude significant coronary artery disease, and invasive studies should not be done nor should a diagnosis of coronary artery disease be made. Coronary arteriography may be considered if the tests suggest a significant amount of myocardium at risk, i.e., strongly positive exercise electrocardiography (especially at low levels of exercise) or a nuclear scan which demonstrates evidence of a large amount of myocardium at risk. Either exercise radionuclide ventriculography or stress thallium imaging can be used. Because the former is considerably cheaper, we use it in most instances. There are some instances, however, when the exercise thallium study is preferable; for example, young adults with insulin-dependent diabetes mellitus may demonstrate a nonspecific abnormal response to exercise radionuclide ventriculography, presumably as a result of myocardial dysfunction attributable to factors other than large vessel coronary arterial disease. Similarly, any individual with primary cardiac muscle dysfunction, hypertension, valvular disease or a ventricular conduction defect such as left bundle-branch block may potentially produce global or local wall motion abnormalities with exercise. Since these latter conditions are unassociated with disease of the larger coronary vessels, the thallium scan would fail to show perfusion defects and thus would correctly be interpreted as negative. However, false positive thallium scans have been reported with left bundle-branch block.

**Individuals with Chest Pain**

As noted above, the type of chest pain syndrome determines the prevalence of coronary artery disease. Typical angina pectoris is defined as chest pain usually touching the sternum, precipitated by effort or emotion, relieved in one or two minutes by nitroglycerin, or in several minutes by rest. The prevalence of atherosclerotic disease of the large coronary vessels exceeds 90 percent in this subgroup. It should be remembered that in order to be classified as typical angina pectoris it should be consistently typical; otherwise, it must be considered atypical. The incidence of coronary disease in this atypical category depends largely upon the skill of the examining physician, and probably will run around 50 percent. Nonanginal chest pain has none of the above characteristics, and most individuals within this group have no coronary artery disease.

Since the incidence of coronary disease in the group with nonanginal chest pain is low, the predictive value of a positive electrocardiographic stress test performed upon an individual with this complaint is correspondingly low, approximately 40 percent. This means that the majority of individuals with a positive test do not have coronary artery disease. It is thus not justifiable to make a diagnosis of coronary artery disease or recommend coronary arteriography on the grounds of a positive exercise electrocardiogram in individuals with nonanginal chest pain. Before one can even presume such a diagnosis, further evaluation is required. For
reasons already mentioned, a negative exercise radionuclide ventriculogram virtually excludes disease. Therefore, both a positive exercise electrocardiogram and an exercise nuclear scan are required before making a diagnosis of coronary disease or performing coronary arteriography.

Since the prevalence of coronary artery disease in middle-aged men with atypical angina pectoris is about 50 percent, the predictive value of a positive test is most helpful. The exercise electrocardiogram has a predictive value of about 85 percent; therefore, most of the patients with positive tests will indeed have coronary artery disease. Because the sensitivity of the exercise electrocardiogram is only about 60 percent, one would anticipate a sizable number of false negative tests in this group. Theoretically, this would mean that many individuals with coronary disease but with negative test results would be falsely labeled as normal and thus denied any further evaluation. This problem is relatively unimportant from a practical standpoint, inasmuch as the low sensitivity of the exercise electrocardiogram is largely accounted for by a high number of false negatives in the group with single vessel disease or in whom small areas of myocardium are ischemic. Therefore, although a negative test result does not exclude significant coronary artery disease, it does make the diagnosis of left main or triple vessel coronary disease, with large areas of myocardium at risk, unlikely. Nevertheless, because exercise radionuclide ventriculography has greater sensitivity than exercise electrocardiography, it is reasonable to begin with the nuclear test in patients with atypical angina pectoris, especially if the patient is already hospitalized.

In patients with typical angina pectoris, the prevalence of coronary artery disease exceeds 90 percent. Although the predictive value of a positive test is extremely high in this subgroup, that of a negative test is low. This means that although a positive test is highly reliable in supporting the diagnosis, a negative test is likely to be falsely negative; therefore, within the group with typical angina pectoris, a negative test has little diagnostic significance. The reason for performing this test in such patients is to screen for high risk lesions with significant myocardium at jeopardy. High risk lesions correlate with a strongly positive treadmill electrocardiogram, especially when appearing at low levels of exertion. They also correlate with exercise radionuclide ventriculograms that have a significant fall in global ejection fraction and a large new wall motion abnormality during exercise, and with large reversible perfusion defects on thallium imaging. On the other hand, absence of such findings in individuals who possess good exercise tolerance indicates a good prognosis, regardless of anatomic lesions. Patients presenting with typical angina pectoris, therefore, should be subjected to coronary arteriography only when symptoms are unacceptable despite medical management or physiologic testing indicates a significant amount of myocardium at risk. It is done in anticipation of a decision to proceed with invasive type therapeutic procedures, ie, surgery or angioplasty.

**Reasons for the Performance of Coronary Arteriography**

Coronary arteriography is rarely needed to make the diagnosis of coronary artery disease. In subgroups of the population with a low prevalence of coronary artery disease, ie, asymptomatic individuals or those with nonanginal pain, both a positive exercise electrocardiogram and stress nuclear scan should be required before cardiac catheterization is recommended. In the subgroup with an intermediate prevalence of coronary artery disease, ie, atypical angina pectoris, a positive stress nuclear scan should be obtained before coronary arteriography is recommended. Diagnostic coronary arteriography may be recommended for patients with inconclusive noninvasive test results to alleviate anxiety created by the uncertainty. Finally, as mentioned above, angiography is performed as a precondition to operative or angioplasty intervention in cases already selected on the basis of intractable symptoms or the presence of a large area of ischemic myocardium.

**Indications for Mechanical Manipulation of Coronary Lesions**

Coronary artery bypass surgery is often indicated in patients who have moderate or severe angina pectoris not controlled by medical therapy, significant left main coronary obstruction or triple vessel disease, especially with impairment of left ventricular function. Data from the recently concluded coronary artery surgical study (CASS) showed that patients who were asymptomatic or mildly symptomatic survived as long with medical therapy as with surgery, regardless of the number of coronary vessels involved. There was a slight trend for patients with triple vessel disease and impaired left ventricular function to have a higher rate of survival with surgery. These data support the conclusion that medical management of most patients is acceptable until worsening symptoms require surgical palliation, and this approach does not carry any mortality penalty. We do not believe that the more recently developed technique of percutaneous coronary arterial angioplasty will alter this scheme for it will likely be indicated for those patients in whom surgery is indicated, but who possess coronary lesions amenable to this approach.

**Management of the Patient after a Myocardial Infarction**

These principles discussed also apply following
acute myocardial infarction. The need to perform coronary arteriography depends upon the presence of postinfarction angina pectoris or a significant amount of residual myocardium at risk as demonstrated by physiologic testing, whether the patient is young or not. The physiologic testing may be accomplished with exercise electrocardiography, radionuclide ventriculography, or thallium imaging within a few weeks after the initial event. Coronary arteriography should be recommended only when symptoms are present or when physiologic testing suggests high risk.27-33 The most favorable timing for such evaluation and resultant therapeutic interventions have yet to be determined. Moreover, the strategy for the employment of arteriography, together with various interventions, during the process of acute myocardial infarction have not yet been well worked out and will not be discussed here.

Patients who sustain myocardial infarction without the development of electrocardiographic Q waves fall within a heterogeneous group. This group includes not only those with completed occlusion of small branch arteries, but also those with high grade but incomplete obstructive lesions of the proximal or mid-left anterior descending artery. This latter category includes many individuals thought to have an increased risk for subsequent fatal myocardial infarction. Patients in this category often have marked ST wave abnormalities in the precordial leads and may continue to manifest an unstable course characterized by recurrence of chest pain and electrocardiographic ST shifts. Recurrent episodes of this nature mandate a more aggressive approach; therefore, coronary arteriography should be performed without physiologic testing. However, in most instances of non-Q wave infarction with a more stable clinical course, the patient can be evaluated for ischemia with physiologic testing. Again, such a patient can be evaluated for significant residual myocardium at jeopardy with a carefully monitored exercise electrocardiogram or exercise nuclear scan in the same way that a patient with a transmural myocardial infarction is evaluated.

Proper Uses of Radionuclide Techniques

As discussed previously, exercise radionuclide ventriculography and thallium imaging have the same sensitivity for detecting coronary artery disease. Because of its lower cost, we use the former whenever possible. Exercise echocardiographic techniques employing digital analysis of wall motion offer considerable promise and may soon provide the clinician with another more cost effective alternative to radionuclide ventriculography. Thallium imaging, however, is more specific for coronary artery disease and may be preferred in certain situations. Such is the case when one evaluates individuals in whom there is a high likelihood of myocardial dysfunction from causes other than large vessel coronary disease, such as diabetes mellitus, various types of cardiomyopathy, or hypertension, and electrical conduction abnormalities within the left ventricle. When cineangiography has already been performed and specific lesions have been demonstrated, we find the exercise thallium test more helpful for accurately evaluating the physiologic significance of these anatomic obstructions. Similarly, we find the stress thallium imaging technique more useful in patients who have undergone bypass grafting or angioplasty in identifying continued adequate blood supply to previously ischemic areas of myocardium.

Summary

1. One should not routinely screen asymptomatic patients for coronary artery disease with exercise electrocardiography because the predictive value of a positive test in this subgroup is too low and a positive test is likely to be a false positive test.

2. Patients with nonanginal chest pain can be evaluated with exercise electrocardiography. A negative test excludes disease but a positive test is not sufficient for a diagnosis of coronary artery disease or to proceed with coronary cineangiography. This requires a positive stress nuclear scan: under most circumstances an exercise radionuclide ventriculogram.

3. Patients with atypical angina pectoris should be evaluated with exercise radionuclide ventriculography. The relative insensitivity of the exercise electrocardiogram will allow individuals with organic disease to go unrecognized within this group.

4. The history of typical angina pectoris is a sensitive indicator for the presence of coronary artery disease.

5. Following a transmural myocardial infarction, the need for coronary arteriography should be based upon symptoms or the presence of significant residual myocardium at risk as determined by physiologic testing, whether the patient is young or not.

6. Following a subendocardial or non-Q wave infarction, many patients can be evaluated with physiologic testing before angiography is recommended.

7. Exercise radionuclide ventriculography (or comparable echocardiographic techniques) are cheaper than exercise thallium imaging and are equally sensitive for the detection of coronary artery disease. Thallium testing is, however, more specific in assessment and may be used more effectively in situations where false positive ventriculography is more likely or in evaluating the physiologic effects of known anatomic lesions, before and/or after such lesions have been treated by surgery or angioplasty.

8. Coronary arteriography is rarely needed for diagnosis of coronary artery disease, no matter what the clinical presentation. It is most properly used as a preoperative evaluation in a patient who has symptoms
uncontrolled by medical management or in whom a significant amount of myocardium is at risk as determined by physiologic testing with exercise electrocardiography or stress nuclear techniques.

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