Controversies in Coronary Artery Disease

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CARDIOVASCULAR CLINICS, Albert N. Brest, Editor-in-Chief

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Controversies in Coronary Artery Disease

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This book is dedicated to those heroes of medicine whose role in the triumphs of medicine is usually not adequately recognized. These include (1) the patients who consent to participate in clinical research, and (2) the physician's family. In my case, to my wife, Shameem; our son, Aly; and our daughters, Nadia and Yasmin.

Editor's Commentary

Coronary heart disease is presently the major cause of mortality in the westernized world. During the past decade, enormous strides have been made in our understanding of this disorder and in the availability of improved diagnostic methods and therapeutic approaches. Despite these advances and the improved outlook for the patient with coronary disease, many clinical challenges remain and significant controversies persist regarding diagnosis and management especially. This monograph deals with the important controversial issues that vex us currently. The contributors to this volume comprise an extraordinary wellspring of information and insight. I am enormously grateful to Shahbudin H. Rahimtoola for his scholarly guidance in the formulation of this book, and both of us are indebted to the participating authors for their exemplary contributions.

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Contents

Should Exercise Electrocardiographic Testing Be Replaced by Radioisotope Methods?

Robert S. Gibson, M.D., and George A. Beller, M.D.

In recent years, much has been written related to the noninvasive detection of coronary artery disease (CAD) in patients with chest pain. Today, the clinician is presented with several alternative approaches to exercise testing and must choose the appropriate test or tests yielding the greatest diagnostic and prognostic information. How should the clinician select the proper test? Is exercise electrocardiography alone no longer indicated? Should a thallium-201 perfusion scan or exercise radionuclide angiogram be performed? In what sequence should the tests be undertaken and what are the cost/benefit ratios involved?

Although previous studies indicate that exercise electrocardiography is a valuable epidemiologic tool when large groups are studied,[1–3] the suboptimal sensitivity of the test in symptomatic patients[4–22] poses certain problems when it is used to detect CAD in the individual patient. With the availability of thallium-201 myocardial perfusion scintigraphy and exercise radionuclide angiography as alternative methods of diagnostic evaluation, the physician is now faced with determining whether these noninvasive nuclear cardiology procedures should replace exercise electrocardiographic stress testing.

Clearly, there are many factors that govern the decision by the physician to order a particular test.[23] As pointed out by Redwood and coworkers,[24] "only when the strengths and weaknesses of a test are fully appreciated, can it be properly employed or rejected in the assessment and management of the individual patient." The purpose of this chapter, therefore, is threefold. First of all, it will explore some basic principles in test selection and interpretation, focusing on the assignment of probabilities for test use and evaluation. Secondly, it will review the value and limitations of exercise electrocardiography, thallium-201 perfusion scintigraphy, and radionuclide angiography for both detecting CAD and staging its severity. Lastly, it will present an approach whereby these tests can be used alone or in combination either for diagnostic purposes or in the estimation of relative risk for future coronary events.

PRINCIPLES OF TEST SELECTION AND INTERPRETATION

The potential of noninvasive testing to detect the presence of significant CAD is now fairly well established. However, the question of when to employ a test for this purpose is deceptively complex and remains somewhat controversial at present. In selecting diagnostic studies, the goal to keep in mind is to acquire the most definitive information concerning the presence or absence of CAD, with the fewest maneuvers and with the

least expense, discomfort, and risk to the patient. The decision for choosing one non-invasive test over another rests on the ability of the test to reliably predict the patient's angiographic coronary anatomy. When a diagnostic test is used to detect CAD, two questions frequently arise: (1) If the test result is positive, what is the probability the patient has disease? (2) If the test result is negative, what is the probability the subject does not have disease? The former probability reflects the predictive accuracy of a positive test result and the latter, the predictive accuracy of a negative test result. In order to answer these questions and thus determine the diagnostic capabilities of the test, two bits of information are needed. First, the operating characteristics of the test need to be known—in particular, its sensitivity, specificity, false-negative rate, and false-positive rate (Fig. 1). Sensitivity measures the fraction of patients with disease that will be detected by the test (a/a + b). This value expresses the probability that patients with disease will have positive test results. Specificity measures the fraction of normal patients that will be correctly identified as having no disease (d/c + d). It reflects the probability that patients without disease will have negative test results. The false-negative ratio is the proportion of negative test results in all patients with disease (b/a + b), and the false-positive ratio is the proportion of positive test results in all patients who do not have disease (c/c + d). Secondly, the prevalence of disease in the population under study has to be known. Once the operating characteristics of the test are known and combined with the pretest likelihood of disease in the population under study, the results of the test can be applied to a particular patient to yield a probability estimate of CAD. A formula called Bayes' theorem[25] is used for this purpose.

Predictive Value and Bayesian Theory

Bayes' theorem states that although the reliability of a diagnostic test is defined by its sensitivity and specificity, a precise measure of the test's predictability cannot be accurately undertaken without reference to the prevalence of disease in the population under study. Since the major issue in clinical practice is knowing the predictive value of

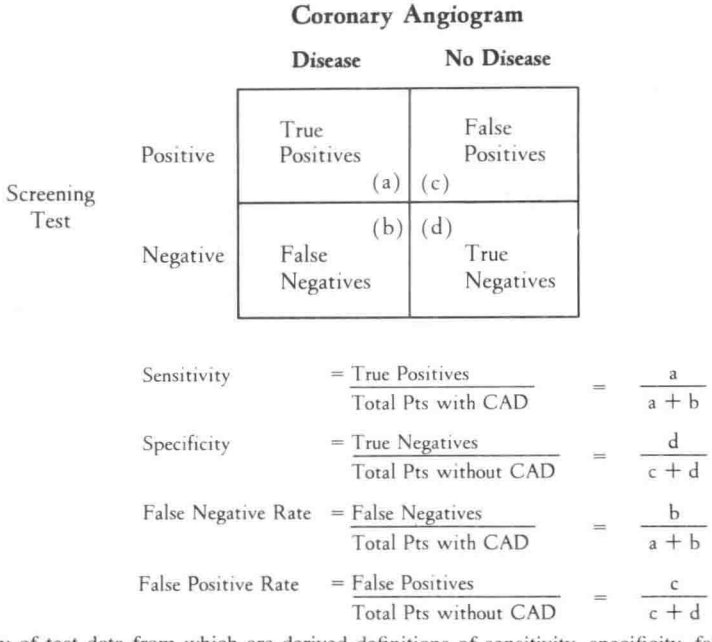

Figure 1. Display of test data from which are derived definitions of sensitivity, specificity, false-negative rate, and false-positive rate.

a positive and negative test result, respectively, these terms deserve further emphasis. The predictive value of a positive test result indicates the percentage of patients with CAD among all patients with positive test results (true-positives/true-positives + false-positives), whereas the predictive value of a negative test result reflects the percentage of patients without CAD among all patients with negative test results (true-negatives/true-negatives + false-negatives).

The importance of integrating a test's sensitivity and specificity with disease prevalence to calculate predictive values is illustrated in the following examples. Assume we have a near-perfect screening test, one with a 92 percent sensitivity (8 percent false-negative rate) and a 98 percent specificity (2 percent false-positive rate). Certainly, this is superior to any noninvasive test currently available for CAD detection. Now consider the results of the test applied to an asymptomatic individual with a 5 percent pretest probability of having CAD (Fig. 2), a patient with atypical chest pain and an estimated prevalence of 50 percent (Fig. 3), and, lastly, a middle-aged man with typical angina pectoris and a disease prevalence of 90 percent (Fig. 4).

In the first example, one would expect 950 normal subjects and 50 patients with CAD, based on a 5 percent disease prevalence. Since our test has a 2 percent false-positive rate and an 8 percent false-negative rate, 19 of 950 normal subjects and 46 of 50 CAD patients would have positive test results, yielding a positive predictive value of 71 percent. Thus, in this population of asymptomatic subjects, a positive test result would provide misleading information in 29 percent of such individuals. Although a negative test result allows one to exclude disease in 99 percent, this is only of marginal benefit considering the pretest likelihood of no disease was already 95 percent. In the second example of an individual with atypical chest pain, calculation of predictive values reveals definite clinical benefit from the test. By applying the test to this population, CAD is correctly identified in 98 percent, a substantial increase over the pretest likelihood of 50 percent. In addition, a negative test result reduced the probability of disease to 7 percent. In the last example of the individual with typical angina, a positive test result increased the likelihood of CAD from 90 percent to 99 percent. A positive test result would add little certainty to an already high likelihood of disease. A negative test result would reduce the likelihood of disease to only the intermediate level,

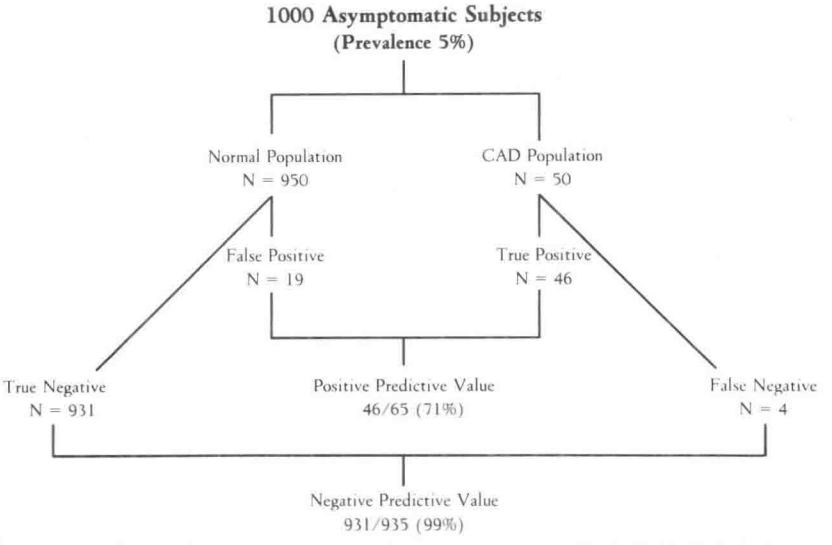

Figure 2. Probability of detecting coronary artery disease in asymptomatic individuals based on hypothetical data, when the pretest likelihood of disease is 5 percent, and the diagnostic test has 92 percent sensitivity and 98 percent specificity.

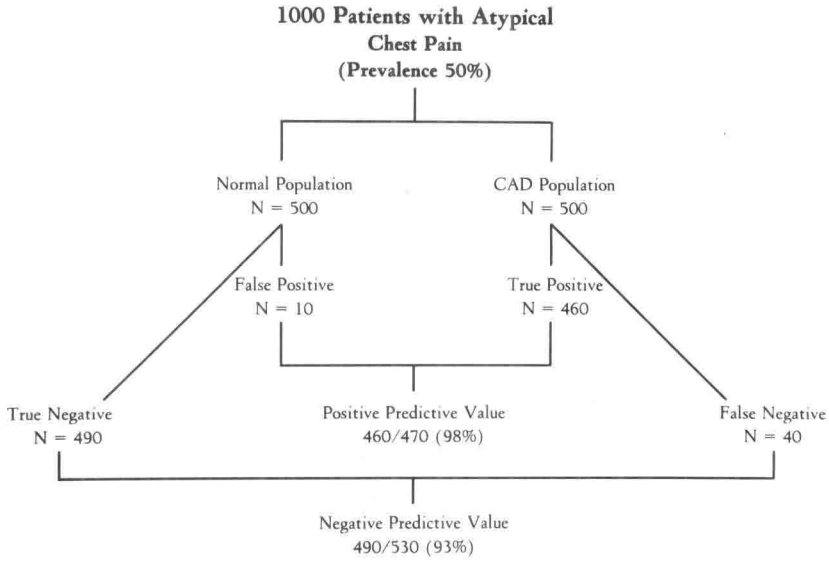

Figure 3. Probability that chest pain is due to coronary artery disease based on hypothetical data, where the pretest likelihood of disease is 50 percent, and the diagnostic test has 92 percent sensitivity and 98 percent specificity.

since the pretest and post-test probabilities were 90 percent and 42 percent, respectively. As will be discussed in the final section of this chapter, it is in this instance that a second noninvasive test is extremely useful.

These examples illustrate several points worthy of emphasis: (1) Sensitivity and specificity figures do not indicate the predictability of a positive or negative test result when applied to a specific mixed population or to an individual patient. Such figures tell us only what percentage of patients with and without CAD will have a positive and negative test result, respectively. When applying the test to a clinical population, con-

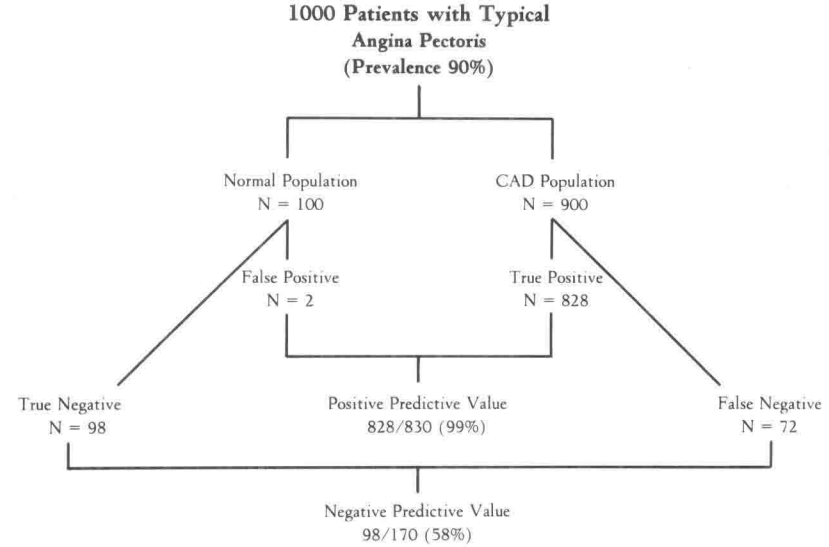

Figure 4. Probability that chest pain is due to coronary artery disease based on hypothetical data, when the pretest likelihood of disease is 90 percent, and the diagnostic test has 92 percent sensitivity and 98 percent specificity.