How Can We Diagnose Coronary Heart Disease in Hypertensive Patients?

SYMPTOMS of angina occur in patients with essential hypertension both with and without coronary artery disease. No noninvasive screening test has been found to adequately discriminate between hypertensive patients with and without associated coronary atherosclerosis. The 1983 projection of prevalence of hypertension in the United States (defined as a blood pressure measurement greater than 140/90 mm Hg taken as the average of three readings on one occasion or self-reported taking of antihypertensive agents) estimates 58 million persons to be at increased risk of morbidity and premature mortality. Because essential hypertension is highly prevalent and myocardial infarction remains the major cause of death in the United States, more clinical research needs to be directed toward the evaluation or development of effective noninvasive tools to diagnose significant obstructive epicardial coronary artery disease resulting in myocardial ischemia in this large population of patients.

Definitions and Mechanisms

Both hypertensive heart disease and coronary heart disease may result in similar clinical events. Furthermore, both diseases frequently occur in the same patient. It is well established that progressive increments in blood pressure, especially systolic blood pressure, increase the risk for the development of atherosclerosis, resulting in anatomical coronary artery disease. Coronary heart disease (stable angina pectoris, unstable angina, myocardial infarction, and sudden death) is a manifestation of ischemic heart disease due to obstructive atherosclerotic epicardial coronary artery disease.

The diagnosis of hypertensive heart disease requires evidence of left ventricular hypertrophy or left ventricular failure and sustained systemic arterial systolic and diastolic hypertension. This older definition of hypertensive heart disease does not integrate the concepts of Doppler left ventricular diastolic filling abnormalities, which may predate echocardiographic left ventricular hypertrophy, and hypertensive hypertrophic cardiomyopathy of the elderly associated with supernormal systolic function. However, it is the presence of left ventricular hypertrophy that alters the supply (coronary blood flow) and demand (myocardial oxygen requirement) equation, resulting in angina even when the epicardial coronary arteries appear normal by arteriography. Reduced coronary reserve, demonstrated by a reduction of dipyridamole-induced coronary vasodilation, is suggested as being an important contributor to angina pectoris in hypertensive patients with left ventricular hypertrophy. Light and electron microscopic examinations of biopsied left ventricular endomyocardial tissue from these patients did not demonstrate any evidence of small-vessel disease. Researchers using the regional xenon-133 washout technique measured reduced myocardial blood flow per unit mass of tissue in controlled hypertensive patients with left ventricular hypertrophy, which they believed to be a consequence of a lower level of wall stress due to both hypertrophy of the left ventricular wall and reduced systolic pressure. Although the resting coronary vascular resistance was elevated in these patients compared with normal subjects, there was a significant decrease in resistance during atrial pacing, suggesting improved perfusion.
The presence of electrocardiographic left ventricular hypertrophy increases the risk of myocardial infarction, sudden death, and congestive heart failure.13-16 Electrocardiographic left ventricular hypertrophy also increases the risk of these events in normotensive patients, but the level of jeopardy is higher in hypertensive patients. Moreover, repolarization changes (left ventricular hypertrophy "strain" pattern) independently increase the risk of cardiovascular events, but definite electrocardiographic left ventricular hypertrophy (voltage) with left ventricular hypertrophy "strain" pattern is associated with a higher (sixfold) increase in death from coronary heart disease.13 More recently, echocardiographic left ventricular hypertrophy (anatomical left ventricular hypertrophy) has been determined to be a marker predictive of premature cardiovascular mortality.17

Diagnostic Methods

The distinction between angina pectoris caused by coronary heart disease and that caused by hypertensive heart disease is important because treatment goals and management may be different for each entity. If the presence of epicardial coronary artery disease can be established by noninvasive techniques, the risks and expense of coronary arteriography can be avoided. Moreover, even if obstructive coronary artery disease is documented by arteriography, the resulting knowledge of anatomy may not accurately reflect physiological importance, that is, prove that angina is related to the arterial narrowing rather than to left ventricular hypertrophy.

Although it is not unreasonable to perform exercise stress testing to assess the blood pressure response to exercise and functional aerobic capacity, its use for determining the probability of obstructive epicardial coronary artery disease lacks specificity.18-21 Systemic hypertension, even without resting electrocardiographic changes, may result in ST segment depression without obstructive epicardial coronary artery disease.19-21 Although electrocardiographic left ventricular hypertrophy may result in a false diagnosis of obstructive epicardial coronary artery disease, the sensitivity of the electrocardiogram for detecting left ventricular hypertrophy is low (although the specificity is high) when using the Romhilt-Estes point score system.22,23 Therefore, undiagnosed anatomical left ventricular hypertrophy may be present when electrocardiographic criteria are absent, and diagnostic ST depression at peak stress may result from ischemia due to left ventricular hypertrophy and abnormal coronary blood flow rather than obstructive epicardial atherosclerotic coronary artery disease.21,22 Also, electrocardiographic left ventricular hypertrophy often is associated with resting ST and T wave repolarization changes. These changes are associated with a higher likelihood of a false-positive electrocardiographic response. Currently, echocardiography is the most sensitive and specific method to define the presence of anatomical left ventricular hypertrophy.23-25 Wroblewski et al.21 studied 31 hypertensive patients with anginal chest pain by exercise stress testing and coronary arteriography. None of the patients had electrocardiographic left ventricular hypertrophy, but all had anatomical left ventricular hypertrophy by echocardiography. There were 10 (32%) false-positive diagnoses of obstructive epicardial coronary artery disease in this group. These factors suggest that the use of exercise stress testing to diagnose coronary artery disease in hypertensive patients with chest pain should be abandoned.

Radionuclide left ventricular angiography in normotensive patients has been reported to be an excellent indicator of ischemia due to coronary artery disease.26 However, a recent study documents that it is a poor way to detect obstructive epicardial coronary artery disease in hypertensive patients.27 Coronary arteriography and exercise radionuclide angiography studies were performed in 37 hypertensive and 109 normotensive patients with chest pain. When the traditional criteria (failure of the ejection fraction to increase by 5% and/or the development of new wall motion abnormalities with exercise) were used, the predictive accuracy was poor in the hypertensive group (46%) as compared with the normotensive group (89%). Thus, stress nuclear angiography does not help in the diagnosis of coronary artery disease in hypertensive patients.

The sensitivity, specificity, and predictive values of exercise thallium-201 myocardial perfusion imaging for detecting obstructive epicardial coronary artery disease is superior to routine exercise stress testing.28,29 Bayes' theorem of conditional probability shows that the positive predictive accuracy of a test (the ratio of true-positive results to both true-positive and false-positive results) is highly dependent on the pretest probability of disease in a given patient population (Table 1). If we assume that the
average sensitivity for thallium-201 imaging is 94% and the specificity is 71% (unpublished data from our institution, 1987) and consider a hypothetical population of 1000 patients with a low disease prevalence of 10%, then 94 of 100 patients with obstructive epicardial coronary disease present would have a true-positive study result (sensitivity = 94%). Of the 900 disease-free patients, 261 would have a false-positive test result (1 — specificity), since 29% of the patients who were disease-free would have a positive result (see Table 1). Therefore, only 94 (26%) of the 355 patients with positive test results would have true-positive test results. It is in the midrange of disease prevalence that a positive (or negative) test result optimizes the difference between the pretest and posttest probability of disease. However, in patients with a low to intermediate pretest likelihood of obstructive epicardial coronary artery disease, the absence of perfusion defects suggests a good prognosis (i.e., high negative predictive value).3031

The development of quantitative methods for the evaluation of planar thallium-201 images has provided a more objective means by which scan abnormalities may be detected. These methods help to eliminate the subjective biases and interobserver variability that have been noted in visual image interpretation, especially when the readers are not experienced or the volume of studies performed is low. In basic terms, quantitative methods evaluate an individual patient’s myocardial kinetics (uptake and washout) and compare scan regions, using in reference either predetermined normal values or each patient as his or her own control. The overall sensitivity, specificity, and predictive accuracy of planar thallium-201 imaging for the detection of obstructive epicardial coronary artery disease may be improved by these methods.32 Single-photon emission computed tomography, using thallium-201, is a newer modality that has the potential to quantitate and localize ischemic or infarcted myocardium better than standard planar images can, especially in the setting of obstructive epicardial triple-vessel and circumflex coronary artery disease.33 However, the overall utility of this modality, in view of its higher cost and comparable sensitivity and specificity to planar imaging for zero-, one- and two-vessel coronary artery disease, must be better defined.

To our knowledge, no retrospective or prospective studies have assessed myocardial perfusion imaging with thallium-201 in hypertensive patients who have undergone coronary arteriography. Because myocardial thallium uptake is dependent on regional Na⁺-K⁺ pump function, as well as myocardial blood flow, any myocardial pathology may produce an abnormal image. It may thus be postulated that hypertensive patients, especially those with left ventricular hypertrophy, may have perfusion abnormalities unrelated to epicardial coronary artery disease, that serve to alter the kinetics of thallium-201 and result in abnormal images interpreted as representing ischemia or infarction.35 Certainly, it is well documented that there is marked heterogeneity of thallium-201 uptake and washout, even in the normal subjects used to derive the reference values used in quantitative analysis programs.36 One study of thallium-201 myocardial perfusion imaging in aortic stenosis demonstrated focal perfusion defects and wall thinning in five of 11 patients without significant obstructive epicardial coronary artery disease (30% or less narrowing).37 Therefore, whether hypertensive cardiovascular disease with attendant left ventricular hypertrophy will alter the sensitivity, specificity, and predictive accuracy of thallium-201 myocardial imaging remains to be determined by a prospective study.

Coronary arteriography remains the "gold standard" for evaluating anatomical coronary artery disease, but it cannot determine altered blood flow or ischemia. It is now well documented that a less than 50% occlusive lesion demonstrated by arteriography...
may be associated with significant segmental myocardial perfusion defects with exercise testing. The intraoperative Doppler measurement of reactive hyperemia after a brief, complete occlusion of a coronary vessel is an indicator of the severity of anatomical obstruction. This precise technique demonstrates a disturbing dissociation between the angiographic estimation of luminal narrowing and the magnitude of reactive hyperemia. The transstenotic pressure gradient of a coronary stenosis, instead of the percentage (for lesions less than 90%) of luminal narrowing seen at angiography, may be a better predictor of the presence of a reversible thallium defect. Such studies highlight the dilemma of diagnosis and therapy for angina. Should we treat morphological changes, physiological consequences, or clinical manifestations?

Issues

Hypertension and coronary heart disease remain highly prevalent diseases. Complications of coronary heart disease remain the major cause of mortality in the United States. However, the high prevalence of hypertension precludes a general recommendation for coronary arteriography to screen "chest pain of uncertain origin". Furthermore, the morbidity and mortality (not to mention the cost) of cardiac catheterization merit major consideration. A noninvasive technique is needed that can predict with a reasonable degree of accuracy the presence of obstructive epicardial coronary artery disease causing myocardial ischemia in hypertensive patients.

Thallium-201 myocardial perfusion imaging may be the logical screening tool. Prior knowledge of the presence or absence of left ventricular hypertrophy by echocardiography will be important since electrocardiographic left ventricular hypertrophy with or without a "strain" pattern may be measuring something other than hypertrophy. Therefore, careful measurements of echocardiographic left ventricular wall thickness and mass should be performed in hypertensive patients with chest pain so that we may answer these questions: What types, if any, of perfusion defects in the hypertrophied left ventricle of hypertensive patients are characteristic of hypertensive heart disease without significant obstructive epicardial coronary artery disease? Are hypertensive patients with anatomical left ventricular hypertrophy and angina, when compared with those without anatomical left ventricular hypertrophy, more likely to have reversible thallium defects? If so, what types of defects are more likely to be associated with coronary artery disease? Is the left ventricular hypertrophy "strain" pattern a sign of myocardial ischemia or hypertensive heart disease? Will regression of left ventricular hypertrophy by vigorous antihypertensive drug treatment correct perfusion defects if disease of the major epicardial coronary arteries is absent? There are no data to answer these questions about the operational characteristics of thallium-201 scintigraphy in these patients.

Summary and Conclusions

Chest pain is a common complaint among hypertensive patients. Hypertension and coronary heart disease each may present with symptoms and signs that are clinically indistinguishable. Noninvasive testing by routine exercise stress testing and stress radionuclide angiography are not reliably predictive of ischemia resulting from obstructive epicardial coronary artery disease and should be abandoned for that diagnostic purpose. Noninvasive thallium-201 myocardial perfusion imaging for this purpose may prove to be a valuable tool, avoiding the risk and expense of coronary arteriography. However, carefully performed prospective studies are not available. Because of the high prevalence of both diseases, a high priority must be given to obtaining these data and evaluating other noninvasive methods (especially positron emission tomography) if they appear promising.
Acknowledgment
We thank Mrs. Peggy Best for her assistance in the preparation of this manuscript.

References

Address for reprints: L. Michael Prisant, M.D., Room BD-133, Residence III, Medical College of Georgia, Augusta, GA 30912-0425.

(Hypertension 10: 467–472, 1987)
How can we diagnose coronary heart disease in hypertensive patients?
L M Prisant, M J Frank, A A Carr, T W von Dohlen and A M Abdulla

_Hypertension_. 1987;10:467-472
doi: 10.1161/01.HYP.10.5.467

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/10/5/467

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in
_Hypertension_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Hypertension_ is online at:
http://hyper.ahajournals.org//subscriptions/