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Editorial Comment

Isn't It Time to Reevaluate the Sensitivity of Noninvasive Approaches for the Diagnosis of Coronary Artery Disease?*

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The study by Legrand et al. (1) confirms other studies (2,3) that indicate that measurements of percent stenosis of lesions demonstrated by coronary angiography correlate poorly with the functional significance of the obstruction. The weak correlation between percent stenosis and vasodilator capacity noted by Legrand et al. (1) might have been even worse if the angiograms had been analyzed by visual interpretation as opposed to the more reliable computer based analysis that was employed. It is unfortunate that most of our present knowledge about the sensitivity of noninvasive approaches to diagnosing coronary obstructions (stress thallium scintigraphy, exercise electrocardiography, exercise radionuclide angiography, and so on) is based on comparisons between the noninvasive test result and percent stenosis estimated from the visual interpretation of an angiogram by one or more cardiologists. It is even more unfortunate that this error—utilizing an estimate of percent stenosis to validate the noninvasive imaging techniques—continues to be frequently repeated. Because the study by Legrand et al. utilized a physiologic index of coronary dilator capacity as one standard, this is a step forward.

This editorial will focus on two aspects of this problem: 1) reasons for the poor correlation between percent stenosis and coronary vasodilator reserve in patients with multivessel coronary disease, and 2) important design features of future studies aimed at assessing the sensitivity of noninvasive tests for detecting the presence and severity of coronary disease.

Problems with percent stenosis. There are five reasons why percent stenosis is a poor predictor of the functional significance of coronary lesions particularly when they occur in patients with multivessel coronary disease. 1) Gould (4) and Young et al. (5) have repeatedly demonstrated in a convincing manner that many geometric parameters in addition to percent stenosis—exit angle, entrance angle, length, absolute cross-sectional area—influence the hydraulic effects of an obstruction. Hence, the use of percent stenosis or any other single anatomic feature of an obstructure has a weak theoretical foundation. 2) If angiograms are visually interpreted, intraobserver and interobserver variability are substantial (6,7). 3) Diffuse disease, undetected by angiography, can be quite severe and is frequent in patients with multivessel coronary disease (3,8). This severely limits the usefulness of measurements of percent stenosis which tacitly assume that the vascular segment adjacent to the obstruction is normal. Because diffuse disease is less of a problem in patients with single vessel coronary artery disease, percent stenosis determinations of isolated obstructions, utilizing quantiative techniques, are useful in predicting coronary vasodilator reserve in this special, highly selected subgroup of patients (9). 4) Active coronary vasomotor tone or passive distension of coronary vessels can be a complicating factor particularly in patients with Printzmetal's angina (10) or alterations in systemic pressure that may influence lesion dimensions (11). 5) Finally, other factors that limit coronary reserve or alter the physiologic function of the coronary circulation (left ventricular hypertrophy, infarction, anemia, hypoxia, hypotension, coronary collateral flow, antianginal medications, and so on) can amplify or blunt the physiologic effects of the given coronary obstruction. In view of these reasons, it is not surprising that percent stenosis has turned out to be of limited value in predicting the physiologic significance of coronary obstructions in most patients with coronary artery disease. It is also important to emphasize that the interpretation of direct measurements of flow reserve must also take into account factors other than the stenosis which can limit the vasodilator capacity of coronary vessels.

Ideal study design. If we are to reevaluate the sensitivity of noninvasive tests for detecting coronary artery disease or characterizing the severity of such disease, first and foremost it will be important to quantitatively characterize the physiologic effects of the coronary obstructions being examined. Measurements of maximal vasodilator reserve in individual vessels are best accomplished with intracoronary papaverine and a coronary Doppler catheter (12,13). Approaches that do not produce maximal dilation or cannot measure maximal increases in flow (about fivefold in normal patients) (14,15) are not ideal. Second, the anatomic features of the obstruction that should be measured with quantitative techniques include percent stenosis, absolute cross-sectional area and length (4,5). If possible, measurements of the entrance and exit angle of the stenosis should also be obtained (4,5).

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Third, measurement of the size of the perfusion field of the obstructed vascular segment are important. One promising approach to accomplishing this involves the injection of intracoronary technetium-99m–labeled microspheres (16) or intracoronary thallium-201 (17). The likelihood of identifying physiologic abnormalities in perfusion or function is related to both the magnitude of the perfusion deficit and the size of the perfusion field of the obstructed vessel (18). Factors that confound the analysis of noninvasive tests (13)—hypertrophy, infarction, collateral flow, multivessel coronary disease, hypoxia, anemia, antianginal drugs, and so on—should be avoided until the sensitivity of the test under more easily interpretable conditions has been defined. In this regard, studies should be done ideally in patients with a single proximal coronary obstruction in the absence of infarction, hypertrophy, coronary collateral vessels, left ventricular dysfunction and antianginal medications. The noninvasive test being examined should be carefully performed and interpreted not only visually but also with the assistance of a computer-based analysis system.

Implications. There is a great need to develop clinically useful noninvasive approaches to the diagnosis of physiologically significant coronary obstructions. The studies by Legrand et al. (1) and others (19) suggest that conventional approaches frequently validated with the now tainted reference standard, percent stenosis, are less sensitive than what is commonly appreciated. Only with studies that have a nearly ideal design will it be possible to determine the true sensitivity, specificity and cost effectiveness of both conventional (stress thallium scintography, exercise electrocardiography, exercise radionuclide angiography) and new approaches (positron imaging, cine computed tomography, SPECT imaging) for the noninvasive diagnosis of coronary disease. At the very least, future studies must avoid endless repetition of past errors. Investigation utilizing inappropriate standards waste valuable resources, confuse the novice and are quickly discarded by sophisticated investigators.

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