Coronary Artery Disease is More Than Just Coronary Lumen Disease

For decades researchers have argued about the accuracy of reading percent diameter stenosis (%DS) from coronary angiograms.[1–5] Despite understanding some of the reasons for misinterpreting %DS[6–9] from angiographic results, the fact remains that the findings from "lumenograms" represent coronary "lumen" disease, and does not exclude coronary artery disease.[10,11] As my late teacher, Dr. Mel Marcus from the University of Iowa, taught me, coronary arteriography/angiography should be thought of as lumenography. As he pointed out more than 2 decades ago, and as we and others have since proven, the ability to detect disease in the walls of the arteries of the heart, or any artery for that matter, is dependent on either (1) our ability to look directly into the wall of the artery itself or the consequences of plaque buildup, which if sufficiently present, will be detectable as lumen disease or %DS, and/or (2) our ability to elicit a response from the artery that is either "normal" or "abnormal"), which subsequently tells us there is disease within the artery itself.

Dr. Marcus was very interested in ultrasound and computer tomography (CT) applications for detecting coronary artery disease and was a staunch advocate of following things through to their logical conclusion, which probably explains why he and I got along so well. Indeed, as a student of his at Iowa, I got to see and be involved in both of these technologies/approaches in their infancies. Intravascular ultrasound (IVUS) has come a long way since then, allowing investigators like Eric Topol and many others, to uncover coronary artery disease when angiography fails to do so. CT applications (cine CT, ultrafast CT, and so forth), used to detect calcium deposits within arteries, like angiography itself, does not exclude coronary artery disease (CAD) if calcium is undetected or absent. Again, as I learned as an Internal Medicine Honor Student at Iowa, the absence of a positive finding on a test doesn't exclude disease; it simply means you didn't find any.

It was this perspective and training that "drove" me to find a better method for detecting heart disease, i.e., to find heart disease if it is present and to be as certain as possible that if present it will be found, treated, and not just missed. The question for all of us cardiologists and noncardiologists alike is, how do you find CAD when it hasn't shown up as lumen disease (%DS), but is nonetheless affecting coronary blood flow? It is this regional coronary blood flow difference that results in the presence or absence of angina. In fact, coronary artery lumen (%DS) disease is one, but not the only, cause of regional blood flow difference re-

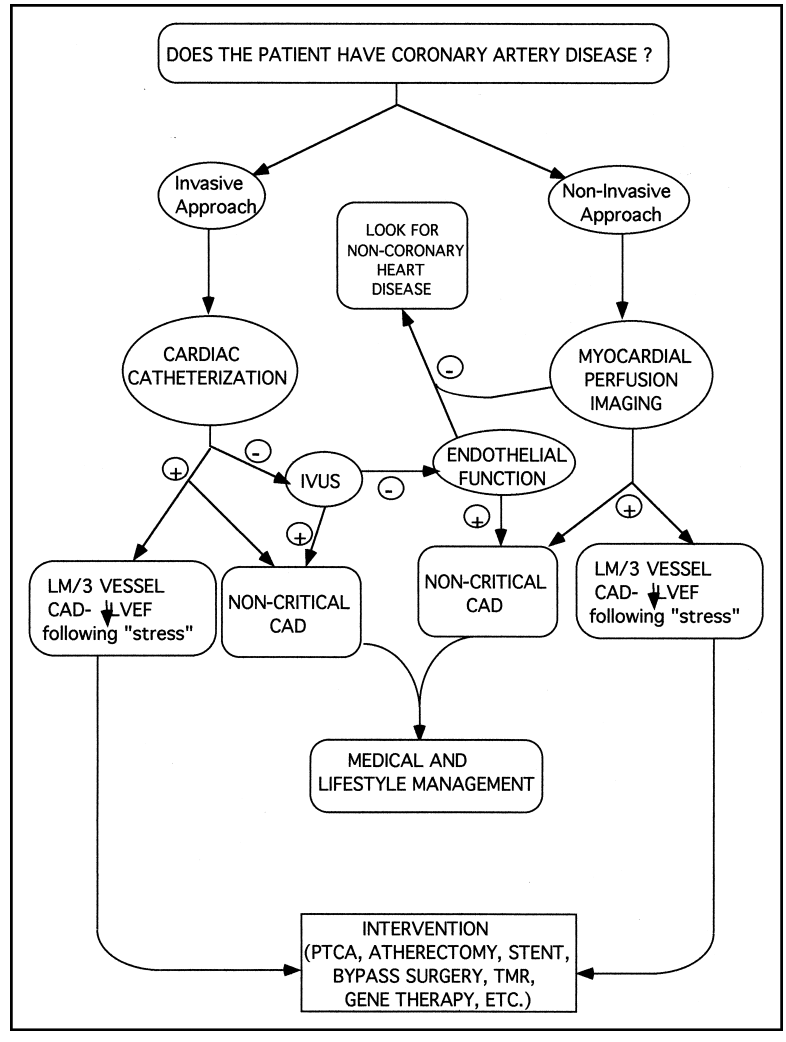

FIGURE 1. Algorithm to determine if patients have coronary artery disease. Patients with coronary artery disease can be assessed through 1 of 2 pathways. The first option is the "invasive" approach in which diagnostic studies include angiography, intravascular ultrasound, and endothelial dysfunction studies. The second option is "non-invasive" and includes assessment of regional wall motion abnormalities and myocardial perfusion imaging.

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sponsible for angina. These differences in regional coronary blood flow can be elicited by pharmacologic[12,13] "stress" and to a lesser extent by physical exertion,[12,14–16] which can then be quantified using either single-photon emission computed tomography or positron emission tomography myocardial perfusion imaging. Both methods indirectly measure coronary flow reserve which Poiseuille,[17] Fleming et al,[5,19] and Gould et al[18] previously demonstrated. In fact, it is a change in coronary flow reserve that can be found when endothelial function studies are performed. These studies expose the coronary endothelium to vasoactive substances designed to determine the responsiveness of the coronary endothelium[11,20] by trying to induce vasodilation and increase coronary blood flow; failure to do so implies coronary endothelial dysfunction,[21] which can occur even in the absence of coronary lumen (%DS) disease.

In the year 2001, the detection of coronary artery disease (Figure 1) still requires our ability to (1) detect disease within the artery proper, which in the earlier stages of the disease will not be associated with the lumen narrowing that is seen in the later stages of CAD, thus requiring either IVUS, an endothelial function study, or myocardial perfusion, and/or (2) the ability to (a) elicit regional blood flow differences using myocardial perfusion, (b) demonstrate endothelial disease using IVUS, or (c) demonstrate endothelial dysfunction by revealing impaired vasodilator response to appropriate stimuli. In the past, physicians would have treated all patients with clean lumenograms as those who did not have heart disease. Today we have gone beyond the simple argument of whether the angiogram is a gold standard. Truly, for patients with lumen disease, the angiogram is a remarkable diagnostic tool, but we also now know that CAD isn't found just in the lumen of coronary arteries, and that the search for CAD must extend beyond the lumen to the coronary artery itself.

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