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THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

The Risk Continuum of Atherosclerosis and its Implications for Defining CHD by Coronary Angiography

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ABSTRACT

Patients undergoing coronary angiography for suspected coronary heart disease who are found to have coronary atherosclerotic disease with <50% diameter stenosis may carry a risk of adverse cardiac events similar to that in patients with single-vessel obstructive disease. Yet clinical practice guidelines offer no direction for managing symptomatic patients with nonobstructive coronary atherosclerosis because current diagnostic criteria for coronary heart disease are not met. Accordingly, secondary preventive measures are not endorsed, and their role is not defined in this setting. Available data suggest that we are missing the opportunity to provide effective preventive measures in millions of patients with nonobstructive coronary heart disease. The emergence of noninvasive coronary angiography in patients with suspected coronary heart disease provides the opportunity to transition from a categorical perspective on the presence or absence of coronary heart disease to accepting the risk continuum from atherosclerosis and its implications for diagnosis and management. (J Am Coll Cardiol 2016;68:2467–78)
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A 43-year-old woman presents to a physician's office complaining of intermittent chest discomfort that is not related to identifiable triggers. She carries a history of arterial hypertension and achieved good blood pressure control on a diuretic agent/angiotensin-receptor-antagonist combination. Her physical examination is unremarkable, except for mild obesity. A baseline electrocardiogram is normal. Her serum cholesterol and low-density lipoprotein levels are in a low-risk range. She underwent exercise stress testing with myocardial imaging, which did not provoke symptoms or reveal evidence of myocardial ischemia. The patient's symptoms persisted, and she eventually underwent computed tomography (CT) coronary angiography to conclusively rule out coronary heart disease (CHD). CT angiography revealed noncalcified atherosclerotic disease in her proximal left anterior descending artery (LAD) with an approximately 40% lumen diameter stenosis (Figure 1). Very mild atherosclerotic disease was also noted in her left circumflex and right coronary arteries, both with <30% lumen narrowing. Although her symptoms may or may not be related to these angiographic findings, the question of whether preventive measures (e.g., aspirin and statin therapy) are indicated to lower her risk of adverse cardiac events arises.

DEFINING THE ISSUE

The case example illustrates several problems with our present concept of defining CHD using coronary angiography. According to current practice guidelines, the diagnosis and management of CHD center

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ABBREVIATIONS AND ACRONYMS

CHD = coronary heart disease

CT = computed tomography

FFR = fractional flow reserve

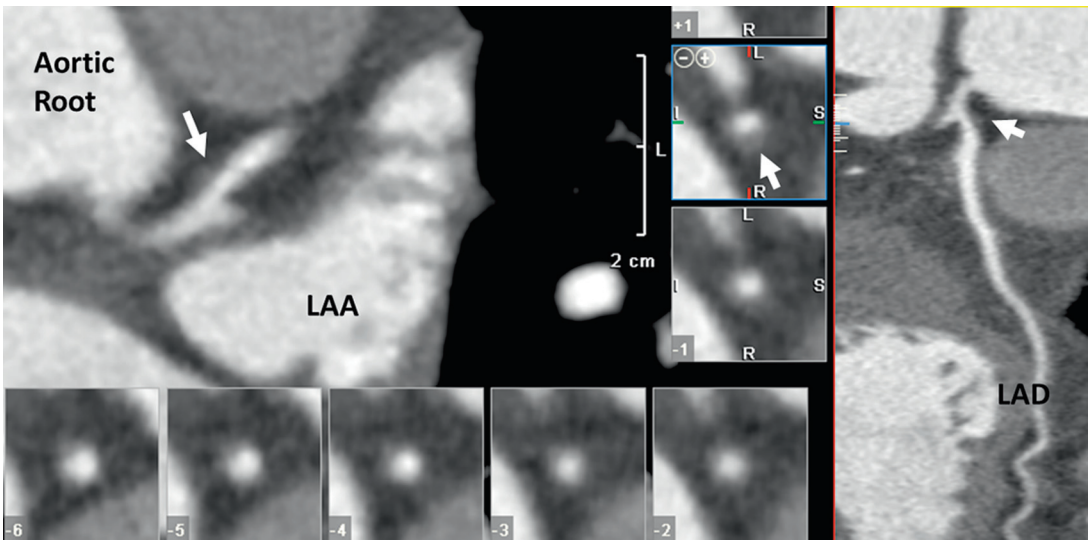
LAD = left anterior descending artery

on the presence of either provocable myocardial ischemia or at least 1 coronary arterial stenosis of 50% or greater (1-3). Such patients are at high risk for adverse cardiac events and are candidates for comprehensive secondary preventive measures (4). Conversely, symptomatic patients without history of myocardial infarction or coronary artery revascularization who have evidence of coronary atherosclerotic disease, but have no provocable ischemia or high-grade stenoses, are presumed to have neither CHD nor clinical atherosclerotic cardiovascular disease (1-5). These patients are considered low risk for death from cardiovascular causes, and the appropriate use of preventive measures (e.g., high-intensity statin therapy) is neither established nor endorsed by practice guidelines (1,4,5). As a result, secondary prevention is less frequently implemented in these patients (6).

Several large clinical datasets, using both conventional and CT coronary angiography, have demonstrated that symptomatic patients with nonobstructive coronary atherosclerotic disease (<50% diameter stenosis) carry risk of myocardial infarction and death, which may be similar to that of patients with single-vessel obstructive disease (7-10). Among more than 11,000 patients undergoing invasive coronary angiography, men and women with diffuse coronary atherosclerotic disease, but without a ≥50% stenosis, had indistinguishable adverse event rates after 7 years compared with patients with single-vessel CHD (**Figure 2**) (10). In a registry of 37,674 Veteran Affairs patients undergoing cardiac catheterization, patients with nonobstructive disease in 3 coronary arteries had an annual risk of myocardial infarction and death exceeding 3% (i.e., consistent with high risk), which was similar to the risk in patients with single-vessel CHD (9). Another large registry demonstrated that the mortality risk gradually increased with the extent of nonobstructive coronary atherosclerotic disease by CT angiography (11). Indeed, these data from more than 80,000 patients consistently demonstrate a risk continuum of adverse events with the extent of atherosclerotic disease without a threshold effect for lumen obstruction or hemodynamically significant CHD (12).

An analysis of chest pain characteristics of 15,888 patients without history of CHD undergoing elective coronary angiography revealed that only 37% had typical angina, whereas most had atypical chest pain or symptoms not ascribed to cardiac disease (13). Yet more than 80% of patients in this cohort had evidence of either obstructive (48%) or nonobstructive (33%) coronary disease by cardiac catheterization. Chest

FIGURE 1 Nonobstructive Coronary Atherosclerotic Disease by Computed Tomography Angiography



A computed tomography angiographic image of coronary atherosclerotic disease in the ostial and proximal left anterior descending artery (LAD) of a 43-year-old woman who presented with atypical chest pain and negative stress test results is shown. The atherosclerotic disease is characterized by a noncalcified plaque that extends from the distal left main coronary artery into the LAD with approximately 40% lumen stenosis. **Arrows** point to the same atherosclerotic plaque displayed in different projections. LAA = left atrial appendage.

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