Use of New Imaging Techniques to Screen for Coronary Artery Disease

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Because coronary artery disease (CAD) is the most frequent cause of death in industrialized nations and its onset is currently unpredictable, there is a need for new methods of screening apparently healthy individuals to identify those at increased risk. Technical advances in the noninvasive imaging techniques of computed tomography (CT), magnetic resonance imaging (MRI), and nuclear imaging now make it possible to image the heart and perform a partial evaluation of the coronary arteries without the need for an invasive procedure such as cardiac catheterization.

Despite these capabilities, prediction of heart attack is likely to require characterization of the amount and composition of atherosclerotic lesions (plaques) within the coronary arteries. At present, CT is the only noninvasive technique in widespread clinical use that can obtain information about the composition of coronary atherosclerotic plaque in living patients. Although the information is currently limited to determination of the presence and amount of calcium in the plaque, the test has already been documented to provide information about the presence of disease or its probability. Thus, many healthy individuals who could be considered at risk for CAD because of age, high cholesterol level, or other factors now wonder if they should undergo CT scanning to determine if their coronary arteries are calcified. The decision to undergo this test is more complicated than might be expected because of conflicting opinions about the significance of coronary artery calcification.

Calcification, Coronary Artery Atherosclerosis, and Coronary Heart Disease

Atherosclerosis is a diffuse disease that affects many arteries of the body, not just the coronary arteries. In the early stages, it causes changes in the walls of the arteries, with increases in cholesterol content and scar tissue. In later stages, it causes plaques that thicken the wall of the artery, and in some cases, narrow the center of the artery so that the flow of blood is gradually reduced. At this stage, calcium is generally present in the plaques.

Plaques that impede flow as well as plaques that do not impede flow are at high risk of rupture. These vulnerable plaques cause most coronary artery events. When a vulnerable plaque ruptures, it stimulates the local formation of a blood clot that can block the flow of blood to the heart muscle and cause the sudden onset of a heart attack (myocardial infarction).

At present, there are no invasive or noninvasive tests in routine use to identify vulnerable plaques in living patients. Vulnerable plaques may or may not be calcified, thus complicating the determination of cardiac risk by screening for calcification.

There is a logical appeal to the approach of a direct evaluation of the coronary arteries, rather than reliance on an indirect measure such as age, the amount of cholesterol circulating in the blood, and other traditional risk factors. Improvements in CT technology now allow the noninvasive visualization of calcification within the walls of the coronary arteries in living patients.

How Are CT Tests for Coronary Calcification Performed?

There are currently two essentially equivalent methods for the visualization and quantification of coronary artery calcification—electron beam computed tomography (EBCT) and multidetector computed tomography

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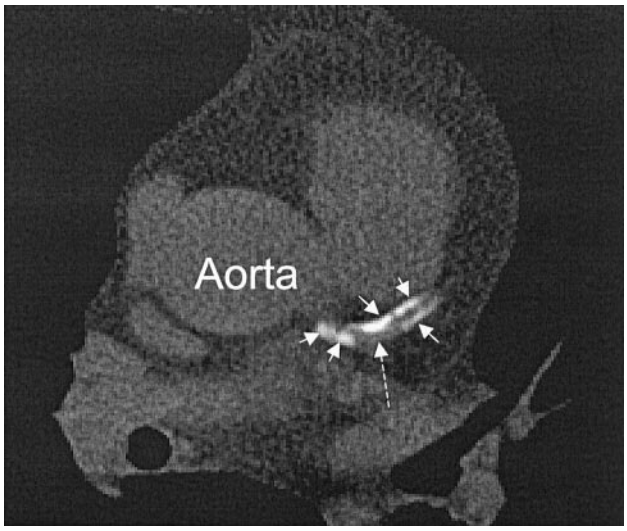

A cross-sectional image through the aorta and the origin of the left coronary artery (dashed arrow). A moderate amount of calcification can be easily identified as bright signals (solid arrows).

(MDCT). Both EBCT and MDCT are large, complex x-ray imaging systems. EBCT has been used for almost two decades to detect and quantify coronary calcification but is not as widely available as MDCT. Because systems must be fast enough to freeze the motion of the heart to obtain accurate information, some MDCT systems are not recommended for coronary calcium measurements.

A scan using the CT technique is relatively simple and convenient for the patient, who needs only to lie quietly in the CT scanner for approximately 10 minutes. No special preparation is required for the test, and there is no restriction on the types of medication taken before or during the test. The patient is asked to hold his/her breath for 10 to 30 seconds, depending on heart rate and the CT scanner type. The total door-to-door time is approximately 15 minutes.

The test exposes the patient to a limited amount of ionizing radiation (0.7 to 3 mSv [milli-Sieverts—a unit for the effective radiation dose]) that is equivalent to 25% to 100% of the natural background radiation exposure that an individual in the United States receives per year (2.5 to 3 mSv). This is less than the dose received during a diagnostic cardiac catheterization (approximately 4.5 mSv) and only a fraction of the occupational exposure limit for a radiation worker in the United States (50 mSv per year). The amount of calcium is usually expressed as an Agatston Score, which is based on the area and the density of the calcified plaques. A typical report provides an Agatston Score for every major coronary artery, a total Agatston Score for the patient, and a few representative images (see the Figure).

What Is the Meaning of the Results of the Test for Coronary Calcification?

All experts agree that CT testing can determine if calcifications are present in the walls of the coronary arteries. If calcification of any amount is present, it follows that atherosclerosis is present in the coronary artery. Hence, patients with no symptoms but with detectable calcification can be said to have CAD not detectable by the usual clinical tests (subclinical CAD). However, there is controversy about the relation of the calcification score to the cardiac events of unstable angina, myocardial infarction, and sudden cardiac death.

The Agatston Score in Apparently Healthy Individuals

The distribution of calcification scores in populations of individuals without known heart disease has been studied extensively. From those data we know that the amount of calcification increases with age. Men develop calcifications about 10 to 15 years earlier than women. Furthermore, in the majority of asymptomatic men over 55 years of age and women over 65 years of age, calcification can be detected. These data have been used to create tables that compare the amount of calcium of an individual to a group of people of similar age and gender (percentiles).

The Predictive Value of the Agatston Score

A Positive Test

A test is considered to be positive if calcification is detected within the coronary arteries. Absolute Agatston scores of less than 10, 11 to 99, 100 to 400, and above 400 have been proposed to categorize individuals into groups having minimal, moderate, increased, or extensive amounts of calcification, respectively. The amount of calcification can give, to some extent, an indication of the overall amount of atherosclerosis.

It is well established that individuals with Agatston Scores above 400 have an increased occurrence of coronary procedures (bypass, stent placement, angioplasty) and events (myocardial infarction and cardiac death) within the 2 to 5 years after the test. Individuals with very high Agatston scores (over 1000) have a 20% chance of suffering a myocardial infarction or cardiac death within a year. Even among elderly patients (over 70 years), who frequently have calcification, an Agatston Score above 400 was associated with a higher risk of death.

This is an impressive ability to identify vulnerable patients for a technique that does not detect vulnerable plaques, as described earlier. This paradox is presumably explained by the

greater frequency of vulnerable plaques in patients with calcification.

In addition, a greater amount of calcification and a higher Agatston score increase the likelihood that coronary angiography will detect a significantly narrowed coronary artery stenosis. However, there is not a 1-to-1 relationship between a high score and the presence of coronary artery stenosis. In addition, the stenosis might not occur at sites that are calcified.

A Negative Test

A test is considered to be negative if no calcifications are detectable within the coronary arteries. Although this does not absolutely exclude the presence of atherosclerotic deposits within the coronary arteries, it does indicate that there is nothing more than minimal atherosclerosis, and the risk of a coronary event over the next 2 to 5 years is very low. The likelihood that a significant coronary artery narrowing is present is also very low.

What Does the Test Tell You?

A positive test: Calcifications are detected in the coronary arteries

- Indicates that subclinical CAD is present
- Is more frequent with increasing age and may be found in the majority of men over 55 years of age and women above 65 years of age
- Can, according to the amount of calcification and your age and sex, indicate a substantially increased risk for myocardial infarction or cardiac death, even if no symptoms are present.

A negative test: No calcifications are detected in the coronary arteries

- Predicts a very low likelihood of experiencing myocardial infarction or cardiac death in the near future
- Does not exclude the presence of atherosclerosis in the coronary arteries

Does the Agatston Score Provide Independent Predictive Value?

Although there is little controversy that Agatston scores can provide information on the risk of future events, there is considerable debate as to whether the Agatston score provides predictive information beyond that obtained from traditional risk factors. Preliminary studies suggest that coronary calcification does add information in the subset of individuals who are considered to be at intermediate risk because they have a number of traditional risk factors. Several large studies (such as the Multiethnic Study of Atherosclerosis [MESA]) are underway to further clarify this and related issues.

Furthermore, detection of calcification must also compete with newly discovered risk factors. C-reactive protein (CRP), a marker of inflammation that can be determined by a simple blood test, has been shown to add prognostic information in those at intermediate risk. In the future, it can be expected that genetic variations will also be identified that will improve the prediction of cardiac risk.

Which Healthy Individuals Should Be Tested for Coronary Artery Calcification?

The American Heart Association and the American College of Cardiology (AHA/ACC) provide guidelines for testing for coronary calcification that are updated yearly and are available online (http://www.ahajournals.org/misc/sci-stmts_topindex.shtml). These guidelines currently suggest, and we agree, that screening for calcification may be of value for an individual who is considered to be at intermediate 10-year risk, which is defined as a 10% to 20% likelihood of a cardiac event within the next 10 years.

Steps Your Doctor Will Take in Considering Whether You Should Have a Test for Coronary Artery Calcification

Your doctor will calculate your 10-year risk of a cardiac event on the basis of "traditional" risk factors.

If you are at an intermediate 10-year risk (10% to 20% chance of a cardiac event), your physician will discuss the value of undergoing the test.

The discussion with your physician will help to determine if coronary artery calcium screening will assist in your preventive care.

Patients with an intermediate risk profile should be willing to start preventive therapy without an expensive test. However, if necessary, the test for coronary calcification is available to support more intensive efforts to reduce traditional risk factors through improved diet, increased exercise, or smoking cessation, all of which are always desirable ways to improve continued cardiovascular health. In some patients, the test may also lead to more intensive diagnostic efforts, such as performing an exercise stress test (treadmill) or even cardiac catheterization.

In summary, the availability of a noninvasive technique to detect coronary calcification makes it possible to obtain direct information on the presence of atherosclerosis in the coronary arteries. The test is of greatest value in individuals judged to be at intermediate risk on the basis of traditional risk factors. In the future, CT and other methods are likely to improve the noninvasive assessment of the level of vulnerability of the coronary arteries, knowledge that

could greatly assist in the prevention of cardiac events.

Additional Resources

Ten-Year Cardiac Risk Calculators Online

Framingham Risk Score. Available at: http://circ.ahajournals.org/content/vol97/issue18/images/large/hc1881494003.jpeg. Accessed July 18, 2003.

National Cholesterol Education Program Score. Available at: http://hin.nhlbi.nih.gov/atpiii/calculator. asp?usertype=prof. Accessed July 18, 2003.

Prospective Cardiovascular Münster (PROCAM) Study Score. Available at: http://www.chd-taskforce.com/risk-english.htm. Accessed July 18, 2003.

Other Web Sites

AHA Journals. Scientific Statements Indexes. Available at: http://www.ahajournals.org/misc/sci-stmts_topindex.shtml. Accessed July 18, 2003.

HeartCenter Online for Patients. The Risk Factor Center. Available at: http://www.heartcenteronline.com/myheartdr/Articles_about_the_heart/The_Risk_Factor_Center.html. Accessed July 18, 2003.

National Heart, Lung and Blood Institute. Framingham Heart Study. Available at: http://www.nhlbi.nih.gov/about/framingham/. Accessed July 18, 2003.