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Coronary Artery Disease

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Coronary artery disease is the number one cause of death in the United States, affecting 1.5 million Americans yearly. Five hundred thousand people will die annually; half of these people will die suddenly from a heart attack with no previous symptoms. For this reason, markers which could identify persons at risk of developing coronary artery disease (CAD) are extremely important. Unlike other tests which detect abnormal blood flow in the coronary arteries, coronary artery scoring (CAS) by computed tomography attempts to quantify the degree of plaque formation in these vessels before a hemodynamically significant stenosis develops. Blood flow is altered only in advanced disease and therefore most tests will appear normal in early or mild CAD. Only CAS can detect the earliest stages of CAD before the buildup of plaque has progressed to the point that it impedes blood flow to the heart. This is because CAS examines the earliest development of calcium in atherosclerotic plaques, before there is significant narrowing of the coronary arteries. It is therefore suggested that this test can provide a means to predict future coronary events, thereby preventing symptomatic coronary disease, and potentially decreasing morbidity and mortality. However, because this technology is new, there is controversy regarding its most appropriate utilization. The following is a comprehensive review of the literature on this subject to date.

CAD Pathophysiology

The development of atheromata within the coronary artery is usually secondary to an injury to the endothelial lining of the blood vessel. When this occurs, circulating histiocytes lodge on this injured surface and are transformed into macrophages, which in turn accumulate lipids. These lipid layers can be covered with a fibrous cap. If this cap ruptures, it allows circulating blood to come in contact with the lipid and smooth muscle, which can then initiate an intense thrombogenic reaction. This process can result in progression of coronary artery stenosis or occlusion, which in turn leads to myocardial ischemia or infarction. The calcification of the fibrous plaques in the coronary arteries occurs as the macrophages attempt to stabilize the arterial wall during the healing process. Therefore, the calcified, fibrotic plaques appear less prone to rupture than "soft" cellular lesions. There appears to be a correlation between the volume of calcified plaque and soft non-calcified plaque. The quantity of calcification on the endothelial surface of the coronary artery can provide a useful measure of

the amount of soft, relatively unstable plaque that might pose a risk of rupture and subsequent catastrophic coronary events.1 As up to two thirds of patients who have an acute myocardial infarction or unstable angina have only minimal narrowing from the accumulation of lipid streaks, exercise tests which rely on abnormalities of flow through a stenotic artery frequently show no abnormalities. Similarly, although coronary angiography may be helpful in the diagnosis of stenotic disease, the findings of luminal narrowing may not be helpful for accurately predicting the sites of future plaque rupture and occlusion. The quantity of calcification in a patient's coronary artery can be correlated to the extent of atherosclerotic disease. The absence of calcification is likewise a significant indicator of the absence of coronary artery disease.[2,3]

Deposition of calcium has a direct correlation with the atherosclerotic process. Factors contributing to this are genetic predisposition, hematologic alterations, diabetes, smoking and abnormalities of lipid metabolism. Table 1 lists the patient populations who are at risk for CAD.

Table 1. PATIENT POPULATIONS AT RISK FOR CAD

- Age (men 45 or older, women 55 or older)
- Family history of heart disease
- High cholesterol
- History of smoking
- High blood pressure
- High stress levels
- Sedentary lifestyle
- Diabetes

IMAGING OF CORONARY ARTERY CALCIFICATIONS

Coronary calcification is detectable with numerous imaging modalities, including plain-film radiography, fluoroscopy, non-spiral or incremental computed tomography (CT), spiral CT, electron beam CT, intravascular ultrasound, magnetic resonance imaging, and transthoracic and transesophageal echocardiography. Electron beam CT and spiral CT are by far the most sensitive methods of detecting calcification, because of the ability of calcium to attenuate the x-ray beam. Multi-slice spiral computerized tomography is an extremely accurate method of detecting and quantifying coronary artery calcifications because of its high resolution (pixel slices of 0.25mm - 0.50mm2, 3mm thick sections) and fast imaging times (100 msec). With this technology, even minute amounts of calcium can be detected with considerable sensitivity. The total examination time is approximately five minutes, and the dose of radiation is less than 1.1cGy. No contrast media is required. Since this is an anatomic study, there is no need for exercise or pharmacological alteration.

For scoring coronary calcific lesions, an arbitrary value of 130 Hounsfield Units (a measure of x-ray attenuation or HU) and an area greater than 1.0mm2 are used. Regions of interest are placed around the areas of calcifications. Pixel clusters above 130 HU are displayed, and if the cluster lies over the course of a coronary artery and if the volume is greater than two contiguous pixels, the area is scored as a "lesion". Once the regions of interest have been placed, the scanner software displays the peak calcification, the attenuation in HU, and the area in millimeters squared. The volume score is the area of the lesion. This is then multiplied by a factor of 1 through 4, based on the specific HU value for that lesion. The sum of the individual lesion scores is the score for that particular artery. The sum of all lesion scores from all three coronary arteries is the total calcification score.

Numerous clinical and autopsy studies have correlated CAS and the extent of CAD as follows in table 2:

Table 2.

- Autopsy studies have shown that a calcium score of 80 has a sensitivity of 84% and specificity of 84% for predicting significant stenosis somewhere in the coronary arterial system.[4]
- When compared with coronary angiography, CAS has a sensitivity of 90-99% and specificity of 40-91% for detecting hemodynamically significant stenoses.[3,5,6,7,8,9,10,11,12]
- When compared with coronary angiography, CAS has a positive predictive value of 55-81%, and a negative predictive value of 90-100% for identification of hemodynamically significant stenoses.[3,5,6,7,8,9,10,11,12]
- The absence of calcification reliably predicts the absence of a significant stenosis, and CAD.[13]
- The presence of calcification in multiple vessels and in younger patients correlates with high specificity of CAD.[5,6,7,8,9,10,12]
- The prevalence of coronary calcification in women is half that of men until age 60 when differences diminish. The distributions of coronary calcium in men age 40-69 are virtually identical to those in women age 50-79.[14]
- CAS has been shown to be useful for following the progression and regression of CAD and changes that occur after modification of risk factors.[15]

CORONARY CALCIFICATION AND CLINICAL OUTCOME

Although the detection of coronary calcification by CT has been shown to relate to overall atherosclerotic plaque burden, it is coronary event data (occurrences of angina or myocardial infarction and necessity for angioplasty or bypass surgery) that are important in evaluating the true clinical utility of this examination. Supportive evidence that coronary calcium determination is useful for predicting

future cardiac events has been documented in the literature and is detailed in Table 3:

Table 3.

- Symptomatic patients with calcification seen at fluoroscopy have a markedly diminished 5-year survival compared to those without calcification.[16]
- CAS calcium scores of 100 or more in symptomatic patients are highly predictive in separating patients with cardiac events from those without events. In a recent multicenter study which included calcification score, age, gender, and coronary angiographic findings as independent variables, only calcification scores predicted which patients had subsequent cardiac events.[18]
- Fluoroscopically detectable calcification in asymptomatic patients is associated with an event risk almost three times greater than that in patients without calcification. Also, the presence of coronary calcification helps identify asymptomatic individuals at increased risk for a cardiac event at one to two year follow-up.[17,19]

The early detection of coronary disease is of great importance because of its potential to identify those patients who would benefit from diet modification or lipid-lowering drug therapy, which has the potential to reduce cardiac events by 20-30%.

CLINICAL APPLICATIONS OF CAS

The full importance of coronary artery calcification as a predictor of the likelihood of cardiac events must await ongoing clinical trials. Radiology Medical Group, in conjunction with Scripps Mercy Hospital Cardiology Department, has begun an evaluation of the efficacy of this examination by comparing coronary arterial scores obtained on the latest generation of multi-slice spiral CT scanners (General Electric Lightspeed QXI at the RMG First and Laurel Imaging Center) and findings at coronary angiography (performed in the Scripps Mercy Cardiology Department).

At the present time, some conclusions regarding appropriate utilization of CAS can be made:

1. For asymptomatic patients with few risk factors, the application of CAS as a screening tool holds promise, but additional data is needed.
2. This test can be useful in the evaluation and identification of asymptomatic patients with known risk factors for CAD who might benefit from risk management or further diagnostic work-up.

3. CAS can be useful for following the progression of coronary atherosclerosis in patients receiving pharmacological or nutritional therapy.
4. Symptomatic patients with chest pain of indeterminate nature and equivocal stress EKG findings could benefit from CAS. At present this group of patients may receive additional tests including coronary angiography or risk factor management. CAS would be of use in this setting because of its high (90-100%) negative predictive value. In patients with atypical chest pain, in whom the pre-test likelihood of angina is low, a zero calcium score would be very reassuring. A high calcium score would suggest the need for additional cardiac work-up. The advantages of CAS over stress scintigraphy are that it can be performed regardless of the patient's ability to exercise and regardless of the presence of equivocal EKG abnormalities. Also, CAS is not influenced by cardiac drugs which may confound exercise tests. In addition, CACT is approximately one-third the cost of scintigraphy. Table 4 provides recommendations for patient management based on coronary calcification.

Table 4. RECOMMENDATIONS FOR PATIENT MANAGEMENT BASED ON CORONARY CALCIFICATION SCORING

Calcium Score	Plaque Burden/Risk	Recommendations
0	No identifiable atherosclerotic plaque. CAD risk very low.	Healthy diet (low in saturated fat and cholesterol). Stop smoking. Maintain recommended weight.
1-10	Minimal plaque burden. CAD risk low.	All recommendations above PLUS: Tight control of diabetes and hypertension. Consider use of statins in cases of hypercholesterolemia.
11-100	Mild plaque burden. CAD risk moderate.	All recommendations above PLUS: Estrogen for post-menopausal women. Aspirin use. Use of statins for hypercholesterolemia.
101-400	Moderate plaque burden. CAD risk high.	All recommendations above PLUS: Exercise program. Use of statins in cases of high and borderline cholesterol levels. Consider use of Folic Acid, Vitamin E.
>400	Extensive plaque burden. CAD risk very high.	All recommendations above PLUS: Exercise Test to rule out obstructive disease. Consider angiography for symptomatic patients or those with high stress.

Coronary artery scoring is now available at our RMG First and Laurel Imaging Center and our RMG Encinitas Imaging Center. Examinations may be scheduled by calling 619-849-XRAY(9729). For additional information, contact John M. Doemeny, M.D. at 619-849-XRAY(9729), ext. 6305 or e-mail him at **Raysleuth@covad.net**

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