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CT Coronary Angiography: Defining a High-Risk Asymptomatic Population Through Noninvasive Testing

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LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

1. Explain the principles of CTA and the differences between functional and structural cardiac testing.
2. Describe the difference between calcium scoring and CTA.
3. Identify the criteria for patients who would gain the most valuable information from CTA.
4. Apply knowledge of CTA to real cases in your practice who might benefit from this type of imaging technology.

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Cardiovascular disease is the most widespread, expensive, and devastating disease facing modern societies. Aggressive treatment of patients with risk factors for atherosclerotic disease has been shown to be beneficial in preventing future cardiac events. Patients with hypercholesterolemia who are treated aggressively with cholesterol-lowering medications have fewer cardiovascular events. This has held true for both high- and low-risk populations.[1,2]

Although primary prevention is well proven, even more benefit is achieved with secondary prevention (treating patients with known coronary disease).[3-5] Because these patients have more to gain, it is more cost-effective to treat them. The problem has been in identifying high-risk patients before they have devastating clinical events. Some patients are identified as having coronary disease only when they have begun to have heart failure due to cardiac dysfunction. Even more alarming are patients for whom a heart attack or death is the first indication that they have the disease. Patients with early atherosclerotic disease are often asymptomatic until the time of a myocardial infarction, making them difficult to recognize.[6,7] Treating patients after a cardiac event is imperative, but can sometimes be too late to significantly affect longevity. Conversely, the "shotgun" approach of treating everyone with risk factors for coronary artery disease (CAD) is expensive and potentially dangerous.[4,8]

Figure 1. Calcification of the left main and proximal left anterior descending arteries. Calcification positively demonstrates the presence of atherosclerotic disease in the coronary arteries.

FUNCTIONAL TESTING

Functional tests such as stress echocardiography and nuclear perfusion are highly sensitive and specific in detecting coronary disease in patients who are at moderate risk. For these tests to be positive, the patient must already have sufficient coronary blockage that myocardial perfusion is compromised. For healthy patients who have nonobstructive coronary disease, stress tests may be completely negative.[9]

Therefore, a segment of the population has significant coronary atherosclerosis yet is asymptomatic. Patients with early aggressive atherosclerosis may have no subjective symptoms, and a functional test may give no objective indication that they have a problem. They may have the disease, but a diagnosis is delayed or not made and they may not be treated with appropriate medical therapy and lifestyle modification.

STRUCTURAL TESTING

Invasive coronary angiography has been the gold standard for evaluating coronary anatomy and

TABLE 1. COMPARISON OF CALCIUM SCORING, CTA, AND INVASIVE CORONARY ANGIOGRAPHY

	Calcium score	CTA	Invasive coronary angiography
Hospital stay	One hour (includes time to fill out paperwork)	One hour (similar to calcium score time)	Four to five hours minimum (includes time before procedure and bed rest after)
Procedure time	Less than five minutes	Less than five minutes	Roughly one hour (including patient prep time, but not including recovery area stay)
Level of invasiveness	No IV	IV in antecubital fossa	Femoral/radial/brachial artery puncture
Cost	Around $500	Around $2000	Around $6000
Contrast given	None	Approximately 150 cc	Variable, can be as little as 20 cc
Functional evaluation	No	Yes, ejection fraction	Yes, ejection fraction
Covered by insurance	Rarely	Yes, for certain diagnoses	Yes, for most cardiac diagnoses
Scheduling	Can be performed on the same day it's ordered; may be requested by an individual without a physician order	Can be ordered and performed on the same day in most cases	Can be ordered and performed on the same day in most cases
Risk of procedure	Very small—risks are theoretical and related to small amount of radiation exposure	Very small—only risks are those from contrast-related complications	Very small—however, because test is invasive, there is a chance of death, stroke, bleeding, infection, and contrast-related complications
Exclusionary criteria	• Irregular or fast heart rate • Inability to hold breath for 30 seconds • Inability to hold still or follow instructions	• Irregular or fast heart rate • Inability to hold breath for 30 seconds • Poor IV access • Renal Insufficiency or contrast reactions	• Inability to give consent
Therapeutic options at the time of procedure	Diagnostic modality only	Diagnostic modality only	Ability to transition to a therapeutic modality immediately (i.e., angioplasty) if a significant stenosis is discovered
Availability	Available at some hospitals as well as stand-alone clinics for a fee	Newer modality; available at only a few hospitals around the country	Available at all tertiary-care centers and a large percentage of community hospitals
Who performs and interprets the test?	Technologists perform and score; test is then overread by a staff physician.	Technologists perform the test; nursing staff give beta blocker if necessary; physicians perform the reconstruction and interpret images	Cardiologists perform and interpret the test in the cardiac catheterization lab.

Figure 2. A: Coronary angiogram of a left anterior descending artery. B: 3D reconstruction allows visualization of the same artery in relation to the surrounding structures of the heart. C: Curved reformat reconstruction images allow evaluation of the lumen of the artery as well as atherosclerotic plaque formation (arrow).

determining the presence of coronary atherosclerosis. This is a safe test, with a <1% risk of major complication.[10] "Screening angiograms" could be performed to identify patients who have a high potential risk of coronary disease but in whom functional testing is low yield.[11,12] Of course, the high utilization of resources as well as the potential risk of invasive angiography makes this strategy somewhat prohibitive.[13]

This gold standard has limitations in diagnosing mild disease. Angiography defines only the lumen of a coronary artery without giving detailed information about the pathologic processes inside the artery's wall. Since early atherosclerosis may be associated with compensatory expansion of the overall diameter of the artery (the Glagov effect), the lumen of a diseased coronary artery may remain relatively unaffected.[14] Therefore, early disease or subtle plaque in the coronary arteries may go undetected and the diagnosis of atherosclerosis may be delayed.

Intravascular ultrasound (IVUS) can be used to overcome the limitations of coronary angiography. This involves placing a miniaturized ultrasound catheter, which can fully define the microscopic anatomy of the inner lining of the coronary arteries, into the artery itself.[15,16] While this is the most accurate way of assessing total plaque burden, there are drawbacks to this procedure. It is somewhat time consuming, and only one artery at a time

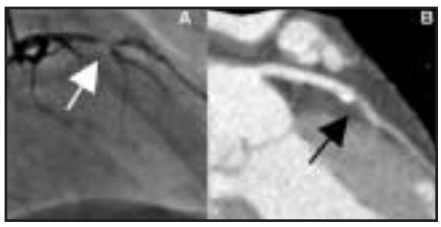

Figure 3. High-grade stenosis of the left anterior descending artery (arrows) visualized by invasive coronary angiography (A) and CTA (B).

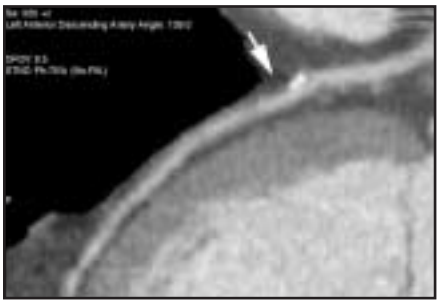

Figure 4. Stenosis (arrow) visualized in the left anterior descending artery by CTA. It consists of both calcified (bright white) and noncalcified (gray) plaque. The patient was asymptomatic and unaware that he had coronary artery disease.

can be imaged. The coronary arteries must be directly instrumented, increasing risk to the patient. Additionally, patients need anticoagulation therapy when undergoing IVUS, which is unnecessary during routine diagnostic coronary angiography.

OTHER OPTIONS

New modalities and tests are expanding the ways practitioners can visualize anatomy and disease.

• *CT scanning* dramatically increased the resolution at which we could visualize the human body. Originally, CT imaging of the heart was problematic because of the significant motion artifact that occurred while the heart was beating.[17] With gating technology and larger array sizes, current multislice CT scanners (MSCT, or spiral CT) are able to image the coronary arteries of a beating heart.

• *Calcium scoring* has been used for several decades as a marker for atherosclerosis.[18,19] Calcium scoring uses gated CT scans of the heart to quantify the amount of calcium present in the coronary arteries (Figure 1). Patients with elevated calcium scores are (by definition) forming plaque in their coronary arteries. That patients with the highest calcium scores have increased associated coronary plaque burden, stenosis, and coronary events is well established.[20-23]

Although lower calcium scores are associated with fewer events, it cannot be said with certainty that these patients do not have CAD. Plaque takes time to calcify and so patients (even symptomatic patients) can have calcium scores of zero but have significant CAD.[24] For patients who are younger and asymptomatic, calcium scoring may give the false impression that no coronary disease is present.

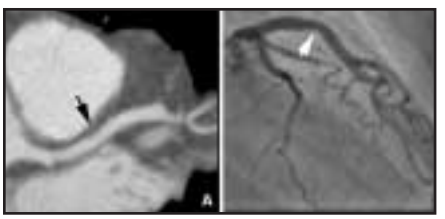

Figure 6. CTA (A) and invasive coronary angiogram (B) of a 33-year-old woman with strong family history of coronary artery disease. The plaque seen on the CTA (black arrow) could easily have been missed on the invasive angiogram (white arrow).

• *CT angiography* can differentiate between the coronary lumen, soft plaque, and calcified plaque, whereas calcium scoring is limited to defining calcified plaque. Although the technique for imaging is similar to calcium scoring, the patient is given an intravenous bolus of contrast material. Images of the heart are gated, and the scan of the heart is timed to coincide with the arrival of the contrast in the coronary arteries.

Patients are required to hold their breath for up to 30 seconds and must lie still for the duration of the scan. In addition, due to the need to time the scan with the beating of the heart, the modality cannot be used in patients who have irregular heart rates. Slow heart rates reduce the amount of artifact in a scan, so beta blockers are routinely given for patients with elevated heart rates.

Raw axial images can be reconstructed so that the coronary arteries may be evaluated in multiple views. Angiographic-type images can be made using "curved reformat" views, which allow detailed evaluation of the lumen and walls of the coronaries. In addition, 3D reconstruction of the coronary arteries allows the practitioner to evaluate for coronary anomalies and to trace the course of the coronaries in relation to the other structures of the heart (Figure 2). Through this technique, a detailed image of the coronary anatomy can be made in a short amount of time without an arterial puncture and without the risk involved in placing a catheter directly into the coronary arteries.

With the recent introduction of faster, higher resolution scanners, CT coronary angiography (CTA) has been shown to have high sensitivity and specificity in detection of coronary disease. It has been shown to be useful in qualifying and quantifying plaque characteristics, detecting stenoses (Figure 3), and evaluating coronary anomalies.[25-27]

CASE STUDIES

The following case studies highlight the ability of CT angiography to assist in the diagnosis of coronary atherosclerosis and to contribute a crucial piece of information to the treatment plan. Patient 1 was a 40-year-old man with no diagnosis of hypertension or diabetes and no history of CAD. He smoked approximately one pack of cigarettes per day and had a family history of diabetes mellitus and CAD. He had no symptoms of angina pectoris, and had had a

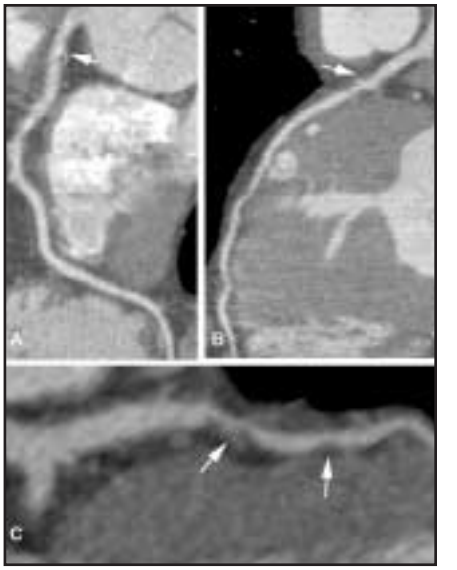

Figure 5. CT coronary angiogram demonstrating atherosclerotic plaques (arrows) in the right coronary (A), left anterior descending (B), and first diagonal (C) arteries. Patient had elevated cholesterol but was asymptomatic and had no previous diagnosis of CAD.

stress test within the last five years, which he stated was "unremarkable."

As part of his workup, he underwent CTA on a 16-slice CT scanner (GE LightSpeed). The images clearly demonstrated a moderate-sized plaque in the proximal portion of his left anterior descending artery (LAD) (Figure 4). It was made up of both calcified and noncalcified plaque, and was not flow-limiting. There was minimal disease in his other arteries.

CTA made the diagnosis of CAD in this otherwise asymptomatic patient. Based on these findings, his physician started him on high-dose statin therapy with a goal of reducing his LDL cholesterol level to ≤70 mg/dL. Seeing the images depicting plaque in his arteries had a

TABLE 2. PATIENTS WHO WOULD BENEFIT FROM CTA

- Patients who are not symptomatic, for early detection
- Patients who have a low to moderate probability of having significant coronary disease
- Patients who have risk factors, but who are reluctant to start on medication
- Patients with symptoms consistent with coronary artery disease, but who are reluctant to undergo invasive testing. CT can be used for both diagnostic as well as prognostic evaluation (can picture normal as well as single-vessel disease)

powerful effect on the patient as well. It convinced him that he needed to make significant lifestyle changes, including smoking cessation, diet modification, and weight loss.

Patient 2 was a 52-year-old man with a history of mild hypertension and mild hypercholesterolemia. He had been on and off his medications for the last few years. He did not smoke and had no symptoms of angina pectoris. He was actually quite fit and active, and underwent the CT angiogram to find out "how he was doing."

CTA clearly demonstrated mild to moderate atherosclerosis in many of his coronary arteries. The RCA had nonobstructive, mildly calcified plaque in the proximal portion. In the LAD distribution there was a mild amount of soft plaque, which was contiguous with plaque in the diagonal arteries (Figures 5A and 5B).

After his scan, the patient went back on his medications. The hope was that with the knowledge that he had already started making plaque in his arteries, he would continue to comply with medical management for the rest of his life.

Patient 3 was a 33-year-old woman with an HDL level >60 mg/dL and an LDL level <100 mg/dL. Previous stress tests had not demonstrated ischemia. Despite this, she was extremely concerned that she had premature CAD. Her mother had her first heart attack at age 35, had a heart transplant at age 40, and died of complications several years after that.

CTA was performed as part of a research protocol. In addition to her noninvasive coronary angiogram, a traditional invasive angiogram was performed. The invasive angiogram demonstrated no significant flow-limiting stenosis. Comparing the two images side by side (Figures 6A and 6B), however, a small amount of plaque was seen in the CT coronary angiogram, which corresponded to "luminal irregularities" seen in the same area on the invasive angiogram.

In a young woman with high HDL and low LDL, early coronary plaque was unexpected. Many physicians would have been satisfied with negative stress testing and, with her cholesterol profile, she would not have been started on medical therapy. Without her strong family history, she would never have been a candidate for invasive coronary angiography.

What is disturbing is that the subtle irregularities seen on the invasive angiogram might be described as "normal" coronary arteries by many cardiologists. However, the CT coronary angiogram clearly demonstrated premature coronary atherosclerosis. Based on the findings from the CT coronary angiogram, the patient's treatment plan was changed to include aggressive lipid therapy as well as a more detailed look into her particle size, lipoprotein, and homocysteine levels. Instead of the false reassurance that "nothing was wrong," her doctor was able to give her concrete evidence that she was at higher risk than her peers. This permitted her physicians to be more watchful and more aggressive with her present and future medical care.

CONCLUSION

Calcium scoring and CTA are two new noninvasive imaging modalities that provide direct visualization of coronary artery atherosclerosis. Compared to invasive coronary angiography, CTA has the ability to quickly assess coronary arteries for both calcified and noncalcified plaque, without need for invasive instrumentation of the heart (Table 1).

Of the many patients who are candidates for CTA (Table 2), those who stand to benefit most are those with the highest potential risk and those who are at the earliest stages of their disease process. A large segment of the population is completely asymptomatic, yet is at higher risk because of lifestyle, comorbidities, or family history. Some of these patients have already begun producing plaque in their coronary arteries but would not be considered for secondary prevention in traditional terms.

For patients with low to moderate risk of coronary disease, CTA can be used as a screening, or "triage," test to evaluate the need for further, invasive testing. For patients who have positive stress tests but very low pretest probable false-positives, it can take the place of invasive angiography as the next logical test.

The ability to detect the presence of plaque in its early stages of formation facilitates earlier intervention in a patient's life, at a time when functional stress tests would not detect disease. For some patients, noninvasive testing with CTA can give direct visualization of their coronary atherosclerosis. This powerful message may mean the difference between quitting and not quitting smoking, staying or not staying on medications, and, ultimately, whether or not they go on to develop myocardial damage.

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