Understanding Cardiac Screening: The Nuclear Stress Test & Coronary Artery Calcium Score

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Abstract

Coronary artery disease (CAD) is a chronic condition that too often presents as a crisis of chest pain, heart attack or even sudden death. CAD begins in early adulthood and progresses silently over decades of life. Once identified it can be interrupted, hence the value of screening for silent, asymptomatic and subclinical disease. Half of all cardiovascular deaths occur in persons who were incorrectly assessed as low risk. Thus, it is imperative that physicians are aware of the importance of screening and the strengths and limitations of available cardiac tests including the Coronary Artery Calcium Score and the Nuclear Stress Test.

Introduction

Two non-invasive cardiac testing modalities are commonly employed in the assessment of coronary artery disease: the Nuclear Stress Test (NST) and Coronary Artery Calcium Score (CAC). Their respective strengths and limitations should be considered in the evaluation of asymptomatic patients with possible coronary artery disease. The test characteristics of positive predictive value (PPV) and negative predictive value (NPV) are clinically relevant to the proper use of cardiac testing modalities.

The Nuclear Stress Test (NST) is limited by a low sensitivity and low positive predictive value (PPV) and is not optimal for screening asymptomatic or low risk patients. The Coronary Artery Calcium Score (CAC) with a high negative predictive value (NPV) is a useful screening tool for an asymptomatic and a low or intermediate risk patient. The CAC has other unique characteristics that make it useful for early identification, risk assessment, prognosis and promoting patient compliance in the management of coronary artery disease.
Cardiovascular disease (CVD) remains the number one cause of death globally.\textsuperscript{1} In the United States (U.S.), CVD kills 600,000 individuals every year and is the leading cause of death for both men and women.\textsuperscript{2} Several traditional risk factors are well known to increase the risk of cardiovascular disease. These factors include smoking, high blood pressure, elevated cholesterol, diabetes and family history.\textsuperscript{3} Physicians have actively sought out these factors to assess an individual’s cardiovascular risk as well as to lower their risk of complications such as heart attack or stroke.\textsuperscript{4} Once identified, simple treatments such as lipid-lowering therapy can significantly lower the risk of complications.\textsuperscript{5,6}

The challenge physicians face in diagnosing CVD is the high incidence of silent or unrecognized CVD with half of all cardiovascular deaths occurring in persons who are assessed as low risk.\textsuperscript{7} Many of the fatalities attributed to CVD were not optimally treated in the U.S. because the disease is unrecognized. Consensus ACC/AHA/ACP statements have noted that the “detection and treatment of risk factors can slow progression of atherosclerosis… and reduce the occurrence of clinical cardiovascular events in both primary and secondary prevention settings. More recently, it has been shown that atherosclerosis can be stabilized or even modestly reversed.”\textsuperscript{3}

Currently, the Framingham Risk Assessment establishes a baseline for determining cardiovascular risk. Coronary Artery Disease (CAD) is an important category of CVD involving the buildup of plaque within the coronary arteries of the heart itself. It is important to establish a diagnosis of coronary artery disease in a stable asymptomatic patient when such a diagnosis does not exist. The early identification of coronary artery disease would often alter therapy and afford clinical benefit to the patient.

Physicians employ specific cardiac testing modalities in patients to further assess their cardiovascular status and future risks. Understanding the strengths and weaknesses of each testing modality is key to their effective use in clinical practice. Two non-invasive cardiac testing modalities are commonly employed in the assessment of coronary artery disease: the NST and CAC. Their respective strengths and limitations should be considered in the evaluation of asymptomatic and symptomatic patients with possible coronary artery disease.

**Discussion**

**Nuclear Stress Test (NST)**

The Nuclear Stress Test is a means of determining which patients do not have high grade coronary obstructive disease with a negative predictive value (NPV) of 90 to 99 percent.\textsuperscript{8,9} The negative predictive value describes the strength of the tests’ negative result in the population studied. The NST is especially useful in the symptomatic patient in the setting of a high prevalence of coronary artery disease. The NST uses a radioactive analog that is associated with metabolic activity. Changes in blood flow within the heart at rest and with exertion are seen by measuring the level of radiation within the heart muscle using an external detector. Areas with lower radiotracer activity suggest blockages in the coronary arteries that supply that part of the heart. Other factors such as overlying gastric contents or breast tissue unfortunately may confound the test, producing a false positive result.
The NST is very limited for the evaluation of low-risk, asymptomatic patients with a positive predictive value (PPV) of as low as 12 percent.\textsuperscript{10,11}

The NST is indicated in the assessment of intermediate or high-risk patients. Nevertheless, it is often used in clinical practice in lower risk populations and is poorly suited to this.\textsuperscript{10,11} If the NST is used in a low risk population, such as pre-operative patients, the likelihood of “false-positive” results will be much higher. This is reflected in the low PPV for the NST.\textsuperscript{10,11} The Nuclear Stress Test is thus of limited utility in a low risk population or as a screening method for coronary artery disease.

**Coronary Artery Calcium Score (CAC)**

The Coronary Artery Calcium Score is an objective means of determining which patients do not have coronary artery disease with a negative predictive value of 96 to 99 percent.\textsuperscript{11} Thus, it is an excellent screening tool for an asymptomatic or low-risk patient and a means of “ruling-out” coronary artery disease. The CAC uses a very low dose of radiation (1mSv) with a computerized tomography (CT) scan that is synchronized to the heartbeat to obtain images without motion artifact. It then measures the amount of calcified hard plaques within the coronary arteries of the heart. The presence of these calcifications correlates with the atherosclerotic burden present. A zero score provides your patient with the best prognosis of any cardiac test including coronary catheterization. When the calcium score is zero, it has both a high sensitivity of 99 percent as well as a high negative predictive value of 99 percent. This makes a score of zero the most clinically useful result of the heart calcium scoring exam.\textsuperscript{12} (Figure 2)

However, the CAC is a poor test for determining which patients do have flow limiting high-grade obstruction. The bulk of calcification seen on calcium scoring is subendothelial and resides within the arterial wall.\textsuperscript{13} It should not be confused with the acute intraluminal thrombosis of acute coronary syndromes.\textsuperscript{1} Nevertheless, the coronary calcium score is useful in the diagnosis and clinical management of stable coronary artery disease.

**The Tests in Use**

The current workhorse of cardiac testing is the NST. The major limitation of the NST is its limited sensitivity and specificity of 80 to 85 percent,\textsuperscript{9} as well as the tests’ inability to detect non-occlusive coronary disease. Due to its limited sensitivity, up to 20 percent of NST negative results can be false negatives. In these patients with false negatives, there exists undetected obstructive coronary disease. These patients have an annualized rate of heart attack or death of 0.8 percent, or an 8 percent 10-year risk.\textsuperscript{14} Furthermore, the NST exam is unable to detect non-occlusive coronary disease. Patients with non-obstructive disease have a risk of death or myocardial infarction that is higher than those without CAD, estimated at 1.4 percent over ten years.\textsuperscript{14}

A subsequent CAC test often confirms coronary disease in those individuals with negative NST results. In this setting, the heart calcium score is a complementary test to the NST. The CAC score has a negative predictive value of 99 percent. If the calcium score is zero, the patient’s
chance of a cardiac death in the next decade is indeed very low (0.4 to 0.6%). Conversely, if the CAC score is very high, aggressive medical management is indicated. Large observational studies have shown 10-year survival in asymptomatic patients with coronary artery disease was 99.4 percent if the CAC score was 0 but was only 87.8 percent in those with a CAC score of greater than 1000. Several studies have confirmed the value of CAC scoring for assessing the risk of future cardiac events. A study of 8,425 men without clinical CVD from 1998-2007 evaluated those who underwent a preventive examination that included a measurement of CAC. In this cohort, the annual risk of a cardiovascular event was only 0.1 percent in those with a CAC of zero and almost 2 percent in those with CAC values ≥400. This twenty-fold increase in risk far exceeds the two to three-fold risk increase represented by traditional cardiovascular risk factors such as high cholesterol, hypertension or diabetes. The powerful prognostic measure of CAC can be adjusted for age, gender and ethnicity to identify individuals at high CVD risk who would benefit from aggressive primary prevention with medical management. Studies have demonstrated that statin-based lipid-lowering therapy can slow or even reverse the progression of atherosclerosis seen on coronary calcium scoring.

In the acute setting, a NST or Left Heart Catherization may be necessary to ensure patient safety. In the future, the coronary CTA (CT Angiogram) or MRA (MR Angiogram) tests will likely impact this use of the NST. There are also refinements to the calcium score such as measures of calcium volume and density that promise to further increase the predictive value of calcium scoring. Notably, calcium density is inversely related to CV risk and may reflect plaque stabilization and the healing process within the arterial wall. More densely calcified plaque appears to contribute less to cardiovascular events and may be more resistant to plaque rupture. Additionally, the newer lesion specific calcium scoring (Voros method) has been shown to better predict the presence of obstructive coronary artery disease compared to the traditional Agaston calcium score. The Agaston score is the standard semiautomated method of assessing a calcium score value. The Agaston score is the weighted density score given to the highest attenuation value or “Hounsfield units” (HU) greater than 130 that are then multiplied by the area of the calcification. Many studies have shown that the Agaston score affords a method of risk stratification with a stepwise increase in risk with higher Agaston score.

Grading of Agaston scores is as follows:

**No evidence of CAD: 0**

**Minimal CAD: 1-10**

**Mild CAD: 11-100**

**Moderate: 101-400**

**High Risk: >400**

These values are proven to be predictive of the risk for future major adverse cardiac events. It should also be pointed out that the positive and negative predictive value of any test is influenced by the prevalence of disease in the population. The values of PPV and NPV are
clinically relevant since the consideration of the disease prevalence and test predictive power is fundamental to the proper use of cardiac testing modalities. The clinical setting of pre-test probability and the symptomatic versus asymptomatic patient also inform which tests are best suited to the question at hand. The use of appropriate testing modalities should afford better differentiation regarding which patients should and which should not require invasive procedures. A screening test result alone should never lead to an invasive procedure that could place a patient at risk; rather, it should inform the physician as to their patient’s condition.

The cardiac calcium score has other unique characteristics. Although many physicians only assess a calcium score as a numeric value, the review of the images of coronary plaque is invaluable. The coronary calcium score comes with a compact disk that will play on most computers. Viewing the plaque within each of the coronary arteries with the patient provides overwhelming visual evidence and compels the patient into an active prevention and treatment mindset. The CT scan images demonstrate bright white hard calcium deposits within the heart that often shock patients from their denial of disease. A meta-analysis of studies with over 11,000 patients has shown a two to three-fold increase in initiation of aspirin, lipid-lowering and anti-hypertensive medications as well as lifestyle changes for those with evidence of coronary calcium compared with patients having none.25 (Figures 1-8)

The CAC test may be of less value in the inpatient setting with symptomatic patients. This is typically where chest pain is evaluated and thus there is concern regarding soft plaque and acute obstruction not seen by calcification scoring. It also can be argued that coronary calcium scoring will prompt inappropriate use of left heart catheterization. These should be reserved for high-risk patients and medical management remains the most effective and safe intervention for all but those in acute coronary syndrome.26

The current problem facing physicians is not the overdiagnosis of cardiovascular disease but the opposite.27 Particularly in young men, there is ample evidence that traditional risk factors cannot adequately predict cardiovascular risk.28

Recent data from the Centers for Disease Control and Prevention (CDC)’s Million Hearts 2022 initiative suggest more should be done to identify cardiovascular disease in asymptomatic individuals.29 The findings suggest that as many as one in three hospitalizations and deaths related to cardiovascular events in 2016 involved adults in middle-age — between the ages of 35 and 64.

During a press briefing, the CDC’s Principal Deputy Director Anne Schuchat, MD stated, "many of these cardiovascular events are happening to middle-aged adults - who we wouldn't normally consider to be at risk. Most of these events can be prevented through daily actions to help lower risk and better manage medical conditions."29

The CAC provides high sensitivity and negative predictive values for identifying cardiovascular disease. Once appreciated in an individual, preventive measures proven to reduce cardiovascular mortality include the use of aspirin and statins, glucose and blood pressure control, as well as smoking cessation and regular exercise.

CAC scoring can also be done at a very low cost similar to that of an EKG. The diagnostic and prognostic power of CAC scoring has been extremely well documented. A recent prospective study by Shaw et al of more than 63,000 asymptomatic patients who were followed over 12
years showed once again the superiority of CAC scoring to the Framingham Risk Score. For a calcium score of zero, keeping with the results of other studies, the observed CV mortality was very low in both men and women at 0.4% over the 12-year follow-up. However, with a calcium score of over 400, the hazard ratio for cardiovascular mortality increased dramatically to 9.1 or a nine times greater risk of cardiovascular death. These results far exceed the prognostic power of Framingham Risk Scores or of any other cardiac test currently available. Also, the risk from coronary calcification was found to be greater in women than in men.30

Conclusion

The Nuclear Stress Test is a useful cardiac testing modality for symptomatic patients and those patients at high risk for obstructive coronary artery disease. However, it is of limited utility in a low risk population or as a screening method for coronary artery disease.

The Coronary Artery Calcium Score is an underutilized test with a cost similar to an EKG that uses less radiation than a mammogram and takes only ten seconds of CT time. It offers useful information in the proper setting and in the hands of an informed physician. The CAC has other unique characteristics that make it useful for early identification, risk assessment, prognosis and promoting patient compliance in the management of coronary artery disease.

If physicians truly intend to impact the unacceptably high morbidity and mortality of cardiovascular disease, its early identification and preventive care should be prioritized. The use of CAC data and CT images that are visually reviewed is a very powerful tool in educating physicians as well as personalizing the disease to the patient.30

A better understanding of cardiac testing modalities will ultimately lead to better care of patients. That is the shared goal of all physicians.
**Figures 1-8: Examples of CAC images**

Figure 1: Proximal Left Anterior Descending Artery calcification demonstrated. The calcium score for this artery alone was 250 per Agaston technique.

Figure 2: Right Coronary Artery without calcification and calcium score of zero is free of calcified plaque.

Figure 3: Right Coronary Artery calcification demonstrated in patient with total CAC score over 1000. Note that calcification involves arterial wall seen in cross section here.

Figure 4: Left Circumflex Artery calcification demonstrated bottom right with score for this artery of 90. Note the normal non-calcified Right Coronary Artery seen at top left.

Figure 5: Left Anterior Descending Artery calcification demonstrated in a patient with mild coronary artery disease with a CAC score of 85.

Figure 6: Proximal Left Anterior Descending Artery calcification is demonstrated in patient with total CAC score of 700.

Figure 7: Proximal Right Coronary Artery calcification demonstrated in patient with RCA calcium score of 900. Note that the sternum is seen at top of image and spine at the bottom. There is also a small area of calcified plaque seen in the wall of the descending aorta. The bright white character of the areas connotes the relative high density of the calcifications.

Figure 8: Left Main Coronary Artery arising from the Aorta with a calcified plaque in the proximal Left Anterior Descending Artery. The CAC score for the LAD is 250.
References:


CME Post-Test
Return by August 1, 2021 by EMAIL to kristy@dcmsonline.org

1. When does the atherosclerotic process of coronary artery disease typically begin?
   A. At birth.
   B. In young adulthood, ages 20s to 30s.
   C. In middle age, ages 50s to 60s.
   D. Only in older adults, over age 65.

2. What is the number cause of death of American women?
   A. Breast cancer
   B. Lung cancer
   C. Motor vehicle accidents
   D. Cardiovascular disease

3. The use of Calcium Artery Calcium Scoring involves high doses of radiation exposure and high costs.
   A. True
   B. False

4. Over half of deaths from cardiovascular disease occur in patients who prior to their death would be assessed as?
   A. High risk
   B. Intermediate risk
   C. Low risk

5. The use of Coronary Artery Calcium Scoring has been shown to change patient behavior in a positive manner.
   A. True
   B. False

6. Which cardiac test provides your patient with the best long-term prognosis?
   A. Normal EKG
   B. Negative Stress Test
   C. Calcium Score of Zero
   D. Normal Coronary Catherization
7. In the SCOT Heart study, the use of CTA (CT Angiography) was associated with lower 5 year death from coronary artery disease or MI when compared to functional stress testing.
   A. True
   B. False

8. The Cardiac Artery Calcium Score measures calcification present:
   A. Within atherosclerotic plaques
   B. Within the arterial wall
   C. Within heart valves
   D. Within acute intracoronary thrombi
   E. Only A &B
   F. Only C & D

9. One third of hospitalizations and deaths in 2016 related to cardiovascular events in adults between the ages of 35 and 64 who were not typically considered high risk.
   A. True
   B. False

10. The Cardiac Artery Calcium Score involves less radiation exposure than a mammogram.
    A. True
    B. False

EVALUATION:

1. What will you do differently as a result of this information?

2. How will you apply what you learned to your practice?

Please evaluate this article. Circle one number using this scale: 1= Strongly Agree to 5= Strongly Disagree

The article met the stated objectives: 1 2 3 4 5

The article was appropriate to my practice: 1 2 3 4 5

The topic was current and well presented: 1 2 3 4 5