Coronary artery calcium scanning: a useful tool for refining heart failure risk prediction?

“While coronary artery calcium has been used extensively to predict future cardiovascular disease events, recent data suggest it may be useful for identifying congestive heart failure in early stages, especially in asymptomatic populations.”

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Heart failure (HF) is a leading cause of morbidity and mortality in the elderly population, both in the developing and the developed nations. Approximately 5.8 million people in the USA currently have HF [1]. About one in five people who have HF die within 1 year after diagnosis as most of them when diagnosed are already at an advanced stage of the disease [1,2]. Unfortunately, physical examination only correctly diagnoses half of the cases. Early diagnosis and treatment of HF can halt the progression of disease and result in better life expectancy. There are some hurdles in accurately diagnosing HF in certain population groups. Diagnosing obese or elderly patients with congestive HF (CHF) can be challenging, especially given comorbidities, use of multiple medications and access to diagnostic services. While coronary artery calcium (CAC) has been used extensively to predict future cardiovascular disease (CVD) events, recent data suggest it may be useful for identifying CHF in early stages, especially in asymptomatic populations.

Background of CAC as a tool for risk prediction in the asymptomatic population

CAC has proved to be a great tool to diagnose and predict future outcome of various CVDs [1–3]. The accuracy of cardiac computed tomography (CT) has allowed identification of early atherosclerotic disease in asymptomatic individuals and prognostically surpassed traditional risk factors for the prediction of coronary artery disease (CAD). CAC as a risk stratification tool has great implications in diagnosing preclinical atherosclerosis [1]. In asymptomatic patients, the absence of CAC predicts excellent event-free survival with 10-year event rates of

approximately 1% [2]. Traditional risk factor evaluation has been shown to underrate coronary risk in certain population groups, particularly in women and young adults [3,4]. This may lead to suboptimal medical management of their coronary risk factors. CAC may help to refine the risk stratification and treatment strategies of these patient populations who are otherwise categorized as intermediate or low risk based on Framingham Risk Score categorization. CAC has consistently demonstrated independent and incremental predictive power for CVD when added to traditional risk factors [5–11].

In the Multi-Ethnic Study of Atherosclerosis (MESA) cohort [12], many traditional cardiovascular risk factors were associated with both the risk of developing cardiovascular events and increases in existing CAC scores. These included older age, male gender, white race/ethnicity, hypertension, higher BMI, diabetes mellitus and a family history of heart attack. Diabetes mellitus was the strongest risk factor for CAC progression. CAC progression is associated with mortality even after adjusting for baseline CAC, age, sex, time between scans, hypertension, hypercholesterolemia, diabetes, family history and smoking. Despite excellent cost–effectiveness data and prognostication, concerns have been raised about radiation. With modern CT use, the radiation exposure associated with CAC scans has been significantly reduced, now comparable to one to two mammograms (~1 mSv) [13–15], while providing important information about the coronary risk and cardiac anatomy of the subject. Patient-specific protocols, limited scan length and lowering tube voltage further reduce the radiation dose to the individual patient.

Keywords

- computed tomography
- coronary artery calcification
- HF ■ risk prediction of HF

Use of CAC for diagnosis of CHF

The etiology of HF, whether coronary induced or nonischemic, may be difficult to discern clinically. Differentiation of ischemic from nonischemic etiology is clinically important for both therapeutic and prognostic implications. With its ability to noninvasively discern and quantitate coronary artery calcification, studies originally performed with electron beam tomography correlated well with angiographic stenosis and were shown to be useful in distinguishing ischemic from nonischemic cardiomyopathies [16]. The current standard reference to differentiate between ischemic and nonischemic cardiomyopathy (CM) is invasive angiography. A study was carried out to compare the sensitivity and specificity of CAC testing with angiography in the setting of CHF of unclear etiology. One hundred and twenty-five patients with CM (ejection fraction <0.40) and known coronary anatomy underwent CAC scanning. Of the 72 patients who were found to have ischemic CM, 71 patients had CAC (sensitivity 99%; $p < 0.001$; mean score 798 ± 899). In comparison, among the 53 patients without significant coronary artery disease (nonischemic CM), the mean score was significantly lower (17 ± 51 ; $p < 0.0001$), and 44 patients had a CAC score of 0 (no CAC present). Overall accuracy for determining the etiology of CM (differentiating ischemic from nonischemic) was 92% for this technique.

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Determining the etiology of the CM in a patient presenting with HF can be difficult. Both dilated and ischemic CM may have identical clinical presentations with cardiomegaly, reduced left ventricular function and CHF. The treatment and prognosis of these two diseases are different, and therefore diagnosis is critical for optimal management. Noninvasive studies have shown that perfusion defects could distinguish between ischemic and nonischemic CM with only fair accuracy, and that perfusion defects can occur in idiopathic dilated CM as well as in ischemic CM. Nuclear imaging may have artifacts and attenuation variations that can lead to incorrect diagnoses, and the common presence of left bundle branch block in CM, which can

also make interpretation of nuclear imaging difficult. CAC testing was compared with nuclear testing in this population, and the overall diagnostic accuracy was significantly higher with CT, as compared with nuclear stress testing (84 vs 64%; $p = 0.009$). Given the high sensitivity of CAC (97–99%), this may prove to be an effective screen prior to angiography in patients with CHF of unclear etiology [17]. In another study, the accuracy of CAC was compared with that of echocardiography in 111 patients undergoing angiography for the evaluation of HF. Electron beam tomography-derived coronary calcium correctly identified 61 out of 63 patients (97%) with obstructive coronary artery disease, significantly higher than the 43 out of 63 patients (68%) with segmental wall motion abnormalities identified by echocardiography ($p < 0.001$) [18]. The authors found that the presence of CAC is superior to that of segmental wall motion abnormalities by echocardiography to distinguish ischemic from nonischemic CM.

Use of CAC in risk prediction of CHF

With advances in CVD treatment, more people now survive heart attacks but are left with a weakened heart. Effective treatment of HF not only reduces the mortality but also slows the progression of the disease. Newer prognostic studies in asymptomatic cohorts have started to demonstrate the ability of CAC testing to identify those individuals who develop CHF. Recently, CAC has been shown to have a clear association with the risk of HF [19]. In the Rotterdam Study, a population-based cohort, 1897 asymptomatic participants (mean age 69.9 years; 58% women) underwent CAC scoring and were followed for 6.8 years for the occurrence of HF and CHD. After adjustment for cardiovascular risk factors, increasing CAC scores were associated with HF (p for trend < 0.001), with a hazard ratio of 4.1 (95% CI: 1.7–10.1) for CAC scores >400 compared with CAC scores of 0–10. Moreover, adding CAC to cardiovascular risk factors substantially improved the risk classification of subjects (continuous net reclassification index: 34.0%). Because HF is highly prevalent in the elderly, it might be valuable to include HF as an outcome in future risk assessment programs incorporating CAC. One hypothesis is that CAC may predispose to CHF, as a marker of endothelial function, independent of overt CAD. Alternatively, those with more CAC may just have more cardiovascular events and, thus, if they survive, will ultimately develop CHF as a sequelae of multiple heart attacks (CAC as

a marker of ischemic CM). The Health ABC HF model adequately predicted 5-year HF risk in a large community-based study, providing support for the external validity of the model. This tool may be used to identify individuals in whom to target HF prevention efforts [20]. The Health ABC HF prediction model uses common clinical variables to predict HF incident risk in the elderly, an approach that may be used to target and treat high-risk individuals, and consideration should be made to add CAC to this model to make it more robust in identifying preclinical cases of HF. Further long-term outcome studies in the elderly will need to be

performed to validate the current observations, but the robust net reclassification offered by CAC is appealing.

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