Coronary Artery Calcium Score: Where Do We Stand? Current Uses and Implications in Asymptomatic Patients

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The coronary artery calcium (CAC) score is a measurement of the calcium burden in coronary arteries, via low-radiation, non-contrast computed tomography of the heart. The initial quantification and work on CAC measurement was performed by Agaston and colleagues in the 1980s [1]. Since that initial publication, this imaging technique has been extensively investigated as a means of non-invasive assessment of atherosclerotic disease and as a predictive marker of cardiovascular disease, mostly in asymptomatic individuals. Dr. Robert Bonow, past president of the American Heart Association, referred to CAC stating, "It's not a risk factor, it's the actual disease" [2]. More precisely, it is actually the subclinical disease.

CAC testing has been found to be one of the strongest predictors of major adverse cardiovascular events among patients and has an incremental predictive value over that of standard coronary risk factors, specifically in patients with no known coronary heart disease [3].

One of the most prominent and cited studies on the characteristics of subclinical cardiovascular disease is the Multi-Ethnic Study of Atherosclerosis (MESA) [3]. Detrano et al. [4] investigated CAC as a predictor of coronary events among 6722 individuals without cardiovascular disease at baseline during a mean follow-up of 3.9 years. The patients were chosen from four different racial and ethnic populations. They found that the higher the CAC score, the higher the risk of a coronary event. In comparison to participants with no documented coronary calcium, the adjusted risk of a coronary event was increased by a factor of 7.73 among participants with coronary calcium scores between 101 and 300, and by a factor of 9.67 among participants with scores above 300 ($P < 0.001$) [4]. Many other studies found a similar correlation.

Subsequent work has shown that the absence of CAC in asymptomatic individuals confers a very low risk of cardiovascular events. A recent review article on CAC referred to this test as the "Mammogram of the Heart" due to its significant potential value as a screening tool for cardiovascular disease [5]. Blaha et al. [6] investigated the absence of coronary artery calcification and all-cause mortality in 44,052 asymptomatic patients with a mean follow-up of 5.6 years. They found that the absence of CAC predicted excellent survival with a 10 year event rate of approximately 1%. In this cohort almost half of those aged 50 to 60 years old had no coronary artery calcification on imaging [6]. Substantial data have further reinforced this prognostic score of zero [7].

CAC has both a strong positive and negative predictive value, but what is its clinical implication and when should it be used?

The 2013 American College of Cardiology/American Heart Association (ACC/AHA) Cholesterol Management Guidelines have significantly broadened the scope of patients eligible for statin therapy [8]. As a result of these guidelines, there is concern that physicians may potentially over-initiate lifelong preventive therapy. If CAC scoring is utilized in the screening of patients, a CAC score of zero could almost halve the pre-CAC cardiovascular risk estimate of patients and reclassify approximately one-half of candidates as not eligible for statin therapy [9]. These results highlight the potential use of a CAC of zero as a method to downwardly reclassify risk and accurately identify those individuals who are truly at low risk for cardiovascular disease. This risk-reduction approach has been termed "interventional prevention" [10]. CAC scoring may also be a useful risk assessment tool in specific target groups such as those with an increased cardiovascular risk based purely on advanced age, in those averse to taking lifelong statin treatment, and in those who suffer from the adverse effects of statin treatment. A CAC of zero would validate the decision to minimize or even avoid lifelong pharmacotherapy in those individuals who are indeed at low risk.

Conversely, a positive CAC score can support initiation of a statin. Both the American and European guidelines recommend using CAC > 300 AU as a high risk factor to support statin initiation [8]. A practical clinical approach is to incorporate the MESA risk score, utilizing the CAC number, which calculates a 10 year risk estimation, similar to the Framingham Risk Scoring. The physician may initiate statin therapy if the 10 year risk is above 7.5% [11].

Furthermore, several studies have shown CAC score to positively enhance patient adherence to both pharmacological and non-pharmacological treatments, such as dietary changes and exercise. It has also been shown that patients with coronary calcification have better initiation and are more compliant to various therapeutic interventions compared to those with baseline zero calcium score [12].

WHAT ARE THE CURRENT GUIDELINE RECOMMENDATIONS?

The AHA/ACC and other American guidelines consider CAC as a IIb indication in patients at low to moderate risk [13]. The European guidelines suggest using CAC as an atherosclerotic imaging assessment tool in asymptomatic adults at moderate risk, as a IIa indication [14]. Both the Israeli Heart Society and Israeli Society of Radiology have adopted the European approach. They further emphasized that since CAC does not assess the vulnerability of atherosclerotic plaques, it should not be used as a screening tool. It should be used in those patients at moderate risk where there is uncertainty of statin initiation and cardiovascular disease-prevention targets [15]. An obstacle to the use of CAC is that this modality is currently not recognized as part of the Israeli Health Basket. However, it is useful to note that the coronary calcium burden can be roughly estimated on high resolution computed tomography of the chest (HRCT). This procedure is used in some centers as an early lung cancer screening modality, and there should be emphasis on documenting and reporting CAC on each HRCT done, especially in light of concurrent risk factors in smokers for both disease processes.

In light of the currently available data, our recommendation to physicians in Israel is to consider the use of CAC in the following circumstances:

- to help enhance shared decision making between physician and patients with moderate cardiovascular risk, where there is uncertainty of statin initiation and cardiovascular disease-prevention targets (as per current Israel Heart Society recommendations)
- to help tailor individual therapy, both pharmacological and non-pharmacological, in those patients who are:
  - at an increased cardiovascular risk based purely on advanced age
  - averse to taking lifelong treatment
  - suffering from the adverse effects of statin treatment.

In summary, CAC scoring is an excellent marker of subclinical atherosclerotic disease in asymptomatic individuals.

Physicians should be aware of both its strong positive and negative prognostic value and added benefit in estimating cardiovascular risk.

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> **"Those who profess to favor freedom and yet deprecate agitation are men who want crops without plowing the ground "**
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> Frederick Douglass (1817-1895), African-American social reformer, abolitionist, orator, writer, and statesman. After escaping from slavery in Maryland, he became a national leader of the abolitionist movement, known for his dazzling oratory