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Is There a Role for Coronary Artery Calcium Scoring for Management of Asymptomatic Patients at Risk for Coronary Artery Disease?: Clinical Risk Scores Are Sufficient To Define Primary Prevention Treatment Strategies Among Asymptomatic Patients

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Introduction

Adequate screening for identifying individuals at risk of developing cardiovascular disease (CVD) is important because vascular disorders are a preventable cause of morbidity and mortality worldwide. Furthermore, the lifetime risk of developing CVD is high (an estimated 66% for men and >50% for women) and often the first symptom of disease is a sudden death, thereby occurring without an opportunity for intervention.^{1–3} Conventional risk factors aggregated as risk scores (such as the National Heart, Lung, and Blood Institute report on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Adult Treatment Panel III, based on the Framingham risk score]) have shown to predict the 10-year risk of developing coronary heart disease (CHD) in most individuals,^{4, 5} and the predictive capability of these risk factors extends over a 30-year time horizon.⁶ However, established risk scores may underestimate CVD risk in some individuals.⁷ In addition, it is also recognized now that even among those with an optimal risk factor profile at age 55 years, the residual lifetime risk of CVD remains substantial (40% in men and 30% in women).³ These observations have motivated the search for additional risk factors (including imaging tests that detect subclinical atherosclerosis) that can enhance the predictive utility of conventional risk factors.

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Conflicts of Interest Disclosures

None.

The underestimation of CVD risk may be especially evident in people with a family history of premature CVD.^{8–10} Independent of established risk factors, a positive family history has been associated with a greater prevalence of subclinical atherosclerosis (such as an increased coronary artery calcium [CAC] score, obtained by coronary computerized tomography [CCT]).^{11, 12} Estimation of the CAC score is, therefore, currently considered a valuable supplement to the Framingham Risk Score for the assessment of CVD risk in individuals with a familial history of premature vascular disease^{11, 12} and among patients classified as having an intermediate 10-year risk of coronary heart disease (CHD) based on Framingham Risk Score.^{13, 14}

Undoubtedly, biomarkers (including imaging tests such as CCT) may aid the risk-stratification of asymptomatic people at risk of developing CVD. Yet, several criteria must be satisfied before any such biomarker can be incorporated into clinical practice at primary care settings. Table 1 summarizes the American Heart Association guidelines for the evaluation of biomarkers for screening for CVD risk.¹⁵ A comprehensive evaluation of which criteria are met by a putative screening biomarker assumes specific importance when a candidate test is expensive or not easily obtained (as it is in the case of imaging tests). The present article focuses on the clinical utility of CAC scores derived by CCT (as the prototype imaging test) because it is the most commonly used and best studied imaging modality that is used for screening asymptomatic individuals in the community. To put the discussion into a clinical context, we present 2 clinical cases in Table 2, which should serve as an appetizer for reflection. The 2 examples reflect relevant scenarios where CCT testing is appropriate according to guidelines, but where the interpretation of CAC scores may be challenging.

CAC score as an independent risk factor in asymptomatic individuals: Some Challenges

Data on Long-Term Outcomes

Several population-based cohort studies with a typical follow-up time of 3–5 years have consistently demonstrated that elevated CAC scores are associated with increased risk of new-onset CVD independent of standard risk factors and the Framingham Risk Score.^{16–23} However, there are very limited data available on CVD risk over a longer time horizon (such as 10-, 20- or 30-year risk of CVD).²⁴ It seems likely that a high CAC score will continue to maintain a strong adverse prognostic value, but it is less clear if a CAC score of 0 will continue to maintain a strong favorable prognostic value over a longer time period. A CAC score of 0 is associated with a low risk of CVD during the subsequent 3–5 years and event rates may be as low as the event rates for those with a low Framingham Risk Score (<10% risk of coronary death or myocardial infarction within the next 10 years). The reported coronary death or myocardial infarction event rates were 11 of 1322 (0.8%) for those with a CAC score of 0 vs. 26 of 2230 (1.2%) for those with a Framingham Risk Score <10% during a mean follow-up of 5.0 years in the Heinz Nixdorf Recall Study.²⁵ During a mean follow-up of 7 years corresponding numbers were 14 of 316 (4.4%) for those with a CAC score of 0 vs. 1 of 98 (1.0%) for those with a Framingham Risk Score <10% in the South Bay Heart Watch study. Moreover, during a follow-up of 7 years, 7 of 75 individuals (9.3%) with a

CAC score of 0 but a Framingham Risk Score of 21 experienced an event in the South Bay Heart Watch study. Investigating a cohort of 442 individuals with a CAC score of 0 annually for 5 consecutive years, Min et al. reported that 106 patients (25.1%) converted to a CAC >0 during the study period, but that such a conversion was very uncommon before year 4 and escalated at the end of the study period.²⁶ Additional studies are, therefore, clearly needed to establish the longer-term prognosis associated with a CAC score of 0.

Although not recommended in guidelines (for several reasons), one theoretical possibility to overcome the issue of limited follow-up time for currently available data could be to re-screen individuals at select time intervals, e.g., every 5 years to define management strategies. Longitudinal data indicate that individuals who have rapid increases in CAC scores over time are at markedly greater risk of CVD.^{24, 27} For example, 1 study showing that an increase of the CAC score >15% per year translated into a 17-fold increased risk of CHD, compared to those who did not have a progression in CAC scores.²⁷ Recent data from the Multi-Ethnic Study of Atherosclerosis (MESA) confirm the prognostic significance of change in CAC.²⁸ However, another recent study noted that progression of CAC score by >50 over a 5-year period was noted in only 2% of individuals.²⁹ Thus, the use of changes in CAC scores is challenged by the limited variability over shorter periods of follow-up, relative to levels of other CVD risk factors.

Effect of Demographic Factors Including Race

It is unclear if the interpretation of CAC scores should be age- or ethnicity-specific. For example, it has been argued by Pletcher et al.³⁰ that a CAC score of 50 may be unusually high for a 40-year-old woman without other CHD risk factors, but unusually low for a 70-year-old man with hypertension, and that the same CAC score, therefore, may affect risk assessment (post-test probability) in opposite directions for these two individuals. Likewise, the prevalence and possible prognostic importance of a high CAC score may vary by ethnicity. For instance, the MESA study reported that in women, whites had the highest CAC percentiles followed by the Chinese and blacks, whereas the Hispanics had the lowest percentiles of CAC scores. In men, the rank ordering of CAC scores was slightly different: whites had the highest percentiles followed by the Hispanics, with the lowest CAC scores being observed in blacks at the younger ages and in Chinese at the older ages.³¹ However, no differences in the prevalence of a CAC score >10 Agatston units were reported in asymptomatic whites versus blacks in the Dallas Heart Study.³² The prognostic importance of race in the risk assessment of CAC scores has not been firmly established yet, but data from the MESA study suggested that there were no significant race-related differences in the prognostic importance of a specific CAC score and that the predictive utility of CAC scores was independent of race.^{18, 33}

Test-Retest Variability

The concept of reproducibility is important for all biomarkers, and CAC scores are no exception. Whereas earlier studies reported a high variability in repeat CCT scans to measure CAC, more recent studies have noted mean interscan variability of 15 to 20% with a median of 4 to 8%.^{34–36} Others have reported that variability of CAC scores is greatest in the low score range and least in the high score range.³⁷ The interpretation of low CAC

scores must, therefore, take into account variability in the measurements, especially when interpreting serial scans. The clinical consequences of such variability in CAC scores are not known. Specifically, it is not known if such variability will translate into individuals falling into different risk categories (e.g. CAC score of 0, 1–50, 51–100, 101–300, and >300) and, as a result, if such variability would impact treatment decisions.

Incremental Predictive Use of CAC Scores in a Primary Screening Program

To validate a new biomarker in the setting of screening of asymptomatic individuals, several metrics should be evaluated beyond measures of association (i.e., relative risks). These include a change in discrimination (c statistic), the net reclassification improvement (NRI), and the integrated discrimination improvement (IDI).^{15, 38} For the screening of asymptomatic individuals, there is evidence that CAC scores improve both the c statistic and the NRI. The MESA study demonstrated that CAC provided a net reclassification improvement of 25% ($p < 0.001$) compared with a model including only the Framingham Risk Score, with 23% of those with events being reclassified to a high-risk category, and 13% of those without events being reclassified to a low-risk category when CAC scores were added to the multivariable model.²² These analyses were, however, limited to estimating the 5-year risk of CHD and excluded participants with diabetes mellitus.²² A more recent analysis of the MESA study with follow-up extended to 7.6 years yielded a much higher NRI of $\approx 66\%$.³⁹ The Heinz Nixdorf Recall Study yielded a NRI of $\approx 31\%$.²⁵ Similarly, data from the Rotterdam study of subjects >55 years showed an improved predictive capability of the 10-year risk of CHD by addition of CAC scores to the Framingham Risk Score. In total, 51% and 53% of the men and women were reclassified, with the greatest proportion of reclassifications in the intermediate risk group.¹⁹ C statistics were significantly improved from 0.72 to 0.76 and NRI was 14% ($p < 0.01$).¹⁹ The St. Francis Heart Study reported a NRI of $\approx 70\%$ (as cited by Budoff).^{16, 40} These data indicate that CAC scores consistently improve model discrimination and NRI, yet the range of improvements in the latter varied widely between 14% (weak to intermediate) and 70% (strong),⁴¹ highlighting the need for additional studies.

A final concern related to newer biomarkers includes the risk of overestimating their predictive use. In this context, a recent review suggests substantial publication bias associated with most of the newer biomarkers, including measurements of CAC, underscoring the notion that published reports based on observational studies may overestimate their prognostic utility.⁴²

Do Imaging Tests (Such as CAC Scoring) Translate Into a Change in Management and Better Clinical Outcomes in Asymptomatic Individuals?

When considering the value of a new biomarker as a supplement to conventional risk-prediction scores, we need to consider not only the ability for a new biomarker to reclassify CVD risk in patients, but we must evaluate whether the results of the biomarker test will affect treatment decisions and patient outcomes. Three potential benefits from a biomarker test have been suggested by Pletcher and Pignone.⁴³ These include: (1) better patient understanding of the risk of disease, (2) healthier patient behavior, and (3) better clinical

decisions. Studies regarding the impact of CCT on patient understanding and behavior are sparse. The Early Identification of Subclinical atherosclerosis by Noninvasive imaging Research (EISNER) prospective randomized trial assigned 2,137 volunteers to undergo vs. not to undergo CCT scanning (2:1) before risk factor counseling. The trial illustrated that those who were offered a CCT scan improved their risk factors more than those who did not undergo CCT.⁴⁴ The improvements were further shown to be dose dependent with greater improvements in people with higher CAC scores.⁴⁴ Other studies have failed to report changes in patient behavior upon being provided CAC score results.^{45–47} Whether CAC testing will translate into beneficial clinical outcomes is, therefore, yet to be determined, and currently data on hard endpoints from randomized trials (i.e., CCT vs. no CCT) are lacking.⁴⁴ Also, of note, randomized trials of statins have reported clinical benefit without a change in CAC scores, suggesting that regression of CAC may not be a therapeutic target or a tool for monitoring benefits of treatment strategies (as opposed to other risk factors such as high blood pressure, or dyslipidemia).^{16, 48} It may be reasoned that this argument could be extended to standard risk scoring and biomarkers as well. In this context, a recent meta-analysis suggested that there may be a modest beneficial impact on lifestyle and prophylactic pharmacotherapy associated with the use of global risk scores, perhaps indicating that improving risk factors and patient behaviour with use of any tests is challenging in general.⁴⁹

It is currently not well established whether the CAC scores modify treatment decisions for the individual people. For individuals with low 10-year risk of CHD, the likelihood of finding a CAC score >0 is so small that the tests are currently not recommended; further, prophylactic treatment is not recommended beyond lifestyle measures to maintain optimal levels of CVD risk factors.¹⁴ For people with high risk of CHD (i.e., 20% risk of developing CHD within the next 10 years) and possible for selected intermediate-risk individuals (i.e., 10–20% risk) non-pharmacological lifestyle management advice and appropriate pharmacological treatment (based on guidelines) should be offered irrespectively of their CAC status.⁵⁰ More precisely, guidelines recommend consideration of aspirin treatment for all patients with a 10-year risk of CHD 10% without contraindications; statin treatment for those with dyslipidemia (threshold for initiation of treatment depends on risk factor burden with primary goal as follows: LDL-C <160 mg/dL if 1 risk factor is present; LDL-C <130 mg/dL if 2 risk factors are present and 10-year CHD risk is <20%; or LDL-C <100 mg/dL if 2 risk factors are present and 10-year CHD risk is 20% or if the patient has diabetes mellitus); and antihypertensive medications for those with hypertension.⁵⁰ Thus, for most asymptomatic patients, CCT is unlikely to change clinical decision-making with the exception of patients with an intermediate risk who may be managed more aggressively if they have a high CAC score (although randomized clinical trial data are lacking to justify this strategy).

As for the example with Mrs. X and Mr. Y (Table 2), therapies would possible not be affected by CCT findings. Mrs. X had an estimated low risk of CHD based on the Framingham Risk Score (calculated risk 7%), but she had an adverse risk factor profiles including a positive family history of premature CVD, which in reality puts her at a higher risk than estimated by the Framingham Risk Score. Acknowledging this, current guidelines consider a CAC scan appropriate in such an individual.¹⁴ However, despite her burden of

risk factors, the CAC score turned out to be 0. Based on the low CAC score, the question is whether Mrs. X should be treated less aggressively than if her CAC score was unknown. There is currently lack of data to answer this question, but perhaps a low CAC score should be considered an excellent opportunity for prevention of future CVD rather than declare her to be at lower risk than if her CAC score was unknown? Mr. Y is being classified as having an intermediate risk of CHD based on the Framingham Risk Score (calculated risk 14%) and, therefore, the indication for his CCT was appropriate according to the guidelines. Because his CAC score turned out to be high, the question is whether he should be treated more aggressively than if he had no CCT scan performed? The answer is probably not because current guidelines recommend consideration of aspirin use in all individuals at an intermediate or high 10-year risk of CHD.⁵⁰ Because Mr. Y had an optimal lipid profile and blood pressure, other prophylactic medications are probably not indicated in his case beyond maintaining healthy lifestyle measures. It is, however, possible that, if his CAC score had turned out to be low aspirin could be omitted (but there are no randomized clinical trial data to support this strategy).

Follow-up Testing after CCT

Concerns have been raised that referral to stress test or coronary angiography after CCT might occur more often than is necessary and that the results from CAC scans may raise additional questions rather than provide easy answers in some cases.^{51, 52} Yet, the EISNER trial did not show a difference in downstream medical testing between those who did and did not undergo CAC scanning.⁴⁴ Current guidelines state that stress myocardial perfusion imaging may be considered in asymptomatic individuals at high risk of coronary heart disease, such as those with a CAC score >400 (class IIb recommendation).⁵³ When considering the risk of having significant stenosis based on CAC scores, it is critical to consider the sensitivity, specificity, positive and negative predictive values. The notion of positive predictive value is particularly important in the primary prevention setting. When the prevalence of a disease or a trait is low in the community, it is desirable to have a high specificity. This is because we want to avoid unnecessary anxiety associated with a false positive test, limit unnecessary treatment (and related side effects) and costs. When the setting is one of a high pretest probability (example, individuals with chest pain), we want to maximize sensitivity so as to avoid falsely reassuring someone with a negative test. Data on the sensitivity, specificity, positive, and negative predictive values of a CAC score below and above 0 for predicting coronary atherosclerosis and significant stenoses in asymptomatic people are sparse. Data from the MESA study indicated that a CAC score >0 was associated with a reasonable sensitivity (91%) but a low specificity of 51% and a very low positive predictive value of 2% for having significant stenoses creating the challenge of anxiety related to a false positive test (as cited by Budoff).^{33, 40} Ho et al.⁵⁴ reported that the frequency of CT angiographic stenoses increased as CAC scores increased with a significant stenosis (>60% lesion) found in 7.9%, 8.3%, 14.5%, and 27.2% of those with CAC scores of 1 to 100, 101 to 400, 401 to 1,000, and >1,000, respectively. The extent to which individuals shown to have significant angiographic coronary stenosis are referred for invasive revascularizations downstream in a real-world clinical practice is not known. One caveat to be remembered when interpreting predictive values is that, unlike most screening tests in the case of CAC we are predicting events into the future. As such, predictive values of CAC

testing may be sensitive to the duration of follow-up. Importantly, however, it is unclear if asymptomatic individuals with higher CAC scores should be referred for coronary angiography, given that there is currently little evidence to support revascularization of asymptomatic people.⁵⁵

Cost-effectiveness of Imaging Tests

The economic evaluation of any screening or diagnostic test is complex, but a generally accepted measure in this context is the amount spent money on tests per quality-adjusted life years (QALY) gained. Because there are currently no data available that evaluate the improvements in long-term outcomes for screening with CCT, the cost-effectiveness of CCT is somewhat difficult to estimate. The economic value of CCT has, however, been evaluated both in young and middle-aged/older asymptomatic individuals. Using data from the Prospective Army Coronary Calcium (PACC) project of young volunteers recruited from the U.S. army (aged 40–50 years) Taylor et al.⁵⁶ evaluated the cost-effectiveness of screening of young asymptomatic individuals with CCT.⁵⁶ Based on the expected relative risk reduction associated with preventive medications and the numbers considered at pre-test risk, the authors estimated that adding CCT to the conventional Framingham risk score was associated with \$11,500 to > \$1,000,000 per QALY gained.⁵⁶ One potential interpretation of these data is that in a group of low-risk individuals CCT screening may not be cost-effective. van Kempen et al.⁵⁷ evaluated the cost-effectiveness associated with CCT screening based on data from the Rotterdam study of middle-aged and elderly individuals at intermediate risk of developing CVD. The study sample had a mean age of 70 and 74 years in men and women. The authors took into consideration economic costs of CCT, cost of preventive medications, benefits and risk of adverse effects of medications (e.g., bleedings with aspirin therapy), and cancer-related risk associated with CCT (see section below). They concluded that screening of intermediate risk patients (i.e., 10% risk of coronary heart disease within 10 years) is probably cost-effective in men but unlikely to be so in women (Figure 1).⁵⁷ Two other recent studies have reported cost-savings associated with CAC screening.^{21, 44} Another interesting point of view from a public-health perspective illustrated in Figure 1 relates to the wide gap between current practice and current guidelines. If full adherence to the current guidelines would be reached in clinical practice, this would translate into a much larger gain in quality-adjusted life expectancy compared with the additional gain in quality-adjusted life expectancy associated with introduction of CCT beyond the full adherence to current guidelines. Perhaps these data therefore suggest that an improved focus on ‘getting with the guidelines’ may be an effective alternative to implementing CCT for CAC scoring.

Other Concerns Associated with Use of CCT: Radiation Exposure and Risk of Incidental Findings Associated with Testing

When tests are performed on asymptomatic individuals, there is a hazard of incidental findings particularly with the use of imaging tests. If the indications for the tests are appropriate, the risk-benefit ratio is favorable. A retrospective review of 1356 individuals referred for CAC screening reported that 278 (20.5%) of the individuals had 1 non-cardiac finding on the scanning. Of these 57 (4.2%) individuals were recommended diagnostic CT

follow-up.⁵⁸ To our knowledge, the economic and psychosocial consequences associated with incidental findings in CCT scan screenings have not been adequately investigated.

When using CCT for screening, the risk of cancer induced by radiation exposure must be considered.⁵⁹ The radiation exposure associated with a typical chest CT examination is $\approx 3\times$ times the amount of annual natural background radiation exposure and is estimated to be 30x that received from a routine chest x-ray (estimated effective radiation doses are 3 mSv for CCT and 0.1 mSv for a posteroanterior and lateral chest x-ray). It has been suggested that as much as 1.5 to 2% of all cancers in the U.S. are currently attributable to CT scans, a number that has raised from 0.6% in 1996 and may be increasing further as a result of the increase in numbers of procedures performed.⁶⁰ Although the amount of radiation for 1 scan is small, it will inevitably lead to a significant number of cancers, especially among younger patients and women (who are generally more susceptible to radiation compared with older men). Because the association between radiation and incidence of solid cancers seems to be cumulative, risks increase for each scan performed, arguing that in the setting of primary screening of asymptomatic individuals repetitive scans are inappropriate.⁶¹ In this context, it should be noted that more recent protocols have been reported to be associated with radiation exposure of <1 mSv to as low as 0.6 mSv (lower than mammography).^{62, 63} Clearly additional longitudinal data are warranted as experiences with these newer protocols accrue.

Other Concerns Associated with Use of CCT: That CAC Scores “Override” Clinical Risk Factors in Evaluation and Management

It may be argued that CAC scores should not be viewed as a risk factor but rather a marker of subclinical disease. Yet, even as a marker of subclinical disease, its presence (or absence) does not guarantee an adverse (or better) outcome. First, we do not know the long-term prognosis of a low CAC score; second, individuals with a low CAC score but high risk factor burden may still have a high CVD risk; and third, an elevated CAC score in individuals without other risk factors may not be associated with an adverse prognosis in all people, and may theoretically cause unnecessary anxiety and medical therapy (e.g., increased risks of bleeding with aggressive antiplatelet therapy). Of note, the predicted 7-year risk of coronary heart death or nonfatal myocardial infarction for a particular CAC score seemed to differ for the different categories of Framingham Risk Score in the South Bay Heart Watch study.²⁰ As seen in Figure 2, individuals with a CAC score >300 but a Framingham Risk Score of $<10\%$ seem to have a much lower risk of suffering from an event than individuals with a CAC score of zero but a Framingham Risk Score of $>20\%$. Thus, it seems important not to consider CAC scores as an absolute key for the future risk of developing overt cardiovascular disease, but rather as a clinical risk marker in line with the Framingham Risk Score.

Conclusions

Whereas the use of imaging tests in people deemed to be at intermediate risk of coronary disease may be useful in some cases, the routine use of such tests in primary care settings is challenged by lack of data on long-term risk associated with CAC scores, and a lack of

evidence that such screening results in a change in patient outcomes. The routine application of such testing in primary care settings is also challenged by the potential psychological burden associated with tests, incidental findings and their implications, radiation exposure (for select imaging tests) and associated cancer risks, and associated costs to the already-stressed health care systems.

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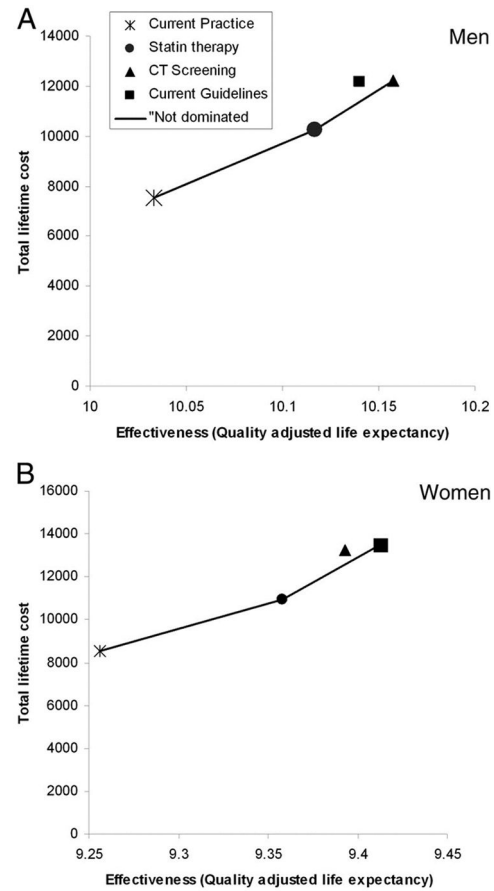


Figure 1. estimated cost-effectiveness associated with CCT screening of middle-age and elderly individuals at intermediate risk of developing CVD. Reprinted from van Kempen et al.⁵⁷ with permission of the publisher. Copyright © 2011, Elsevier. Authorization for this adaption has been obtained both from the owner of the copyright work and from the owner of copyright in the translation or adaption.

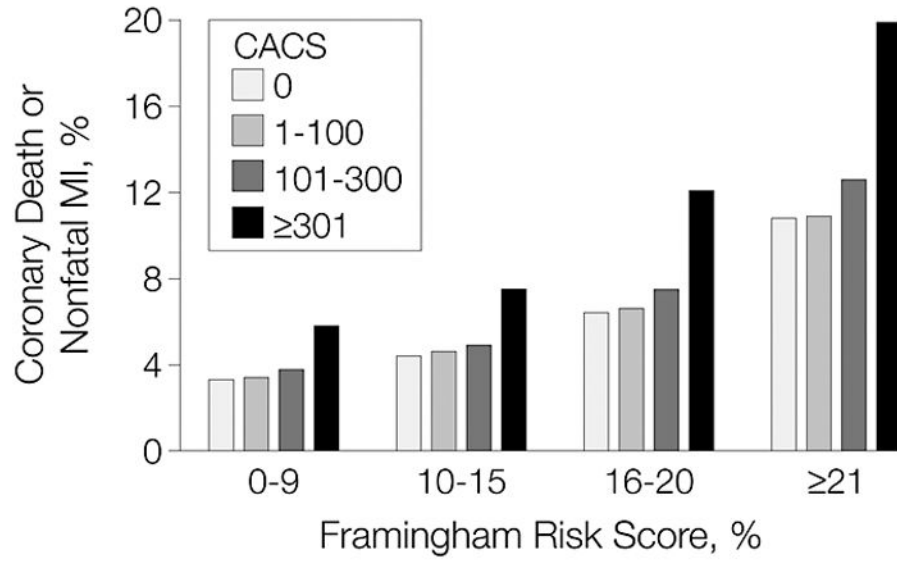


Figure 2. predicted 7-year risk of coronary heart death or nonfatal myocardial infarction for different combinations of coronary artery calcium (CAC) score and Framingham Risk Score in the South Bay Heart Watch study. Reprinted with permission from Greenland et al.²⁰ Copyright © 2004, American Medical Association. Authorization for this adaption has been obtained both from the owner of the copyright work and from the owner of copyright in the translation or adaption.

Table 1

Principles for evaluation of a new biomarker, as suggested by Hlatky et al.¹⁵ in 2009 AHA guidelines of evaluation of a new biomarker.

1	Proof of concept: Do novel biomarkers differ between subjects with and without outcomes?
2	Prospective validation: Does the novel biomarker predict the development of future outcomes in a prospective cohort or nested case-control study?
3	Incremental value: Does the novel biomarker add predictive value to established, standard risk markers?
4	Clinical use: Does the novel risk marker change predicted risk sufficiently to change recommended therapy?
5	Clinical outcomes: Does use of the novel risk marker improve clinical outcomes, especially when tested in a randomized clinical trial?
6	Cost-effectiveness: Does use of the marker improve clinical outcomes sufficiently to justify the additional costs of testing and treatment?

Table 2

Two illustrative cases.

Mrs. X is a 48-year old African American lady who is overweight (body mass index of 29 kg/m²), has a slightly pro-atherogenic lipid profile with a high-density lipoprotein cholesterol value of 42 mg/dL and a total cholesterol value of 235 mg/dL, and a normal blood glucose. She has a normal estimated glomerular filtration rate and no microalbuminuria. Her mother suffered from an ischemic stroke at the age of 61 and her father died from myocardial infarction at the age of 55. She measured her blood pressure at home with an average value of 145/90 mmHg. The blood pressure in clinic is 150/95 mm Hg. She is a smoker and has a stressful life providing care for her two grandchildren aged 1 and 3 years two days a week, along with her fulltime night job at a convenience store. Because of her positive family history and adverse risk profile, her doctor refers her to CCT and her CAC score turns out to be zero.

Mr. Y is a 74-year old white man with an optimal lipid profile (HDL cholesterol 52 mg/dL and total cholesterol 195 mg/dL), normal blood pressure (120/80 mmHg), euglycemia, a normal estimated glomerular filtration rate with no microalbuminuria, and no family history of early-onset cardiovascular disease. He is a non-smoker and swims for 30 minutes 3x each week. Mr. Y has read in the newspaper about this new facility that provides CCT that provokes his interest and he seeks the test to find out his CAC score. His doctor, therefore, refers him to a CCT and the CAC score turns out to be >300.

Based on the given information, the 10-year risk of developing coronary heart disease based on the Framingham Risk Score can be calculated elsewhere (<http://cvdrisk.nhlbi.nih.gov/calculator.asp>).