Marked Discordance Between Coronary Artery Calcium Score and Framingham Risk Score in Middle Eastern and Veteran American Populations

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Introduction

Conventionally, the Framingham Risk Score (FRS) has been used to determine an individual’s 10-year risk for angina, myocardial infarction, and death. It evaluates a number of factors including diabetes mellitus, systolic blood pressure, total cholesterol level, high-density-lipoprotein (HDL-C) level, and smoking [1]. Population studies have indicated that the FRS fails to predict cardiovascular events (CV) in up to 50% of patients [2]. For this reason, it is imperative to find alternative or supplementary tools that allow a more accurate risk stratification. One such tool is the Coronary Artery Calcium Score (CACS). Numerous studies have demonstrated the utility of CACS in predicting risk for CV disease [3-5]. Most risk calculators including CACS and FRS reveal concordant risk scores. The primary objective of this study is to quantify the magnitude of discordance between the risk assessed by FRS and that by CACS in two different population groups, namely Middle Eastern and veteran Americans.

Background: Conventionally, the Framingham Risk Score (FRS) was used as a tool to risk stratify individuals for cardiovascular (CV) events and death. More recently, the coronary artery calcium score (CACS) has been used as a complimentary method for the assessment of CV risk. This study’s objective is to quantify the magnitude of marked discordance (MD) between FRS and CACS. The subjects were from two different ethnic groups, namely, a Middle Eastern population and a veteran American population.

Methods: This is a retrospective observational cohort study of 499 consecutive patients who underwent multidetector cardiac computerized tomography (MDCT) at King Fahd Armed Forces Hospital (KFAFH), Jeddah, Saudi Arabia and Veterans Affairs Loma Linda Health Care System (VALLHCS). CACS was measured using the Agatston method. FRS was calculated by chart review. MD was defined as a CACS of <100 with a high risk FRS or a CACS of >400 with low risk FRS. Patients had CACS between 100 and 400 were excluded from the analysis.

Results: A total of 499 patient CT studies were reviewed with 450 meeting study criteria, 130 patients from the VALLHCS (63 ± 12, 95% males) and 320 from KFAFH (27% males). MD was found in 308 (68%) of the total number enrolled. In the American population, of the 62 patients with a CACS <100, 3% (2 patients) only had discordantly high FRS and of the 69 patients with a CACS >400, 20 patients (29%) had a discordantly low FRS. In the Middle Eastern population, of the 290 patients with a CACS <100, 281 patients (96.9%) had discordantly high FRS and of the 30 patients with a CACS >400, only 5 patients (16.7%) had a discordantly low FRS.

Conclusion: The majority of MD in the Middle Eastern population had a high FRS with a low CACS. In contradistinction, the American veterans with MD had a high CACS and a low FRS.
Coronary Artery Calcium Score (CACS)

The CACS is calculated by multiplying the individual lesion area with a weighing factor which is based on the HU of each lesion. The factor is 1 for a peak lesion of 130 - 199 HU, 2 for 200-299 HU, 3 for 300-399 HU, and 4 for any lesion equal to or greater than 400 HU. The sum of all lesion scores gives the individual vessel score. A total CACS is the sum of all the vessel scores. Once CACS is calculated, CV risk is determined based upon risk strata that have been previously published [4-6]. A total CACS of <100 implies low (2.1%) risk, 101-400 implies intermediate (4.2%) risk, and >400 implies high (>7.2%) risk.

Framingham Risk Score (FRS)

The charts of patients who had undergone a CCT were reviewed to obtain the variables needed to calculate the FRS. These variables include: age, systolic blood pressure, total cholesterol level, HDL-C level, diabetes mellitus, and smoking, on a point system. Separate nomograms designed for men and women define an absolute risk for cardiovascular events based on a total FRS. The absolute risk for a given individual is cross referenced with age to determine the relative risk [1].

<table>
<thead>
<tr>
<th>CACS</th>
<th>Veteran American Population</th>
<th>Middle Eastern Population</th>
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<tbody>
<tr>
<td></td>
<td>Total (n=131)</td>
<td>Discordance (n=22, 17%)</td>
</tr>
<tr>
<td>&lt;100</td>
<td>62</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>&gt;400</td>
<td>69</td>
<td>20 (29%)</td>
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<tr>
<td>Concordance</td>
<td>0.001344</td>
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Discussion

To the best of our knowledge, this is the first study comparing concordance and discordance between FRS and CACS in 2 different ethnic groups (Middle East and veterans Americans). The study showed that MD is significantly higher in Middle Eastern patients compared with veteran American patients (89% vs. 17%). The pattern of MD also differed in both populations. The Middle Eastern population showed discordantly low CACS and high risk FRS in 96.9% while in veteran Americans, 29% had CACS >400 and low risk FRS.
Coronary arterial calcification is thought to be a response to chronic inflammation from the atherosclerotic process [7,8]. As this calcification is easily detected and measured by CCT, it has become an excellent surrogate marker for CAD. Large scale studies have established the value of CACS in risk stratification independent of the FRS [9-11]. However, low or absent calcification does not exclude the presence of CAD. Many studies have reported that up to 6.2% of individuals with no coronary calcium are found to have soft plaques [12]. These studies have for the most part examined Caucasians. It has been previously shown that African-American males with established coronary artery disease do not manifest coronary calcification as their age matched Caucasian counterparts [11]. To date, epidemiologic data for ethnic groups like Middle Eastern patients is lacking. Our study did show that 96.9% of Middle Eastern patients had a low CACS despite having established coronary artery disease or multiple poorly controlled cardiovascular risk factors i.e., a high FRS. Data review also showed that the most common risk factor in those individuals was Diabetes mellitus. In contradistinction, the vast majority (29%) of the veteran American discordant population had a very high CACS and a low risk FRS. This implies other variables not accounted for by the FRS. These variables may be genetic, environmental or a combination of the two in that ethnic group. Isolating the factors responsible for these discordant populations has important diagnostic and therapeutic implications. Recent studies suggest a role for performing concomitant FRS and CACS when screening an individual for CAD.3 In an individual who is deemed low or even intermediate risk by FRS, a high CACS implies a high risk for future cardiovascular events. Therefore, MD populations are important targets for future investigations into the etiology of atherosclerotic CV disease in the different ethnic groups. These discordant populations should receive aggressive risk factor modification [9].

Our findings suggest that the overall correlation between 10-year absolute risk determined by FRS and CACS is appropriate for the intermediate risk patients whether veteran American or Middle Eastern. However, use of traditional risk factor analysis led to MD classification in 68% of our population. One possible explanation is that these individuals' inflammatory response triggers less calcium deposition or is less chronic in nature. Thus, evaluation of inflammatory markers examining the early age at which Middle Eastern patients present with coronary artery disease may explain the low CACS.

**Study limitation**

One of the limitations of this study is the small overall sample size (450 patients). In particular, the number of veteran Americans (131) was very small resulting in an uneven representation of both groups. Furthermore, we elected to use the FRS because it specifically addresses coronary artery disease. However, there are newer risk stratification algorithms such as the D’Agostino total CVD risk algorithm from 2008 which incorporates risk of CHF and stroke as well as being more comprehensive [13]. Employing such algorithms may lead to different results. Additionally, there is a referral bias. Patients were referred for CCT for diverse reasons including equivocal exercise stress test, abnormal myocardial perfusion imaging, atypical symptoms, and idiopathic cardiomyopathy.

**Conclusion**

Discordance between CACS and FRS is demonstrable in a large percentage of our studied populations. The pattern of discordance differed between the two ethnic groups. In the American veteran group, MD was found in those who had a low risk FRS and a high CACS. In the Middle Eastern individuals, the discordance was primarily in those with a low CACS and a high FRS. The study emphasized the importance of concomitant use of FRS and CACS to risk stratify patients. It also suggests a search for other unconventional environmental or genetic risk factors in those with discordant risk scores.

**References**