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

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Abstract

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.

Keywords: Framingham risk score; Coronary artery calcium score; Discordance; Cardiovascular risk

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.

Methods

This is a retrospective, observational cohort study. Data was collected from the multidetector cardiac computerized tomography (CCT) databases of King Fahd Armed Forces Hospital (KFAFH), Jeddah, Saudi Arabia and the Veterans Affairs Loma Linda Healthcare System (VALLHCS), California, USA. The CCT images were analyzed and the CACS was measured using Agatston method. Subsequently, individual charts were reviewed for FRS calculation. Marked Discordance (MD) was defined as a CACS <100 with a high risk FRS or a CACS >400 with a low risk FRS.

Cardiac Computerized Tomography (CCT)

CCT was performed with a 64-Slice scanner (Siemens Sensation) and a 16-detector-row scanner (Aquilion^{TM} 16-Toshiba Medical Systems Corporation). The CCT protocol has been described in a number of previous publications that were validated by electron beam computed tomography [5-7]. Briefly, prior to contrast infusion, initial ECG triggered 3.0-mm-thick cross-sectional measurements covering the heart with 100 ms exposure time per slice were obtained. The acquired images were then manually processed to quantify the calcium score utilizing the Agatston method. This method employs 20

contiguous 3.0-mm sections of the heart with the most cephalad slice originating at the lower margin of the main pulmonary artery and the most caudad slice terminating at the level of the diaphragm. A threshold of 130 Hounsfield Units (HU) is used to identify calcification. This threshold was selected to exclude artifacts and is 2 standard deviations of the average attenuation of the aorta. Only calcified plaques that are at least 1 mm^2 in size or two adjacent pixels are included in the calculation. Both a Seimens Syngo and vital images, Vitrea 2 workstation were used to calculate the CACS. The software automatically color codes any region with HU more than 130. The operator manually places a region of interest around each lesion and assigns it to a coronary artery. This process is repeated for each axial slice.

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 1for 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].

Statistical analysis

Statistical analysis was performed using SPSS software (14.0, SPSS Inc., Chicago, IL, USA). Quantitative variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as frequencies or percentages. Comparison of CACS and FRS in both groups was first performed using the linear regression. Agreement between CACS and FRS was assessed using Pearson correlation with 95% confidence Interval. Logistic regression analysis was evaluated to understand the predicting variables e.g. age, gender, and diabetes for each score (Tables 1 and 2).

Results

A total of 499 patient records were reviewed (330 were Middle Eastern patients studied at KFAFH and 160 were studied at the VALLHCS). The study enrolled 450 patients after exclusion of 49 due to incomplete data. Middle Eastern patients were younger than the veteran Americans (45 yrs vs. 63 ± 12 yrs) with a higher predominance of female gender (73% vs. 5%). Based on CACS, the enrolled patients were divided into two groups. The first group included 312 patients with a CACS <100 (290 Middle East patients and 62 veteran American patients). Marked discordance was detected in 283 patients (90.7% of the total studied population). MD was detected in 281 out of 290 (96.9%) of the Middle Eastern patients. However, only 2 out of 62 (3%) of the veteran American patients had a high risk FRS and low CACS. The second group included 99 patients with a CACS >400 (69 veteran Americans and 30 Middle East patients). MD was detected in 25 patients (25%). Twenty out of 69 (29%) of the veteran American patients had a CACS >400 with a low risk FRS while only 5 out of 30 (16.7%) of the Middle Eastern patients had a discordantly high CACS and low FRS (Table 1).

	Veteran American Population			**Middle Eastern Population**		
	Total (n=131)	Discordance (n=22, 17%)	Concordance (n=109, 83%)	Total (n=320)	Discordance (n=286, 89%)	Concordance (n=34, 11%)
CACS						
<100	62	2 (3%)	60 (97%)	290	281 (96.9%)	9 (3.1%)
>400	69	20 (29%)	49 (71%)	30	5 (16.7%)	25 (83.3%)
Concordance	0.001344			0.02335		

Table 1: Distribution of concordance and discordance for both Middle Eastern and veteran American patient groups.

Veteran American Population 131				**Middle-Eastern Population 320**			
DM	HTN	Smoker	Dyslipidemia	DM	HTN	Smoker	Dyslipidemia
37	71	50	77	175	161	120	77

Table 2: Logistic regression analysis.

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 10year 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.

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