Quantifying the impact of using Coronary Artery Calcium Score for risk categorization instead of Framingham Score or European Heart SCORE in lipid lowering algorithms in a Middle Eastern population

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Background: The use of the Coronary Artery Calcium Score (CACS) for risk categorization instead of the Framingham Risk Score (FRS) or European Heart SCORE (EHS) to improve classification of individuals is well documented. However, the impact of reclassifying individuals using CACS on initiating lipid lowering therapy is not well understood. We aimed to determine the percentage of individuals not requiring lipid lowering therapy as per the FRS and EHS models but are found to require it using CACS and vice versa; and to determine the level of agreement between CACS, FRS and EHS based models.

Methods: Data was collected for 500 consecutive patients who had already undergone CACS. However, only 242 patients met the inclusion criteria and were included in the analysis. Risk stratification comparisons were conducted according to CACS, FRS, and EHS, and the agreement (Kappa) between them was calculated.

Results: In accordance with the models, 79.7% to 81.5% of high-risk individuals were down-classified by CACS, while 6.8% to 7.6% of individuals at intermediate risk were up-classified to high risk by CACS, with slight to moderate agreement. Moreover, CACS recommended treatment to 5.7% and 5.8% of subjects untreated according to European and Canadian guidelines, respectively; whereas 75.2% to 81.2% of those treated in line with the guidelines would not be treated based on CACS.

Conclusion: In this simulation, using CACS for risk categorization warrants lipid lowering treatment for 5–6% and spares 70–80% from treatment in accordance with the guidelines. Current strong evidence from double

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randomized clinical trials is in support of guideline recommendations. Our results call for a prospective trial to explore the benefits/risks of a CACS-based approach before any recommendations can be made.

Introduction

The Coronary Artery Calcium Score (CACS), measured in Agatston units (AU), is a non-invasive method of measuring calcification in the coronary arteries [1]. It is used to assess the overall coronary calcified plaque burden thereby providing prognostic information regarding the occurrence of future cardiovascular (CV) events [2,3]. A high CACS indicates that individuals are at high risk for cardiovascular events even if they were classified as having low or intermediate risk using traditional risk assessment tools such as the Framingham risk score (FRS), as adopted by the Canadian Cardiology Society (CCS) [4], or the European Heart SCORE (EHS) [5]. These individuals may necessitate aggressive preventive lipid lowering therapy [6].

Historically, incorporating the traditional CV risk factors such as blood pressure, age, gender, smoking, and cholesterol levels into the FRS and EHS models aided clinicians in risk classification and in decisions on initiating therapeutics [5]. However, experience – supported by various studies – has demonstrated the shortcomings of these models in predicting coronary heart disease (CHD) [7,8]. CACS has become a well-established surrogate marker of coronary atherosclerosis [9]. Despite the fact that the mechanism underlying CAC deposition within atherosclerotic plaque is not yet entirely clear, CAC has been shown in autopsy studies to significantly correlate with the overall coronary tree plaque burden [10]. Improvement in CHD risk prediction using CACS in comparison to traditional risk factors is well documented. Five major studies have significantly and favorably influenced the opinions of scientific communities on the usefulness of CACS as a predictor of events. These are the Multi-Ethnic Study of Atherosclerosis (MESA) [11], the Heinz Nixdorf Recall (HNR) study [12], the Rotterdam study [13], the JUPITER-MESA study [14], and the publications from the CONFIRM Registry [15]. These studies showed that CACS is an independent predictor for CHD

Abbreviations	
AU	Agatston units
CACS	Coronary Artery Calcium Score
CCS	Canadian Cardiology Society
CHD	Coronary Heart Disease
CV	Cardiovascular
EHS	European Heart SCORE
ESC	European Society of Cardiology
FRS	Framingham Risk Score
NRI	Net Reclassification Index

[16] and has added value over the FRS tool in that it performs similarly in multiple ethnicities and works well in both women and men. Currently, the AHA categorizes CAC scoring as a Class 2B recommendation among asymptomatic persons at intermediate risk for cardiac events by the FRS tool [17].

The clinical utilization of CACS has been validated in several areas, with varying levels of evidence in the area of reclassifying an individual's risk for CHD events and in improving adherence with preventive therapeutic recommendations. Recent evidence suggests that reclassification of patients from intermediate risk as per Framingham risk score to high-risk status based on CACS warrants aggressive preventive therapy, especially as treatment decisions for this group are indecisive [2]. However, no evidence-based guidelines currently exist on how to implement CACS risk categorization in treatment algorithms. The utilization of CACS for risk stratification is gaining wide acceptance [18], and appears to impact both the patient at the individual level and the healthcare system at large. Whereas the net reclassification index is the most consulted measure in the literature, the initiation of therapeutics amongst all up-classified individuals remains a current practice. This may be justified since there is no proof that intensive preventive interventions can be safely reduced in persons at high Framingham risk and low risk by CACS [13]. Hence, quantifying the impact of up and down-classification on initiating therapeutics will enable improved clarification of the cost–benefits to CACS utilization [19].