Analysis of three risk stratification systems in a Saudi population

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Introduction: Coronary artery disease is the leading cause of death worldwide. Although there are a number of algorithms in use for determining the risk of coronary artery disease and thus predicting future cardiovascular events, the data available regarding their validity among the Saudi population are insufficient.

Objective: We studied the validity of three clinical score systems in predicting a high risk population defined as having excessive coronary calcification: the American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Risk Equation, the Framingham Risk Score, and the European Systematic Coronary Risk Evaluation.

Methods: We analyzed data from 462 patients aged $\geqslant$ 40 years. High-risk features were if the Coronary Calcium Score was either >400 or in the $\geqslant$ 75th percentile using Multi-Ethnic Study of Atherosclerosis (MESA) score. The scores for the three algorithms were then calculated using the participants' clinical data.

Results: A total of 87 (18.8%) patients were positive for coronary calcification. Among them, 60 (13%) were classified as being at high risk according to the MESA score. Analyzing these patients by the ACC/AHA Pooled Cohort Risk Equation resulted in nine (15%) as being at low risk, 12 (20%) at intermediate risk, and 39 (65%) at high risk. The Framingham Risk classification resulted in 14 (23%) being at low risk, 13 (22%) at intermediate risk, and 33 (55%) at high risk. The European Systematic Coronary Risk Evaluation risk classification showed 24 (40%) at low risk, 12 (20%) at intermediate risk, and 24 (40%) at high risk, with $p < 0.0001$.

Conclusion: The ACC/AHA Pooled Cohort Risk Equation has superior risk calibration compared to the other two risk-score algorithms in a Saudi population.

Introduction

Coronary artery disease (CAD) is the most common cause of death worldwide, representing a disease burden in both developing and underdeveloped countries [1]. In the USA, mortality due to cardiovascular diseases accounted for 34.3% of all deaths in 2006. Furthermore, it was reported that in 2010 an American experienced a coronary event approximately every 25 seconds while someone died from a coronary event

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approximately every minute. The total direct and indirect costs of CAD and stroke in the USA are estimated to be $503.2 billion—higher than for any other diagnostic group [2].

The best strategy for the management of CAD is early detection and control of risk factors such as diabetes mellitus, hypertension, dyslipidemia, and cigarette smoking. In addition, risk stratification for future cardiovascular events has an important role in identifying patients at higher risk.

Multiple risk score algorithms are available that can predict the 10-year risk of atherosclerotic cardiovascular diseases (ASCVD), the most commonly utilized being the Framingham Risk Score (FRS), the European Systematic Coronary Risk Evaluation (SCORE), and the American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Risk Equation [3,4].

In Saudi Arabia, patients with acute coronary syndrome are almost a decade younger than those in developed countries [5], warranting early detection of those at high risk. However, to date no data testing the validity of risk stratification systems in the Saudi population have been published. The aim of this study was to analyze and compare the accuracy of these systems in identifying patients at higher risk for ASCVD.

Methods

Study settings and participants

A cross-sectional analysis of 918 patients underwent multidetector row computed tomography (MDCT) scan between January 2010 and December 2014 to evaluate the validity of three risk stratification systems in identifying patients at higher risk defined by the Coronary Calcium Score (CCS). Four hundred and sixty two patients older than 40 years were enrolled for the final analysis, while 456 patients were excluded (Fig. 1). The study protocol was approved by the Institutional and Regional Ethical Committee.

Patients' characteristics

Variables such as sex, race, and ethnicity were obtained by self-reporting. Risk factors for CAD such as hypertension, diabetes mellitus, dyslipidemia, family history of premature CAD, and smoking history were obtained. Total cholesterol, low-density lipoprotein, and high-density lipoprotein were recorded before MDCT scan. In addition, systolic blood pressure, weight, height, waist and hip circumference, and waist–hip ratio were measured, and body mass index calculated.

Abbreviations	
ACC/AHA	the American College of Cardiology/American Heart Association
CAD	Coronary artery disease
FRS	Framingham Risk Score
CCS	Coronary Calcium Score
MDCT	multidetector computed tomography
MESA	Multi-Ethnic Study of Atherosclerosis
SCORE	the European Systematic Coronary Risk Evaluation
ASCVD	atherosclerotic cardiovascular disease

CT protocol

Participants underwent a noncontrast, low-radiation calcium-scoring scan (dual-source, Definition Flash; Siemens Healthcare, Forchheim, Germany) with a gantry rotation time of 0.28 seconds. Imaging parameters included $2 \times 128 \times 3$-mm slice collimation with 3-mm slices of a field of view extending from the tracheal bifurcation to the diaphragm. The scan was taken with breath-hold and a prospectively electrocardiography-triggered protocol with image acquisition initiated at 70% of the cardiac cycle. The imaging parameters were 120 kVp, 0.33-seconds temporal resolution, and 3-mm slice thickness.

CT image analysis

Images were reconstructed and analyzed using an Advantage Windows AW4 (GE Healthcare, Waukesha, WI, USA) to measure the calcium score using the Agatston method.
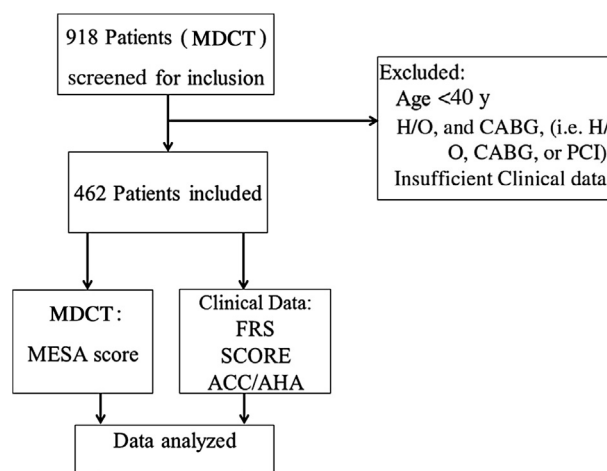

Figure 1. Methods of patient enrollment to the analysis. ACC/AHA = American College of Cardiology/American Heart Association; MDCT = Multidetector computed tomography; FRS = Framingham Risk Score; MESA = Multi-Ethnic Study of Atherosclerosis; SCORE = European Systematic Coronary Risk Evaluation.

Identification of high-risk groups

All patients with either a CCS $\geqslant$ 400 or a CCS in the $\geqslant$ 75th percentile using the online sex-specific Multi-Ethnic Study of Atherosclerosis (MESA) score calculator [6] were identified as high risk.

Calculation of clinical risk scores

Patients' clinical data and lipid profiles were used to calculate the three clinical risk scores, namely sex-specific FRS, sex-specific SCORE, and sex- and race-specific ACC/AHA Pooled Cohort Risk Equation, using age, diabetes mellitus, total cholesterol level, high-density lipoprotein level, smoking status, systolic blood pressure, and use of antihypertensive medication [4,7,8].

Table 1. Baseline characteristics.

Variables	
Age (y), mean ±SD	52 ± 8
Male sex, n (%)	315 (68)
Body mass index (kg/m^2), mean ± SD	29.9 ± 4.7
Body weight (kg), mean ± SD	83.2 ± 13
Diabetes mellitus, n (%)	128 (27.5)
Hypertension, n (%)	207 (44.7)
Dyslipidemia, n (%)	24 (5)
Family history of coronary artery disease, n (%)	33 (7)
Current smoking, n (%)	80 (17.4)
Cholesterol (mmol/L), mean ± SD	4.2 ± 1.3
Low-density lipoprotein (mmol/L), mean ± SD	2.6 ± 1.1
High-density lipoprotein (mmol/L), mean ± SD	1.2 ± 0.3
Coronary calcium score	31 ± 136

SD = standard deviation.

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation and categorical variables were expressed as frequencies or percentages. For normally distributed continuous variables a two-sample t test was performed, and Chi-square exact tests were run for categorical variables to compare the high- and low-risk groups defined by MESA score. A value of $p < 0.05$ was considered statistically significant for all tests. All statistical analyses were performed using SPSS for Windows (Version 19.0; SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics

Baseline characteristics of the 462 patients are shown in Table 1. The mean age of the patients was 52 ± 8 years, with 315 (68%) of them being men. Coronary artery calcification was present in 87 (18.8%), of whom 69 (14.9%) were men and 18 (3.9%) were women.

MESA score and high-risk patients

Using the MESA score calculator, 60 (13%) patients were in the $\geqslant$ 75th percentile and comprised the high-risk group. Chi-square exact test analysis showed a significantly higher prevalence of Diabetes mellitus and Hypertension in the high-risk than in the lower-risk group (Table 2).

Ten-year calculated risk

The expected 10-year risk for each system was stratified into three categories as low, intermediate, and high. Analysis of all patients using the ACC/AHA Pooled Cohort Risk Equation resulted in 264 (57%) classified as low risk, 60 (13%) as

Table 2. Comparison between the high- and low-risk group.

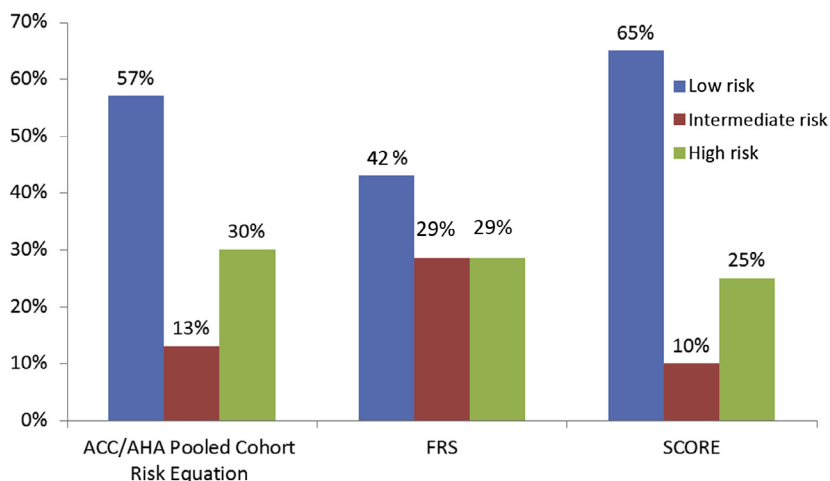| Variables	High-risk group	Low-risk group	p
No. of patients	60 (13)	402 (87)	
Age (y), mean ± SD	54 ± 10	51 ± 8	0.09
No. of men, n (%)	45 (75)	270 (14)	0.3
Diabetes, n (%)	32 (53)	96 (24)	<0.0001
Hypertension, n (%)	42 (70)	165 (41)	0.001
Smoking, n (%)	8 (13)	72 (18)	0.27
Dyslipidemia, n (%)	5 (8)	19 (4.7)	0.3
Family history of coronary artery disease, n (%)	8 (13)	25 (6.2)	0.1
Coronary calcium score, mean ± SD	230 ± 315	1 ± 6	<0.0001

SD = standard deviation.

Figure 2. Risk stratification of all participants. ACC/AHA = American College of Cardiology/American Heart Association; FRS = Framingham Risk Score; SCORE = European Systematic Coronary Risk Evaluation.

intermediate risk, and 138 (30%) as high risk. With FRS, 198 (42%) were classified as low, 132 (29%) as intermediate, and 132 (29%) as high risk. Using the SCORE system, 300 (65%) were classified as low, 48 (10%) as intermediate, and 114 (25%) as high risk (Fig. 2).

The three scoring systems overestimated the predicted cardiovascular risk by 130% for the ACC/AHA pooled cohort risk equation, 120% for FRS, and 90% for SCORE.

Patients with a high MESA score

Analyzing these patients using the ACC/AHA Pooled Cohort Risk Equation resulted in nine (15%) as being at low risk, 12 (20%) at intermediate risk, and 39 (65%) at high risk. The FRS risk classification showed 14 (23%) at low risk, 13 (22%) at intermediate risk, and 33 (55%) at high risk. The SCORE risk classification demonstrated 24 (40%) at low risk, 12 (20%) at intermediate risk, and 24 (40%) at high risk ($p < 0.0001$; Fig. 3).

Discussion

In the present study, we tested the utility of three different risk stratification systems in predicting patients with a high 10-year ASCVD risk. We found the ACC/AHA Pooled Cohort Risk Equation to be more sensitive than FRS and SCORE in identifying patients at high risk among the Saudi population. In addition we found that diabetes mellitus and hypertension were the
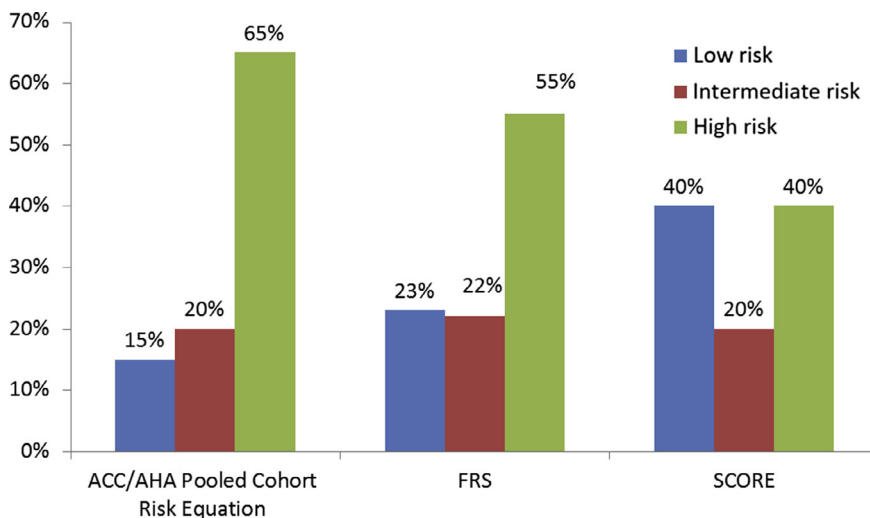

Figure 3. Risk stratification of high risk group showed that American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Risk Equation to be more sensitive than Framingham Risk Score (FRS) and the European Systematic Coronary Risk Evaluation (SCORE) in identifying patients at high risk.

predominant risk factors in the high risk group, defined by higher coronary calcification.

Cardiovascular diseases is a major health issue in Saudi Arabia, with approximately 5.5% of the population in the age group 30–70 years having CAD [9]. Furthermore, the Saudi Project for Assessment of Coronary Events registry has reported a higher prevalence of CAD risk factors among patients presenting with acute coronary syndrome and a higher prevalence of diabetes mellittus in comparison with individuals in developed countries [5].

Cardiovascular risk stratification is considered an important strategy that aims to classify the general population into either low-, intermediate-, or high-risk groups, which may help in identifying individuals susceptible to hard cardiovascular events and in predicting persons who might benefit from preventative measures, thus resulting in less cardiovascular mortality by decreasing the prevalence of risk factors for CAD [10,11] and increasing the implementation of various primary prevention methods, such as the use of aspirin, lowering of blood pressure and low-density lipoprotein cholesterol in the indicated group, and reduction of body weight in cases of adiposity [12,13].

At present there are multiple risk stratification algorithms in use. For decades FRS was the most widely used for the calculation of 10-year risk in asymptomatic individuals. However, the FRS underestimates the lifetime risk, especially in younger individuals with multiple risks and in women; moreover, it does not predict the incidence of stroke [14,15]. This necessitated the introduction of the ACC/AHA Pooled Cohort Risk Equation to overcome these limitations. In this system diabetes mellitus was included as a predictor variable, and fatal and nonfatal stroke were added to the ASCVD end points [16,17].

Many studies showed that coronary calcification detected using noncontrast MDCT can accurately predict the coronary plaque burden, with a high correlation of >0.9 between CCS and coronary plaque area [18]. In addition, CCS can provide prognostic information regarding the risk of hard cardiovascular events. With a CCS $\geqslant 400$ there is 2.5-fold increase in cardiovascular diseases risk when compared with a CCS <10. CCS is considered an independent predictor, and superior to the traditional risk factor of CAD in the assessment of subclinical CAD and future ASCVD events [6,19,20].

In the present study, we found that all the three risk stratification systems tend to overestimate the predicted cardiovascular risk by 90% to 130%. A recent study by DeFilippis et al. [21] investigated five different risk scores and reported findings consistent with the present study. These investigators found that the ACC/AHA Pooled Cohort Risk Equation system and the FRS tended to overestimate the risk by 86% and 53%, respectively, while the SCORE was not tested. Similar findings were reported by Muntner et al. [22], who found that the observed and predicted 5-year cardiovascular diseases events in their cohort in the REasons for Geographic and Racial Differences in Stroke and ACC/AHA Pooled Cohort Risk Equation were similar, but found an apparent overestimation of risk mainly in the group with a 10-year ASCVD risk $\geqslant 10\%$.

Risk overestimation may lead clinicians to start patients on medications for primary prevention that is not indicated, which may expose them to otherwise avoidable adverse effects. However, it may negatively affect the cost-effectiveness of the primary prevention program. For these reasons, further studies with long-term follow-up of ASCVD events are needed for a better assessment of risk stratification algorithms.

The present study indicated that the ACC/AHA Pooled Cohort Risk Equation is more sensitive than other risk scores in the Saudi population, so its use in asymptomatic individuals should provide valuable information regarding future cardiac risk, and may indicate persons who might benefit from measures taken to prevent ASCVD.

Our study has certain limitations: it is a single-center study and is a cross-sectional analysis that depends mainly on the CCS as the gold standard approach to identify the high-risk group, with no follow-up of patients for any ASCVD events. In this study the sample size was relatively small and the high-risk group consisted of a small percentage of the total patient cohort.

Conclusion

Among the Saudi population, the ACC/AHA Pooled Cohort Risk Equation has a higher sensitivity than FRS and SCORE in predicting patient's future risk driven by the MESA score. Further evidence is needed to verify the validity of the test in formulating preventive measures for ASCVD.

Acknowledgement

References

[1] Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001;104:2746–53.

[2] WRITING GROUP MEMBERS, Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, et al. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. Circulation 2010;121:e46–e215.

[3] Goff Jr DC, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2935–59.

[4] Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24:987–1003.

[5] Alhabib KF, Hersi A, Alfaleh H, Alnemer K, Alsaif S, Taraben A, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients with acute coronary syndromes: results of the Saudi project for assessment of coronary events (SPACE) registry. J Saudi Heart Assoc 2011;23:233–9.

[6] Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, et al. Multi-ethnic study of atherosclerosis: objectives and design. Am J Epidemiol 2002;156:871–81.

[7] Risk Assessment Tool for estimating your 10-year risk of having a heart attack. National Heart, Lung, and Blood Institute. <http://cvdrisk.nhlbi.nih.gov/>.

[8] Arteriosclerotic cardiovascular disease risk estimator. American College of Cardiology and the American Heart Association. <http://tools.acc.org/ASCVD-Risk-Estimator/>.

[9] Al-Nozha MM, Arafah MR, Al-Mazrou YY, Al-Maatouq MA, Khan NB, Khalil MZ, et al. Coronary artery disease in Saudi Arabia. Saudi Med J 2004;25:1165–71.

[10] Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. Circulation 2011;123:933–44.

[11] Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, et al. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet 2006;368:647–58.

[12] Kahn R, Robertson RM, Smith R, Eddy D. The impact of prevention on reducing the burden of cardiovascular disease. Circulation 2008;118:576–85.

[13] Akosah KO, Schaper A, Cogbill C, Schoenfeld P. Preventing myocardial infarction in the young adult in the first place: how do the National Cholesterol Education Panel III guidelines perform? J Am Coll Cardiol 2003;41:1475–9.

[14] Schlendorf KH, Nasir K, Blumenthal RS. Limitations of the Framingham risk score are now much clearer. Prev Med 2009;48:115–6.

[15] Marma AK, Lloyd-Jones DM. Systematic examination of the updated Framingham Heart Study general cardiovascular risk profile. Circulation 2009;120:384–90.

[16] Preiss D, Kristensen SL. The new pooled cohort equations risk calculator. Can J Cardiol 2015;31:613–9.

[17] Karmali KN, Goff Jr DC, Ning H, Lloyd-Jones DM. A systematic examination of the 2013 ACC/AHA pooled cohort risk assessment tool for atherosclerotic cardiovascular disease. J Am Coll Cardiol 2014;64:959–68.

[18] Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area: a histopathologic correlative study. Circulation 1995;92:2157–62.

[19] Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology 2003;28:826–33.

[20] McClelland RL, Jorgensen NW, Budoff M, Blaha MJ, Post WS, Kronmal RA, et al. 10-Year coronary heart disease risk prediction using coronary artery calcium and traditional risk factors: derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) with validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study). J Am Coll Cardiol 2015;66:1643–53.

[21] DeFilippis AP, Young R, Carrubba CJ, McEvoy JW, Budoff MJ, Blumenthal RS, et al. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. Ann Intern Med 2015;162:266–75.

[22] Muntner P, Colantonio LD, Cushman M, Goff Jr DC, Howard G, Howard VJ, et al. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. JAMA 2014;311:1406–15.