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Original Article

A cross-sectional validation study comparing the accuracy of different risk scores in assessing the risk of acute coronary syndrome among patients in a tertiary care hospital in Kerala

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ABSTRACT

Background: There are many cardiovascular disease (CVD) risk score calculators in practice, which are not based on Indian population data.
Objectives: To identify the best CVD risk score calculator applicable in the Indian population.
Materials and methods: A total of 1000 patients presenting with acute coronary syndrome (ACS) were included in the study and their CVD risk score, had they presented before the event, was calculated. The Framingham risk score (FRS—body mass index [BMI], FRS—fasting lipid profile [FLP]), the American College of Cardiology/American Heart Association pooled cohort equation risk calculator (ACC/AHA PCE), Joint British Society risk calculator 3 (JBS3) and the World Health Organization (WHO) risk prediction charts (WHO TC and WHO without TC [WHO NO TC]) were used.
Results: It was seen that among the 1000 people included in the study, the FRS-BMI (59.2%), FRS-FLP (61.5%), ACC/AHA (70.1%) and the JBS3 (62.5%) identified a majority as having a risk of ≥20%, whereas both the WHO TC (65.3%) and the WHO NO TC (64.5%) identified a majority of the ACS patients as having a risk of <20%. The sensitivity was highest for the ACC/AHA (87.8%), FRS-FLP (85.1%) and then JBS3 (80.1%), whereas the specificity was highest for the WHO TC (83.6%) and the WHO NO TC (82.1%). When looking at the accuracy, the FRS-FLP was the most accurate with 80.1%, whereas the ACC/AHA and the JBS3 followed at 74.7% and 73.1%, respectively.
Conclusion: The ACC/AHA seems to be an acceptable risk prediction system to be used in the Indian population and is also relatively easy and cheap to use.

1. Introduction

Cardiovascular diseases (CVD) are among those that are leading the causes of mortality and morbidity having a prevalence that is seen to be increasing day by day and has a negative effect on health care economics and quality of life worldwide, and the focus has shifted from treatment to prevention of symptomatic CVD. The recognition of those at risk of developing CAD and subsequent CVD is essential in the prevention strategies.[1] The landmark Framingham study helped define the field of preventive cardiology and identification of modifiable risk factors for CVD and the Inter Heart Study from which knowledge of nine modifiable risk factors was widely gained. The life-time risk of developing myocardial infarction or coronary insufficiency or death from a CVD was found to be 48.6% in men and 31.7% in women at the age of 40 years. At the age of 70 years, it was 34.9% of men and 24.2% in women. It has been also found that CVD burden is large and growing in the South Asian population with the occurrence of myocardial infarction a good 10 years earlier in these countries than in other countries.

Abbreviations: ACC/AHA PCE, American College of Cardiology/American Heart Association pooled cohort equation; ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; CCU, Cardiac Care Unit; CVD, cardiovascular disease; FLP, fasting lipid profile; FRS, Framingham risk score; HDL, High Density Lipoprotein; JBS3, Joint British Society 3; JNC, Joint National Congress; LDL, Low Density Lipoprotein; NSTEMI, Non-ST Segment Elevation Myocardial Infarction; STEMI, ST Segment Elevation Myocardial Infarction; VLDL, Very Low Density Lipoprotein; WHO RPC, Who Health Organization Risk Prediction Chart.

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1.1. Role of prevention

The increasing disease burden is preempted by substantial increase in plaque burden, which may have accumulated even before there is significant luminal narrowing of coronary vasculature causing a reduction of blood flow, resulting in CAD.[1] The aim of cardiovascular screening is identification of intermediate and high risk individuals for initiating of interventions to reduce the occurrence of ischemic events and cardiovascular deaths.[2] The incidence of CVD is increasing in the South Asian population and the average age of first coronary event is on an average less than 10 years as compared to the Western average.[4] The major challenges faced while optimizing the risk factor system for South Asians, especially Indians is that the incidence of risk factors such as Diabetes is comparatively greater than in the Western population.[3] It is seen that smoking is less in the men and almost unheard of in women in India, while the HDL are lower and triglycerides are higher with LDL being smaller and denser. Thus the risk for CVD based on the same risk factors is different in Indians.[5] The CAD rates in rural Indian populations has increased to 6% from 2% and in the urban populations up to 12% from 4% in about 30 years.[6] The mortality from CVD is set to increase by 103% in men and 95% in women in India.[7]

2. Methods

This is a single-centre, cross-sectional validation study including 1000 patients with Acute Coronary Syndrome (ACS). The diagnosis of myocardial infarction was based on the 4th universal definition of myocardial infarction.[8] The ACS was labelled as STEMI, NSTEMI or unstable angina.[9] All the patients were admitted to the CCU and managed as per current recommendations.

2.1. Variables analyzed and data collected

Detailed history of demography, socio-economic status and clinical details of the patient was obtained using a questionnaire. Careful clinical examination of vitals, anthropometry and systemic examination was done. Blood samples for HbA1c, renal functions, Random blood sugar values were drawn at the time of hospitalization and the subsequent morning after 8 hours of overnight fasting, the fasting blood sugarlipid profile (FLP) were tested. Electrocardiograms, echocardiograms and coronary angiograms, in necessary cases, were done and analyzed by an individual observer.

2.2. Estimation of CVD risk

Based on the data collected, the estimated 10-year risk for each person was calculated using the Framingham model, ACC/AHA Pooled cohort's equation, the JBS 3 risk calculator and the WHO Risk prediction charts. It is noteworthy that the FRS risk calculators do not give a risk beyond 30% while the WHO risk prediction charts give a range of risk. Thus, for the ease of comparison, the values were also dichotomized into <20% and ≥20% of CVD risk. The Framingham calculator has two subsets, one of which relies only on history and examination (FRS-BMI) while the other incorporates biochemical test (Fasting Lipid profile- FRS-FLP). Likewise, the WHO risk Prediction Charts are also two in number for each region, based on whether lipid profile is incorporated in the calculation of the score or not (WHO TC and WHO NO TC). For both the Framingham and the WHO models, both the charts were used.

2.3. Statistical analysis

The results were entered and managed on Microsoft Excel and statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) Software. The standard statistical analysis of the baseline characteristics of the study population was done. The results were described as mean ± standard deviation or percentage. The McNemar's Chi square test was applied to the dichotomized variables and the Pearson coefficient was calculated for each of the risk scores to calculate the correlation between the scores. A p value <0.05 was considered significant.

3. Results

The baseline characteristics of the study population are presented in Table 1. Considering the ACC/AHA's recent classification of hypertension, an additional 7.1% of people were identified as hypertensive, while the JNC7/8 classification identified 21.1% less as being hypertensive. The total cholesterol, Triglycerides, LDL and VLDL were normal in a majority of the study population, while the HDL was low. A majority (50.6%) had a normal BMI. There were 188 STEMI, 414 unstable angina and 398 NSTEMI. A total of 646 patients underwent Coronary angiogram and of them 221 had significant Single single vessel disease, 183 had double vessel disease and 242 had triple vessel disease. A majority had anterior wall involvement with Left Anterior Descending Coronary Artery (LAD) disease being the maximum. The traditional risk factors of diabetes, hypertension, dyslipidaemiashowed significant correlation with a higher risk estimate with p being <0.001. The incidence of newer risk factors such as autoimmune diseases, Connective tissue disease and history of atrial fibrillation were low in the study population.

3.1. 10-year CVD risk

When the scores were dichotomized, it was seen that the FRS BMI (59.2%), FRS FLP (61.5%), ACC/AHA (70.1%) and the JBS3 (62.5%) identified a majority as having a risk of ≥20 percentage while the WHO TC (65.3%) and WHO NO TC (64.5%) identified a majority of the ACS patients as having a risk of <20 percentage (Ref-Table 2 and Fig. 1). Considering the distribution of the scores, the JBS3 identified the maximum as having highest risk when the scores were divided (Ref-Table 3 and Fig. 2). In both diabetic and nondiabetic individuals,

Table 1
Baseline characteristics of the study population.

Parameters	Values
Age (years)	62 ± 10.9
Gender	
Male	737
Female	263
Smoking	355
History of ethanol intake	284
Diabetes	611
Hypertension	624
Dyslipidaemia	513
Chronic kidney disease	234
Premature CAD in family	130
Autoimmune/connective tissue disease	65
Atrial fibrillation	52
BMI (%)	25 ± 4.3
Pulse rate (min)	75 ± 14.4
Systolic BP (mmHg)	128 ± 22.6
Diastolic BP (mmHg)	77 ± 12
Total cholesterol (mg/dl)	173 ± 49.8
TGL (mg/dl)	138 ± 63.3
HDL (mg/dl)	40 ± 12.6
LDL (mg/dl)	111 ± 42.9
VLDL (mg/dl)	28 ± 13.8
Fasting blood sugar (mg/dl)	149 ± 63.9
Postprandial blood sugar (mg/dl)	229 ± 103.1
Random blood sugar (mg/dl)	171 ± 84.6
HbA1c (%)	7 ± 1.8

Table 2
Dichotomised CVD risk.

10-year CVD risk (%)	FRS-BMI ($n = 1000$)	FRS-FLP ($n = 1000$)	ACC/AHA ($n = 1000$)	JBS3 ($n = 1000$)	WHO TC ($n = 1000$)	WHO NO TC ($n = 1000$)
<20	408	385	299	375	653	645
≥20	592	615	701	625	347	355

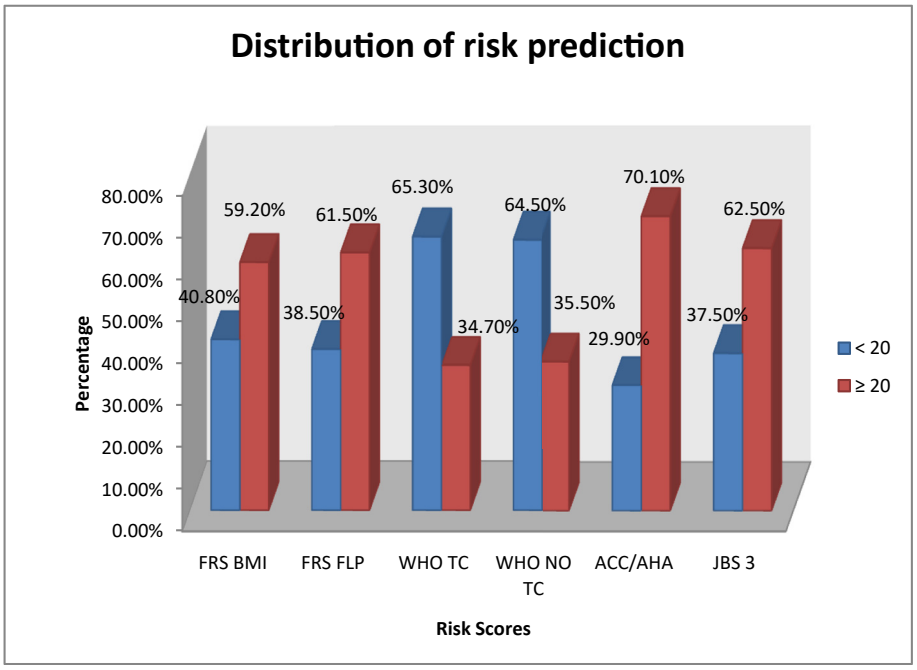

Fig. 1. Dichotomized 10 year risk.

Table 3
Calculated CVD risk.

10-year CVD risk (%)	FRS-BMI ($n = 1000$)	FRS-FLP ($n = 1000$)	ACC/AHA PCE ($n = 1000$)	WHO TC ($n = 1000$)	WHO NO TC ($n = 1000$)	JBS3 ($n = 1000$)
<10	115	146	232	412	389	136
10–<20	293	239	67	241	256	214
20–<30	159	181	276	135	160	184
30–<40	433	434	188	78	64	119
≥40			237	134	131	347

ACC/AHA identified the maximum as having a higher risk, while the WHO charts performed the worst in both diabetic and non diabetic population. FRS performed poorly in the diabetic population compared to the nondiabetic population. The ACC/AHA also identified a maximum of hypertensive and people with dyslipidaemia as having higher risk. Overall, the risk scores were comparable with significant p of <0.001. The sensitivity was highest for ACC/AHA (87.8%), FRS-FLP (85.1%) and then JBS3 (80.1%), while the specificity was highest for WHO TC 83.6% and WHO NO TC (82.1%). When looking at the accuracy, FRS-FLP was the most accurate with 80.1%, while ACC/AHA and the JBS 3 followed at 74.7% and 73.1%.

3.2. Classification as hypertensive

A total of 624 people were known hypertensive and the ACC/AHA identified a majority of the hypertensive (48.9%) and the nonhypertensive (21.2%) population as having a higher overall risk. Considering the classification of hypertension by the JNC 7/8, a total of 587 were identified as having normal blood pressure, while the ACC/AHA classification identified 695 people as having Hypertension. When comparing with the risk scores, the ACC/AHA Pooled Cohort"s Equation identified a majority of those identified as having normal blood pressure and those identified as hypertensive as having a higher risk of developing ACS (Fig. 3).

4. Discussion

On statistical analysis, ACC/AHA had the highest sensitivity and the second highest accuracy. While a good specificity is essential, the trade up of missing patients is not worth it. Hence, a greater sensitivity while sacrificing specificity is acceptable when dealing with a disease such as the CAD. The ACC/AHA model also had statistical significance with a majority of the risk factors. It has been reported that the Pooled Cohorts Equation has better discriminative ability for future primary CVD events in a multiethnic cohort when compared with the FRS.[10,11] The JBS model and the FRS model employing the Fasting lipid profile came second when the scores were dichotomised. Previous studies[4,12] have shown these two risk

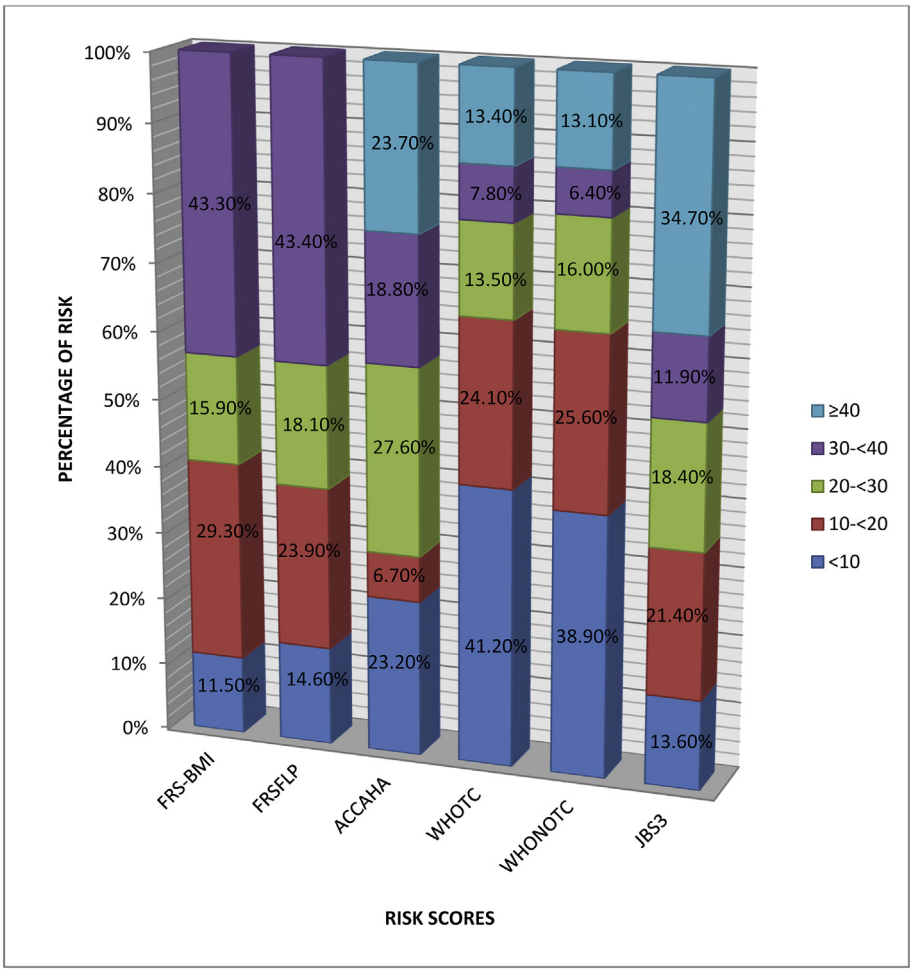

Fig. 2. Estimated 10-year cardiovascular risk according to the studied risk assessment models. *The two highest risk categories have been combined for FRS-BMI and FRS-FLP as it does not provide absolute risk value if the estimated 10-year risk exceeds 30%.

scores to have been superior in the Indian population. Individually, the JBS3 came closest to ACC/AHA in the study population with a high-risk prediction of 62.5%. The JBS3 also predicted a greater number of the study population as having a risk of ≥40% when compared to the other scores.

Presence of and Connective tissue disease has been linked to CVD previously[13] and the JBS, which includes a majority of the newer risk factors, socio economic status performed admirably highlighting the importance of the inclusion of these newer risk factors in the risk calculation systems. But the fact that FRS FLP and ACC/AHA performed identically and better, respectively, also brings to light the fact that CVD is no longer just a disease of the affluent and the importance of the traditional risk factors still outweighs the newer risk factors. One of the main reasons is the poor implementation of resources for the screening of these factors in developing countries. The Framingham study estimates the 10-year risk of (fatal or nonfatal) CVD for men and women separately, according to a subject's individual risk factors and profile.[14] The FRS has been found to under predict by 0.43 in high risk population and over predict by 2.87 ratios in low-risk population, although many of the factors which caused this are also applicable to other risk prediction systems.[15] The FRS has been shown to have good predictive accuracy in populations from United States, New Zealand and Australia, while it is not so in the European.[16] The FRS FLP underlines the importance of biomarkers in the prevention of ACS. As reported in previous studies4[,12,4,12]), it was noticed that the WHO risk prediction charts performed the worst in the Indian population. The simple nature of the chart thought makes it easy to be employed in the field, does not make up for the poor performance in picking the individuals at high risk. Considering the fact that among all the disease, worldwide, CVD are among those that are the leading causes of mortality and morbidity with a prevalence that is seen to be increasing day by day, the need of the hour is a greater coverage of preventive strategies.

4.1. CVD risk in India

To predict the incidence of Acute Coronary Syndrome in Indians with traditional risk models based on Western population and risk profile data is a challenge. The Framingham risk score prediction was overestimated in Asian population who has a low incidence of coronary artery disease and a disproportionately higher incidence of stroke[17] The 2013 ACC/AHA new pooled cohort equation is also purportedly reported to overestimate the incidence of CVD in Asian Americans.[18] It was reported by Barzi et al.[19] that the simplified version of the FRS needs recalibration as it overestimated the risk of cardiovascular events. It has been noted that the disease is often more extensive, intense and associated with more adverse outcomes in South Asians, compared to American, European and other Asian counterparts.[20] Thus, the risk for CVD based on the same risk

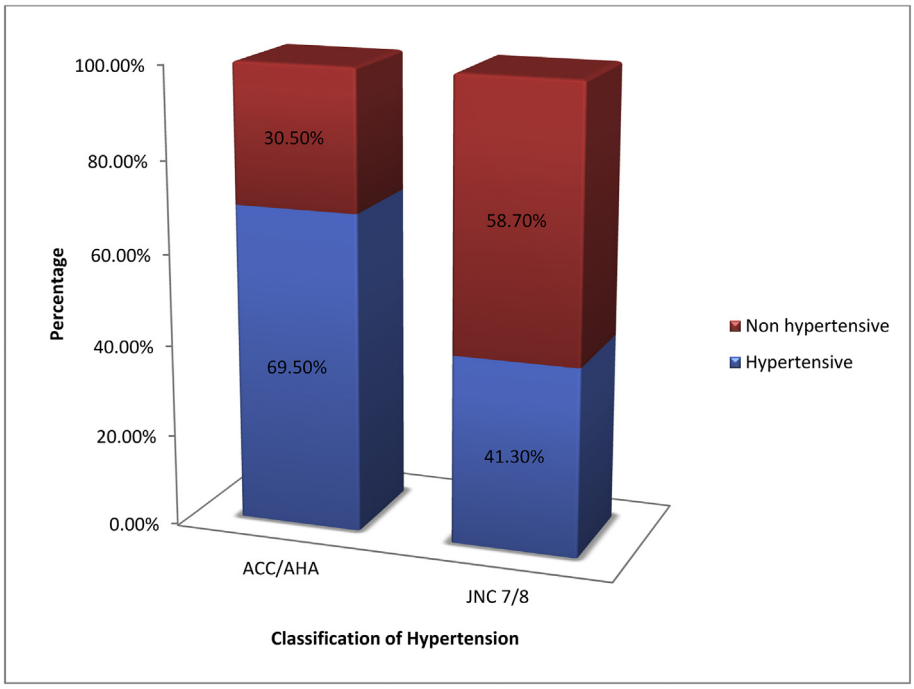

Fig. 3. Distribution of hypertensive people by ACC/AHA and JNC 7/8 classification.

factors is different in Indians.[21] A previous study showed that the old FRS model identified only 5% of high risk individuals[22] and a recent retrospective study done showed that the JBS3 performed the best.[12] Recently, another study has shown that the FRS-CVD was better for predicting the risk for CVD in Indian population.[4] Several studies have also shown that the risk assessment systems which have been developed based on Western population, actually underestimate the risk of CVD in Indians,[23,24,25]

4.2. Classification of hypertension

Another important fact identified in this study is the fact that the ACC/AHA classification of hypertension identified a greater number of previously undiagnosed people as having hypertension. Several studies have shown that the ACC/AHA classification overestimates the number of hypertension.[26,27,28] However, considering the fact that the risk of ACS increases across the range of blood pressure with no safe range, in the present scenario of CAD being a Pandemic, not sparing any age group and with racial differences blurring, a more aggressive approach at identification of at risk and appropriate use of resources in preventive strategies is not only justified but also long since overdue.

5. Limitations

The major limitation of this study is that the risk score systems are intended for use in high-risk population at risk for developing CVD but also at the same time free of CVD. Most of the patients had previously been on statins which would have already lowered their cholesterol values which would have been further reduced in the event of an acute coronary syndrome though the effect is less well studied.

6. Conclusion

The results show that the ACC/AHA Pooled Cohort"s Equation identified a greater number of people as having a higher risk of developing Acute Coronary Syndrome in the study population. Thus the ACC/AHA seems to be an acceptable risk prediction system to be used in the Indian population which is also relatively easy and cheap to employ.

7. Perspectives

7.1. Competency in patient care and procedural skill

The use of the ACC/AHA classification for hypertension and the ACC/AHA PCEPooled Cohorts Equation would help in better stratification of people at risk for Coronary Artery Disease aiding in appropriate resource deployment in Primary prevention.

7.2. Translational outlook

Further research in the form of prospective studies are required to establish the benefit and need to include emerging newer risk factors to strengthen the predictive capability.

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Disclosures

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Conflicts of interest

All authors have none to declare.

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