



Comparison of Framingham, JBS3 Heart, WHO/ISH and ACC/AHA ASCVD risk scores in South Indian women with first cardiovascular event

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Abstract

Background

There is a substantial burden of cardiovascular disease in women and primary prevention is desirable. Risk prediction models validated in western populations need to be assessed for applicability in Indian women.

Materials and Methods

Women who presented with first myocardial infarction were assessed using Framingham 2008, Framingham Adult Treatment Panel III, World Health Organisation International Society of Hypertension risk prediction chart, 3rd Joint British Societies risk calculator and American College of Cardiology/American Heart Association Atherosclerotic Cardiovascular disease risk calculator to see which model could correctly identify maximum number of patients as being at risk if they had presented prior to the acute coronary event.

Results and Conclusions: 152 women of mean age 64.80 ± 13.35 were included in the study. In those aged ≤65, only Framingham 2008 categorized >50% individuals as being at more than low risk. In those aged above 65 all scoring systems categorized >50% individuals to be at more than low risk. When all ages were considered, ASCVD and Framingham were found to be the more appropriate predictors to assess cardiovascular risk in

South Indian women. In those aged below 65 years, even an intermediate score should probably be a target for intervention and any score other than low should be advised diet and lifestyle modification. The accuracy of all scoring systems is reasonably adequate in those aged above 65.

Keywords: Cardiovascular Disease, Risk Assessment, Women.

Introduction

More than three million Indians die from Cardiovascular disease (CVD) every year. Studies from various parts of India put the prevalence of CVD at 7% - 13% in urban and 2% -7% in rural populations.¹⁻⁸ By 2030, CVD will be the main cause of death throughout India, accounting for more than 35% of all deaths as per World Health Organisation (WHO) estimates.⁹ Evidently, there is a pressing need for aggressive risk assessment and primary prevention of CVD.

The World Health Organisation International Society of Hypertension (WHO – ISH) published risk prediction charts, dedicated to different ethnic-geographic regions statistically derived using extrapolated risk factor prevalence data. The 3rd Joint British Societies risk calculator (JBS3) risk score is applicable to UK populations but also provides risk estimates for non-

resident Indians. The other important cardiovascular risk prediction models are Framingham 2008, the later Framingham Adult Treatment Panel (ATP) III, and the American College of Cardiology American Heart Association Atherosclerotic Cardiovascular disease (ACC AHA ASCVD) risk estimator.

These models are derived from western populations. Actual performance of these models in Indians merits study in view of the following.

Most CVD in the west occurs among in persons aged ≥ 65 . Conversely, of the 47 million Indians with CAD in 2010, 60% are < 50 , 37% < 40 and 18% < 30 according to official estimates by Government of India and WHO.¹⁰ The average age of first MI has decreased by > 10 years in India but increased by > 10 years in the US. In those < 65 , CVD causes 19% deaths in Americans and $> 50\%$ deaths in Indians.¹¹⁻¹⁵

There is a substantial burden of CVD amongst women as well. Angiographic studies in Indian women show high prevalence of severe and extensive disease including three-vessel disease (40%) despite the fact that majority of these women (56%) were premenopausal.¹⁶

In a nutshell, incidence and mortality from CVD is two-fold higher¹⁷⁻²⁰ and occurs 5 – 10 years earlier among Asian Indians than Caucasians.

Among women, differences between Indian and western are exacerbated. Women have higher prevalence of obesity, abdominal obesity and diabetes than men.²¹⁻

²³ Tobacco use is very infrequent.²² Women with MI have more than double the mortality compared to men (23% vs 9%). Diabetic women have even higher mortality.²¹

The present study applied Framingham 2008, Framingham ATP III, JBS3 Heart Risk, WHO/ISH risk prediction charts and ACC/AHA ASCVD Risk estimator in women without prior known cardiovascular disease who presented with first MI. The predicted 10 year risk for

atherosclerotic cardiovascular disease was estimated in a hypothetical scenario where the patient had visited the hospital just before the event occurred. The study sought to evaluate the accuracy of various cardiovascular models in South Indian women. The objective of the study was to identify the risk predictor that categorized maximum number of women correctly as being at risk for major cardiovascular events.

Materials and Methods

Study design was cross sectional.

Adult females without prior known cardiovascular disease who present with first acute myocardial infarction within 24H of onset of symptoms confirmed by elevated troponin levels were included in the study.

All included patients underwent detailed clinical examination, medical history taking, blood investigations and electrocardiogram. Fasting lipid profile was obtained within 24 H of onset of chest pain, as lipid levels are not substantially altered by the occurrence of the acute coronary syndrome in this time interval.

Study parameters recorded were age, gender, history of diabetes, smoking history, family history of premature CVD, history of atrial fibrillation, history of chronic kidney disease, history of rheumatoid arthritis, history of blood pressure treatment, systolic blood pressure, body mass index, total cholesterol, HDL cholesterol.

Risk of having a major CV event was calculated for each patient using the different risk scores. The Framingham 2008 (F 2008), Framingham ATP III (F ATP III), ACC/AHA ASCVD and JBS3 online calculators are available for download from the respective websites. The WHO risk prediction charts were taken from the 'Guideline for assessment and management of cardiovascular risk' available at the WHO website. The chart applicable for South- East Asian region D (which includes Bangladesh, Bhutan, Democratic People's Republic of Korea, India,

Maldives, Myanmar and Nepal) was used. The highest age group analyzable in WHO/ISH is 79, so all individuals aged ≥ 80 were evaluated using the table for 70 – 79. The lowest cholesterol level in WHO is 4 mmol/L which was utilized for all those with lower cholesterol values.

Data was entered into Microsoft excel sheet and analysis done using SPSS version 16. Quantitative variables were expressed using mean with standard deviation / percentages. Fisher’s exact test with p values < 0.05 were taken as statistically significant.

The study was approved by the Institutional Research and Ethics Committees. Informed written consent was obtained from all patients participating in the study and their relatives.

Results

152 women satisfied the inclusion criteria within the duration of the study. Baseline characteristics of the study population are given in Table I. All patients were nonsmokers. Most were of average socioeconomic status, obese and health conscious. The youngest patient was 38 years old. 34.21% were diabetics, 73.03% had systemic hypertension, and 25.66% had positive family history of premature CVD. More than half of the population was already on statins and antihypertensives. 24.34% were admitted with STEMI and 75.66% had non STEMI. At presentation, mean heart rate was 78.70 ± 08.67

Table I. Baseline characteristics		
Parameters	(n = 152)	Percentage
Family History	39	25.66
Diabetes mellitus	52	34.21
Hypertension	111	73.03

STEMI	37	24.34
Non STEMI	115	75.66
Mortality	6	03.95
Statins	79	51.97
ACEI or ARB	78	51.32
Beta blockers	65	42.76
Parameters	Mean \pm SD	
Age (years)	64.80 \pm 13.35	
BMI (kg/m2)	26.46 \pm 03.57	
Heart rate (beats/min)	78.70 \pm 08.67	
Systolic BP (mm Hg)	151.71 \pm 28.10	
Diastolic BP (mm Hg)	87.57 \pm 10.95	
Total cholesterol (mg/dl)	189 \pm 62.80	
HDL cholesterol(mg/dl)	51.20 \pm 04.62	

beats/min, systolic blood pressure 151.71 ± 28.10 mm Hg and diastolic blood pressure 87.57 ± 10.95 mm Hg. Mean age of patients was 64.80 ± 13.35 years, age distribution given in Table II. 41 patients developed severe LV dysfunction. Six patients died. All others were hemodynamically stable at discharge. Mean hospital stay was 5.9 days. Prolonged hospital stay more than 5 days was due to recurrent angina and cardiac failure.

The estimated 10 year risk of major CVD was calculated with collected data according to the four scoring systems in all patients (Table III) and stratified according to age. Since age >65 alone is a risk factor for CVD in females, the patients were grouped into those ≤65 and those >65 and the most accurate scoring system determined (Table IV). There were comparably equal numbers of individuals in both age groups - ≤65 years : 74 (48.68%) and >65 years : 78 (51.32%). In the <65 age group none of the scoring systems correctly categorized more than 50% of patients as being at high risk (Table V). Percentages of high risk individuals identified were Framingham 2008 (41.89%) > ASCVD (36.49%) > JBS3 (20.27%) > Framingham ATP III = WHO/ISH (0%). Accuracy markedly improved with increasing age >65 in all scoring systems: ASCVD (91.03%) > JBS3 (75.64%) > Framingham 2008 (67.95%) > WHO/ISH (39.74%) > Framingham ATP III (38.46%) (Table V). Overall accuracy in all age groups was: ASCVD (64.47%) > Framingham 2008 (55.26%) > JBS3 (48.68%) > WHO/ISH (20.39%) > Framingham ATP III (19.74%) (Table V).

Since the the high risk identification rate was <50% in all scoring systems in those <65, all who had been categorized as being at more than low risk (ie., intermediate/high risk) were grouped together on the grounds that the cutoff should be lowered to increase the yield. This meant inclusion of those with calculated CVD

40-49	21	13.82
50-59	23	15.13
60-65	26	17.11
	> 65 years (N = 78)	51.32
66-69	14	9.21
70-79	42	27.63
≥80	22	14.47

risk ≥10% for Framingham and WHO/ISH, ≥5% for ASCVD and ≥20% for JBS3 respectively.

In those aged ≤65, only Framingham 2008 categorized >50% individuals as being at more than low risk. (Table VI). The yields were Framingham 2008 (56.76%) > ASCVD (36.49%) > JBS3 (20.27%) > Framingham ATP III (14.86%) > WHO (12.16%). In those aged above 65 all scoring systems categorized >50% individuals to be at more than low risk as follows. ASCVD (100%) > Framingham 2008 (78.21%) > JBS3 (75.64%) > WHO/ISH (69.23%) > Framingham ATP III (66.67%). When all ages were considered, ASCVD and Framingham had the highest frequencies of more than low risk : ASCVD (69.08%) > Framingham 2008 (67.76%) > JBS3

Table II. Age distribution

Age (years)	No. of Individuals	Percentage
	< 65 years (N = 74)	48.68
30-39	04	2.63

Table III. Calculated 10 year CVD risk% stratified according to age in different scoring systems

Age	N	F ATP III*			F 2008*			ASCVD**			JBS3***		WHO/ISH*		
		L	I	H	L	I	H	L	I	H	L	H	L	I	H
30-39	04	04	0	0	04	0	0	04	0	0	04	0	04	0	0
40-49	21	21	0	0	21	0	0	21	0	0	21	0	21	0	0
50-59	23	23	0	0	07	04	12	15	0	08	23	0	23	0	0
60-65	26	15	11	0	0	07	19	07	0	19	11	15	17	09	0
66-69	14	11	03	0	07	0	07	0	07	07	11	03	12	02	0
70-79	42	11	08	23	07	08	27	0	0	42	08	34	10	09	23
≥80	22	04	11	07	03	0	19	0	0	22	0	22	02	12	08

*Low(L):<10, Intermediate(I):10-<20, High(H): ≥20,**L: <5, I: 5-<7.5, H: ≥7.5,***L:<20, H: ≥20

Table IV. Calculated 10 year CVD risk stratified amongst those <65 and those >65

Age	F ATP III			F 2008			ASCVD			JBS3		WHO/ISH		
	L	I	H	L	I	H	L	I	H	L	H	L	I	H
≤65	63	11	0	32	11	31	47	0	27	59	15	65	9	0
>65	26	22	30	17	8	53	0	07	71	19	59	24	23	31

Table V. Patients correctly categorized as high risk according to the various scoring systems

Age	F ATP III		F 2008		ASCVD		JBS3		WHO/ISH	
	N	%	N	%	N	%	N	%	N	%
≤65	0	0	31	41.89	27	36.49	15	20.27	0	0
>65	30	38.46	53	67.95	71	91.03	59	75.64	31	39.74
All	30	19.74	84	55.26	98	64.47	74	48.68	31	20.39

Table VI. Patients categorized as being at more than low risk (Intermediate + High) in various scoring systems

Age	F ATP III		F 2008		ASCVD		JBS3		WHO/ISH	
	N	%	N	%	N	%	N	%	N	%
≤65	11	14.86	42	56.76	27	36.49	15	20.27	9	12.16
>65	52	66.67	61	78.21	78	100	59	75.64	54	69.23
Total	63	41.45	103	67.76	105	69.08	74	48.68	63	41.45

Table VII. Comparison between ASCVD, Framingham 2008, JBS3

Age	Scoring system	Detected	Missed	Fisher's exact test. Two tailed P value
≤ 65	F 2008	42	32	F 2008 Vs ASCVD : P = 0.027, statistically significant. ASCVD Vs JBS3: P = 0.0442, statistically significant
	ASCVD	27	47	
	JBS3	15	59	
> 65	ASCVD	78	0	ASCVD Vs F 2008 : P<0.0001, statistically significant F 2008 Vs JBS3 : P = 0.8495, not statistically significant
	F 2008	61	17	
	JBS3	59	19	
All ages	ASCVD	105	47	ASCVD Vs F 2008 : P = 0.9018, not statistically significant F 2008 Vs JBS3 : P = 0.0011, very statistically significant ASCVD Vs JBS3: P = 0.0004, extremely statistically significant
	F 2008	103	49	
	JBS3	74	78	

(48.68%) > Framingham ATP III = WHO/ISH (41.45%) (Table VI).

The three highest scoring systems namely ASCVD, Framingham 2008 and JBS3 were compared.(Table VII) In the <65 group, Framingham 2008 was statistically better than ASCVD and both Framingham and ASCVD were better than JBS3. In the >65 group, ASCVD was significantly better than both Framingham and JBS3, whereas there was no statistical difference between Framingham and JBS3. Overall, there was no statistical difference between ASCVD and Framingham 2008, and both were better than JBS3.

Discussion

In the similar study in North Indian men and women by Bansal M et al,²⁴ JBS3 most correctly identified North Indian patients with MI as high-risk, ACC/AHA and Framingham were intermediate, and WHO/ISH had the lowest accuracy. In another study by the same group,²⁵ JBS3 had best correlation with coronary calcium score while ACC/AHA and WHO significantly underestimated CV risk.

Kanjilal S et al²⁶ compared Framingham, SCORE and JBS and all 3 risk scores identified <5% Indians as being at

high-risk. Khanna et al²⁷ found that Framingham grossly underestimated risk while metabolic syndrome more strongly correlated in young Indians with angiographically proven CVD.

In a retrospective case-control study by Guha S et al,²⁸ Framingham identified 14.29% diabetics and 19.91% nondiabetics with ACS as high risk, and the mean risk score was statistically significantly different between patients and controls. However, Framingham failed to identify a large proportion of high-risk nondiabetic patients and in diabetics there was no significant difference in the projected risk between those with ACS and controls.

Selvarajah et al²⁹ found that Framingham but not the WHO/ISH model can be used to identify high cardiovascular risk in Asians. Kandula et al³⁰ found that South Asians in US with high 10-year predicted ASCVD risk had significantly greater coronary artery calcium than those with low 10 year risk.

Studies applying the risk scores to CVD free Indians have reported varying results.

In the study by Guha et al²⁸ Framingham criteria were applied to disease free controls. Diabetic subjects without

ACS were 3.26% high risk, 54.35% moderate, and 42.39% low risk. Nondiabetic subjects were 9.95%, 21.89%, and 68.16%, respectively.

Ghorpade AG et al³¹ identified 17% rural population as high risk as per WHO ISH. WHO-ISH predicted that 1.7% of hospital staff had >10% risk of CVD event within 10 years.³²

The cutoff points of high risk and population studied in the present study account for differences in findings from the above mentioned studies.

This study is unique in that it deals exclusively with women who were all nonsmokers. This study showed that in South Indian women ASCVD and Framingham 2008 performed best. In those aged below 65 years, where the benefits of prevention are expected to be the greatest, only Framingham 2008 could identify more than 50% individuals as being at more than low risk. 43.24% women younger than 65 years and 30.92% of all ages were wrongly categorized as low risk even with the best performing risk prediction models.

Possible explanations include the following. The large INTERHEART³³ study showed that higher risk for CVD in South Asians in younger ages is mostly due to traditional risk factors covered in most risk prediction models. But there are still many factors emphasized by INTERHEART but not included in most models, namely abdominal obesity, psychosocial factors, non protective effect of alcohol, inadequate consumption of fruits & vegetables, physical inactivity, positive family history possibly mediated through genetically elevated levels of lipoprotein(a) found in 35-40% of Asian Indians and most importantly, abnormal Apo-B/ApoA-1 ratio. Apo B/ApoA1 ratio is said to be a reliable biomarker that can predict the future risk among individuals³³. This laboratory test is expensive and not widely available. In this study the women themselves were nonsmokers, but

43.6% had family members who were smokers and therefore were potential victims of passive smoking. 16.45% of women were in the so called protected premenopausal age group. However seven of these women had premature surgical menopause. None of the scoring systems take into account premature menopause or effects of passive smoking. Even though Indians may not be as well served by screening protocols originating in the west and all models underestimate risk especially in younger individuals, large long-term prospective Indian studies are not feasible due to economic and other constraints. Therefore falling back on the well established risk scores, we conclude that a lower threshold for intervention is probably appropriate in the population aged <65. The accuracy of all scoring systems is comparably adequate in those aged above 65.

Conclusions

Myocardial infarction occurs with alarming frequency in women. Age below 65 or nonsmoking status do not seem to be protective, emphasizing the need for aggressive cardiovascular primary prevention in our population. The mean BMI of the study population was 26.46 ± 03.57 , despite all patients being extremely well informed on cardiovascular health, and despite the fact that more than 50% was already under followup for hypertension, diabetes and dyslipidemia before their acute coronary event occurred. This underscores the need to promote physical activity and dietary modification in our populations. ASCVD and Framingham 2008 are the most appropriate models to assess cardiovascular risk in South Indian women. In those aged below 65 years, even an intermediate score should probably be a target for intervention and any score other than low should at least be advised diet and lifestyle modification. The accuracy of all scoring systems are comparably adequate in those aged below 65.

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