Original Article

Cardiovascular Risk Scores in Women Undergoing Stress Myocardial Perfusion Scan and Comparison with Scan-Predicted Risk

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Abstract

Background: Death due to cardiovascular disease is a major concern in the field of noncommunicable disease. Assessment of cardiovascular risk score using Framingham score and WHO/ISH score is a noninvasive, easier method of predicting the adverse cardiovascular event in the general population. **Aims and Objectives:** The aim of the study was to assess the cardiovascular risk using Framingham score and WHO/ISH in women undergoing stress myocardial perfusion imaging (MPI) and comparison with scan-predicted risk. **Materials and Methods:** Adult females with suspected coronary artery disease referred to the department of nuclear medicine for 2 months were included in the study. Data pertaining to the risk score assessment were collected, and the risk scores were calculated. Subsequently, the patients underwent scheduled Tc-99m methoxy-isobutyl-isonitrile myocardial stress imaging, and scan-predicted risks were calculated. Then, the risk score of Framingham and WHO/ISH methods were compared with stress myocardial perfusion score using Cohen's kappa statistic. **Results:** The mean age of the sample was 52 years (standard deviation: 11). Framingham and WHO/ISH risk scores predicted low, intermediate, and high risk in 62.2%, 28.9%, and 8.9% and 68.9%, 22.1%, and 8.89% of the population. The two scoring methods showed moderate agreement (κ =0.59). However, the scores showed only slight and fair agreement, respectively, with risk predicted by stress MPI. **Conclusion:** Although the risk scores have been shown to benefit in screening general population, they may not perform well in symptomatic patients with suspected angina. Out of the two methods, WHO/ISH fares better than Framingham score in this population.

Keywords: *Cardiovascular risk in women, Framingham score, myocardial perfusion imaging, WHO/ISH risk chart*

Introduction

Coronary artery disease (CAD) is a noncommunicable vascular disease that clinically manifests as myocardial ischemia, angina, heart failure, or sudden cardiac death. CAD is the leading cause of death in women.[1] There is a rise in the development of CAD due to increase in life expectancy, sedentary lifestyle, dietary habits, smoking, urbanization, and other factors that have a major impact on vascular system. This rise is more marked in women than men in the last 20 years.[2] The major risk factors are hypertension, diabetes, dyslipidemia, smoking, obesity, and insulin resistance, and they play a significant role in the pathogenesis of CAD. In spite of the traditional risk factors, the high prevalence of CAD in women is not completely understood. The development of new risk factors such as lipoprotein (a), homocysteine levels, and C-reactive protein levels play a role in assessment of CAD.[3] Gender-specific risk factors such as low estrogen level, pregnancy, menopause, and combined oral contraceptive pills also have a role in the development of CAD in women.[4] Only a few studies have analyzed the use of risk scores in women and far less of Indian women. Their access to health care is limited, and therefore, the current study intends to focus on the risk factors in Indian women who are suspected to have CAD.

Several risk scores are available for assessment of development of CAD in an individual, such as Framingham score, WHO/ISH risk prediction chart, PROCAM score, and Reynolds risk score. Out of the abovementioned scoring systems, Framingham score that uses easily available parameters is widely applied for screening large population, shows consistent results,

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and is being used in clinical and research field for prediction of cardiovascular risk events.[5,6] WHO/ISH risk scoring is prescribed by the Indian guidelines for risk prediction. It has the advantages of availability of low information as well as high information models, simplicity in calculation, and provision of regional scoring system.[7] Both these systems predict adverse cardiovascular events over the next 10 years. The limitation of the Framingham score is that it underestimates the cardiovascular risk in women and that of WHO/ISH is that the low information model slightly overpredicts the risk compared to high information model.[6,8] Coronary angiography is the gold standard for diagnosis and confirmation of CAD but is an invasive technique. Treadmill test is a noninvasive method to screen patients for CAD but suffers from low sensitivity and specificity. Stress myocardial perfusion imaging (MPI) is a noninvasive method used in the assessment of CAD and has a high negative predictive value of 98.8%. It is more accurate than stress echocardiography.[9] It also has the advantage of predicting the risk without any gender disparity.[10] It can be used for risk assessment stratification with consistent results in women with suspected CAD.[11,12] The use of clinical risk assessment score has reduced since the advent of the nuclear modalities, which are, however, expensive. The relevance of these scores in this scenario is less studied. The study will help us to know the performance of Framingham and WHO/ISH risk scoring system in female patients with suspected ischemic heart disease and referred for stress MPI and to compare the risk scores with the scan results.

Methodology

An analytical observational study was conducted in the department of nuclear medicine at a tertiary care hospital from July to August 2019. The inclusion criteria were consecutive women aged more than 18 years of age with suspicion of CAD and referred to the department of nuclear medicine for stress MPI.

Procedure

After obtaining consent from the participants, history of risk factors and lipid profile results were obtained from them. Demographic details including age, sex, height, weight, history of smoking, history of alcohol intake, history of diabetes, history of hypertension, history of intake of antihypertensive medications, history of asthma, and history of dyslipidemia were collected. Levels of total cholesterol, blood glucose, and high-density lipoprotein were noted down. Framingham score for 10-year cardiovascular risk and WHO/ISH score for 10-year cardiovascular risk were calculated using the Canadian Cardiovascular Society chart for Framingham risk score and WHO/ISH risk prediction chart (2014), respectively. The patients then underwent stress MPI as scheduled. Patients underwent stress by either treadmill exercise or pharmacological agent (dobutamine or adenosine), and Tc-99m methoxy-isobutyl-isonitrile was the radiopharmaceutical used. Poststress images were acquired on a single-photon emission computed tomography/computed tomography scanner as per the routine protocol, 45 min after stress. Based on the findings of poststress scan, a rest study was done either on the same or a different day. The images were processed on Symbia.net workstation (Siemens Healthcare). Summed stress scores was represented as percentage abnormal myocardium. The results of stress MPI were represented as low risk, intermediate risk, and high risk for annual CAD-related mortality by nuclear physician based on summed scores and defect characteristics. Risk scores from Framingham scoring and WHO/ISH charts were compared with the risk obtained from stress MPI.

The Framingham risk scores in percentage are calculated from risk chart provided by the Canadian Cardiovascular Society. The risk stratifications were low risk (10%), intermediate risk (10%–19%), and high risk (>19%). According to WHO/ISH score, the scores were low risk (<10%), intermediate risk (10%–<30%), and high risk (≥30%), while risk scores for stress MPI were categorized as low, intermediate, and high risk based on physicians' interpretation.

Statistical analysis

Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables were expressed as proportions. Risk scores estimated by Framingham risk scoring and WHO/ISH chart were expressed as low, intermediate, and high risk for developing major cardiovascular events. The results of stress MPI were interpreted to provide the risk of major cardiovascular events (low, intermediate, and high risk). The estimated risks from scoring method and scan were compared for agreement or discordance with Cohen's kappa statistic. The data were analyzed using the software STATA version 14.2 (StataCorp LP, College Station, Texas, USA).

Results

A total of 51 female patients who had come to the nuclear medicine department for MPI scan were included in the study. Six participants were excluded due to nonavailability of total cholesterol values. Data of 45 female patients were taken for final analysis.

Demographical and biochemical data

The mean age of 45 patients was found to be 52 years (SD: 11). The mean value of body mass index (BMI) was 25.56 (SD: 6.23). The study population had a median blood glucose value of 107 mg/dl (IQR: 88,145). The mean values (SD) of high density lipoprotein (HDL), low density lipoprotein (LDL), and total cholesterol 1.14 mmol/L (SD: 0.29), 2.87 mmol/L (SD: 1.16), and 4.37 mmol/L (SD: 1.40), respectively. The mean systolic blood pressure

of the population was found to be 143 mmHg (SD: 24.83) [Table 1].

Morbidity and behavioral data

No participant had a history of smoking or alcohol intake. Among the 45 patients, 26 (57.8%) had diabetes mellitus. Fifteen (34%) out of 44 patients had a history of hypertension, and among them, 10 patients had a history of hypertension for more than 5 years. Data were not available for one patient. Among the 41 patients with available data, 5 (12.19%) patients had a previous history of myocardial infarction [Table 1].

Association scores

The Cohen kappa statistics was used in the analysis of agreement to detect the strength of the association. The kappa coefficient was estimated by categorization of the variable into low risk, intermediate risk, and high risk between the study test and the reference test [Table 2].

It was found from the table that there was a moderate agreement between Framingham and WHO/ISH risk scores (agreement = 80%; $\kappa = 0.59$; $P < 0.001$) in the assessment of risk factors among women. However, it was found that there is only slight agreement between Framingham and stress MPI score scores (agreement = 60%; $\kappa = 0.09$; $P > 0.001$) in assessing the risk factors among the women. There was a fair agreement between WHO/ISH and Stress MPI score scores (agreement = 71.11%; $\kappa = 0.25$; $P > 0.001$) [Table 3].

Discussion

This cross-sectional observational study was conducted in women referred to the department of nuclear medicine. The study population had a mean age of 52 years and BMI of 25.56. The study population had no smoking habits and no history of alcohol intake. Majority of the population had normal levels of blood glucose and serum total cholesterol. However, more than half of the patients had decreased HDL cholesterol level, which is considered to lower the risk of CAD. Hence, majority of the patients are dyslipidemic. About 25 people had hypertension (history as well as newly diagnosed) and 26 people had diabetes (history as well as newly diagnosed). Five patients had a previous history of myocardial infarction, and among them, three had a history of hypertension. The proportion of population found to have high risk for ischemic heart disease-related events as assessed by stress MPI was about 8.89%.

In our sample population, the Framingham and WHO/ISH risk score charts had a moderate agreement and produced similar results. Framingham risk score categorized slightly less number of people under low-risk group than WHO/ISH risk score, whereas the former categorized more patients into intermediate-risk group. There was no change in categorizing high-risk patients ($n = 4$) with either of these methods.

Table 1: Demographical and biochemical characteristic of the study population (n=45)

Characteristics	Mean/median (SD/IQR)
Age (years)	52 (11)
BMI	25.56 (6.23)
Blood glucose (mg/dl)	107 (88-145)
HDL (mmol/L)	1.14 (0.29)
LDL (mmol/L)	2.87 (1.16)
Total cholesterol (mmol/L)	4.37 (1.40)
Systolic blood pressure (mmHg)	143 (24.83)
Characteristics	**Number of people (%)**
Diabetes*	
Present	19 (42.2)
Absent	26 (57.8)
Hypertension*	
Present	15 (33.33)
Absent	29 (64.44)
Data unavailable	1 (2.22)
Antihypertensive use among hypertensives* (n=15)	
Yes	14 (93.33)
No	1 (6.66)
Hypertensive years* (n=15)	
<5	5 (33.33)
>5	10 (66.66)
Previous history of myocardial infarction*	
Present	5 (11.11)
Absent	36 (80)
Not available	4 (8.89)
Smoking*	
Smokers	0
Nonsmokers	42 (93.33)
Data unavailable	3 (6.67)
Alcoholism*	
Alcoholics	0
Nonalcoholics	43 (95.56)
Data unavailable	2 (4.44)

*Self-reported (n=15) denotes the 15 hypertensive patients for which data were analyzed. SD: Standard deviation, IQR: Interquartile range, HDL: High-density lipid, LDL: Low-density lipid

Table 2: Distribution of low-risk, intermediate-risk, high-risk people by Framingham score, WHO/ISH score, and myocardial perfusion imaging

Risk scores	Low risk (%)	Intermediate risk (%)	High risk (%)
Framingham score	28 (62.22)	13 (28.89)	4 (8.89)
WHO/ISH score*	31 (68.89)	10 (22.22)	4 (8.89)
Stress myocardial perfusion score	39 (86.69)	2 (4.44)	4 (8.89)

*Risk stratification for WHO/ISH score: Low risk - <10%, Intermediate risk - 10%–<30%, High risk - ≥30

There is only slight agreement between Framingham risk score and stress MPI score. Out of the four patients

Table 3: Agreement values between the risk scores used in this study (*n*=45)

Scales	Agreement (%)	K	*P*
Framingham and WHO/ISH	80.00	0.5994	0.0000
Framingham and stress MPI scores	60.00	0.0909	0.1463
WHO/ISH and stress MPI scores	71.11	0.2500	0.0042

MPI: Myocardial perfusion imaging

categorized as high risk by Framingham risk score, MPI scan showed abnormality in only two of them. The remaining two patients had normal stress scan findings, indicating that they have a low risk for developing major adverse cardiac events.

There is a fair agreement between WHO/ISH risk score and stress MPI score. Moreover, risk predictions in low and intermediate population are comparatively better than Framingham risk score. However, similar to Framingham score, there was concordance in high-risk prediction in only two of the four patients. Of the remaining two, one was categorized as low risk and the other as intermediate risk by MPI scan results.

Two patients who were categorized as low and intermediate risk, respectively, as per the two scoring methods had a history of previous myocardial infarction and were found to have defects on the MPI scan and thereby categorized as high risk.

The variation in the performance of Framingham score could be attributed to the characteristics of the sample population being different from the reference population.[13] A systematic review by Stacey Sheridan showed that Framingham had less precision in calculation of hypertension, particularly in women, not consideration of diabetes mellitus and left ventricular hypertrophy as a cause for variation in the risk score. Our study population had a mean age of women in 52 years; the status of menopause leading to low estrogenic state, LDL levels, and increased plasma glucose level are independent risk factors for cardiovascular events that are not taken into account for assessing cardiovascular risk score by the Framingham method.[14]

Limitations

Sample size of the population is relatively small. Random sampling could not be done due to resource and time restrictions.

Conclusion

In a sample population of women with suspected CAD, Framingham and WHO/ISH risk scores were applied and about 9% of the patients were found to have high risk for development of adverse cardiac events. There was a moderate agreement in risk estimation between the two scoring methods (κ = 0.59). The agreement of these scores with stress MPI was slight for the former and fair for the latter. Although the risk scores have been shown to benefit in screening general population, they may not perform well in symptomatic patients with suspected angina. Out of the two methods, WHO/ISH fares better than Framingham score in this population.

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Conflicts of interest

There are no conflicts of interest.

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