

# Applying the Framingham risk score for prediction of metabolic syndrome: The Kerman Coronary Artery Disease Risk Study, Iran

Gholamreza Yousefzadeh<sup>(1)</sup>, Mostafa Shokoohi<sup>(2)</sup>, Hamid Najafipour<sup>(1)</sup>,  
Mitra Shadkamfarokhi<sup>(1)</sup>

## Original Article

### Abstract

**BACKGROUND:** There has been a few studies about the predictability of metabolic syndrome (MetS) based on the Framingham risk score (FRS) as a tool for predicting the risk of 10-years cardiovascular diseases (CVD) in Iranian population. The aim of this study was to compare the risk stratification obtained with the FRS and MetS in a cohort of the Iranian population.

**METHODS:** In this population-based study Kerman Coronary Artery Disease Risk study, Iran, MetS was diagnosed as defined by the revised National Cholesterol Education Program definition criteria (ATPIII) and the FRS was calculated using a computer program, previously reported algorithm.

**RESULTS:** Overall, the prevalence 10-years risk of CVD for patients with MetS was significantly different with those without MetS (74.3 vs. 86.4% for low-risk patients, 18.1 vs. 12.3% for intermediate-risk people, and 7.6 vs. 1.3% for high-risk individuals) ( $P < 0.001$ ). The frequency of intermediate-risk and high-risk for 10-year CVD in men with MetS (39.5 and 18.3%, respectively) was considerably higher than women with MetS (3.2 and 0.1%, respectively). Using multiple logistic regression, the odds ratio of MetS in intermediate-risk and high-risk FRS group was 1.7 and 6.7, respectively ( $P < 0.001$ ).

**CONCLUSION:** Significant association between the presence of MetS and high risk for CVD based on FRS was revealed in both men and women indicating a good concordance between MetS and FRS in predicting the risk of CVDs. However, the odds ratio of the development of risk of cardiovascular events among women was higher than men with MetS.

**Keywords:** Metabolic Syndrome, Framingham Risk Score, Cardiovascular Disease, Ischemic Heart Disease

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### Introduction

The Framingham risk score (FRS) is a simplified and common clinical tool for assessment of the risk level of coronary artery disease (CAD) as well as for identifying individuals who were candidate for risk factors modification.<sup>1</sup> This tool consists of various coronary risk components including gender, age, smoking, systolic blood pressure, and lipid profile state. FRS is the most applicable method for predicting a person's chance of developing cardiovascular disease (CVD) in long-term.<sup>2,3</sup> Because this risk score give an indication of the likely benefits of prevention, it can be effectively useful for both the patient and for the clinicians in deciding whether lifestyle modification and preventive medical treatment,<sup>4,5</sup> and for patient education, by identifying men and women at

increased risk for future cardiovascular events.<sup>6</sup> However, despite the applicability of this tool, it is powerless to evaluate some key factors, which influenced by dietary and metabolic patterns modification. Proverbially, it remained unknown whether the FRS is a good predictor of metabolic disturbances underlying ischemic heart disease.<sup>7</sup> Moreover, the FRS has been shown to overestimate coronary disease risk in Europeans and thus its recalibration in special populations is recommended.<sup>8</sup>

Because of metabolic syndrome (MetS) defined as a complete cluster of cardiovascular metabolic risk factors even diabetes mellitus, insulin resistance, and abdominal obesity, it may offer a better view of the prediction of coronary heart disease in suspected individuals.<sup>7,9-11</sup> However, findings of

1- Physiology Research Center, Institute of Nourpharmacology, Kerman University of Medical Sciences, Kerman, Iran

2- Research Center for Modeling in Health, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

Correspondence to: Mostafa Shokoohi, Email: shokoohi.mostafa@gmail.com

previous studies on comparing the predictive value of FRS versus MetS have been varied widely. Although the MetS score with age included has been identified to be a valid tool for predicting CVD and its predictive ability was as good as the FRS,<sup>12</sup> some others have emphasized inferiority of MetS toward the FRS.<sup>13-16</sup>

There has been no study about the predictability of MetS according to FRS in Iranian population. The aim of this study was to compare the risk stratification obtained with the FRS between individuals with and without MetS in a cohort of the Iranian population.

### Materials and Methods

This population-based study is a great part of The Kerman, Iran, CAD Risk study that scheduled for a cohort of 5874 individuals aged 15-75 years and residence in Kerman city addressing the information of the risk profile of CAD including serum lipids, physical activity, alcohol and drugs addiction, mental disorders like stress and depression, hypertension as well as dietary regimens. The study was approved by the research and ethics committees of the Kerman University of Medical Sciences, Iran, and informed consent was obtained from all participants.

In this survey, a detailed interview regarding social demographics and risk profile was administered and all subjects underwent a clinical examination that included measurement of body composition, systolic and diastolic blood pressure, serum blood sugar and serum lipids. We examined weight and standing height expressed as a body mass index (weight in kilograms divided by height in meters squared). The waist circumference (WC) was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. Blood pressure was recorded using an automatic oscillometric blood pressure recorder after at least 5 min of rest in a chair and arm supported at heart level. Systolic blood pressure was measured at the point where the first of two or more sounds was heard (Phase 1), and diastolic blood pressure before the disappearance of sounds (Phase 5). For biochemical analysis, blood samples of 5 ml were drawn after 12 h overnight fasting for measuring lipid profile, fasting blood sugar, and hemoglobin A1c. Plasma glucose was measured using the glucose oxidase-peroxidase method. The level of serum lipid profile was also determined by standard enzymatic procedures.

MetS was diagnosed as three or more of the following five factors as defined by the revised National Cholesterol Education Program definition criteria for Asian population: (1) fasting triglycerides > 150 mg/dl or lipid medications; (2) systolic blood pressure > 130 mmHg, diastolic blood pressure > 85 mmHg, or antihypertensive medications; (3) fasting plasma glucose > 5.6 g/dl or diabetes medications; (4) high-density lipoprotein (HDL) cholesterol < 40 mg/dl (men) or < 50 mg/dl (women); and (5) WC > 102 cm (men) or > 88 cm (women).<sup>17</sup>

The FRS was calculated using a computer program<sup>18</sup> and based on using a previously reported algorithm,<sup>2</sup> which takes into account age, sex, total cholesterol, HDL cholesterol, systolic and diastolic blood pressure, smoking and the presence of diabetes. The participants were then classified into groups according to cardiovascular risk consistent with the obtained score that individuals with low risk had 10% or less coronary disease risk at 10 years, with intermediate-risk 10-20%, and with high risk 20% or more.<sup>19</sup>

Results were presented as mean  $\pm$  standard deviation for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of < 5 were observed. Quantitative variables were also compared using t-test. Statistical significance was determined as a  $P < 0.050$ . All statistical analysis was performed using SPSS software for Windows (version 20, SPSS Inc., Chicago, IL, USA).

### Results

The mean age for the entire cohort was  $44.34 \pm 16.32$  years (range 10.87 years). Among, MetS was diagnosed in 2346 subjects (39.7%). The baseline demographics comparing subjects with and without MetS are shown in table 1. Compared to non-MetS group, those with MetS were older, were more female, had higher systolic and diastolic blood pressure, had higher fasting blood sugar, and also had different lipid profile status as higher serum total cholesterol, serum triglyceride, and lower HDL.

Overall, 74.3% patients with MetS were low-risk, 18.1% were intermediate-risk, and 7.6% were high-risk for 10-year CVD. Besides, the 10-year risk for cardiovascular disorders according to FRS scoring was significantly lower in those without MetS that 86.4% were low-risk, 12.3% were intermediate-risk, and only 1.3% of them were high-risk for cardiovascular disorders (Table 2). This

significant association between the presence of MetS and high risk for CVD based on FRS was revealed in both men and women indicating a good concordance between MetS and FRS in predicting the risk of CVD s. However, the prevalence intermediate- and high-risk for 10-years risk of CVD in men (39.5 and 18.3%, respectively) was significantly much more compared with those in women (3.2 and 0.1%, respectively) ( $P < 0.001$ ) (Table 2). In other words, the frequency of low-risk category in women was significantly high than men (96.8 vs. 42.1%, respectively).

As shown in table 3, using multiple logistic regression modeling and considering low-risk group as the reference, the odds ratio of risk for MetS was 1.7 in intermediate-risk FRS group and was 6.7 in high-risk FRS group ( $P < 0.001$ ). The odds ratios of intermediate-risk and high-risk among men respectively were 2.63 and 11.4 ( $P < 0.001$ ) and among women were 12.02 and 22.01 ( $P < 0.001$ ). The 10-year increased risk for CVDs according to FRS risk categories was significantly associated with the number of MetS definitional components (Figure 1) that 10-year high risk of cardiovascular disorders was predict in 0.6% of patients with one MetS component,

2.6% in two MetS components group, 7.1% in three MetS components group, 8% in individuals with four or five components group ( $P < 0.050$ ).

## Discussion

Our study performed on a great sample of the Iranian population revealed a prevalence of 39.7% for MetS that is nearly consistent with the previous reports. In a recent report, the overall prevalence of MetS in different Iran areas ranged between 30% and 45%<sup>20-23</sup> that is nearly in the range that reported in neighbor country of Iran including Saudi (39.3%)<sup>24</sup> and Turkish (33%) populations.<sup>25</sup> However, the global prevalence of this phenomenon varies widely so that the published reports from western countries and from southeastern nations documented MetS prevalence of 24.0 and 14.2%, respectively.<sup>26,27</sup> The observed discrepancy might be due to the different in used MetS definitional criteria and also to the differences in genetic predisposition, various lifestyle patterns as well as different nutritional behaviors leading variance in the prevalence of MetS for different communities and ethnic groups.

**Table 1.** Baseline characteristics in individuals with and without metabolic syndrome (MetS)

Characteristics	Group with MetS (n = 2346)	Group without MetS (n = 3528)	P
Female gender (%)	1392 (58.9)	1846 (52.2)	
Age (year)	53.14 ± 13.16	38.48 ± 15.57	
Systolic blood pressure (mmHg)	128.85 ± 20.40	109.97 ± 20.14	
Diastolic blood pressure (mmHg)	82.07 ± 10.54	74.22 ± 9.01	
WC (cm)	93.06 ± 10.99	79.61 ± 10.90	< 0.001
Fasting blood sugar (mg/dl)	121.59 ± 48.96	91.23 ± 22.53	
Serum triglyceride (mg/dl)	198.43 ± 113.34	113.07 ± 75.35	
Serum total cholesterol (mg/dl)	208.47 ± 45.73	181.84 ± 40.50	
Serum HDL (mg/dl)	35.01 ± 8.54	40.58 ± 10.91	

MetS: Metabolic syndrome; WC: Waist circumference; HDL: High-density lipoprotein

**Table 2.** The comparison of 10-year risk for cardiovascular disorders [according to Framingham risk score (FRS) scoring] between two groups of with and without MetS (results reported for the whole population and gender subgroups)

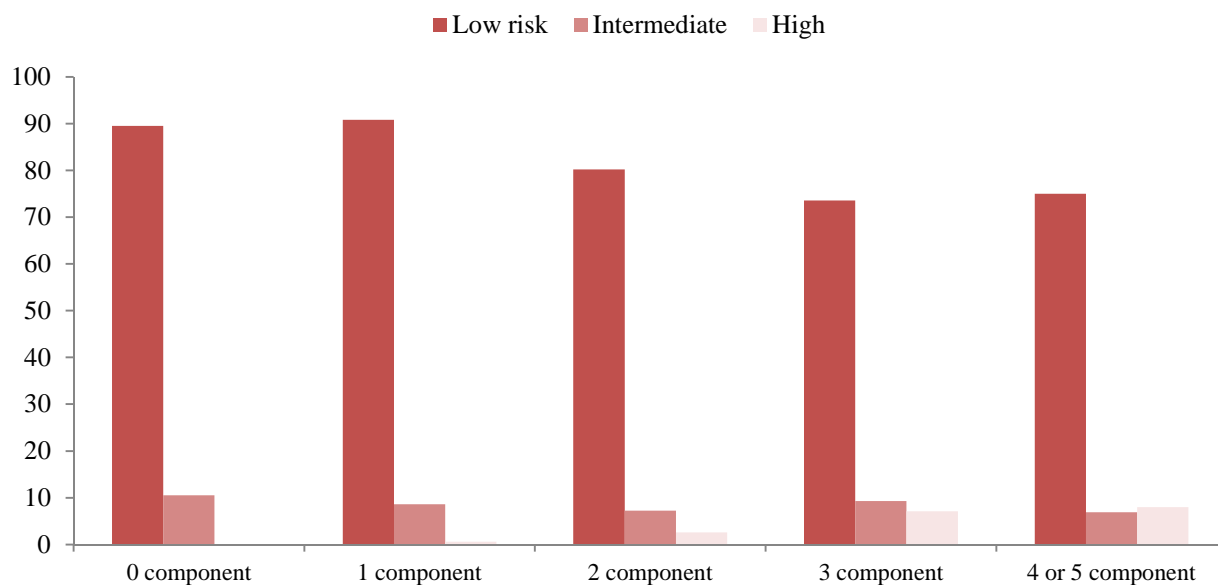
Characteristics	Group with MetS (n = 2346)	Group without MetS (n = 3528)	P
Total			
Low-risk	1756 (74.3)	3056 (86.4)	
Intermediate-risk	428 (18.1)	435 (12.3)	
High-risk	179 (7.6)	46 (1.3)	
Men			
Low-risk	409 (42.1)	1215 (71.9)	< 0.001
Intermediate-risk	384 (39.5)	430 (25.4)	
High-risk	178 (18.3)	46 (2.7)	
Women			
Low-risk	1347 (96.8)	1841 (99.7)	
Intermediate-risk	44 (3.2)	5 (0.3)	
High-risk	1 (0.1)	0 (0.0)	

MetS: Metabolic syndrome

**Table 3.** Multiple logistic regression models for assessing the odds ratio of metabolic syndrome (MetS) in the levels of Framingham risk score (FRS) risk scores

FRS risk categories	Odds ratio	95% CI	P
Total			
Low-risk (ref)	1	-	-
Intermediate-risk	1.712	1.480-1.981	< 0.001
High-risk	6.772	4.872-9.413	< 0.001
Men			
Low-risk (ref)	1	-	-
Intermediate-risk	2.653	2.222-3.168	< 0.001
High-risk	11.495	8.157-16.199	< 0.001
Women			
Low-risk (ref)	1	-	-
Intermediate-risk	12.027	4.757-30.412	< 0.001
High-risk	22.009	10.151-46.790	< 0.001

CI: Confidence interval; FRS: Framingham risk score

**Figure 1.** Association between Framingham risk score risk categories and number of metabolic syndrome components

Several studies have been conducted in past to assess the relative merits of MetS and FRS for prediction of cardiovascular risk, but have shown inconsistent results.<sup>9,13,16</sup> Furthermore, numerous studies attempted to evaluate the concordance between these two predicting tools confirming the superiority of one method over the other. Our study showed a strong correlation between these tools so that higher-risk FRS status has been expressed to be associated with the presence of MetS and its numbers of components. On the other hand, both MetS and FRS can be effectively used for predicting the long-term appearance of cardiovascular events. However because of some potential limitations of FRS such as heavy dependent on age factor and underestimation of cardiovascular disorders in the

young,<sup>28,29</sup> and lack of coverage several prominent features of MetS such as obesity, hypertriglyceridemia and elevated high sensitivity-C reactive protein levels,<sup>17</sup> the use of MetS is more preferred to predict occurrence of CVDs. Yu et al. showed that MetS score, including age appeared greater association with CVD than FRS on the same exposed subjects and thus can have more validation than FRS and, therefore, its predictive ability can be higher than the latter tool.<sup>12</sup> In contrast, because of short-term modification of some life-style-related risk factors such as blood sugar state or obesity, MetS may be an independent determinant of significant CAD only among those individuals at low 10-year risk for future coronary events.<sup>30</sup> Moreover, MetS was found to be less effective at

predicting heart disease than the FRS according the two recent US reports showing the syndrome to be less predictive of CVD than the FRS.<sup>13,14</sup> Meanwhile, the combined use of these two tools did not result in more benefits. In the recent report of the National Heart, Lung, and Blood Institute and American Heart Association conference proceedings, analysis of the Framingham data indicated that no advantage is gained in risk assessment by adding the components of MetS to the FRS.<sup>9</sup> Thus, it still remains to be determined whether FRS or MetS is a better risk assessment tool in young individuals.

This study had some potential limitations. First, its cross-sectional nature and the lack of patients with the angiographically established CVD did not allow us to evaluate whether MetS is a better marker of cardiovascular risk than FRS in our individuals. It was preferred to assess this concordance considering both CVD and healthy subgroups. In addition, our study only covered a local population in eastern Iran and did not include a great sample from all regions of the country. Therefore, results are not generalized to all parts of the country.

In the present study, we found that in spite of increasing frequency of moderate- and high-risk for 10-year cardiovascular events in men, but the odds ratio of development of MetS among women in both moderate- and high-risk groups compared with low-risk group as reference group was remarkably higher in men. The present findings seem to be consistent with other research in the literature review, which found somehow the similar results. In a meta-analysis, patients with the MetS had approximately 60% increased risk of CVD than those without the MetS and that the MetS could be a stronger risk factor for CVD in women compared to men.<sup>31</sup> In another study among a group of people with low prevalence of coronary heart disease (CHD), stroke, and diabetes, the probability to develop CHD after controlling other serious risk factors, among women with the MetS (2 times) was greater than that in men (1.5 times).<sup>14</sup> There have found an association between the MetS and an increased number of CVD events.<sup>32,33</sup> The MetS worsens the development of some main non-communicable diseases like diabetes, CAD, myocardial infarction, stroke, and heart failure. It has indicated that the MetS can be a stronger predictor of CVD events even than diabetes. The studies have shown the discrepancies between men and women concerning the role of the MetS on the development of diseases events. The MetS was

related to an increased prevalence of coronary heart disease.<sup>34-37</sup> In Marroquin *et al.*'s study, which conducted only in women, the MetS deteriorated the prognosis of CVD. The hazard ratio of the impact of the MetS on the prognosis of cardiovascular events was 4.93, almost 5 times higher than that in women without CAD, which was 1.41.<sup>38</sup> There was a strong association between the MetS and CVD mortality among women compared with men (more than twice) based on the data from the San Antonio Heart Study.<sup>39</sup> Dekker *et al.*<sup>40</sup> also suggested that associations of MetS with non-fatal CVD generally were stronger in women than in men. Although the recent study concluded that the FRS can underestimate absolute coronary heart disease risk in older adults, especially among women by 51% compared to 8% in men.<sup>41</sup>

### Conclusion

In conclusion, both MetS and FRS predicting tools can serve as simple clinical approaches to identifying cardiovascular vulnerable and at-risk patients in order to its acceptable concordance. However, because of covering some important metabolic components, including obesity, blood sugar changes as well as pro-inflammatory status, the use of MetS for predicting CVDs is preferable.

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### Conflict of Interests

Authors have no conflict of interests.

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