Metabolic Syndrome versus Framingham Risk Score for Association of Self-Reported Coronary Heart Disease: The 2005 Korean Health and Nutrition Examination Survey

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Background: Several studies in Western populations have indicated that metabolic syndrome (MetS) is inferior to the Framingham risk score (FRS) in predicting coronary heart disease (CHD). However, there has been no study about the predictability of MetS vs. FRS for CHD in Korea.

Methods: Among the 43,145 persons from the third Korea National Health and Nutrition Examination Survey in 2005, laboratory test and nutritional survey data from 5,271 persons were examined. Participants were also asked to recall a physician’s diagnosis of CHD.

Results: The median age was 46 (range, 20 to 78) years in men (n=2,257) and 44 (range, 20 to 78) years in women (n=3,014). Prevalence of self-reported CHD was 1.7% in men and 2.1% in women. Receiver operating characteristic curves and their respective area under the curve (AUC) were used to compare the ability of the FRS and the number of components of MetS to predict self-reported CHD in each sex. In men, AUC of FRS was significantly larger than that of MetS (0.767 [0.708 to 0.819] vs. 0.677 [0.541 to 0.713], P<0.01). In women, AUC of FRS was comparable to that of MetS (0.777 [0.728 to 0.826] vs. 0.733 [0.673 to 0.795]), and was not significant.

Conclusion: The data suggested that FRS was more closely associated with CHD compared to MetS in Korean men.

Keywords: Coronary artery disease; Metabolic syndrome; Risk assessment

INTRODUCTION

Metabolic syndrome (MetS), defined as a cluster of cardiovascular risk factors, has been considered to be a useful concept for prevention of the rapidly growing incidence of coronary heart disease (CHD) [1-3]. The concept of MetS has also been widely used for the co-management of multiple cardiovascular risk factors including diabetes, hypertension, and dyslipidemia in high risk persons for optimal outcomes [1,4]. Furthermore, it has been widely promoted as a means of identifying patients for lifestyle modification to reduce risk factors and disease incidence, in particular CHD [5-8].

Many studies have shown that whether defined on the basis of National Cholesterol Education Program (NCEP) criteria [9-21] or World Health Organization (WHO) criteria [2,10,11,18-22], MetS is associated with significantly increased risk of developing CHD. Several recent studies conducted in Western populations have indicated that MetS is inferior to the Framingham risk score (FRS), a traditional risk scoring system, in predicting CHD [5,19,21,23]. However, there has been no study...
examining the predictability of MetS vs. FRS with regard to CHD in Korea.

The Korean Ministry of Health and Welfare has conducted the Korean National Health and Nutrition Examination Survey (KNHANES) since 1998. We assessed the relative associations of MetS using NCEP criteria [24] vs. FRS with self-reported CHD in a national representative cohort of Republic of Korea.

METHODS

Study population
This study was based on data obtained from the third KNHANES (KNHANES III) among non-institutionalized civilians in the Republic of Korea, conducted by the Korean Ministry of Health and Welfare in 2005. This survey was a nationwide representative study using a stratified, multistage probability sampling design for the selection of household units. The survey consisted of a health interview, health behavior, health examination, and nutrition components. A total of 34,145 individuals from these sampling frames were included in the health interview survey. The FRS can be applied to persons aged 20 to 79 years, so we excluded persons under 20 years and over 79 years. Among this group, 5,271 persons aged 20 to 79 years were identified as participants, using laboratory tests and nutritional survey data.

Health examination survey and laboratory test
Trained interviewers visited each participant’s dwelling and administered a standardized questionnaire on smoking and regular exercise. A dietary recall method was used to collect data on food items consumed by participants during the past 24 hours. The participants were also asked to recall a physician’s diagnosis of CHD (angina or myocardial infarction). Height and weight were obtained using standardized techniques and equipment. Height was measured to the nearest 0.1 cm using a portable stadiometer (Seriter, Bismarck, ND, USA). Weight was measured to the nearest 0.1 kg using a calibrated balance beam scale (Giant-150N; Hana, Seoul, Korea). Body mass index (BMI) was calculated by dividing weight by height squared (kg/m²). Waist circumference (WC) was measured on standing participants with a soft tape midway between the lowest rib and the iliac crest. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by standard methods using a sphygmomanometer with the patient in a sitting position. Three measurements were made on all subjects at 5-minute intervals; the average of the second and third measurements was used in the analysis. Blood samples were collected in the morning after fasting for at least 8 hours. Fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), and high density lipoprotein cholesterol (HDL-C) levels were measured in a central and certified laboratory; an Advia 1650 (Siemens, Tarrytown, NY, USA) was used. Low density lipoprotein cholesterol (LDL-C) was estimated indirectly using the Friedwald formula: LDL-C = TC – [HDL-C + (TG/5)], for subjects with TG levels < 400 mg/dL.

Definitions of MetS and FRS
MetS as defined by NCEP criteria comprises three or more of the following [24]: 1) FPG level of at least 100 mg/dL or current anti-diabetes medication; 2) serum TG level of at least 150 mg/dL; 3) serum HDL-C level lower than 40 mg/dL for men and 50 mg/dL for women; 4) SBP of at least 130 mm Hg or DBP of at least 85 mm Hg or current anti-hypertensive medication; and 5) WC of at least 90 cm for men and 80 cm for women [25]. The FRS for CHD was calculated for each participant [26,27], and participants were categorized according to quintiles of risk score in each sex.

Statistical analyses
Data are presented as mean ± standard deviation or percent. Statistical analysis was performed using SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL, USA). Independent t-test and χ² test was done for comparison of clinical and biochemical characteristics between each sex (Table 1). Independent t-test and χ² test was done for comparison of clinical characteristics according to self-reported CHD in each sex (Table 2). Receiver operating characteristic (ROC) curves and their respective area under the curve (AUC) were used to compare the ability of the FRS and the number of metabolic abnormalities to predict self-reported CHD in each sex (Fig. 1) [28]. Logistic regression analysis for self-reported CHD was done to compare R² between model 1 with variables of five components of MetS and model 2 with variables of age, current smoking, and those variables in model 1 (Table 3). All probability values were two-tailed, and statistical significance was defined as P < 0.05.

Ethics statement
This study was approved by the Institutional Review Board of the Ilsan Paik Hospital (IB-2-1105-013).
Table 1. Clinical characteristics of the study population

| Characteristic                        | Men (n = 2,257) | Women (n = 3,014) | P value |
|---------------------------------------|-----------------|-------------------|---------|
| Age, mean (range), yr                 | 46 (20-78)      | 44 (20-78)        | NS      |
| Current smoking, %                    | 45.9            | 4.3               | <0.001  |
| Exercise 3x/wk, %                     | 33.6            | 34.4              | NS      |
| Daily calories intake, kcal           | 2,351±916       | 1,807±686         | <0.001  |
| Daily fat intake, g                   | 49.0±36.7       | 36.7±28.3         | <0.001  |
| Daily alcohol intake, g               | 17.8±45.0       | 2.6±11.3          | <0.001  |
| BMI, kg/m²                            | 24.0±3.1        | 23.5±3.4          | <0.001  |
| Waist circumference, cm               | 84.3±8.7        | 78.4±9.5          | <0.001  |
| SBP, mm Hg                            | 122.7±16.0      | 116.0±18.1        | <0.001  |
| DBP, mm Hg                            | 80.7±10.3       | 74.7±10.3         | <0.001  |
| Anti-hypertensive medication, %       | 11.3            | 12.6              | NS      |
| Total cholesterol, mg/dL              | 185.2±34.6      | 184.5±35.5        | NS      |
| LDL-C, mg/dL                          | 113.3±30.2      | 115.0±30.3        | NS      |
| Triglyceride, mg/dL                   | 163.4±157.8     | 115.0±80.5        | <0.001  |
| HDL-C, mg/dL                          | 42.4±10.2       | 47.2±10.9         | <0.001  |
| Anti-lipid medication, %              | 1.4             | 1.4               | NS      |
| FPG, mg/dL                            | 98.1±26.1       | 92.9±19.5         | <0.001  |
| Anti-diabetes medication, %           | 7.3             | 5.1               | <0.001  |
| Hormone replacement therapy, %        | 7.0             |                   |         |
| MetS, %                               | 30.9            | 27.8              | 0.016   |
| Self-reported CHD, %                  | 1.7             | 2.1               | NS      |

Values are presented as mean± standard deviation or percent. NS, not significant; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; FPG, fasting plasma glucose; MetS, metabolic syndrome; CHD, self-reported coronary heart disease.

RESULTS

Table 1 summarizes the comparison of clinical characteristics in both genders of the study population. There was no difference in age between men (mean, 46 years; range, 20 to 78 years) and women (mean, 44 years; range, 20 to 78 years). Frequency of current smoking in men was markedly higher compared to women (45.9% vs. 4.3%, P <0.001). Men were more obese compared to women in comparison of BMI and WC. SBP and DBP in men were higher than in women. However, there was no difference in chance of current anti-hypertensive medications between men and women. Serum TG in men was higher and serum HDL-C in men was lower than in women. However, there was no difference in chance of current anti-lipid medications between men and women. FPG and chance of currently taking anti-diabetes drugs in men was higher than in women. Prevalence of MetS defined by NCEP-Adult Treatment Panel III (ATP III) criteria in men was higher than that in women (30.9% in men vs. 27.8% in women, P = 0.016). Contrary to comparison of MetS, there was no difference in CHD prevalence between genders. Prevalence of self-reported CHD was 1.7% in men and 2.1% in women.
Table 2. Clinical characteristics according to self-reported coronary heart disease in each sex

| Characteristic          | Men (n=2,257) |       |       | Women (n=3,014) |       |       |
|-------------------------|---------------|-------|-------|----------------|-------|-------|
|                         | CHD (-) (n=2,219) | CHD (+) (n=38) | P value | CHD (-) (n=2,952) | CHD (+) (n=62) | P value |
| Age, yr                 | 46.5±14.0     | 62.1±8.3 | <0.001 | 45.9±14.7     | 60.6±11.0 | <0.001 |
| Current smoking, %      | 46.1          | 34.2   | NS    | 4.3           | 4.8     | NS    |
| Exercise 3x/wk, %       | 33.3          | 50.0   | 0.037 | 34.3          | 37.1    | NS    |
| Daily calories intake, kcal | 2,357±919     | 2,057±697 | 0.016  | 1,813±689     | 1,541±469 | 0.003  |
| Daily fat intake, g     | 49.2±36.7     | 33.9±37.9 | 0.021 | 37.1±28.5     | 21.7±13.8 | <0.001 |
| Daily alcohol intake, g | 18.0±45.2     | 8.9±29.4 | NS    | 2.6±11.4      | 1.7±6.2 | NS    |
| BMI, kg/m²              | 24.0±3.1      | 24.5±3.2 | NS    | 23.5±3.4      | 24.3±3.1 | 0.044  |
| Waist circumference, cm | 84.3±8.7      | 87.3±9.7 | NS    | 78.3±9.5      | 83.6±9.5 | <0.001 |
| SBP, mm Hg              | 122.5±15.8    | 134.4±22.6 | <0.001 | 115.6±18.0    | 130.7±19.5 | <0.001 |
| DBP, mm Hg              | 80.8±10.3     | 81.7±10.1 | NS    | 74.6±10.2     | 80.9±10.4 | <0.001 |
| Anti-hypertensive medication, % | 10.8 | 36.8 | <0.001 | 11.7 | 54.8 | <0.001 |
| Total cholesterol, mg/dL | 185.3±34.7    | 182.1±29.7 | NS    | 184.3±35.0    | 200.1±53.2 | 0.001  |
| LDL-C, mg/dL            | 113.4±30.2    | 111.5±29.9 | NS    | 114.7±29.9    | 126.8±44.0 | 0.042  |
| Triglyceride, mg/dL     | 163.8±158.9   | 150.3±67.8 | NS    | 114.0±78.0    | 164.2±140.7 | <0.001 |
| HDL-C, mg/dL            | 42.4±10.2     | 40.5±10.7 | NS    | 47.3±10.9     | 42.1±10.6 | <0.001 |
| Anti-lipid medication, % | 1.2           | 10.5   | 0.002 | 1.3           | 8.1     | 0.002 |
| FPG, mg/dL              | 98.0±26.1     | 106.1±24.4 | NS    | 92.7±19.3     | 102.5±26.4 | <0.001 |
| Anti-diabetes medication, % | 7.0           | 26.3   | <0.001 | 4.8           | 21.0    | <0.001 |
| Hormone replacement therapy, % | 6.9 | 8.1 | NS    |               |         |       |
| FRS                     | 8.11±6.23     | 13.31±2.59 | <0.001 | 4.68±7.64     | 12.02±4.75 | <0.001 |
| MetS, %                 | 30.6          | 50.0   | 0.013 | 27.1          | 61.3    | <0.001 |

Values are presented as mean±standard deviation or percent.

CHD, self-reported coronary heart disease; NS, not significant; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; FPG, fasting plasma glucose; FRS, Framingham risk score; MetS, metabolic syndrome.

Table 2 summarizes the data concerning clinical characteristics according to self-reported coronary heart disease in each sex. In men, participants with CHD were older, and showed higher SBP and FPG, and greater probability of current anti-hypertensive medications, anti-lipid medications, and anti-diabetes medications than participants without CHD. In women, participants with CHD were older, and showed higher SBP, cholesterol, TG, FPG, and greater probability of current anti-hypertensive medications, anti-lipid medications, and anti-diabetes medications than participants without CHD. There was no difference in chance of hormone replacement therapy between women with CHD and women without CHD (6.9% vs. 8.1%). In participants with self-reported CHD, prevalence of MetS was 50.0% in men and 61.3% in women. FRS was 13.31±2.59 in men and 12.02±4.75 in women.

ROC curves and their respective AUC were used to compare the ability of the FRS and the number of components of MetS predicting CHD in both genders (Fig. 1). In men, AUC of FRS (mean, 0.767; range, 0.708 to 0.819) was significantly larger than that of MetS (mean, 0.677; range, 0.541 to 0.713) (P<0.01). In women, AUC of FRS was comparable to that of MetS (mean, 0.777; range, 0.728 to 0.826 vs. mean, 0.733; range, 0.673 to 0.795) (not significant). When using a different criterion of FPG of 110 mg/dL or WC for MetS, similar results of ROC analyses were observed (data not shown).

In men, in the logistic regression analysis model with variables of five components of MetS (model 1), hypertension and abnormal glucose were significant determinants for CHD. However, after adjusting for age, current smoking (model 2), hypertension and abnormal glucose were not significant de-
In this nation-wide representative cohort of Koreans, MetS was comparable to the predictability of FRS in the ROC analysis for CHD in Korean women. However, the data showed that the FRS was more closely associated with CHD compared to MetS in Korean men, which suggests the limitation of MetS for the prediction of CHD in Koreans.

There have been a few reports comparing MetS and FRS for the prediction of CHD. FRS was a better predictor of CHD than MetS in a 20-year prospective study of 5,128 men in the United Kingdom aged 40 to 59 years with no history of CHD [23]. Results from a 13.7-year follow-up cohort study including 1,471 men and women in Scotland suggested that MetS is not a useful tool for predicting the risk of CHD [29]. In that study, the authors reported that the AUC for MetS was lower than that of FRS (0.576 vs. 0.752, P<0.001). Both results were applicable across nations.

MetS has been widely used for predicting CHD in clinical practice. Disappointingly, MetS was not superior to FRS for prediction of CHD in our Korean population. Especially in men, MetS was inferior to FRS. Considering that FRS is quite easily calculated compared to MetS, MetS has doubtful clinical usefulness for CHD. These results could be easily anticipated considering each criterion of MetS and FRS. In present study, the $R^2$ of the logistic regression analysis model for CHD with variables of five components of MetS was only 0.048 in men. However, after including age and current smoking as additional variables, the $R^2$ increased from 0.048 to 0.148 in men (Table 3). In women, hypertension was the only significant determinant for CHD in model 1 and even after adjusting for age and current smoking, the significance persisted in model 2. In model 2, age and hypertension were significant determinants for CHD in women. Contrary to the finding that the $R^2$ increased when age and current smoking were included as additional variables in men, in women, the $R^2$ in model 2 was comparable to that in model 1 (model 1, $R^2=0.124$; model 2, $R^2=0.147$) (Table 3).

DISCUSSION

In this nation-wide representative cohort of Koreans, MetS was comparable to the predictability of FRS in the ROC analysis for CHD in Korean women. However, the data showed that the FRS was more closely associated with CHD compared to MetS in Korean men, which suggests the limitation of MetS for the prediction of CHD in Koreans.

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Table 3. Logistic regression analyses for self-reported coronary heart disease in each sex

| Variable               | Model 1 (each variable of MetS) | Model 2 (age, current smoking, and variables of model 1) | Model 1 (each variable of MetS) | Model 2 (age, current smoking, and variables of model 1) |
|-----------------------|--------------------------------|------------------------------------------------------|--------------------------------|------------------------------------------------------|
|                       | OR (95% CI) | P value | OR (95% CI) | P value | OR (95% CI) | P value | OR (95% CI) | P value |
| Hypertension          | 2.23 (1.08-4.63) | 0.031 | 1.31 (0.63-2.73) | 0.405 | 6.42 (3.40-12.14) | <0.001 | 3.56 (1.78-7.12) | <0.001 |
| High triglyceride     | 0.83 (0.42-1.66) | 0.596 | 1.19 (0.59-2.42) | 0.631 | 0.99 (0.56-1.75) | 0.962 | 0.94 (0.53-1.65) | 0.817 |
| Low HDL-C             | 1.17 (0.60-2.30) | 0.647 | 1.13 (0.58-2.23) | 0.719 | 1.80 (0.93-3.47) | 0.083 | 1.71 (0.88-3.31) | 0.115 |
| Abnormal glucose      | 2.59 (1.31-5.10) | 0.006 | 1.70 (0.86-3.37) | 0.127 | 1.57 (0.91-2.74) | 0.108 | 1.37 (0.79-2.39) | 0.261 |
| Abdominal obesity     | 1.08 (0.53-2.20) | 0.844 | 1.02 (0.50-2.09) | 0.953 | 1.22 (0.68-2.19) | 0.506 | 1.10 (0.62-1.96) | 0.744 |
| Age                   | 1.09 (1.06-1.13) | <0.001 | 0.88 (0.44-1.77) | 0.716 | 1.04 (1.02-1.07) | <0.001 | 0.88 (0.27-2.91) | 0.833 |
| Current smoking       | 0.148 | 0.124 | 0.124 | 0.147 |

Definition of each component of metabolic syndrome: hypertension, systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or current anti-hypertensive medication; high triglyceride, serum triglyceride ≥150 mg/dL; low HDL-C, serum HDL-C <40 mg/dL for men and <50 mg/dL for women; abnormal glucose, fasting plasma glucose ≥100 mg/dL or current anti-diabetes medication; abdominal obesity, waist circumference ≥90 cm for men and 80 cm for women.

MetS, metabolic syndrome; OR, odds ratio; CI, confidence interval; HDL-C, high density lipoprotein cholesterol.
be explained by the fact that age was not included in the NCEP-ATP III criteria for MetS. It has been presumed that MetS is a positive stimulus of CHD prevention and effective management. However, the present results suggest that the main role of the concept of MetS may be greater public awareness and education of the necessity of co-management of CHD risk factors. Traditional risk factors, including age, smoking, and cholesterol, which are not included in the criteria for MetS, should be continuously stressed for CHD.

We did not consider current anti-lipid medications for detection of high TG or low HDL-C to define MetS. Because exact history for anti-lipid medication was not available in the KNHANES 2005, we could not distinguish anti-cholesterol medication from anti-triglyceride medication from the dataset. This may affect the study results. However, considering that the number of participants taking anti-lipid medications was relatively small (1.4%) and that anti-lipid medication could affect the prevalence of both FRS and MetS, we did not think this affected the major finding of this study. As other studies have reported that hormone replacement therapy is associated with CHD [30,31], we should consider the presence of hormone replacement therapy in the study of CHD.

In our study, there was no difference in hormone replacement therapy between participants with CHD and those without CHD (8.1% vs. 6.9%).

In-depth analyses of the KNHANES 2005 by the Centers for Disease Control and Prevention (KCDC) and the Korea Institute of Health and Social Affairs (KIHASA) [32] reported that age-adjusted self-reported CHD prevalence in men was 16.6/1,000 persons and 21.6/1,000 persons for women. In our analyses there was no difference in chances of taking anti-hypertensive medication or anti-lipid medication between men and women. However, SBP, DBP, serum TG, and FPG in men were higher than in women. A larger proportion of men took anti-diabetes medication compared to women. Moreover, about 46% of men were current smokers. In spite of the higher accompanying rate of CHD risk factors in men compared to women, there was no difference in self-reported CHD between genders. The reason for this finding is not clear. Further study is needed to elucidate the reason. There are also some limitations to this study. First, this was not a longitudinal follow-up study, but a cross-sectional observational study. In this study, we evaluated clinical and biochemical parameters of participants with past history of CHD in 2005 KNHANES. The relatively low $R^2$ in logistic regression analyses for CHD using well-established risk factors as variables suggests that this study has limitations. The second limitation could be recall bias. The presence of CHD was based on a questionnaire concerning a previous diagnosis of CHD, which was not confirmed by medical records. Neither an electrocardiogram nor a questionnaire concerning heart symptoms (e.g., Rose questionnaire) was available. If there was a difference in the degree of recall bias between genders, this difference could affect the prevalence of self-reported CHD. The strength of this study is that it was conducted based on nationally representative data of the civilian, non-institutionalized Korean population. However, with these limitations, we could not confirm the results of this study and another well-designed follow-up study will be needed.

In conclusion, we observed the inferiority of MetS compared to FRS for prediction of self-reported CHD using ROC analysis in Korean men. The usefulness of MetS for the prediction of CHD in the Korean population should be confirmed in another longitudinal follow-up study.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Metabolic syndrome, Framingham risk score, and CHD

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