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Original Article

Validity of muscle-to-fat ratio as a predictor of adult metabolic syndrome

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Abstract. [Purpose] This study was aimed at determining the validity of the muscle-to-fat ratio as an indicator for the prevention and management of metabolic syndrome by establishing an optimal cutoff value. [Subjects and Methods] Data from the first and second year of the fifth Korea National Health Nutrition Examination Survey, conducted by the Korean Ministry of Health and Welfare and Korean Centers for Disease Control and Prevention, were used. A total of 6,256 subjects were included in the study. Diagnostic accuracy was measured by using the area under the receiver operating characteristic curve. [Results] The receiver operating characteristic curve for the muscle-to-fat ratio, which represents the diagnostic power for predicting metabolic syndrome, was 0.713 in men and 0.721 in women. The optimal cutoff value for the prediction and diagnosis of metabolic syndrome was 3.09 kg/kg in men and 1.83 kg/kg in women. Intergroup differences based on the muscle-to-fat ratio indicated that the low-ratio group had higher values for all indicators of metabolic syndrome than the high-ratio group. [Conclusion] The muscle-to-fat ratio can be used as an indicator for the prediction and diagnosis of metabolic syndrome, and early prevention and management of metabolic syndrome can help in improving public health.

Key words: Metabolic syndrome, Body mass index, Waist-to-hip ratio

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INTRODUCTION

Recently, many countries have experienced an increase in the incidence of adult diseases due to overconsumption of nutrients, lack of exercise, and a westernized lifestyle. According to the 2010 Korean statistical report, the main causes of death in South Korea were cerebrovascular disease, heart disease, diabetes, and hypertensive diseases, accounting for 25.4% of all deaths; these conditions showed an advanced country-type disease pattern, and hence have emerged as an important national health issue. In the past, these diseases were managed independently. However, recent findings have revealed that they do not occur independently; that is, they are associated with each other. This has given rise to a new concept of the metabolic syndrome (MetS), which has recently gained much attention.

MetS is a cluster of diseases that can appear simultaneously: it includes insulin resistance or impaired glucose regulation, abdominal obesity, hypertension, and atherogenic dyslipidemia caused by elevated triglyceride and low-density lipoprotein cholesterol (LDL-C) levels. Moreover, MetS can lead to increased risks of diabetes and cardiovascular disease[1)]. Recent studies have reported that the odds of developing cardiovascular diseases and type 2 diabetes increase with MetS[2)], and this finding is significant from a clinical point of view. In South Korea, the prevalence of MetS in adults aged ≥30 years was 31.9% in men and 25.6% in women[3)]. Considering the current overconsumption of nutrients, westernization of food culture, lack of exercise, and aging population, the prevalence of MetS and onset of cardiovascular diseases caused by MetS is expected to continue increasing[4)], as is already observed in children and adolescents[5)]. Thus, there may be a rapid increase in the prevalence of MetS among young adults in the future. Therefore, it is important to prevent and treat MetS through early diagnosis, and the prevention and management of MetS-related risk factors are an important national public health issue.

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Although the pathogenesis of MetS has not been clearly identified, insulin resistance and abdominal obesity are known to play major roles. Abdominal obesity induces insulin resistance by increasing the free fatty acid level in the plasma, and when onset of hyperinsulinemia occurs from such insulin resistance, metabolic disorders such as dyslipidemia, hypertension, hyperuricemia, and coagulation disorder may develop6).

The risk factors of MetS are closely associated with obesity, which is showing an increasing trend worldwide. For the assessment of obesity, which is the primary cause of MetS, indicators such as body mass index (BMI) and waist circumference (WC) are most widely used as diagnostic criteria in most clinical and epidemiological studies. Recently, the waist-to-hip ratio and waist-to-height ratio are also used as indicators of obesity7–9).

The indicators currently used to predict MetS are the BMI, WC, and body fat percentage. Among these, BMI is the most commonly used owing to its convenience of use. However, studies have reported that BMI does not adequately reflect abdominal obesity and is not appropriate for predicting MetS10, 11). As BMI only considers the height and weight, it is limited in assessing muscular versus obese body types with the same weight. For example, even with a normal BMI, a person might have a high body fat percentage and abdominal obesity, whereas a person with a BMI in the obese range may have high muscle mass and low body fat. It is also difficult to accurately determine whether weight loss is due to loss of muscle or fat. Moreover, there has been a sudden recent increase in the number of persons with normal weight; however, their conditions are accompanied by metabolic complications. In such cases, BMI has several limitations as an indicator.

Studies have reported that WC tends to increase faster than does BMI during the same period, which makes WC inaccurate12, 13), and the odds ratio (OR) of developing MetS can be underestimated in shorter persons, and conversely, the OR can be overestimated in taller persons, depending on the height of persons with similar WC14). The BMI, WC, and body fat percentage are focused solely on body fat mass and do not consider the body muscle mass, which accounts for a large portion of the body composition.

Muscles, which account for approximately 40–50% of the body, play a major role in glucose metabolism and insulin resistance. Recently, studies have reported correlations between low muscle mass and risk factors for cardiovascular disease such as diabetes, hypertension, and dyslipidemia. A decrease in muscle mass has been elucidated as a risk factor for MetS and cardiovascular diseases15–17). Moreover, sarcopenic obesity, a condition involving both sarcopenia and obesity, increases the OR for diabetes and MetS more than does general obesity18). Moreover, relative muscle loss is associated with insulin resistance and the risk of diabetes19), and patients with a normal BMI but low muscle mass showed a higher rate of hypertension and glucose tolerance than did obese persons with high muscle mass20). Body fat mass and body muscle mass are believed to have a significant influence on MetS. However, studies on the effects of muscle mass on MetS have mostly been conducted in elderly subjects with sarcopenia, and no such studies have thus far been conducted on a wide range of age groups including the entire adult population. Therefore, to increase the diagnostic accuracy of the standard for predicting MetS, not only body fat mass, which is known to influence MetS, but also body muscle mass should be considered for the diagnosis of this condition.

Recently, measuring devices that use bioelectrical impedance analysis with proven accuracy have been widely used in the field, and these devices can easily measure body fat and muscle mass, which can be employed to calculate the muscle-to-fat ratio (MFR). Therefore, the MFR can be easily used to predict MetS, and MetS can be predicted easily without a clinical examination such as a blood test. Moreover, such prediction can lead to the early detection and preventive management of MetS, and can help improve national health.

The present study used raw data from the Korean National Health and Nutrition Examination Survey (KNHANES) to examine the validity of the MFR as an indicator for predicting MetS in Korean adults. With the validity confirmed, this study aimed to help improve the predictive index for the prevention and management of MetS by determining an optimal cutoff value.

SUBJECTS AND METHODS

Subjects

This study used the raw data from the first and second year (2010 and 2011, respectively) of the fifth KNHANES, conducted by the Korean Ministry of Health and Welfare and Korean Centers for Disease Control and Prevention. The study participants were selected by using a stratified multistage probability sampling method based on residential area, gender, age group, and housing type. Health behavior, medical examination, and nutrition surveys were conducted on a total of 384 sample lots, consisting of 7,600 households. Among the 21,527 residents, 17,476 responded to the survey (response rate, 81.2%). Among the respondents who were between the ages of 20 and 64 years and met the inclusion criteria of the study, 11,219 (64.2%) were excluded for the following reasons: noncompliance with the fast time, pregnancy, or missing data in any of the analysis parameters. Finally, 6,256 participants (35.8%; 2,648 men, 3,608 women) were selected for the study. The study was approved by the institutional review board (IRB) of the Korea Centers for Disease Control and Prevention (IRB approval no. 2010-02CON-21-C for 2010, 2011-02CON-06-C for 2011).

Methods

The diagnostic criteria for MetS used in the present study were based on the criteria from the National Cholesterol

Education Program Adult Treatment Panel III, which were revised. In addition, the patients had to meet three or more of the following five criteria for MetS to be diagnosed: (i) WC: Asian WC criteria, ≥90 cm for men and ≥85 cm for women; (ii) blood pressure: systolic, diastolic pressure of 130/85 mm Hg or higher, or currently taking hypertension medications; (iii) triglycerides: triglyceride level ≥150 mg/dL or currently taking medications for the treatment of hyperlipidemia, (iv) high-density lipoprotein (HDL): HDL level ≤40 mg/dL in men and ≤50 mg/dL in women; (v) blood glucose: fasting blood glucose ≥100 mg/dL or currently taking diabetes medication or insulin.

For the demographic characteristics of the subjects, including age, gender, history of smoking, total calorie intake, and alcohol consumption level, self-reported data based on the questionnaire were used. For physical activity level, the Korean version of condensed International Physical Activity Questionnaire (IPAQ) was used. The IPAQ comprises vigorous, moderate, and walking activities, and its reliability and validity as a self-reporting physical activity questionnaire are widely recognized[21)]. With the data collected through the IPAQ, the total physical activity level was calculated by using the equations shown in Table 1.

An experienced evaluator measured the subjects, who took off their clothes and wore a gown, according to the anthropometric measurements guidelines specified in the KNHANES. Height was measured with a height-measuring instrument (seca225; Seca, Germany) with the participant in the upright position, and weight was measured with a scale (GL-6000-20; G-tech, Korea) while the participant was barefooted and inhaling. The BMI was calculated as the weight divided by the square of the height (kg/m^2), whereas the WC was measured by feeling for the bottom of the rib cage and top of the iliac ridge to wrap a tape measure (Seca 200; Seca, Germany) around the waist in the middle of the two reference points, making sure that the tape measure was parallel to the floor, and then measuring the value in the exhaled state with the tape measure not pressing down on the skin. Hip circumference was measured from the widest part of the rear hip, with the tape placed parallel to the floor.

Blood pressure measurements were taken from the right arm of the participant while in the sitting position, by using a mercury sphygmomanometer (Baumanometer Desk model 0320; Baum, USA), with the systolic and diastolic blood pressures measured twice each. Moreover, for biochemical blood analysis, the participants were instructed to fast from 7 PM on the day before blood collection and not to drink or eat anything, except water, on the day of blood collection. Blood was drawn from the median cubital vein of the participants, and the collected blood was centrifuged on site to separate the plasma, after which the samples were stored in a refrigerator. Blood analysis was conducted at the Neodin Medical Institute. Subsequently, triglyceride, fasting glucose, total cholesterol, LDL-C, and HDL-C levels were measured by using an automatic analyzer (Hitachi Automatic Analyzer 7600; Hitachi, Japan) and by means of an enzymatic method.

The muscle and fat mass of the participants were measured by using a measuring device (Discovery-W; Hologic, USA) that utilized dual-energy x-ray absorptiometry. The MFR was calculated on the basis of the measured muscle and fat mass.

To confirm the predictive power of MFR on MetS, the analysis of receiver operating characteristics (ROCs) was conducted by using the MedCalc version 15.8 program (MedCalc Software bvba, Belgium).

An ROC curve is defined by both sensitivity, which represents the probability of actually finding a person with the disease by using a certain diagnostic methods, and specificity, which represents the probability of actually finding a nondiseased person. An ROC curve is drawn by marking the 1-specificity and sensitivity of each cutoff point on the X- and Y-axes, respectively, and the accuracy of diagnosis is measured with the area under the ROC curve (AUC). An AUC of 1 indicates a perfect diagnostic examination, whereas a value of ≤0.5 indicates an inaccurate diagnostic examination[22)]. The present study used the curve to calculate the AUC value, sensitivity, specificity, and optimal prediction cutoff points.

On the basis of the calculated optimal cutoff points, the mean and standard deviation were calculated by means of statistical analysis (SPSS version 21.0; IBM Corp, USA), and the χ^2-test and independent t-test were used to investigate intergroup differences. To identify the relative risk of MetS based on the MFR, ORs were derived through logistic regression analysis with adjustment for various influencing factors; all statistical significance levels were set to 0.05.

RESULTS

The general characteristics of the participants are shown in Table 2. On analyzing the differences between men and women for each variable, the results showed that men had a significantly higher height; weight; BMI; WC; triglyceride level; total cholesterol level; LDL-C level; fasting blood glucose level; systolic blood pressure; diastolic blood pressure; total physical

Table 1. Calculation of physical activity level

Category	Calculation method
Walking exercise (MET-min/wk)	3.3 * walking exercise time (min) * walking exercise reps (reps/wk)
Moderate exercise (MET-min/wk)	4.0 * moderate exercise time (min) * moderate exercise reps (reps/wk)
Vigorous exercise (MET-min/wk)	8.0 * vigorous exercise time (min) * vigorous exercise reps (reps/wk)
Total physical activity level (MET-min/wk)	Walking exercise + moderate exercise + vigorous exercise

MET: metabolic equivalent of task; min: minutes; wk: week; reps: repetitions activity level; Alcohol Use Disorder Identification Test (AUDIT) score; total muscle mass; MFR; current smoking rate; abdominal obesity; and rates of hypertriglyceridemia, hyperglycemia, hypertension, and MetS than women. On the other hand, the HDL-C level, total fat mass, and LDL-C were significantly higher in women than in men.

The results of the ROC analysis on the MFR for the diagnostic prediction of MetS are shown in Table 3. The AUC value of the MFR for MetS prediction was 0.713 (95% confidence interval [CI]: 0.696–0.730) in men and 0.721 (95% CI: 0.706–0.736) in women, indicating a relatively accurate prediction. Moreover, the optimal prediction cutoff point was 3.09 kg/kg for men and 1.83 kg/kg for women, with a sensitivity and specificity of 68.62% and 63.76% for men and 76.04% and 58.40% for women, respectively. Furthermore, the AUC value of the MFR for MetS prediction for men was 0.787 in the 20s age range, 0.771 in the 30s, 0.748 in the 40s, 0.686 in the 50s, and 0.699 in the 60s. In addition, the AUC value of the MFR for MetS prediction for women was 0.887 in the 20s age range, 0.776 in the 30s, 0.679 in the 40s, 0.693 in the 50s, and 0.654 in the 60s. The AUC value of MFR for MetS prediction tends to decrease with age.

The intergroup differences based on optimal cutoff points for the diagnostic prediction of MetS are shown in Table 4. To analyze the differences in each indicator, for men, the optimal cutoff point of 3.09 kg/kg was used to categorize those

Table 2. General characteristics of the participants

Variables	Men (n = 2,648)	Women (n = 3,608)
Age (years)	43.7 ± 12.1	43.4 ± 12.2
Height (cm)	171.0 ± 6.2	158.1 ± 5.8***
Weight (kg)	70.8 ± 10.6	57.8 ± 8.9***
BMI (kg/m^2)	24.2 ± 3.1	23.1 ± 3.5***
Waist circumference (cm)	84.4 ± 8.9	77.2 ± 9.7***
Triglyceride (mg/dL)	162.6 ± 42.5	105.1 ± 69.1***
Total cholesterol (mg/dL)	189.8 ± 37.2	187.8 ± 35.5*
LDL cholesterol (mg/dL)	114.2 ± 32.4	111.4 ± 31.1*
HDL cholesterol (mg/dL)	46.0 ± 10.5	51.8 ± 11.1***
Fasting blood glucose (mg/dL)	98.9 ± 23.8	93.2 ± 17.8***
Systolic blood pressure (mmHg)	121.1 ± 15.1	114.8 ± 16.9***
Diastolic blood pressure (mmHg)	80.8 ± 10.5	74.5 ± 10.0***
Total physical activity level (MET-min/wk)	2,819.8 ± 4,040.4	2,071.3 ± 3,325.7***
Total calorie intake (kcal/day)	2,555.5 ± 1,018.4	1,771.0 ± 657.5***
AUDIT (points)	10.4 ± 7.4	3.8 ± 4.6***
Total muscle mass (kg)	51.2 ± 6.4	35.8 ± 4.5***
Total body fat mass (kg)	16.4 ± 5.6	19.6 ± 5.4***
Muscle-to-fat ratio (kg/kg)	3.5 ± 1.3	1.9 ± 0.5***
n (%)		
Smoking	1,233 (46.7%)	191 (5.3%)***
Abdominal obesity	669 (25.4%)	737 (20.6%)***
High triglyceride	1,088 (41.1%)	710 (19.7%)***
Low HDL cholesterol	854 (32.8%)	1,622 (46.1%)***
Elevated blood glucose	804 (30.4%)	598 (16.6%)***
Elevated blood pressure	1,169 (44.1%)	965 (26.7%)***
Metabolic syndrome	800 (30.2%)	651 (18.0%)***

Data are presented as mean ± SD or number (percentage). *Significant difference between men and women (*$p < 0.05$, ***$p < 0.001$). BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; MET: metabolic equivalent of task; AUDIT: Alcohol Use Disorder Identification Test

Table 3. ROC analysis of muscle-to-fat ratio for diagnostic prediction of metabolic syndrome

	AUC (95% CI)	Cutoff	Sensitivity	Specificity
Men	0.7 (0.7–0.7)	3.1	68.6	63.8
Women	0.7 (0.7–0.7)	1.8	76.0	58.4

AUC: area under curve (or receiver operating characteristic); CI: confidence interval who were ≤3.09 kg/kg as the low-ratio group (LRG) and those who were >3.09 kg/kg as the high-ratio group (HRG). The results showed that the weight, BMI, WC, triglyceride level, total cholesterol level, LDL-C level, fasting blood glucose level, systolic blood pressure, diastolic blood pressure, body fat mass, abdominal obesity, hypertriglyceridemia, hyperglycemia, hypertension, low HDL-C level, and MetS were significantly higher in the LRG, whereas the HDL-C level, MFR, total physical activity level, total calorie intake, and smoking rate were significantly lower in the LRG than in the HRG.

For women, the optimal cutoff point of 1.83 kg/kg was used for categorizing those who were ≤1.83 kg/kg as the LRG and those who were >1.83 kg/kg as the HRG. The results showed that age, weight, BMI, WC, triglyceride level, total cholesterol level, LDL-C level, fasting blood glucose level, systolic blood pressure, diastolic blood pressure, body fat mass, abdominal obesity, hypertriglyceridemia, hyperglycemia, hypertension, low HDL-C, and MetS were significantly higher in the LRG, whereas the height, HDL-C level, total calorie intake, and MFR were significantly lower in the LRG than in the HRG.

To identify the effects of each factor of MetS on the OR according to the MFR groups, logistic regression analysis was performed by adjusting for influencing factors such as age, height, weight, AUDIT score, total physical activity level, total calorie intake, and smoking status (Table 5).

Table 4. Intergroup differences based on optimal cutoff points for the diagnostic prediction of metabolic syndrome

Variables	Low ratio group	High ratio group
Men	(n = 1,217)	(n = 1,431)
Age (years)	44.1 ± 11.8	43.4 ± 12.4
Height (cm)	171.0 ± 6.0	171.00 ± 6.4
Weight (kg)	75.4 ± 10.3	66.9 ± 9.1***
BMI (kg/m^2)	25.7 ± 2.9	22.8 ± 2.6***
Waist circumference (cm)	89.1 ± 7.7	80.4 ± 7.9***
Triglyceride (mg/dl)	184.5 ± 135.6	143.8 ± 145.7***
Total cholesterol (mg/dl)	195.3 ± 37.5	185.0 ± 36.3***
LDL cholesterol (mg/dl)	119.4 ± 33.1	110.1 ± 31.3***
HDL cholesterol (mg/dl)	43.7 ± 9.4	48.0 ± 11.0***
Fasting blood glucose (mg/dl)	101.1 ± 22.3	97.0 ± 25.0***
Systolic blood pressure (mmHg)	122.4 ± 14.6	119.9 ± 15.5***
Diastolic blood pressure (mmHg)	82.1 ± 10.3	79.6 ± 10.5***
Total physical activity level (MET-min/wk)	2,460.9 ± 3,401.1	3,126.1 ± 4,495.0***
Total calorie intake (kcal/day)	2,467.9 ± 980.3	2,627.0 ± 1,043.5***
AUDIT (points)	10.5 ± 7.4	10.3 ± 7.5
Total muscle mass (kg)	51.4 ± 6.5	51.0 ± 6.4
Total body fat mass (kg)	20.8 ± 4.4	12.7 ± 3.3***
Muscle to fat ratio (kg/kg)	2.5 ± 0.4	4.3 ± 1.2***
n (%)		
Smoking	541 (44.6%)	692 (48.6%)*
Abdominal obesity	523 (43.3%)	145 (10.2%)***
High triglyceride	652 (53.6%)	435 (30.4%)***
Low HDL cholesterol	493 (40.9%)	361 (25.8%)***
Elevated blood glucose	452 (37.1%)	352 (24.6%)***
Elevated blood pressure	628 (51.6%)	540 (37.7%)***
Metabolic syndrome	548 (44.9%)	252 (17.6%)***
Women	(n = 1,724)	(n = 1,880)
Age (years)	45.7 ± 12.3	41.3 ± 11.7***
Height (cm)	157.1 ± 5.6	159.1 ± 5.8***
Weight (kg)	61.8 ± 9.1	54.0 ± 6.8***
BMI (kg/m^2)	25.0 ± 3.4	21.4 ± 2.5***
Waist circumference (cm)	82.1 ± 9.3	72.6 ± 7.5***
Triglyceride (mg/dl)	120.8 ± 74.2	90.7 ± 60.7***
Total cholesterol (mg/dl)	195.3 ± 36.3	180.9 ± 33.3***
LDL cholesterol (mg/dl)	120.5 ± 31.4	103.3 ± 28.4***
HDL cholesterol (mg/dl)	49.7 ± 10.5	53.8 ± 11.2***
Fasting blood glucose (mg/dl)	95.4 ± 18.4	91.2 ± 16.8***

Table 4. Continued

Variables	Low ratio group	High ratio group
Systolic blood pressure (mmHg)	118.2 ± 17.3	111.8 ± 15.8***
Diastolic blood pressure (mmHg)	76.3 ± 10.2	72.8 ± 9.5***
Total physical activity level (MET-min/wk)	2,125.4 ± 3,356.1	2,016.6 ± 3,286.7
Total calorie intake (kcal/day)	1,702.9 ± 622.1	1,834.4 ± 683.3***
AUDIT (points)	3.7 ± 4.7	3.9 ± 4.5
Total muscle mass (kg)	35.9 ± 4.9	35.6 ± 4.1
Total body fat mass (kg)	23.5 ± 4.6	16.00 ± 3.2***
Muscle to fat ratio (kg/kg)	1.6 ± 0.2	2.3 ± 0.4***
n (%)		
Smoking	97 (5.7%)	94 (5.0%)
Abdominal obesity	626 (36.5%)	111 (5.9%)***
High triglyceride	487 (28.3%)	222 (11.8%)***
Low HDL cholesterol	910 (54.0%)	710 (38.8%)***
Elevated blood glucose	381 (22.1%)	215 (11.5%)***
Elevated blood pressure	612 (35.5%)	352 (18.7%)***
Metabolic syndrome	494 (28.7%)	156 (8.3%)***

Data are presented as mean ±SD or number (percentage). *Significant difference between the low-ratio group and the high-ratio group (*$p < 0.05$, ***$p < 0.001$). BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; MET: metabolic equivalent of task; AUDIT: Alcohol Use Disorder Identification Test

Table 5. Logistic regression analysis for metabolic syndrome

			High-ratio group	Low-ratio group	
				Odds ratio	95% CI
Men	Hypertension	Unadjusted	1.0 (Reference)	1.75***	1.50–2.05
		Adjusted		1.19	0.96–1.97
	Diabetes	Unadjusted		1.80***	1.53–2.13
		Adjusted		1.08***	1.07–1.09
	Abdominal obesity	Unadjusted		6.73***	5.48–8.27
		Adjusted		2.66***	1.93–3.68
	Hypertriglyceridemia	Unadjusted		2.64***	2.25–3.09
		Adjusted		1.79***	1.45–2.21
	Low HDL-C level	Unadjusted		1.99***	1.69–2.35
		Adjusted		1.45***	1.16–1.81
	Metabolic syndrome	Unadjusted		3.82***	3.20–4.55
		Adjusted		1.98***	1.55–2.54
Women	Hypertension	Unadjusted	1.0 (Reference)	2.38***	2.05–2.78
		Adjusted		1.05	0.83–1.33
	Diabetes	Unadjusted		2.19***	1.83–2.63
		Adjusted		1.05***	1.04–1.06
	Abdominal obesity	Unadjusted		9.08***	7.32–11.26
		Adjusted		2.10***	1.48–2.98
	Hypertriglyceridemia	Unadjusted		2.94***	2.46–3.50
		Adjusted		1.55***	1.21–1.99
	Low HDL-C level	Unadjusted		1.85***	1.61–2.11
		Adjusted		1.23*	1.02–1.47
	Metabolic syndrome	Unadjusted		4.43***	3.60–5.39
		Adjusted		1.46*	1.09–1.96

Adjusted data were tested by using multivariate logistic regression analysis after adjustment for age, height, weight, AUDIT score, total physical activity level, total calorie intake, and smoking. *: Significant difference compared with the high-ratio group (*$p < 0.05$, ***$p < 0.001$). LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol

In men, logistic regression analysis without adjusting for influencing factors showed that compared with the group with a higher MFR, the group with a lower MFR had significantly higher ORs for developing diseases related to MetS, such as hypertension (1.759 times), diabetes (1.809 times), abdominal obesity (6.735 times), hypertriglyceridemia (2.640 times), low HDL-C level (1.998), and MetS (3.820). After adjusting for each of the influencing variables, logistic regression analysis showed that compared with the group with a higher MFR, the group with a lower MFR had significantly higher ORs for developing diseases related to MetS, such as diabetes (1.084 times), abdominal obesity (2.668 times), hypertriglyceridemia (1.795 times), low HDL-C level (1.451 times), and MetS (1.988 times). The OR for hypertension was 1.193 times higher in the group with a lower MFR than in the group with a higher MFR; however, this result was not statistically significant.

In women, logistic regression analysis without adjusting for influencing factors showed that compared with the group with a higher MFR, the group with a lower MFR had significantly higher ORs for developing diseases related to MetS, such as hypertension (2.389 times), diabetes (2.197 times), abdominal obesity (9.080 times), hypertriglyceridemia (2.940 times), low HDL-C level (1.851 times), and MetS (4.438 times). On adjusting for each of the influencing variables, logistic regression analysis showed that compared with the group with a higher MFR, the group with a lower MFR had significantly higher ORs for developing diseases related to MetS, such as diabetes (1.055 times), abdominal obesity (2.106 times), hypertriglyceridemia (1.559 times), low HDL-C level (1.231 times), and MetS (1.463 times). The OR for hypertension was 1.052 times higher in the group with a lower MFR than that in the group with a higher MFR; however, this result was not statistically significant.

DISCUSSION

MetS refers to metabolic disorders accompanied by abdominal obesity, dyslipidemia, hypertension, and hyperglycemia[23)]. Prevention of MetS is important because this condition can acutely diminish the quality of life and shorten a person's life expectancy by causing cardiovascular disease, type 2 diabetes, and various cancers[24)]. To prevent MetS, early prediction and diagnosis are important, and the indicators currently used for such purposes are the BMI, WC, and body fat mass.

Although the BMI is the most commonly used indicator for predicting obesity, it does not adequately reflect the percentage of muscles or fat distribution within the body according to a person's weight, which has an impact on the person's health[25)]. Even among persons with the same BMI, the muscle mass or abdominal fat mass may vary, and premenopausal women are known to have abdominal fat mass that is about half of that in men[26)]. Moreover, the use of WC as the only indicator has shortcomings: the ORs for diseases may be underestimated or overestimated depending on the height of persons with a similar WC[14)]. Therefore, although the amount and distribution of fat are important factors in expressing and predicting the OR for obesity and MetS-related diseases, new indicators should be tested.

Muscles, which account for a major portion of the body, are quantitatively important and involved in the metabolism of glucose and fat, and hence, determination of the body muscle mass may help in preventing and treating obesity and insulin resistance. When body muscle mass is low or has decreased, it can cause resistance to insulin, and may ultimately facilitate the onset of MetS[27)]. Therefore, muscle mass, in addition to fat mass, is an important factor that must be considered in the prediction and diagnosis of MetS. Thus, the MFR, which simultaneously considers both body fat and muscle mass, may be a potential indicator for the prediction and diagnosis of MetS.

The present study used raw data from the KNHANES, which are nationally representative. The hypothesis in this study was that MFR could predict MetS. Therefore, the present study verified whether the MFR is capable of predicting and diagnosing MetS, and identified the optimal cutoff values of the MFR, which were then used to analyze the effects of the MFR on the components of MetS. The results of the study showed that in the ROC analysis of the MFR for the prediction of MetS, the AUC, which indicates the accuracy of diagnosis, was 0.713 in men and 0.721 in women. Normally, tests can be categorized on the basis of the AUC values as perfect (AUC = 1.0), very accurate ($0.9 < \text{AUC} < 1$), moderately accurate ($0.7 < \text{AUC} \leq 0.9$), less accurate ($0.5 < \text{AUC} \leq 0.7$), or noninformative (AUC = 0.5)[22)], and as the results of the present study corresponded to a moderately accurate diagnostic test, the MFR was found to be useful in the prediction and diagnosis of MetS.

The prediction cutoff point of MFR was found to be 3.09 kg/kg in men and 1.83 kg/kg in women, with high sensitivity and specificity at the cutoff points for both genders. Thus, these cutoff points can be used for predicting MetS. When comparisons were made by categorizing the participants into LRG and HRG on the basis of each cutoff point, all MetS-related indicators and the prevalence of MetS-related diseases were significantly higher in the LRG than in the HRG. Moreover, when influencing factors such as age, height, weight, AUDIT score, total physical activity level, total calorie intake, and smoking status were adjusted to determine the relative OR for MetS based on MFR groups, men and women showed 1.988 and 1.463 times higher ORs, respectively, for MetS in the LRG than in the HRG. These findings demonstrated that an MFR lower than the cutoff point had a negative effect on MetS-related factors, resulting in easy exposure to MetS, whereas an MFR higher than the cutoff point decreased the OR for MetS. Consequently, to prevent MetS, it is important to decrease body fat; however, an adequate amount of or an increase in muscle mass should be present. These findings were similar to the results of other studies that reported that a 10% increase in the skeletal muscle mass reduced the OR for prediabetes by 12% and the homeostatic model assessment for insulin resistance by 11%[19)] among adults with a normal BMI, and that low muscle mass showed a negative effect on cardiovascular risk factors and increased the prevalence of cardiovascular diseases[15)], but low muscle mass and strength elevated the serum insulin level to affect the development of MetS[28)]. In conclusion, for the prevention of MetS, in addition to reduction of body fat mass, an increase in body muscle mass is necessary.

To increase the muscle mass in the body, resistance exercise must be performed. Long-term resistance exercise has been reported to increase muscle mass, enhance insulin sensitivity by increasing glucose transporter protein 4 inside the skeletal muscles, decrease the blood glucose and lipid levels[29, 30], and enhance blood glucose regulation and insulin action in patients with type 2 diabetes[31, 32]. In addition, a recent study reported that resistance exercise is effective for blood glucose regulation in patients with type 2 diabetes[33]. Therefore, an increase in body muscle mass decreases the risk of insulin resistance and diabetes, which ultimately lowers the risk of MetS.

The present study was a cross-sectional study that used data from the KNHANES; the analyses were performed by using government study data that are representative of Koreans, and therefore, the findings of the present study present new indicators for the prediction/diagnosis of MetS that are absolutely needed for the early prevention of this condition. There are no studies to date that verified the validity of our new indicator, MFR, which simultaneously considers both body fat mass and muscle mass, both of which have a major influence on MetS. Thus, to our knowledge, the present study is the first to use MFR as an indicator and is of great significance.

Obesity, a component of MetS that is also a major cause of type 2 diabetes, hypertension, and dyslipidemia, is a risk factor that can be adjusted for. If lifestyle modifications, such as regular exercise and eating habits, can be achieved in the early stages, MetS prevention measures may have a significant impact[34]. For such prevention, early prediction and diagnosis with a simple indicator is necessary, and the MFR may be used as an excellent indicator for this purpose.

The present study has some limitations. Because it was a cross-sectional study, we could not infer on any relations. Furthermore, as the KNHANES data used in the present study were from a self-report questionnaire on demographic variables and patient history, the reliability of responses may be limited. Moreover, the association between obesity and diabetes may differ according to the types of muscle fibers[35]; however, the present study developed the index with only muscle mass and did not consider muscle strength or quality.

Future studies should apply the MFR derived in the present study to different age groups, and compare it to other indicators to determine its capability for diagnostic prediction. Furthermore, the efficacy of using a combination of various predicative indicators on the diagnosis of MetS should be assessed, and continued future studies with application for various ethnic groups are also needed to present more accurate reference points.

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