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ORIGINAL

Association of the leptin to high-molecular-weight adiponectin ratio with metabolic syndrome

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Abstract. Recent studies have reported that leptin and adiponectin are associated with metabolic syndrome. The leptin/adiponectin ratio has been suggested as an atherosclerotic index. The objective of this study was to compare the degree of association of metabolic syndrome with adiponectin levels, leptin levels, leptin/adiponectin ratio, and leptin/high-molecular-weight (HMW) adiponectin ratio. The study population included 3272 Koreans (men: 1915, women: 1357; age, 30–84 years), who had visited the Health Examination Center. Adipokines were divided into quartiles, and metabolic syndrome was defined by the National Cholesterol Education Program Adult Treatment Panel-Ⅲ (NCEP ATP Ⅲ). A logistic regression model was fitted to establish the association between adipokines and metabolic syndrome. Adipokines, such as adiponectin, HMW adiponectin, and leptin, were found to be statistically related to metabolic syndrome. Compared to the lowest quartile, the leptin/HMW adiponectin ratio in the highest quartile was associated with a 5-fold increase in the probability of prevalent metabolic syndrome, which was independent of age, smoking status, exercise, low-density lipoprotein (LDL) cholesterol, and body mass index. There was a linear increase in the leptin/HMW adiponectin ratio as the number of metabolic syndrome components increased. The leptin/HMW adiponectin ratio had the highest odds ratio in women. In addition, compared to adiponectin or leptin alone, the AUC of the leptin/adiponectin ratio and leptin/HMW adiponectin ratio was higher for metabolic syndrome. We may suggest that the leptin/HMW adiponectin ratio is not superior to other adipokine markers, but is as effective as the leptin/total adiponectin ratio.

Key words: Adiponectin, High-molecular-weight adiponectin, Leptin, Leptin/adiponectin ratio, Metabolic syndrome

THE RECENT increase in the prevalence of cardiovascular disease is regarded as an important medical problem in Korea. In general, metabolic syndrome affects approximately one-quarter of Koreans [1] and has become a leading health concern due to its link to cardiovascular disease. Metabolic syndrome occurs concurrently in people with conditions such as abdominal obesity, dyslipidemia, hypertension, and elevated insulin levels. Furthermore, it increases the risk of cardiovascular disease [2-4]. As a result, scientific interest has increased with respect to traditional and alternative factors that may be related to metabolic syndrome, such as subclinical inflammation, microalbuminuria, nonalcoholic fatty liver disease, and adipokines [5].

Leptin and adiponectin are considered to have a role in the regulation of energy metabolism. This is because both leptin and adiponectin are adipokines that are closely associated with insulin resistance [6-10]. Leptin is involved in the regulation of body weight and energy expenditure, with increased levels being recorded in cases of obesity [11-13]. High levels of circulating plasma leptin are associated with many features of metabolic syndrome, such as abdominal obesity, insulin resistance, and high blood pressure. In comparison, increased adiponectin levels cause a reduction in abdominal fat levels, and are associated with insulin sensitivity [14-20]. Adiponectin is an adipocyte-specific secretory protein, which possesses antidiabetic and antiatherosclerotic properties. Adiponectin exists in multimeric form in serum, and high-molec-

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ular-weight (HMW) adiponectin is considered as the major active form of the protein.

A combination of adiponectin and leptin as an index of insulin sensitivity was first proposed in 2003 [21]. Subsequently, many investigators have reported that the adiponectin/leptin ratio (or leptin/adiponectin ratio) is a relevant and reliable marker of insulin resistance in comparison with other parameters [20]. However, the effect of adipokines on metabolic syndrome and insulin resistance seems to stem from the influence of a combination of adipokines, rather than from the effect of a single adipokine [22]. Recent studies have suggested that the leptin/adiponectin ratio may be a useful parameter for assessing insulin resistance in patients with and without diabetes [23, 24]. However, previous studies on the association between the leptin/adiponectin ratio and metabolic syndrome had several limitations, including a small sample size and very specific sample populations, such as groups with only children [25], elderly subjects [10], or male subjects [26]. In addition, few studies have reported a relationship between metabolic syndrome and adiponectin, leptin only, or leptin to total adiponectin ratio. Furthermore, HMW adiponectin is a better indicator of metabolic syndrome than is total adiponectin [27]. The association between the leptin to HMW adiponectin ratio and metabolic syndrome is poorly understood, owing to limited reports on this issue. Therefore, it is necessary to investigate whether the leptin/HMW adiponectin ratio is associated with metabolic syndrome. This study attempts to determine whether the leptin/HMW adiponectin ratio has a stronger association with metabolic syndrome.

The purpose of this study was to examine the association between the serum leptin/adiponectin ratio and metabolic syndrome, and to compare the strength in the relationship of metabolic syndrome with respect to adiponectin, leptin, and the leptin/HMW adiponectin ratio in the Korean population.

Patients and Methods

Study participants

Between 2006 and 2007, 9995 Korean men and women over the age of 20 years participated in the Korean Metabolic Syndrome Research Initiative, with routine health examinations at the Health Promotion Center of University Hospitals [28, 29]. Of the participants, 3487 individuals were randomly selected for the measurement of serum leptin, total adiponectin, and HMW adiponectin. The analysis excluded subjects for whom information was missing with respect to the components of metabolic syndrome, such as waist circumference, triglycerides, high-density lipoprotein (HDL) cholesterol, and/or blood pressure. In addition, subjects with a history of cardiovascular disease, stroke, or any type of cancer were also excluded. As a result, the final study population comprised 3272 participants (1915 men and 1357 women). The Institutional Review Board of Yonsei University College of Medicine approved the design of study, and all the participants provided written informed consent for the study.

Clinical and biochemical assessment

For clinical chemistry assays, serum samples were obtained from peripheral venous blood samples obtained after a 12-hour fast, and then stored at -70 °C for 2 hours. Biomarkers for fasting blood glucose, total cholesterol, triglyceride, and HDL cholesterol levels were measured using a Hitachi-7600 analyzer (Hitachi Ltd., Tokyo). In 2006 and 2007, information was obtained through self-administered questionnaires on reproductive history, medical history, and lifestyle factors, including smoking, alcohol consumption, and physical activity. The participant's weight and height were measured while they wore light clothing. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). Waist circumference was measured midway between the lower rib and iliac crest.

Definition of metabolic syndrome

The standard definition of metabolic syndrome requires the presence of at least 3 of the 5 associated components according to the Third Adult Treatment Panel (ATP III) of the National Cholesterol Education Program (NCEP) [30]. However, waist circumference cutoffs as an index of abdominal obesity have been modified for Asian populations [31].

The following factors were used to define metabolic syndrome:

(1) Abdominal obesity: a waist circumference of ≥90 cm for men and ≥80 cm for women.
(2) Triglyceride: a triglyceride level of ≥150 mg/dL.
(3) Low HDL cholesterol: HDL cholesterol of <40 mg/dL for men and <50 mg/dL for women.
(4) High blood pressure: a systolic blood pressure of ≥130 mmHg or a diastolic blood pressure of ≥85

mmHg.

(5) Hyperglycemia: fasting plasma glucose levels of ≥110 mg/dL.

Statistical analysis

All adipokines were categorized into quartiles, including leptin, total adiponectin, HMW adiponectin, and their ratios. Serum leptin levels were categorized into quartiles according to leptin levels (<1.61, 1.61–3.15, 3.16–5.62, ≥5.63 ng/mL). Serum adiponectin levels were categorized into quartiles according to adiponectin levels (<3.08, 3.08–4.40, 4.41–6.34, ≥6.35 μg/mL). The data are presented as the mean ± S.D. The partial correlation coefficient was used to describe the association between adipokines and other continuous variables of interest controlling for the effect of age. The odds ratios and 95% confidence intervals (CIs) of adipokine levels for metabolic syndrome were calculated. A multivariate logistic regression model was used to test the independent association of adipokines with metabolic syndrome, while adjusting for potentially confounding variables such as age, smoking status, exercise, low-density lipoprotein (LDL) cholesterol, and BMI. A logistic regression model was fitted to establish the association between adipokines and metabolic syndrome. Receiver operating characteristic (ROC) analysis was performed and the area under the curve (AUC) was compared by using a nonparametric approach for adiponectin, leptin, the leptin/adiponectin ratio, and leptin/HMW adiponectin ratio. We performed additional analysis to obtain the *Akaike's information criterion* (*AIC*) estimates for adipokines. The *AIC* is a way of selecting a model from a set of models. All statistical tests were two-sided, and statistical significance was accepted for *p*-values of <0.05. All analyses were conducted using STATA version 9 and SAS version 9.1 software package (SAS Institute Inc, Cary, NC, USA).

Results

The mean age of the study population was 44.3 years for men and 46.3 years for women. The mean leptin/HMW adiponectin ratio was 1.97 in men and 2.81 in women. Compared to men, women were less likely to be current or former smokers. Of 1915 men and 1357 women, 336 (17.6%) men and 166 (12.2%) women had metabolic syndrome (Table 1).

The adiponectin, HMW adiponectin, and leptin levels were found to be correlated with the components

Table 1 General characteristics of the study population

	Total (n = 3,272)	Men (n = 1,915)	Women (n = 1,357)
	Mean ± SD	Mean ± SD	Mean ± SD
Age, years	45.0 ± 9.3	44.3 ± 8.8	46.3 ± 9.9
Body mass index, kg/m^2	23.6 ± 2.9	24.4 ± 2.7	22.5 ± 2.9
Waist circumference, cm	80.8 ± 9.3	84.6 ± 7.8	75.5 ± 8.4
Systolic blood pressure, mm Hg	118.6 ± 14.5	121.7 ± 13.4	114.4 ± 14.9
Diastolic blood pressure, mm Hg	77.1 ± 12.0	80.6 ± 11.2	72.4 ± 11.4
Triglyceride, mg/dL	127.5 ± 81.8	145.5 ± 88.3	102.8 ± 63.7
HDL cholesterol, mg/dL	52.1 ± 12.7	48.8 ± 11.5	56.9 ± 12.8
Insulin, μg/mL	4.1 ± 2.3	4.3 ± 2.5	3.8 ± 2.1
HOMA	0.98 ± 0.64	1.04 ± 0.68	0.89 ± 0.56
Adiponectin, μg/mL	5.1 ± 2.9	4.1 ± 2.3	6.4 ± 3.1
HMW adiponectin, μg/mL	2.7 ± 2.1	2.0 ± 1.5	3.7 ± 2.3
Leptin, ng/mL	4.3 ± 3.8	2.6 ± 2.0	6.6 ± 4.5
HMW:total adiponectin ratio	0.50 ± 0.13	0.46 ± 0.12	0.55 ± 0.13
Leptin:adiponectin ratio	1.04 ± 1.10	0.81 ± 0.85	1.35 ± 1.31
Leptin:HMW adiponectin ratio	2.32 ± 2.79	1.97 ± 2.31	2.81 ± 3.29
Smoking status, %			
Ex-smoker	23.5	39.0	1.8
Current smoker	23.7	39.1	1.9
Metabolic syndrome, %	15.3	17.6	12.2

Abbreviations: SD, standard deviation; HMW, high-molecular-weight; HDL, high-density lipoprotein; HOMA, homeostatic model assessment

Table 2 Correlations (*P*-value) of adiponectin and leptin with cardiometabolic risk factors

	Adiponectin	HMW adiponectin	Leptin	HMW/total*	Leptin/adiponectin	Leptin/HMW
Adiponectin	-	0.92 (<.0001)	−0.10 (<.0001)	0.32 (<.0001)	−0.46 (<.0001)	−0.44 (<.0001)
HMW adiponectin	0.91 (<.0001)	-	−0.12 (<.0001)	0.62 (<.0001)	−0.43 (<.0001)	−0.46 (<.0001)
Leptin	−0.10 (<.0001)	−0.12 (<.0001)	-	−0.10 (<.0001)	0.71 (<.0001)	0.63 (<.0001)
Waist circumference	−0.21 (<.0001)	−0.21 (<.0001)	0.49 (<.0001)	−0.13 (<.0001)	0.47 (<.0001)	0.44 (<.0001)
Body mass index	−0.22 (<.0001)	−0.22 (<.0001)	0.55 (<.0001)	−0.13 (<.0001)	0.51 (<.0001)	0.47 (<.0001)
Systolic blood pressure	−0.08 (<.0001)	−0.07 (<.0001)	0.20 (<.0001)	−0.04 (0.0197)	0.18 (<.0001)	0.16 (<.0001)
Diastolic blood pressure	−0.06 (0.0015)	−0.05 (0.0043)	0.14 (<.0001)	−0.03 (0.0575)	0.13 (<.0001)	0.12 (<.0001)
Triglyceride	−0.19 (<.0001)	−0.19 (<.0001)	0.21 (<.0001)	−0.13 (<.0001)	0.27 (<.0001)	0.27 (<.0001)
HDL cholesterol	0.26 (<.0001)	0.25 (<.0001)	−0.14 (<.0001)	0.10 (<.0001)	−0.22 (<.0001)	−0.21 (<.0001)
LDL cholesterol	−0.06 (0.0002)	−0.08 (<.0001)	0.17 (<.0001)	−0.07 (<.0001)	0.14 (<.0001)	0.13 (<.0001)
Insulin	−0.18 (<.0001)	−0.18 (<.0001)	0.50 (<.0001)	−0.13 (<.0001)	0.49 (<.0001)	0.46 (<.0001)
HOMA	−0.19 (<.0001)	−0.19 (<.0001)	0.47 (<.0001)	−0.13 (<.0001)	0.48 (<.0001)	0.45 (<.0001)

Abbreviations: HMW, high-molecular-weight; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HOMA, homeostatic model assessment *HMW/total, HMW to total adiponectin ratio; Leptin/adiponectin, Leptin to total adiponectin ratio; Leptin/HMW, Leptin to HMW adiponectin ratio Values are age- and gender-adjusted Spearman correlation coefficients and *P* values for correlations of adiponectin and leptin with cardiometabolic risk factors

Table 3 Odds ratios (95% CI) and ROC analysis for the association between metabolic syndrome and markers in men

Variable	OR* (95% CI)	AUC (SE)
Adiponectin (Q4 *vs*. Q1)	0.33 (0.18–0.61)	0.6324 (0.0396)
HMW adiponectin (Q4 *vs*. Q1)	0.37 (0.20–0.71)	0.6492 (0.0345)
Leptin (Q4 *vs*. Q1)	2.78 (1.63–4.73)	0.7275 (0.0291)
HMW/total adiponectin ratio (Q4 *vs*. Q1)	0.66 (0.42–1.05)	0.5484 (0.5130)
Leptin/adiponectin ratio (Q4 *vs*. Q1)	3.69 (2.18–6.25)	0.7496 (0.0137)
Leptin/HMW adiponectin ratio (Q4 *vs*. Q1)	3.65 (2.23–5.99)	0.7379 (0.0140)

Abbreviations: CI, confidence interval; AUC, area under the curve; SE, standard error; HMW, high-molecular-weight; Q4, highest quartile; Q1, lowest quartile *Adjusted for age, smoking status, exercise, LDL cholesterol, and body mass index

Table 4 Odds ratios (95% CI) and ROC analysis for the association between metabolic syndrome and markers in women

Variable	OR* (95% CI)	AUC (SE)
Adiponectin (Q4 *vs*. Q1)	0.18 (0.10–0.34)	0.6492 (0.0345)
HMW adiponectin (Q4 *vs*. Q1)	0.23 (0.13–0.42)	0.6534 (0.0516)
Leptin (Q4 *vs*. Q1)	1.22 (0.34–4.30)	0.6177 (0.6530)
HMW/total adiponectin ratio (Q4 *vs*. Q1)	0.28 (0.16–0.47)	0.7120 (0.0164)
Leptin/adiponectin ratio (Q4 *vs*. Q1)	5.03 (1.71–14.79)	0.7332 (0.0199)
Leptin/HMW adiponectin ratio (Q4 *vs*. Q1)	6.08 (2.41–15.34)	0.7331 (0.0204)

Abbreviations: CI, confidence interval; AUC, area under the curve; SE, standard error; HMW, high-molecular-weight; Q4, highest quartile; Q1, lowest quartile *Adjusted for age, smoking status, exercise, LDL cholesterol, and body mass index

of metabolic syndrome. Of these adipokines, leptin was highly correlated with waist circumference, BMI, insulin, and homeostatic model assessment (HOMA) (Table 2); in particular, leptin showed a higher correlation than adiponectin amongst the adipokines.

The adjusted odds ratio (95% CI) and AUC of metabolic syndrome by quartiles of adipokines are shown in Table 3 and Table 4. The leptin/HMW adiponectin ratio had the highest association (adjusted odds ratio) for metabolic syndrome in women. The leptin/HMW adiponectin ratio in the highest quartile was associated with a 3.65-fold increased probability of prevalent metabolic syndrome in men and 6.08-fold increase in women when compared with the lowest quartile, independent of age, smoking status, exercise, LDL cholesterol, and BMI. Moreover, compared to other markers,

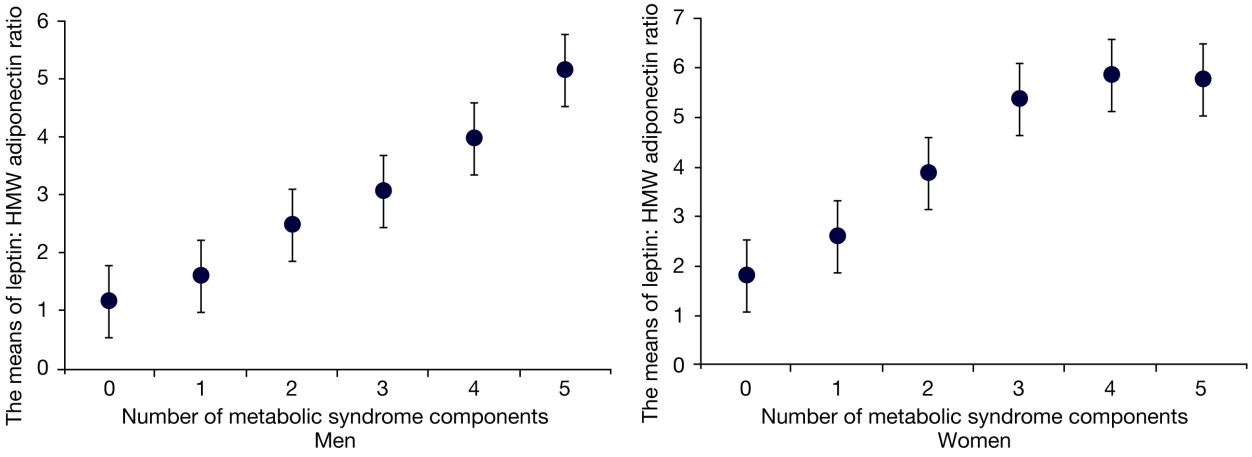

Fig. 1 Mean values of the leptin/HMW adiponectin ratio with respect to the number of metabolic syndrome components

Table 5 Sex-specific odds ratios* (95% CI) for the association between metabolic syndrome and leptin/HMW adiponectin ratio

	Leptin/HMW adiponectin ratio quartiles				
	Quartile 1 (n=818)	Quartile 2 (n=818)	Quartile 3 (n=818)	Quartile 4 (n=818)	P trend
Men					
Metabolic syndrome	1.0	1.83 (1.12–2.99)	2.66 (1.64–4.30)	3.65 (2.23–5.99)	0.0010
Abdominal obesity	1.0	2.25 (1.29–3.90)	2.26 (1.30–3.91)	3.74 (2.13–6.55)	0.0518
High blood pressure	1.0	1.27 (0.97–1.66)	1.35 (1.01–1.79)	1.35 (0.98–1.86)	0.1212
High triglycerides	1.0	1.75 (1.29–2.37)	3.01 (2.20–4.11)	3.68 (2.60–5.20)	0.0071
High glucose	1.0	2.29 (1.45–3.63)	1.57 (0.95–2.61)	3.70 (2.24–6.12)	0.1831
Low HDL cholesterol	1.0	1.07 (0.77–1.49)	1.36 (0.97–1.92)	1.41 (0.97–2.05)	0.0432
Women					
Metabolic syndrome	1.0	2.14 (0.80–5.74)	3.28 (1.28–8.42)	6.08 (2.41–15.34)	0.0294
Abdominal obesity	1.0	1.06 (0.56–1.99)	0.82 (0.44–1.52)	1.59 (0.87–2.92)	0.4034
High blood pressure	1.0	1.32 (0.79–2.21)	1.34 (0.82–2.22)	1.54 (0.93–2.56)	0.0519
High triglycerides	1.0	2.41 (1.00–5.79)	4.39 (1.91–10.07)	6.68 (2.92–15.30)	0.0054
High glucose	1.0	1.09 (0.42–2.81)	1.45 (0.59–3.60)	1.75 (0.71–4.29)	0.0233
Low HDL cholesterol	1.0	1.95 (1.28–2.99)	2.03 (1.33–3.10)	3.32 (2.16–5.10)	0.0461

*Adjusted for age, smoking status, exercise, LDL cholesterol, and body mass index

the AUC of leptin/adiponectin ratio and leptin/HMW adiponectin ratio was higher for metabolic syndrome. The AUC of the leptin/adiponectin ratio and leptin/HMW adiponectin ratio are similar to that of metabolic syndrome. In particular, in women, the AUC for the HMW adiponectin/total adiponectin ratio is similar to those for the leptin/adiponectin and leptin/HMW adiponectin ratios, although the correlation between HMW adiponectin and HMW adiponectin/total adiponectin ratio is not very high. Combination of this ratio with the leptin/HMW adiponectin ratio may result in a more sensitive marker for metabolic syndrome.

Fig. 1 shows the different means of the leptin/HMW adiponectin ratio according to the number of metabolic syndrome components. There was a linear increase in the leptin/ HMW adiponectin ratio with the increase in the number of metabolic syndrome components.

The leptin/HMW adiponectin ratio was positively associated with abdominal obesity, high triglyceride levels, high glucose levels, and low HDL cholesterol levels. In particular, the level of triglycerides was higher than the other metabolic syndrome components in both men and women (Table 5).

Discussion

Adipokines, such as adiponectin, HMW adiponectin, and leptin, were found to be statistically related

to metabolic syndrome. In particular, leptin showed a higher correlation with cardiometabolic risk factors than adiponectin and other adipokines. Moreover, investigation of metabolic syndrome and the leptin/HMW adiponectin ratio showed that the ratio had a higher correlation with metabolic syndrome than did adiponectin or leptin alone. Consistency in the results was also maintained when confounding factors were considered, such as age, smoking status, exercise, LDL cholesterol levels, and BMI. In addition, the higher leptin/HMW adiponectin ratio was correlated with an increase in the number of metabolic syndrome components, which was found in both males and females.

In some studies, it has been suggested that the leptin/adiponectin ratio may be related to metabolic syndrome in specific populations, and may serve as a useful diagnostic marker of metabolic syndrome. Examples include the geriatric population (i.e., people over 65 years in age), a few groups of children and adolescents, and male subjects [10, 26, 32, 33]. A previous study has shown that the leptin/adiponectin ratio has a significantly higher AUC than adiponectin in older adults from China. Hence, the leptin/adiponectin ratio may present a better diagnostic marker of metabolic syndrome in older populations [10]. Likewise, several other studies were conducted by either targeting small groups of subjects or specific groups [25, 32, 33]. In comparison, in this study, we analyzed over 3000 healthy, middle-aged Koreans. As a result, we found that women also show signs of correlation between the leptin/adiponectin ratio and metabolic syndrome. It appears that leptin/HMW adiponectin was not superior to other adipokine markers in this regard, although it is as effective as the leptin/total adiponectin ratio. However, in our data, the leptin/HMW adiponectin ratio evidenced a minimum output of *AIC* and *-2 Log L*, indicating that the leptin/HMW adiponectin ratio is best suited to explaining the dependent variable. Therefore, it will be necessary to confirm our results in large population prospective studies. We performed additional analysis to obtain the best cutoff for metabolic syndrome. The best cut point of leptin/HMW adiponectin ratio for identifying metabolic syndrome was 1.5 in study participants (sensitivity 51.0%, specificity 30.1%). However, the choice of cutoff level for screening depends on the importance of false positive and false negative for disease. In this regard, the cutoff for metabolic syndrome is better to lower the false positive. In our data, the best cutoff level was 5.5 when high specificity (90.9%).

It has also been recently suggested that the leptin/adiponectin ratio may play a role as a marker for insulin resistance [23, 34, 35] and type 2 diabetes [36]. In addition, pulse wave velocity and carotid intima-media thickness, which are surrogate clinical markers of atherosclerosis, are also correlated with the leptin/adiponectin ratio [37, 38]. In an Aboriginal Canadian population, however, incident type 2 diabetes was borderline significant for the leptin/adiponectin ratio [39]. In a prospective study, the leptin/adiponectin ratio showed no association with the risk of coronary heart disease [40].

Several investigations have shown that HMW adiponectin is associated with type 2 diabetes and metabolic syndrome. It has been suggested that the HMW form of adiponectin may be a useful marker and predictor of insulin resistance and metabolic syndrome in healthy Japanese men [27, 41]. Moreover, Nakashima *et al*. reported that compared to total adiponectin, HMW adiponectin is more closely associated with the progression to type 2 diabetes [42]. In our study, the crude correlation of total adiponectin and HMW adiponectin to metabolic syndrome was similar. However, the association of the leptin versus HMW adiponectin ratio was higher (size of adjusted odds ratio) for metabolic syndrome than for leptin versus the total adiponectin ratio.

The correlation between components of metabolic syndrome and the leptin/adiponectin ratio has been recorded in previous studies [22, 43]. In 220 Japanese patients with type 2 diabetes, the adiponectin/leptin ratio was found to be significantly correlated in men and women with high triglyceride ($r = -0.199$ and $r = -0.402$, respectively) and HDL cholesterol levels ($r = 0.235$ and $r = 0.358$, respectively) [24]. Furthermore, the leptin/adiponectin ratio was significantly associated with waist circumference and HDL cholesterol in a healthy male population in Italy [43]. Adiposity levels, including BMI and waist circumference, were found to be inversely correlated with the adiponectin/leptin ratio ($r = 0.70$) in an aboriginal Canadian population [39]. In this study, this ratio showed a significantly positive correlation with HDL cholesterol levels and a significantly negative correlation with triglyceride levels and all metabolic syndrome components.

Adipokines facilitate the participation of the adipose organ in a major regulatory role for energy balance and glucose homeostasis [44]. Thus, any disruption to the secretion of adipokines has many metabolic repercussions [45]. For example, adiponectin and lep-

tin are associated with obesity, and are involved in the process of insulin resistance [7, 9, 20]. Leptin is an adipose-specific hormone contributing to body weight and energy regulation, and it modulates insulin sensitivity and glucose disposal [11, 13, 22, 46, 47]. Leptin production is influenced by nutritional status, stress, body mass, and the activation of the immune system [20, 47, 48]. Adiponectin enhances the action of insulin and decreases serum glucose levels [16-19]. As a result, leptin is associated with an increase in the prevalence of type 2 diabetes [36] and metabolic syndrome [15, 49]. Adiponectin suppresses TNF-α signaling in adipocytes, and protects against the development of insulin resistance. In the event of insulin resistance, the secretion of adiponectin would further decline. The insulin-resistant state may be involved in such a vicious cycle [16].

This study analyzed markers that are measured only once, making it a cross-sectional study design; hence, the interpretation of the results may have some limitations. However, the present study was performed with a relatively larger sample size (over 3000 individuals) of healthy middle-aged Korean men and women, compared to previous studies. In addition, this study is the first investigation that examines the association between the leptin/HMW adiponectin ratio and metabolic syndrome for both men and women in a single study population. However, carefully designed follow-up studies are required to confirm the related mechanisms recorded in the present study.

In conclusion, after adjusting for confounding factors, including BMI, we showed that the leptin/ HMW adiponectin ratio is significantly associated with metabolic syndrome in an adult Korean population. Moreover, the leptin/HMW adiponectin ratio, as well as the leptin/total adiponectin ratio, is better indicators for metabolic syndrome than adiponectin or leptin alone. Therefore, these results show that the leptin/HMW adiponectin ratio is helpful in understanding cardiovascular diseases.

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Conflicts of Interest

The authors declared no conflicts of interest.

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