RELATIONSHIP BETWEEN METABOLIC SYNDROME AND METABOLIC SYNDROME SCORE AND INSULIN RESISTANCE AND BETA CELL FUNCTION IN KOREAN ADULTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

***Introduction**: The present study was conducted to assess the relationship between metabolic syndrome (MetS) and metabolic syndrome score (MSS) and insulin resistance and beta cell function in Korean adults with type 2 diabetes mellitus (T2DM).*

***Material and method**: This study included 541 adults with T2DM using 2010 Korean National Health and Nutrition Examination Survey (KNHANES) data.*

***Results**: The key study results were as follows: First, after adjusted for the related variables [age, gender, smoking, drinking, exercising, TC, 25(OH)D, and BMI], metabolic syndrome (p = 0.967) and MSS increases (p = 0.131) were not significantly associated with the HOMA-IR levels. Second, after adjusting the related variables (except BMI), MetS (p = 0.264) and MSS increases (p = 0.359) were not significantly associated with HOMA-B levels. However, when further adjusted for BMI, MetS (p = 0.004) and MSS increases (p = 0.010) were inversely associated with HOMA-B levels.*

***Conclusion**: Metabolic syndrome and increase of metabolic syndrome score were inversely associated with beta cell function, but were not independently associated with insulin resistance in Korean adults with T2DM.*

***Keywords**: metabolic syndrome, metabolic syndrome score, insulin resistance, beta cell function, diabetes mellitus.*

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Introduction

Diabetes, a disease that results from the interaction of genetic factors and environmental factors, is one of the most common endocrine diseases worldwide[1, 2]. Approximately 90% of diabetes cases can be categorized as Type 2 diabetes mellitus (T2DM), which is caused by both beta cell dysfunction and insulin resistance[3-5]. Subjects with T2DM, which is a state of normoglycemia or hyperglycemia, have poor beta cell function compared with non-diabetic subjects[6].

Metabolic syndrome (MetS) is defined as a disease in which conditions such as hypertension, high blood glucose, plasma lipid abnormality, as well as abdominal obesity occur simultaneously with resistance to insulin and at least three of five coronary risk factors[7, 8]. The de-differentiation and death of beta cells are caused by insulin resistance, such as metabolic syndrome[9].

Research on MetS and insulin resistance and beta cell function is being conducted all over the world. The association between individual MetS components and beta cell function and insulin resistance differs between ethnic groups and countries, and the most subjects are either healthy of have diseases such as obesity, peripheral vascular disease, or coronary heart disease[10-16]. However, research on subjects with T2DM is rare.

Although the Republic of Korea is experiencing an increasing prevalence of diseases such as diabetes and MetS, there remains a lack of research on the association between metabolic syndrome and insulin resistance and beta cell function in the population of Korea. Therefore, the present study aimed to investigate the association between MetS and metabolic syndrome score (MSS) and HOMA-IR and HOMA-B levels in Korean adults with T2DM using data from the fifth Korea National Health and Nutrition Examination Survey (KNHANES), which is representative of the population of Korea.

Materials and methods

Study subjects

This study was based on data from the KNHANES V-1 (2010), which is the most recent data that measured homeostasis model assessment (HOMA) among the KNHANES. The KNHANES is a cross-sectional survey conducted nationwide by the Division of Korean National Health and Welfare. The KNHANES V-1 (2010) was performed from January 2010 to December 2010. The survey includes a representative national sample of the Korean population, selecting from recorded households in the Population and Housing Census in Korea. The survey section is arranged by district and housing type characteristics. Twenty households were selected from each survey section using a stratified, multistage probability cluster sampling method that considers geographical area, age, and gender. In the KNHANES V-1 (2010), 8,958 individuals over 1 year of age were sampled for the survey. Among the 6,665 subjects who participated in the KNHANES V-1, we limited the analyses to adults aged ≥20 years. We excluded 1,864 subjects whose data were missing for important analytic variables, such as HOMA-IR and HOMA-B, and various blood chemistry tests. After the exclusion of those individuals with missing values or who do not have symptoms of diabetes mellitus (4,260 subjects non-diagnosed with diabetes mellitus or with fasting plasma glucose level < 126 mg/dL), 541 adults were included in the analyses. The KNHANES study was approved by the Institutional Review Board of the Centers for Disease Control and Prevention in Korea (IRB No, 2010-02CON-21-C). All participants in the survey signed an informed written consent form.

General characteristics and blood chemistry

Research subjects were classified by sex (men or women), smoking (non-smoker or ex-smoker or current smoker), alcohol drinking (yes or no), and regular exercise (yes or no). In the smoking category, participants who smoked more than one cigarette a day, those who had previously smoked but do not presently smoke, and those who never smoked were classified into the current-smoker, ex-smoker, and non-smoker groups, respectively. Alcohol drinking was indicated as "yes" for participants who had consumed at least one glass of alcohol every month over the last year. Regular exercise was indicated as "yes" for participants who had exercised on a regular basis regardless of indoor or outdoor exercise. (Regular exercises was defined as 30 min at a time and 5 times/wk in the case of moderate exercise, such as swimming slowly, doubles tennis, volleyball, badminton, table tennis, and carrying light objects; and for 20 min at a time and 3 times/wk in the case of vigorous exercise, such as running, climbing, cycling fast, swimming fast, football, basketball, jump rope, squash, singles tennis, and carrying heavy objects). Anthropometric measurements included height, weight, body mass index (BMI), and waist measurement (WM) and final measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP). Blood chemistry included measurements of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs), fasting plasma glucose (FPG), fasting plasma insulin, hemoglobin A1C (Hb A1C), and 25-hydroxyvitamin D [25(OH)D].

HOMA-IR and HOMA-B and T2DM

The homeostasis model assessment of insulin resistance (HOMA-IR) and beta-cell function (HOMA-B) were derived from fasting glucose and insulin levels. The formulas are as follows: HOMA-IR = [fasting insulin (μU/mL) × fasting plasma glucose (mg/dL)]/405; HOMA-B = 360 × fasting insulin (μU/ml) / [fasting plasma glucose (mg/dL) - 63][17]. T2DM was defined as a fasting blood glucose level of ≥ 126 mg/dl or through the subject's self-reported history of diabetes or use of diabetes medications[18].

MetS and MSS

Metabolic syndrome was defined using the diagnostic criteria of the Revised National Cholesterol Education Program Adult Treatment

panel III (Revised NCEP-ATP III) based on common clinical measures[7], including TG, HDL-C, blood pressure (BP), FPG, and WM. A TGs level of over 150 mg/dL or treatment for dyslipidemia was set as the criteria for elevated TGs. The criteria for reduced HDL-C were HDL-C levels of less than 40 mg/dL and 50 mg/dl for males and females, respectively, or treatment for dyslipidemia. A FPG level of over 100 mg/dL or the use of medication for hyperglycemia was set as the criteria for elevated FPG. An SBP level of over 130 mmHg or a DBP level of over 85 mmHg or the use of antihypertensive medication were set as the criteria for elevated BP. The criteria for abdominal obesity were abdominal circumference measurements of over 90 cm and 80 cm for males and females, respectively, according to the Asia-Pacific criteria[19]. The presence of defined abnormalities in any three of these five measures constitutes a diagnosis of metabolic syndrome. The MSS indicates the presence of abdominal obesity, elevated BP, elevated FPG, elevated TGs, or reduced HDL-C. Subjects without any of the five risk factors received a MSS of 0, and those with one, two, three, or four or more of the risk factors received a MSS of 1, 2, 3, or ≥ 4, respectively[20]. However, there was no subject without any of the five risk factors because the participants of the present study were T2DM.

Statistical analysis

The collected data were statistically analyzed using SPSS WIN (ver. 18.0). The distributions of the participant characteristics were converted into percentages, and the successive data were presented as averages with standard deviations. The average difference in HOMA-IR and HOMA-B for general characteristics and blood chemistries were calculated using an analysis of variance and independent t-tests. In the case of analysis of covariance test (ANCOVA), the 4 models constructed were:

1) no adjustment;

2) adjusted for age and gender;

3) further adjusted for smoking, alcohol drinking, regular exercise, TC, and 25(OH)D; 4) further adjusted for BMI. The significance level for all of the statistical data was set as $p < 0.05$.

Results

Clinical characteristics of subjects with T2DM

Clinical characteristics of the research subjects are shown in Table 1. In men subjects, the mean HOMA-IR and HOMA-B levels of subjects were 4.53 ± 3.74 and 66.12 ± 58.59, respectively.

Variables	Category	Males (n=297)	Females (n=244)	p-value
Metabolic syndrome	MSS<3	113 (38.0)	48 (19.7)	<0.001
	MSS≥3	184 (62.0)	196 (80.3)	
Metabolic syndrome score (MSS)	1	15 (5.0)	13 (5.3)	<0.001
	2	98 (33.0)	35 (14.4)	
	3	107 (36.1)	74 (30.2)	
	≥4	77 (25.9)	122 (50.1)	
Age (years)	<40	17 (5.7)	11 (4.5)	0.032
	40-49	39 (13.2)	23 (9.4)	
	50-59	84 (28.3)	46 (18.9)	
	60-69	80 (26.9)	88 (36.1)	
	≥70	77 (25.9)	76 (31.1)	
Smoking	Non-smoker	40 (13.2)	227 (93.4)	<0.001
	Ex-smoker	146 (49.2)	9 (3.7)	
	Current smoker	111 (37.6)	8 (2.9)	
Alcohol drinking	No	80 (27.0)	139 (57.0)	<0.001
	Yes	217 (73.0)	105 (43.0)	
Regular exercise	No	266 (90.1)	219 (89.6)	0.886
	Yes	31 (9.9)	25 (10.4)	
WM (cm)		88.03±9.90	86.12±9.26	0.022
BMI (kg/m^2)		24.60±3.30	25.25±3.44	0.025
SBP (mmHg)		125.08±15.20	129.63±17.46	0.001
DBP (mmHg)		75.64±10.17	75.15±9.64	0.57
HOMA-IR		4.53±3.74	4.57±3.06	0.892
HOMA-B		66.12±58.59	79.29±63.00	0.012
Insulin (μU/mL)		12.32±9.05	13.21±7.40	0.216
Hemoglobin A1C (%)		7.40±1.59	7.32±1.41	0.57
FPG (mg/dL)		147.44±44.69	139.17±40.60	0.026
TC (mg/dL)		182.06±39.25	194.60±43.09	<0.001
TG (mg/dL)		198.99±207.70	160.94±98.14	0.005
HDL-C (mg/dL)		45.39±10.70	50.01±13.27	<0.001
25(OH)D (ng/dL)		19.58±7.17	17.96±7.08	0.009

Table 1: General characteristics of subjects with type 2 diabetes mellitus.

WM: waist measurement, BMI: body mass index, WM: waist measurement, SBP: systolic blood pressure, DBP: diastolic blood pressure, HOMA-IR: Homeostasis model assessment of insulin resistance, HOMA-B: Homeostasis model assessment of beta-cell function, TC: total Cholesterol, TG: triglyceride, HDL-C: HDL-cholesterol, LDL-C: LDL-cholesterol, 25(OH)D: 25-hydroxyvitamin D, FPG: fasting plasma glucose

According to the classification of risk factors for coronary artery disease and the MSS guidelines, 15 (5.0%), 98 (33.0%), 107 (36.1%), and 77 (25.9%) subjects were classified as MSS 1, MSS 2, MSS 3, and MSS ≥ 4, respectively, while the prevalence rate of MetS was 184 of the 297 patients (62.0%). In women, the mean HOMA-IR and HOMA-B levels of subjects were 4.57 ± 3.06 and 79.29 ± 63.00, respectively. According to the classification of risk factors for coronary artery disease and the MSS guidelines, 13 (5.3%), 35 (14.4%), 74 (30.2%), and 122 (50.1%) subjects were classified as MSS 1, MSS 2, MSS 3, and MSS ≥4, respectively, while the prevalence rate of MetS was 196 of the 244 patients (80.3%).

Comparisons of HOMA-IR and HOMA-B levels according to MetS characteristics

Comparisons of the HOMA-IR and HOMA-B levels according to MetS characteristics are shown in Table 2.

Variables	Category	HOMA-IR	p-value	HOMA-B	p-value
WM (cm)	[a]Normal	4.13±3.39	<0.001	61.49±54.73	0.015
	[b]Abdomal obesity	4.93±3.46		81.68±64.64	
BP (mmHg)	[c]Normal	6.32±5.47	0.007	76.28±79.59	0.626
	[d]Elevated blood pressure	4.29±2.98		71.38±51.78	
TG (mg/dL)	[e]Normal	4.18±3.40	0.003	71.62±63.21	0.864
	[f]Elevated triglyceride	5.06±3.46		72.52±57.64	
HDL-C (mg/dL)	[g]Normal	4.32±3.50	0.074	68.17±63.12	0.096
	[h]Reduced HDL-C	4.85±3.37		76.94±57.59	
BMI (kg/m²)	<25.0	4.18±3.57	0.008	67.78±60.34	0.037
	≥25.0	4.98±3.30		78.80±61.20	

Table 2:Comparison of HOMA-IR and HOMA-B levels according to metabolic syndrome characteristics and BMI.

[a]Normal is defined as WM <90 cm in male or <80 cm in female, [b]Abdomal obesity is defined as WM >90 cm in male or >80 cm in female, [c]Normal is defined as SBP <130 mmHg or DBP <85 mmHg, [d]Elevated blood pressure is defined as SBP >130 mmHg or DBP >85 mmHg, [e]Normal is defined as TG <150 mg/dL, [f]Elevated triglyceride is defined as TG >150 mg/dL, [g]Normal is defined as HDL-C >40 mg/dL in male or >50 mg/dL in female, [h]Reduced HDL-C is defined as HDL-C <40 mg/dL in male or <50 mg/dL in female.

In terms of MetS components, the HOMA-IR levels were significantly higher in the abdominal obesity (p < 0.001), and elevated TG (p = 0.003) than in the normal group. However, the HOMA-IR level was significantly lower (p = 0.007) in the elevated BP than the normal group. In addition, the HOMA-IR level was significantly higher (p = 0.008) in the obesity group (BMI ≥ 25.0 kg/m²) than the normal weight group (BMI < 25.0 kg/m²). The elevated BP (p = 0.626), elevated TGs (p = 0.864), and reduced HDL-C (p = 0.096) showed no significant difference in HOMA-B levels. In addition, the HOMA-B level was significantly higher in the abdominal obesity (p = 0.015) and obesity group (p = 0.037) than the normal group.

Comparison of HOMA-IR and HOMA-B levels according to MetS and MSS

Comparisons of the HOMA-IR and HOMA-B levels according to MetS and MSS are shown in Table 3 and 4. In terms of the HOMA-IR levels, after adjusting the related variables [age, gender, smoking, drinking, exercising, TC, 25(OH)D, and BMI], MetS (p = 0.967) and MSS (p = 0.131) were not significantly associated with the HOMA-IR levels. In terms of the HOMA-B levels, after adjusting the related variables (except BMI), MetS (p = 0.359) and MSS (p = 0.264) were not significantly associated with the HOMA-B levels. However, when further adjusted for BMI, MSS was inversely associated with HOMA-B levels (p = 0.004). These were 106.92 ± 11.40 [95% confidence interval (CI), 84.53-129.32] for MSS 1, 78.41 ± 5.47 (95% CI, 67.66-89.15) for MSS 2, 70.52 ± 4.42 (95% CI, 61.83-79.20) for MSS 3, and 62.44 ± 4.44 (95% CI, 53.71-71.16) for MSS ≥ 4. In addition, the HOMA-B level of MetS [66.62 ± 6.14 (95% CI, 60.45-72.79)] was significantly lower (p = 0.010) than the non- MetS [82.63 ± 5.06 (95% CI, 72.69-92.58)].

Discussion

The present study investigated the association between MetS and MSS and HOMA-B levels using data from the fifth KNHANES, which is representative of Koreans. MetS and MSS were inversely associated with beta cell function but were not associated with insulin resistance in Korean adults with T2DM (Tables 3 and 4).

MetS is characterized by insulin resistance[12], and insulin resistance leads to beta cell exhaustion, glucotoxicity, and hyperinsulinemia, which place a massive strain on the endoplasmic reticulum of beta cells[21]. For healthy subjects, most previous studies suggested that insulin resistance is positively associated with MetS or its components. Yamada et al. reported that the MetS and all its components

were associated with HOMA-IR levels in Japanese adults ($p < 0.001$)[22].

	Model 1	Model 2	Model 3	Model 4
MSS 1	4.12±0.91 (2.26-5.98)	4.05±0.64 (2.79-5.31)	4.17±0.62 (2.96-5.38)	4.67±0.63 (3.42-5.92)
2	4.23±0.35 (3.54-4.92)	4.21±0.30 (3.62-4.80)	4.14±0.30 (3.56-4.72)	4.39±0.30 (3.80-4.99)
3	4.27±0.22 (3.84-4.69)	4.25±0.25 (3.76-4.75)	4.13±0.25 (3.64-4.61)	4.11±0.25 (3.63-4.59)
≥4	5.08±0.23 (4.63-5.53)	5.11±0.25 (4.63-5.60)	5.15±0.24 (4.68-5.62)	4.93±0.25 (4.44-5.41)
p-value	0.057	0.042	0.012	0.131
Non-MetS	4.21±0.28 (3.59-4.86)	4.20±0.27 (3.67-4.74)	4.17±0.27 (3.64-4.69)	4.50±0.28 (3.95-5.05)
MetS	4.69±0.19 (4.39-5.01)	4.70±0.18 (4.35-5.04)	4.66±0.17 (4.32-4.99)	4.52±0.17 (4.17-4.86)
p-value	0.137	0.131	0.129	0.967

Table 3: Comparisons of HOMA-IR levels according to metabolic syndrome and metabolic syndrome score.
MSS: Metabolic syndrome score, Non-MetS: Non-metabolic syndrome, MetS: Metabolic syndrome
Model 1 [M±SE (95% CI)], Non-adjusted; Model 2 [M±SE (95% CI)], adjusted for age and gender; Model 3 [M±SE (95% CI)], adjusted for age, gender, smoking, alcohol drinking, regular exercise, TC, and 25(OH)D; Model 4 [M±SE (95% CI)], adjusted for age, gender, smoking, alcohol drinking, regular exercise, TC, 25(OH)D, and BMI

	Model 1	Model 2	Model 3	Model 4
MSS 1	92.08±17.54 (56.07-128.07)	92.57±11.42 (70.14-114.99)	92.75±11.26 (70.63-114.87)	106.92±11.40 (84.53-129.32)
2	92.57±11.42 (70.14-114.99)	72.76±5.34 (62.28-83.24)	71.20±5.38 (60.63-81.77)	78.41±5.47 (67.66-89.15)
3	72.15±4.67 (62.93-81.36)	72.80±4.50 (64.98-81.63)	71.07±4.51 (62.20-79.93)	70.52±4.42 (61.83-79.20)
≥4	70.40±3.07 (64.35-76.44)	68.03±4.37 (59.44-76.61)	68.68±4.34 (60.14-77.21)	62.44±4.44 (53.71-71.16)
p-value	0.215	0.251	0.264	0.004
Non-MetS	74.01±4.87 (62.94-86.76)	76.20±4.83 (66.71-85.70)	75.14±4.86 (65.59-84.68)	82.63±5.06 (72.69-92.58)
MetS	72.06±3.72 (66.03-76.55)	70.30±3.12 (64.17-76.43)	69.78±3.11 (63.66-75.89)	66.62±6.14 (60.45-72.79)
p-value	0.696	0.31	0.359	0.01

Table 4: Comparisons of HOMA-B levels according to metabolic syndrome and metabolic syndrome score.
MSS: Metabolic syndrome score, Non-MetS: Non-metabolic syndrome, MetS: Metabolic syndrome
Model 1 [M±SE (95% CI)], Non-adjusted; Model 2 [M±SE (95% CI)], adjusted for age and gender; Model 3 [M±SE (95% CI)], adjusted for age, gender, smoking, alcohol drinking, regular exercise, TC, and 25(OH)D; Model 4 [M±SE (95% CI)], adjusted for age, gender, smoking, alcohol drinking, regular exercise, TC, 25(OH)D, and BMI

Lee et al. reported that all of the MetS components were associated with HOMA-IR levels in Korean non-diabetic adults ($p < 0.001$)[23]. Yin et al. reported that all of the MetS components were associated with HOMA-IR levels in Chinese children and teenagers ($p < 0.001$)[24].

In addition, these studies have shown that all of the MetS components were positively associated with insulin resistance. However, in subjects with T2DM, the association between MetS components and the HOMA-IR levels may vary across the ethnic groups and countries. Gobato et al. evaluated the association between the HOMA-IR levels and MetS (25). In their findings, TGs ($p = 0.051$), SBP ($p = 0.352$), and DBP ($p = 0.182$) were not significantly associated with insulin resistance. However, MetS was positively associated with HOMA-IR levels. In addition, Saely et al. reported that HOMA-IR levels increased significantly ($p < 0.001$) with an increasing number of MetS risk factors in non-diabetic adults[26]. On the other hand, Sowjanya et al. evaluated the association between insulin resistance and MetS in Indians[27]. They found that MetS was associated with HOMA-IR levels in non-diabetics ($p = 0.017$) but not in diabetics ($p = 0.636$). In addition, Ahmen et al. reported that the association between MetS and HOMA-IR levels in subjects with T2DM differ by gender (men, $p = 0.02$; women, $p = 0.57$)[28]. In the present study, HOMA-IR levels were significantly higher in the abdominal obesity and elevated TGs group than in the normal group but significantly lower in the elevated BP group than in the normal group. However, there was no association between the MetS and MSS and insulin resistance.

These results were similar to those of Sowjanya et al. In our previous study, MetS and MSS were positively associated with HOMA-IR levels[29]. However, the participants of our previous study were subjects with obesity.

Participants of the present study are T2DM patients, and they are already a status that has been advanced insulin resistance. Therefore, despite individual MetS components being increased, the HOMA-IR levels may not increase any more.

There have been few studies on the association between MetS components and beta cell function, and previous results were not consistent according to ethnicity and country or healthy subjects and subjects with disease. Among previous studies on beta cell function and MetS components, Imamura et al. evaluated the association between the risk factors of T2DM and beta cell dysfunction and insulin resistance in the Cardiovascular Health Study. They suggested that beta cell dysfunction was positively associated with the elevated TGs and FBG, but was not associated with the elevated BP and reduced HDL-C[30]. On the other hand, Haffner et al. reported that MetS risk factors were not associated with insulin secretion in Mexican-American and non-Hispanic white subjects with T2DM[15]. However, several studies reported that MetS and MSS were associated with beta cell function. For example, Baez-Duarte et al. reported that MetS and MSS were associated with the reduction of beta cell function in Mexican subjects[13].

Cubeddu et al. reported that the absolute number of MetS risk factors was inversely associated with insulin secretion in Latin-American subjects[14]. In addition, in previous study, the association between MetS and HOMA-B levels in subjects with obesity differ by gender (men, $p = 0.005$; women, $p = 0.616$)[29].

In the present study, in the T2DM group, the HOMA-B level of the obesity and abdominal obesity group were significantly higher than those of the normal group. In addition, the HOMA-B level of the elevated BP, elevated TG, and reduced HDL-C groups were not associated with the normal group. Furthermore, after adjusting the related variables (except BMI), MetS and MSS seems to be not associated with the reduction of HOMA-B. However, when further adjusted for BMI, MetS and MSS were significantly associated with the reduction of HOMA-B. Although, the mechanisms of these results could not be demonstrated in the present study, it may be considered effects by BMI. BMI is a strong risk factor of MetS and MSS. In the present study, BMI was rather positively associated with HOMA-B levels in subjects with T2DM. Therefore, the association between MetS and MSS and HOMA-B levels seem the non-significant, but after adjustment for BMI, MetS and MSS were independently associated with the decreased HOMA-B levels.

In healthy subjects, pancreatic beta cells sense changes in blood glucose concentration and are activated for insulin secretion by corresponding to elevated levels of blood glucose[31, 32], but subjects of the present study are the T2DM population. T2DM patients are already a status that has been advanced insulin resistance and beta cell dysfunction. Therefore, it may not be acted the compensatory mechanisms in the T2DM population. MetS is characterized by insulin resistance[12], and MetS component increases the oxidative stress[33], endoplasmic reticulum stress[34], and free fatty acid[35]. Due to this, it can be accelerated to beta cell apoptosis in T2DM population[9].

The association between MetS and MetS components and HOMA-B levels varies between countries and races. These inconsistencies may be attributed to differences of measurements of beta cell function (e.g., clamps, IVGTT, ISOGTT, and HOMA indices). In this study, we used the HOMA index. Although the HOMA indices are not the "gold-standard" method, the HOMA may be more appropriate for use in large epidemiological studies[36]. In addition, it is difficult determine to the clinical utility in comprehensive study because lacks of standardized insulin assays[37]. Therefore, the introduction of a sustainable insulin assay standardization program is necessary.

As the present study was conducted with T2DM population, in whom there is pre-existing increased insulin resistance and beta cell dysfunction, although individual metabolic syndrome components may be positively associated with HOMA-IR levels, metabolic syndrome and increase of its components were not associated with HOMA-IR levels; In contrast, although individual metabolic syndrome components may not be associated with HOMA-B levels, metabolic syndrome and increase of its components were inversely associated with HOMA-B levels in Korean adults with T2DM.

The present study has a few limitations. First, the OGTTs are more sensitive than the FPG test in the diagnosis of diabetes. However, the OGGTs were not employed in the KNHANES V-1 study (2010). Second, because this study was a cross-sectional study, the ability to establish a causal relationship between metabolic syndrome and increases of its components and beta cell dysfunction was limited.

Despite has these limitations, this is the first reported study to determine the relationship between metabolic syndrome and increase of metabolic syndrome score and the HOMA-IR and HOMA-B levels in Korean adults with T2DM.

Therefore, more accurate results might be obtained by performing a cohort study.

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