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Preliminary report: A serious link between adiponectin levels and metabolic syndrome in a Korean nondiabetic population

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Abstract

This large-scale cross-sectional investigation highlights the relationships between adiponectin levels and a number of metabolic syndrome components in a nondiabetic Korean population (N = 6634). In a multivariate logistic regression model, after adjustment for age, homeostasis model assessment of insulin resistance, body mass index, smoking history, C-reactive protein, and low-density lipoprotein cholesterol, adiponectin levels were inversely related with metabolic syndrome in men and women ($P < .05$). Adiponectin level was found to be a significant contributor to metabolic syndrome. Our findings suggest that adiponectin is an important biomarker even in a nondiabetic population at high risk of metabolic syndrome.

1. Introduction

Metabolic syndrome (MetS) is a common and major public health issue worldwide. Since Reaven and colleagues identified the MetS as a link between insulin resistance and hypertension, dyslipidemia, type 2 diabetes mellitus, obesity, and other associated atherogenic risk factors [1-3], adiponectin has been recognized as a key regulator of insulin sensitivity and a powerful predictor for the development of MetS associated with an increased risk of the occurrence of cardiometabolic diseases [4,5]. However, the exact nature and relative contribution of adiponectin, as a potential surrogate marker, warrant further investigation in a nondiabetic population. Hence, a work such as this, to elucidate the metabolic factors underpinning the association between adiponectin and MetS, has important clinical ramification for the prevention of and intervention against associated cardiometabolic diseases. We undertook this study to determine the association between adiponectin and MetS in a nondiabetic Korean population.

2. Material and methods

We conducted a comprehensive demographic and health survey on 10 114 healthy adults who participated in the

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Korean Genomic Rural Cohort Study from November 2005 to January 2008. All participants provided the investigators with signed consent before participation. The Institutional Review Board of Wonju Christian Hospital approved the study. A comprehensive demographic and health questionnaire including past medical history and treatment was used to obtain information related to exclusion criteria. Exclusion criteria included any known diagnosis of diabetes, hypertension, dyslipidemia, cancer, and the use of prescribed medications for these diagnoses. However, participants who were not diagnosed as such, but had signs of high blood pressure (BP), hyperlipidemia, and high fasting blood glucose (FBG) levels at the time of initial assessment were included in this study.

Of 10 114 adults, 6634 subjects who met the criteria were selected for data collection and analysis. In brief, the *National Cholesterol Education Program Adult Treatment Panel III Report–Asian Pacific Guideline* [6,7] was used for the diagnosis of MetS, which meant that subjects met at least 3 of the following criteria: waist circumference of at least 102 cm (male) or at least 88 cm (female), triglyceride (TG) of at least 150 mg/dL, high-density lipoprotein (HDL) cholesterol less than 40 mg/dL (male) or less than 50 mg/dL (female), BP of at least 130/85 mm Hg, and fasting plasma glucose of at least 110 mg/dL. For biochemical analyses, plasma insulin and adiponectin levels were measured by a radioimmunoassay (Linco Research, St. Charles, MO).

3. Statistical analysis

The data are expressed as frequencies, means, and odds ratio (OR). The *t* test or the Mann-Whitney *U* test, Pearson correlation, and multiple logistic regression analysis were performed using the Windows-based SPSS statistical package (version 12.0; SPSS, Chicago, IL). Multiple logistic regression models were also used to assess the association between adiponectin level and MetS while adjusting for potential confounding variables including age, HOMA-IR, C-reactive protein (CRP), body mass index (BMI), smoking history, LDL cholesterol, and TG. Odds ratios and 95% confidence intervals (CIs) were computed by quartile of adiponectin levels, and analyses were performed for men and women independently. To examine the association between adiponectin levels and cumulative number of metabolic components, multivariate analysis by logistic regression was implemented using the continuation-ratio model for increasing number of metabolic components. All statistical significances were determined at $P < .05$.

4. Results

4.1. Anthropometric and metabolic phenotype

Anthropometric and metabolic characteristics are presented in Table 1. The overall prevalence of MetS was 24.8% in men and 30.4% in women ($P < .05$). Body mass index was significantly greater in the MetS group than in the non-MetS group for men and women ($P < .05$). Median adiponectin level was significantly higher in the non-MetS group than in the MetS group. Insulin, HOMA-IR, and CRP were significantly higher in the MetS group than in the non-MetS group ($P < .05$). However, no significant differences in LDL for men and in smoking history for both men and women, respectively, were observed.

Table 1
Baseline anthropometric and metabolic characteristics of study population (N = 6634)

	Men (n = 2709)			Women (n = 3925)		
	Non-MetS (n = 2036)	MetS (n = 673)	*P*	Non-MetS (n = 2730)	MetS (n = 1195)	*P*
Anthropometric characteristics						
Age (y)	56.73 ± 8.01	55.67 ± 8.02	<.01	53.55 ± 8.15	56.43 ± 7.80	<.01
BMI (kg/m$^{2)}$	23.09 ± 2.64	25.84 ± 2.92	<.01	23.48 ± 2.99	26.12 ± 3.12	<.01
Systolic BP (mm Hg)	127.84 ± 16.20	138.79 ± 17.29	<.01	122.66 ± 16.24	135.48 ± 16.38	<.01
Diastolic BP (mm Hg)	81.88 ± 10.77	88.10 ± 10.89	<.01	77.58 ± 11.17	85.04 ± 10.47	<.01
Current smoker (n [%])	814 (40.14)	249 (37)	.28	55 (2.02)	15 (1.27)	.17
Metabolic characteristics						
Total cholesterol (mg/dL)	195.80 ± 36.19	203.10 ± 40.67	<.01	201.11 ± 36.40	213.30 ± 39.07	<.01
TG (mg/dL)	134.09 ± 84.84	247.95 ± 153.79	<.01	104.98 ± 49.73	191.89 ± 98.08	<.01
HDL cholesterol (mg/dL)	48.07 ± 11.82	37.98 ± 8.50	<.01	49.99 ± 10.98	41.72 ± 7.36	<.01
LDL cholesterol (mg/dL)	112.55 ± 31.27	114.15 ± 33.64	.26	119.35 ± 31.01	128.59 ± 33.85	<.01
FBG (mg/dL)	92.68 ± 12.22	104.19 ± 29.19	<.01	88.85 ± 8.78	94.50 ± 16.80	<.01
Waist circumference (cm)	83.00 ± 7.14	90.9 ± 7.27	<.01	77.92 ± 7.73	86.40 ± 7.04	<.01
Insulin (μIU/mL)	6.90 ± 3.53	10.01 ± 6.45	<.01	7.92 ± 3.76	9.79 ± 5.67	<.01
HOMA-IR[a]	1.41 (1.09, 1.84)	2.11 (1.60, 2.94)	<.01	1.54 (1.24, 2.01)	2.00 (1.52, 2.70)	<.01
CRP (mg/L)[a]	0.80 (1.44, 1.79)	1.24 (0.65, 2.33)	<.01	0.53 (0.30, 1.12)	0.92 (0.49, 1.73)	<.01
Adiponectin (μg/mL)[a]	8.12 (5.72, 1.27)	5.88 (4.81, 8.15)	<.01	12.20 (8.99, 15.78)	9.88 (7.32, 13.04)	<.01

Values are expressed as mean ± SD or number (percentage).

[a] Values are expressed as median (lower quartile-upper quartile). *P* value from Mann-Whitney *U* test at $P < .05$.

Table 2
Sex-adjusted Pearson correlation of study variables

	Waist	TG	HDL	FBG	SBP	HOMA-IR	Adiponectin	CRP
Waist	1.0							
TG	0.276*	1.0						
HDL	−0.178*	−0.350*	1.0					
FBG	0.135*	0.160*	−0.055*	1.0				
SBP	0.189*	0.178*	−0.003	0.128 *	1.0			
HOMA-IR	0.360*	0.244*	−0.152*	0.456*	0.181*	1.0		
Adiponectin	−0.221*	−0.228*	0.233*	−0.133*	−0.055*	−0.221*	1.0	
CRP	0.067*	−0.015	−0.031*	0.037*	0.017	0.046*	−0.027*	1.0

SBP indicates systolic blood pressure.
* $P < .05$.

4.2. Relationship between adiponectin level and metabolic components

The relationships between the adiponectin level and metabolic components are shown in Table 2. The adiponectin levels were inversely related to waist circumference ($r = -0.22$), TG ($r = -0.23$), BP ($r = -0.06$), FBG ($r = -0.13$), HOMA-IR ($r = -0.22$), and CRP ($r = -0.03$), but positively associated with HDL cholesterol ($r = 0.23$).

4.3. Multivariable adjusted OR for MetS by quartile of adiponectin

As shown in Table 3, the multivariable adjusted OR (95% CI) of MetS with the highest quartile compared with that of a lower quartile of adiponectin showed that adiponectin was significantly associated with MetS for men (OR, 4.8; 95% CI, 3.62-6.34) and women (OR, 4.2; 95% CI, 3.38-5.22). Further adjustment for age and smoking history (pack years), BMI, and LDL cholesterol attenuated this association; and adiponectin remained significantly connected with an increased risk of MetS in men (OR, 2.4; 95% CI, 1.7-3.4) and women (OR, 1.8; 95% CI, 1.4-2.4).

4.4. Multivariate analysis by logistic regression using the continuation-ratio model for increasing number of metabolic components

In the continuation-ratio model, cumulative number of metabolic components was inversely associated with adiponectin level (OR, 0.48; 95% CI, 0.41-0.55 in men and OR, 0.42; 95% CI, 0.37-0.48 in women) and directly associated with HOMA-IR (Table 4). Fig. 1 also highlights a trend of adiponectin and HOMA-IR according to number of MetS components.

5. Discussion

This is the first large cross-sectional study to highlight the important relationship between adiponectin levels and MetS of a nondiabetic Korean general population in rural areas, whereas other population-based studies have primarily focused on hospital-based population [8-10]. Certainly, our findings demonstrate that MetS is common even among the nondiabetic Korean adults, as evidenced by an association with adiponectin levels. In addition, serum adiponectin levels were significantly associated with the individual components of MetS, CRP, and HOMA-IR. These results could further strengthen the notion that adiponectin mediates insulin-sensitizing, anti-inflammatory, and antidyslipidemic activities as an important biomarker [10-13]. Another novel finding of this present study revealed an inverse trend between the adiponectin levels and increasing number of MetS components, further corroborating a possible serious link with an increased risk of coronary artery heart disease and diabetes [14]. A significant sex difference in adiponectin levels was observed in this study. Women's adiponectin levels were substantially higher than men's despite a higher

Table 3
Multivariable-adjusted ORs for MetS by quartile of adiponectin level

		Model I, OR (95% CI)	P	Model II R (95% CI)	P	Model III OR (95% CI)	P
Men	4th quartile (>10.67)	1		1		1	
	3rd quartile (≤10.67)	1.5 (1.10-2.03)	<.01	1.47 (1.07-2.02)	.02	1.18 (0.81-1.71)	.39
	2nd quartile (≤7.45)	2.92 (2.20-3.89)	<.01	2.57 (1.91-3.48)	<.01	1.56 (1.10-2.26)	.01
	1st quartile (≤5.19)	4.79 (3.62-6.34)	<.01	3.86 (2.87-5.18)	<.01	2.42 (1.70-3.44)	<.01
Women	4th quartile (>14.98)	1	1	1			
	3rd quartile (≤14.98)	1.73 (1.38-2.15)	<.01	1.64 (1.31-2.05)	<.01	1.2 (0.92-1.58)	.18
	2nd quartile (≤11.46)	3.07 (2.48-3.80)	<.01	2.73 (2.19-3.40)	<.01	1.72 (1.32-2.29)	<.01
	1st quartile (≤8.31)	4.2 (3.38-5.22)	<.01	3.33 (2.66-4.16)	<.01	1.82 (1.39-2.40)	<.01

Model I: adjusted for age. Model II: adjusted for age, HOMA-IR, and CRP. Model III: adjusted for age, HOMA-IR, CRP, BMI, smoking history (pack years), LDL cholesterol, and TG.

Table 4
Multivariable-adjusted ORs for number of MetS components by logistic regression using continuation-ratio model

		Model I			Model II			Model III		
		OR	95%CI	*P*	OR	95%CI	*P*	OR	95%CI	*P*
Men	Adiponectin	0.41	(0.36-0.47)	<.01	0.41	(0.36-0.47)	<.01	0.6	(0.52-0.69)	<.01
	HOMA-IR	1.71	(1.60-1.82)	<.01	1.71	(1.60-1.83)	<.01	1.27	(1.19-1.35)	<.01
Women	Adiponectin	0.36	(0.32-0.41)	<.01	0.36	(0.32-0.41)	<.01	0.55	(0.48-0.63)	<.01
	HOMA-IR	1.55	(1.46-1.64)	<.01	1.54	(1.45-1.63)	<.01	1.18	(1.12-1.25)	<.01

Model I: adjusted for age and adiponectin (log transformed) or HOMA-IR. Model II: adjusted for age, adiponectin (log transformed) or HOMA-IR, and CRP. Model III: adjusted for age, adiponectin (log transformed) or HOMA-IR, CRP, BMI, smoking history (packs years), LDL cholesterol, and TG.
* $P < .05$.

prevalence of MetS in women. This sex difference has been linked to androgen levels, which have an inhibitory effect on adiponectin [15].

This study has limitations because of the cross-sectional nature and the fact that we have examined total adiponectin levels rather than high–molecular weight adiponectin. Hence, it is unknown whether the high molecular form is more strongly associated with MetS than is total adiponectin levels. It may be of interest to elucidate this potential mechanism in the context of the low or high molecular forms and determine the direction of causality in a future longitudinal study.

In conclusion, our findings demonstrate that adiponectin is an important surrogate marker to determine the increasing risk factors associated with MetS in a nondiabetic Korean population. Clinically, this study provides useful information with which clinicians can identify individuals at high risk of MetS, potentially contributing to the development of effective prevention and treatment strategies for cardiometabolic diseases.

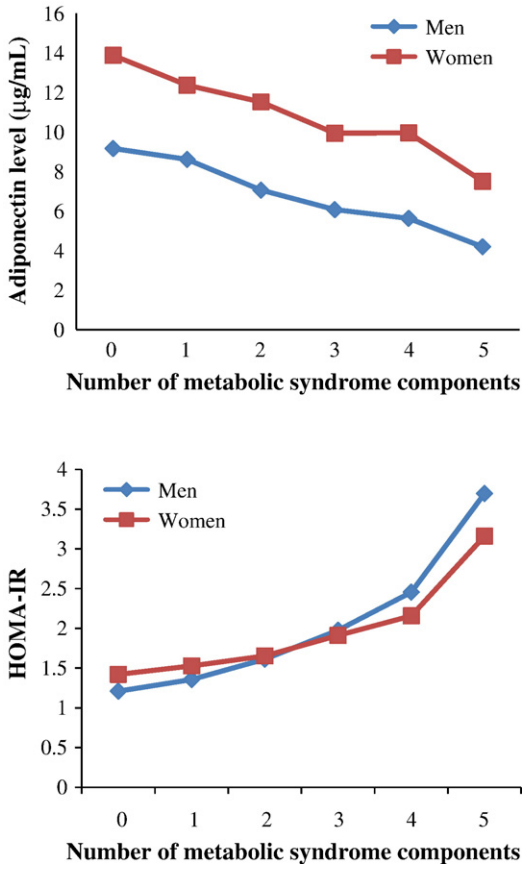

Fig. 1. Trend lines of adiponectin levels and HOMA-IR according to increasing number of MetS components.

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