



Associations Between Lipid Measures and Metabolic Syndrome, Insulin Resistance and Adiponectin

– Usefulness of Lipid Ratios in Korean Men and Women –

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Background: Several reports have raised the possibility that newly addressed lipid measures might be superior to the traditional ones for cardiovascular risk prediction. However, data on the associations between these lipid measures with metabolic syndrome (MetS) is limited.

Methods and Results: A cross-sectional study of participants in routine health examinations was performed. The associations between lipid measure variables (total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), TC/HDL-C, LDL-C/HDL-C, TG/HDL-C ratio and non-HDL-C) and MetS, insulin resistance (IR) by homeostatic model assessment (HOMA) and adiponectin were analyzed in 6,546 participants (3,820 men; mean age 46.0±9.2 years in men, 44.6±9.5 years in women). In multivariable adjusted regression analysis, the 3 lipid ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C showed significant association with the number of MetS components, HOMA and log adiponectin level in both men and women without MetS ($P<0.001$, respectively), though these relations were weaker in participants with MetS. The mean levels of the lipid ratios also associated with increasing numbers of the MetS components, quartiles of HOMA and adiponectin.

Conclusions: Lipid ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C, as well as TG and HDL, were consistently associated with MetS and IR in participants without MetS. Lipid ratios might be used as integrated and simple lipid measures. (*Circ J* 2010; **74**: 931–937)

Key Words: High-density lipoprotein; Insulin resistance; Lipids; Metabolic syndrome; Triglycerides

Metabolic syndrome (MetS) is known as the cluster of changes associated with resistance to insulin, which plays an important role in patients with coronary heart disease (CHD).^{1,2} Increased all-cause and cardiovascular disease (CVD) mortality with the MetS have been reported repeatedly in previous studies.^{3–8} However, the certainty of pathogenesis of insulin resistance (IR) and the predictive value for CVD of MetS has been challenged because of the insufficiency of conclusive evidence.⁹

Dyslipidemia is another well-known major risk factor for CHD, as well as a component of MetS, and the role of low-density lipoprotein cholesterol (LDL-C) in CVD is well established. Over the past several years, a number of clinical trials that have primarily targeted LDL-C have demonstrated clinical benefits of lipid-lowering therapy, with a significant reduction in cardiovascular events. However, 60–70% of CVD

events continue to occur despite LDL-lowering therapy. Therefore, a need for new targets to complement the measures of LDL lowering has been suggested.¹⁰

Several reports have raised the possibility that newly addressed lipid measures might be superior to the traditional ones used for cardiovascular risk prediction. Triglycerides (TG)¹¹ and high-density lipoprotein cholesterol (HDL-C)¹² are not only independent risk factors of CVD, but also components of MetS.¹³ Several lipid ratios have been proposed as simple, convenient clinical indicators because of the integrative information of the multiple variables. The TG/HDL-C ratio has been advocated as an indicator of IR,^{14–16} and the total cholesterol (TC)/HDL-C ratio has shown a predictive value for CVD.^{17,18} The LDL-C/HDL-C ratio has shown similar predictive potential for CHD as the TC/HDL-C ratio, though the published reports are not entirely consistent.¹⁹

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Table 1. General Characteristics of the Study Participants According to the Presence or Absence of MetS

	Men (n=3,820)		Women (n=2,726)	
	With MetS (n=740)	Without MetS (n=3,080)	With MetS (n=283)	Without MetS (n=2,443)
Age, years	47.8±9.4	45.6±9.2***	52.3±10.4	43.7±9.0***
BMI, kg/m ²	27.0±2.6	24.1±2.4***	26.2±2.9	22.4±2.7***
WC, cm	92.3±6.6	83.8±6.7***	85.4±6.7	74.2±7.4***
FBG, mg/dl	108.2±30.6	92.9±14.3***	102.3±27.8	87.3±9.7***
Fasting insulin, μ U/ml	6.4±3.7	3.8±2.6***	6.2±3.7	3.6±2.4***
HOMA	1.7±1.1	0.9±0.7***	1.6±1.1	0.8±0.6***
Adiponectin, μ g/ml	5.6±3.4	7.2±4.1***	8.6±5.3	11.0±5.9***
No. of MetS components	3.3±0.6	0.9±0.8***	3.4±0.6	0.6±0.7***
SBP, mmHg	131.7±12.4	121.8±13.0***	129.9±13.5	114.2±13.3***
DBP, mmHg	85.5±28.6	76.6±10.2***	80.6±10.1	70.9±9.8***
Nonsmoker	159 (21.5)	806 (26.2)	267 (94.4)	2,289 (93.7)
Ex-smoker	268 (36.2)	1,069 (34.7)	5 (1.8)	61 (2.5)
Current smoker	313 (42.3)	1,205 (39.1)*	11 (3.9)	93 (3.8)
Drinker	657 (89.9)	2,726 (89.2)	159 (58.7)	1,113 (46.7)**
Regular exercise†	344 (67.2)	1,385 (66.7)	109 (56.2)	896 (56.1)
Hypertension	416 (56.2)	669 (21.7)***	151 (53.4)	261 (10.7)***
Diabetes	168 (22.7)	142 (4.6)***	54 (19.1)	29 (1.2)***
Dyslipidemia	56 (7.6)	135 (4.4)**	23 (8.1)	67 (2.7)***

Data are mean \pm SD or n (%).

*P between 0.05 and 0.01, **P between 0.01 and 0.001, ***P<0.001 with MetS vs without MetS in men and women, respectively.

†Data available for 2,590 men and 1,792 women.

Hypertension defined as SBP \geq 140mmHg, DBP \geq 90mmHg or history of the disorder; diabetes defined as FBG \geq 126mg/dl (7.0mmol/L) or history of the disorder; dyslipidemia defined as self-reported past history or taking medication.

MetS, metabolic syndrome; BMI, body mass index; WC, waist circumference; FBG, fasting blood glucose; HOMA, homeostatic model assessment; SBP, systolic blood pressure; DBP, diastolic blood pressure.

However, data on the associations between these lipid measures, especially the lipid ratios, with MetS is limited. To improve the understanding of the association between the lipid variables and MetS, we analyzed the associations between potentially valuable lipid measures and MetS, as well as IR and adiponectin. IR has been described as a major etiology of MetS,^{1,2} and adiponectin is known to be closely related.²⁰ Though several lipid measures have been introduced as useful indicators of CVD risk, it is also necessary to refine their meaning in relation to MetS. Our present analysis of Korean men and women was to assess the value of lipid measures within the common core area of MetS, IR and adiponectin.

Methods

Subjects

A cross-sectional study of participants in routine health examinations at the health promotion center of Severance Hospital and Ewha Womans University Mokdong Hospital was performed from April 2006 to June 2007. All the 6,546 subjects (3,820 men, 2,726 women) who completed an annual health evaluation completed a structured questionnaire that collected demographic and clinical characteristics including serum insulin and adiponectin levels. The Institutional Review Board of Human Research of Yonsei University approved this study and written informed consent was given by all the participants before enrollment.

Data Collection

The examinations were performed according to a standard protocol. The structured questionnaire were used to investigate smoking, alcohol and exercise habits and other demographic characteristics. Participants were also asked if they had any disease or if they were taking any medication. The data were checked and cleaned again during the analysis. Weight and height were measured by experienced medical staff and we calculated the body mass index (BMI, kg/m²). Diabetes was defined as a self-reported history of the disorder or when the fasting blood glucose (FBG) level was \geq 126mg/dl. Hypertension was defined as a self-reported history of the disorder or when systolic blood pressure (BP) was \geq 140mmHg or diastolic BP \geq 90mmHg. Dyslipidemia was defined as a self-reported past history or medication for dyslipidemia. MetSs was defined as the presence of at least 3 of the 5 components described by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III),¹³ except waist circumference, the cutoff value of which was modified for Asian populations:²¹ (1) waist circumference $>$ 90cm for men and $>$ 80cm for women; (2) TG level \geq 150mg/dl; (3) HDL-C $<$ 40mg/dl for men and $<$ 50mg/dl for women; (4) systolic BP \geq 130mmHg or diastolic BP \geq 85mmHg; (5) FBG level \geq 110mg/dl.

Laboratory Methods

Peripheral venous blood samples were collected at 08.00h after 12h of fasting and were stored at -80°C within 2h until analysis. FBG, TC, TG, HDL-C, LDL-C and other biomarkers were measured with a Hitachi-7600 analyzer (Hitachi Ltd,

Table 2. Clinical Characteristics of the Study Participants by Lipid Measures

Characteristics	Men (n=3,820)		Women (n=2,726)	
	With MetS	Without MetS	With MetS	Without MetS
TC, mg/dl	193.4±34.5	186.7±30.3***	193.7±34.6	181.4±32.3***
TG, mg/dl	235.2±145.0	126.5±74.6***	173.3±83.9	82.8±42.2***
HDL-C, mg/dl	42.1±8.5	51.3±10.7***	45.5±8.7	60.6±12.4***
LDL-C, mg/dl	114.7±30.3	115.9±28.2	119.0±30.9	107.1±29.8***
TC/HDL-C	4.7±1.1	3.8±0.9***	4.4±0.9	3.1±0.8***
LDL-C/HDL-C	2.8±0.8	2.4±0.7***	2.7±0.8	1.8±0.7***
TG/HDL-C	6.0±4.7	2.7±2.0***	4.0±2.1	1.5±1.0***
Non-HDL-C	151.3±33.5	135.4±30.7***	148.2±33.2	120.8±31.6***

Data are mean±SD.

***P<0.001 with MetS vs without MetS in men and women, respectively.

TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol. Other abbreviation see in Table 1.

Table 3. Regression Analysis of the Lipid Measures With the Number of MetS Components and Insulin Resistance in Participants Without MetS

	β (SE)		
	No. of MetS components	HOMA	Log adiponectin
Men (n=3,080)			
TC, mg/dl	0.0007 (0.000)	0.020 (0.007)**	−0.001 (0.000)**
TG, mg/dl	0.0040 (0.000)***	0.031 (0.003)***	−0.001 (0.000)***
HDL-C, mg/dl	−0.018 (0.001)***	−0.127 (0.019)***	0.010 (0.001)***
LDL-C, mg/dl	−0.0001 (0.000)	0.022 (0.007)**	−0.0002 (0.000)
TC/HDL-C	0.240 (0.013)***	1.780 (0.227)***	−0.122 (0.011)***
LDL-C/HDL-C	0.198 (0.017)***	1.817 (0.280)***	−0.096 (0.014)***
TG/HDL-C	0.154 (0.005)***	1.075 (0.099)***	−0.039 (0.005)***
Non-HDL-C	0.0029 (0.000)***	0.036 (0.007)***	−0.002 (0.000)***
Women (n=2,443)			
TC, mg/dl	−0.001 (0.000)**	−0.001 (0.006)	−0.0001 (0.000)
TG, mg/dl	0.005 (0.000)***	0.042 (0.005)***	−0.001 (0.000)***
HDL-C, mg/dl	−0.018 (0.001)***	−0.075 (0.016)***	0.010 (0.001)***
LDL-C, mg/dl	0.001 (0.000)*	0.013 (0.007)	−0.001 (0.000)**
TC/HDL-C	0.294 (0.015)***	1.229 (0.275)***	−0.161 (0.016)***
LDL-C/HDL-C	0.291 (0.018)***	1.415 (0.311)***	−0.161 (0.019)***
TG/HDL-C	0.258 (0.011)***	1.774 (0.196)***	−0.082 (0.012)***
Non-HDL-C	0.002 (0.000)***	0.012 (0.007)	−0.002 (0.000)***

With adjustment for age, WC, SBP, smoking status, and alcohol drinking.

*P between 0.05 and 0.01, **P between 0.01 and 0.001, and ***P<0.001. Adiponectin was log-transformed to achieve normal distribution.

SE, standard error. Other abbreviations see in Tables 1, 2.

Tokyo, Japan). Insulin was analyzed by solid-phase 2-site chemiluminescent immunometric assay with IMMULITE 2000 (Diamond Diagnostics, Holliston, MA, USA). The homeostatic model assessment of IR (HOMA-IR) was calculated as: $\text{HOMA} = \text{FBG (mg/dl)} \times \text{fasting serum insulin } (\mu\text{U/ml}) / 405$.²² Adiponectin levels were measured using an enzyme-linked immunosorbent assay (Mesdia Co, Ltd, Seoul, Republic of Korea). The intra- and interassay variances of adiponectin were 6.3–7.4% and 4.5–8.6%, respectively.²³

Statistical Analysis

The results are presented as mean±standard deviation (SD) or number (%). Differences in general and clinical characteristics between the with and without MetS groups were compared with Student's t-test (continuous variables) or the chi-square test (categorical variables) in men and women, respectively. The associations between lipid variables [TC, TG, LDL-C,

HDL-C, TC/HDL-C, LDL-C/HDL-C, TG/HDL-C and non-HDL-C] and MetS, IR measured by HOMA, and adiponectin were analyzed. Linear regression analysis was performed to test associations between lipid measures and the number of MetS components, HOMA and log adiponectin with adjustment for age, waist, systolic BP, smoking²⁴ and alcohol status. Log-transformed adiponectin was used to achieve a normal distribution. Mean levels and standard deviations of lipid ratios were calculated according to the number of MetS components, HOMA quartiles, and adiponectin quartiles in men and women, respectively. The differences between each mean value of the lipid ratio levels were assessed by ANOVA tests.

All statistical tests were 2-sided, and differences with a P<0.05 were considered to be statistically significant. All analyses were conducted using SAS statistical software, version 9.1 (SAS Institute Inc, Cary, NC, USA) for statistical analysis.

Table 4. Regression Analysis of the Lipid Measures With the Number of MetS Components and Insulin Resistance in Participants With MetS			
	No. of MetS components	β (SE)	
		HOMA	Log adiponectin
Men (n=740)			
TC, mg/dl	0.0004 (0.001)	0.054 (0.022)*	−0.001 (0.001)
TG, mg/dl	0.001 (0.000)***	0.019 (0.005)**	−0.0002 (0.000)
HDL-C, mg/dl	−0.023 (0.002)***	−0.039 (0.088)	0.011 (0.002)***
LDL-C, mg/dl	0.002 (0.001)**	0.029 (0.024)	0.001 (0.001)
TC/HDL-C	0.389 (0.014)***	1.233 (0.657)	−0.068 (0.018)**
LDL-C/HDL-C	0.089 (0.025)**	0.903 (0.908)	−0.046 (0.025)
TG/HDL-C	0.031 (0.004)***	0.461 (0.155)**	−0.008 (0.004)
Non-HDL-C	0.152 (0.017)***	0.060 (0.022)**	−0.001 (0.001)*
Women (n=283)			
TC, mg/dl	0.0004 (0.001)	0.104 (0.035)**	0.000 (0.001)
TG, mg/dl	0.002 (0.000)***	0.083 (0.014)***	−0.005 (0.000)
HDL-C, mg/dl	−0.017 (0.004)***	0.032 (0.139)	0.007 (0.004)
LDL-C, mg/dl	−0.0003 (0.001)	0.068 (0.039)	0.001 (0.001)
TC/HDL-C	0.122 (0.036)**	2.951 (1.281)*	−0.070 (0.038)
LDL-C/HDL-C	0.074 (0.043)	2.487 (1.522)	−0.028 (0.046)
TG/HDL-C	0.095 (0.016)***	2.528 (0.582)***	−0.032 (0.018)
Non-HDL-C	0.002 (0.001)	0.109 (0.036)**	−0.000 (0.001)

With adjustment for age, WC, SBP, smoking status, and alcohol drinking.
*P between 0.05 and 0.01, **P between 0.01 and 0.001, and ***P<0.001. Adiponectin was log-transformed to achieve normal distribution.
Abbreviations see in Tables 1–3.

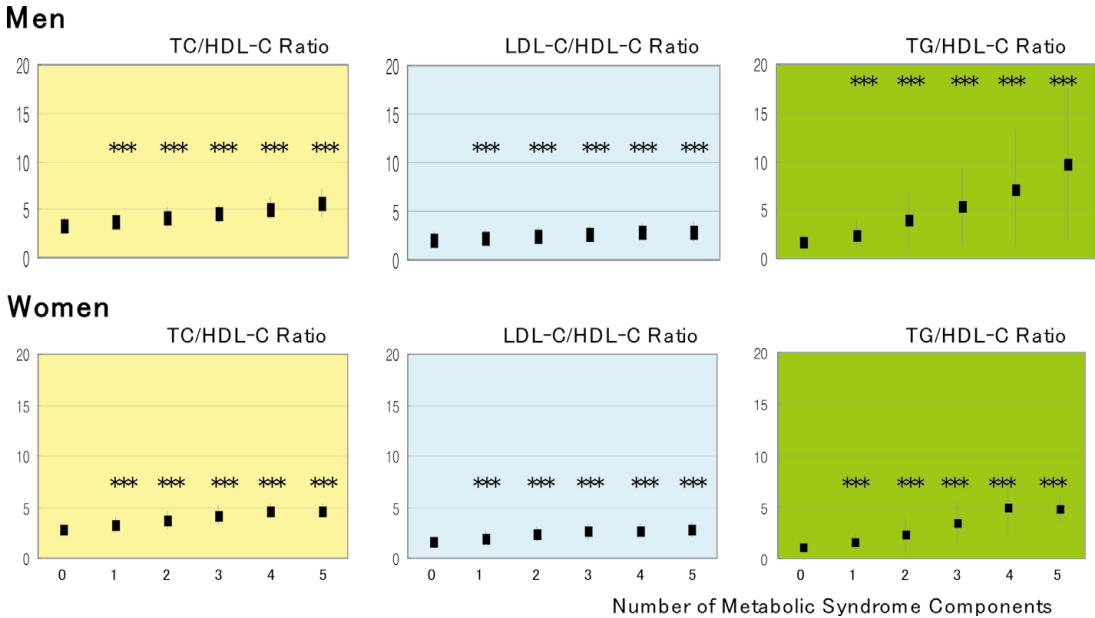


Figure. Lipid ratio levels according to the number of metabolic syndrome components in men and women. Mean \pm standard deviation of the lipid ratio levels. ***P<0.001, compared with the lipid ratio level without any metabolic syndrome component. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

Results

The baseline characteristics of the study population are shown in Table 1. Mean age was 46.0 \pm 9.2 years in men and 44.6 \pm 9.5 in women. The mean age, BMI, waist circumference,

FBG, fasting insulin, HOMA, BP and the number of MetS components showed differences between the groups with and without MetS, both in men and women. The number of MetS components was 3.3 \pm 0.6 in men with MetS and 0.9 \pm 0.8 in men without MetS (Table 1).

Table 5. Lipid Measure Levels According to the Quartiles of Insulin Resistance in Men and Women

	HOMA				Adiponectin			
	0≤Q1<4.8	4.8≤Q2<7.3	7.3≤Q3<10.8	10.8≤Q4	0≤Q1<8.8	4.8≤Q2<14.2	14.2≤Q3<22	22≤Q4
Men (n=3,080)								
TC/HDL-C	3.5±0.9	3.8±0.9	4.1±1.0	4.4±1.0***	4.3±1.1	4.0±1.0	3.8±1.0	3.5±0.9***
LDL-C/HDL-C	2.2±0.7	2.3±0.7	2.5±0.7	2.7±0.8***	2.6±0.8	2.5±0.7	2.4±0.8	2.2±0.7***
TG/HDL-C	2.2±2.2	2.7±2.0	3.4±2.7	4.6±4.0***	4.0±3.6	3.3±2.8	2.9±2.7	2.3±1.5***
Women (n=2,443)								
TC/HDL-C	2.9±0.7	3.1±0.8	3.3±0.9	3.7±1.0***	3.5±1.0	3.4±0.9	3.2±0.8	3.0±0.8***
LDL-C/HDL-C	1.7±0.6	1.8±0.7	2.0±0.7	2.3±0.8***	2.1±0.8	2.1±0.8	1.9±0.7	1.8±0.7***
TG/HDL-C	1.3±0.9	1.5±1.1	1.8±1.3	2.6±1.9***	2.2±1.9	2.0±1.5	1.7±1.3	1.5±1.1***

***P<0.001 with vs without MetS in men and women, respectively.
Abbreviations see in Tables 1,2.

Mean TC levels were 188.0±31.3 mg/dl in men and 182.7±32.8 mg/dl in women. The mean TC/HDL-C was 4.0±1.0 and 3.2±0.9 and TG/HDL-C was 3.3±3.0 and 1.7±1.4 for men and women, respectively (Table 2).

In regression analysis of the lipid measures with MetS and IR after adjustment for multiple covariables in participants without MetS, TC/HDL-C ($\beta=0.240$ with number of MetS components, $P<0.0001$; 1.780 with HOMA, $P<0.001$), LDL-C/HDL-C ($\beta=0.198$ with number of MetS components, $P<0.0001$; 1.817 with HOMA, $P<0.0001$) and TG/HDL-C ($\beta=0.154$ with number of MetS components, $P<0.0001$; 1.075 with HOMA, $P<0.0001$) showed significant positive associations with both the number of MetS components and HOMA in men. TC and LDL-C failed to show significant correlation with all 3 of the MetS-associated variables. TG, HDL-C, and non-HDL-C had statistically significant correlations; however, all their β estimates were lower than 0.127 (0.001–0.127). These results were similar in women without MetS. The 3 lipid ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C consistently showed significant negative correlations with the number of MetS components, HOMA and log adiponectin (Table 3). When we repeated the regression analysis after exclusion of participants with past history of or medications for dyslipidemia, there was no difference in the results (data not shown). However, these relations were weaker in participants with MetS (Table 4).

The mean level of TC/HDL-C was 3.4 (SD 0.7) in participants without any MetS components, whereas it was 5.7 (SD 1.4) in participants with 5 MetS components. The mean levels of LDL-C/HDL-C and TG/HDL-C also increased with increasing number of MetS components. Every mean level of the 3 lipid ratios in participants with any MetS components was significantly higher than those in participants without any components ($P<0.0001$). In men, the TC/HDL-C and TG/HDL-C levels were significantly ($P<0.0001$) different among all of the 6 groups of MetS components (0–5). However, in our analysis of LDL-C/HDL-C, the groups with 2–4 components failed to show a significant difference with the 5 components group. In women, the TC/HDL-C and LDL-C/HDL-C levels were significantly ($P<0.0001$) different between the group with 0–2 components and the 5 components group. In the TG/HDL-C analysis, all groups except those with between 4 and 5 components, showed differences with each other (data not shown) (Figure). The mean levels of single lipid measures (TC, HDL-C, LDL-C, TG) were also associated with increasing number of MetS components (data not shown) Table 5 shows the lipid measure levels according to the levels of IR, which were consistently associated with the

levels of the HOMA and adiponectin quartiles.

Discussion

In our results, 3 lipid ratios were prominent and consistent measures associated with MetS, IR and adiponectin.

Among several proposed lipid markers, TG and HDL-C are key metabolic abnormalities in patients with IR. The TG level was an associated factor with ischemic heart disease, independent of HDL-C concentrations,¹¹ and there is a large body of experimental evidence to suggest that augmenting HDL-C can have major protective effects, from prevention to stabilization and regression of vascular abnormalities, independent of TC or non-HDL-C levels.¹⁰ After 10-year follow-up of 12,339 middle-aged participants in the Atherosclerosis Risk in Communities (ARIC) Study, LDL-C, HDL-C, lipoprotein(a), and in women but not men, TG, were all independent CHD predictors.¹² In terms of sex differences, the levels of TG or TG/HDL-C ratio seemed to be higher in the men in our study. However, the correlations between MetS and TG or TG/HDL-C levels in the regression analysis showed similar results in men and women.

TG/HDL-C has advantages for standardization and identification of patients with an atherogenic lipoprotein profile as a convenient indicator of IR.^{13,14} The necessity to evaluate the value of the TG/HDL-C ratio to predict not only IR but also MetS was suggested in a recent study;²⁵ however, the predictive value of the TG/HDL-C ratio is not completely understood. In a recent prospective study, the TG/HDL-C ratio was an imperfect surrogate for IR and its associated CHD risk, and was only slightly better than the TC/HDL-C ratio for this purpose.²⁶ In our study, the TG/HDL-C ratio showed possibility as a useful marker; however, its range appeared wider than that of the other ratios and we could not directly compare the predictive power of the measures in this cross-sectional study. Further studies are needed to evaluate the strength of TG/HDL-C as a predictor.

Other lipid measures have shown their own predictive value for CVD. Apolipoprotein B (ApoB) and the ApoB/apolipoproteinA-1 (ApoA-I) ratio were strongly and positively related to increased risk of fatal myocardial infarction in both men and women. They are thought to be useful predictors, especially for patients with normal LDL cholesterol levels;²⁷ however, the TC/HDL-C ratio was as good as or better than the apolipoprotein fractions in predicting CVD in a prospective cohort study of over 15,000 US women who were followed over 10 years.¹⁷ According to a recent cohort study, measurement of ApoB or ApoA-I in clinical practice

was not supported when TC and HDL-C results are available.¹⁹

In our study, the correlations between MetS and single lipid measures were relatively low. The LDL-C or TC level has been widely used to assess lipid atherogenesis, but its utility for IR is not well known, in contrast to TG or HDL-C. Though non-HDL-C is suggested to have predictive value for CVD in prospective studies,¹⁷ the relation of non-HDL-C to MetS seemed to be weaker than that of TG/HDL-C or HDL in Korean women.²⁸ Lipid ratios that include information on at least 2 measures might have a more integrated and concentrated explanation than single lipid measures, even TG or HDL-C.

The lipid ratios showed a close correlation not only with MetS, but with IR and adiponectin as well, though the relation was weaker in MetS patients, which might support the consistency of the present results. Adiponectin is known as an inverse predictor of CVD,²⁰ so the negative correlation in the present results is coincident with previous reports.

There is the possibility of racial difference in lipid measures. In African-Americans, TG levels and the TG/HDL-C ratio are not reliable markers of IR.²⁹ In a Taiwanese cohort study, the ApoB or TC/HDL-C concentration was a better predictor of CHD than other lipid markers in Chinese.¹⁸ In Korean women, HDL-C, TG/HDL-C and TG correlated with MetS, based on definitions by the NCEP and IDF without adjustment for important variables including smoking and alcohol status.²⁸ The present study provides additional information about lipid measures in both male and female Asians.

Study Limitations

First, although the study subjects were a general population, they might have better health-related behavior or higher socioeconomic status than others because they chose to take a routine health examination. Second, this study had a cross-sectional design, so we cannot exclude potential biases. Third, TG and HDL-C are included in the criteria of MetS, so the usefulness of TG/HDL-C has limitations, though the analysis with IR and adiponectin also revealed similar results. Fourth, data on ApoB and ApoA-I levels were not collected in our study.

In conclusion, lipid ratios of TC/HDL-C, LDL-C/HDL-C and TG/HDL-C, as well as TG and HDL levels, were consistently associated with MetS and IR in participants without MetS. Lipid ratios might be useful as integrated and simple lipid measures. Further long-term prospective research is needed to reveal the predictive value of the lipid ratios for CVD in association with MetS and to find their optimal cut-off values.

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References

- Reaven GM. Banting Lecture 1988: Role of insulin resistance in human disease. *Diabetes* 1988; **37**: 1595–1607.
- Reaven GM. Role of insulin resistance in human disease (Syndrome X): An expanded definition. *Annu Rev Med* 1993; **44**: 121–131.
- Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; **24**: 683–689.
- Meigs JB. Epidemiology of the metabolic syndrome, 2002. *J Manag Care* 2002; **8**: S283–S292; quiz S293–S296.
- Kajimoto K, Kasai T, Miyauchi K, Hirose H, Yanagisawa N, Yamamoto T, et al. Metabolic syndrome predicts 10-year mortality in non-diabetic patients following coronary artery bypass surgery. *Circ J* 2008; **72**: 1481–1486.
- Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002; **288**: 2709–2716.
- Saito I, Iso H, Kokubo Y, Inoue M, Tsugane S. Metabolic syndrome and all-cause and cardiovascular disease mortality: Japan Public Health Center-based Prospective (JPHC) Study. *Circ J* 2009; **73**: 878–884.
- Tseng CH, Chong CK, Tseng CP, Shau WY, Tai TY. Hypertension is the most important component of metabolic syndrome in the association with ischemic heart disease in Taiwanese type 2 diabetic patients. *Circ J* 2008; **72**: 1419–1424.
- Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: Time for a critical appraisal: Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia* 2005; **48**: 1684–1699.
- Shah PK, Kaul S, Nilsson J, Cercek B. Exploiting the vascular protective effects of high-density lipoprotein and its apolipoproteins: An idea whose time for testing is coming. Part I. *Circulation* 2001; **6**: 2376–2383.
- Egger M, Smith GD, Pfluger D, Altpeter E, Elwood PC. Triglyceride as a risk factor for ischaemic heart disease in British men: Effect of adjusting for measurement error. *Atherosclerosis* 1999; **143**: 275–284.
- Sharrett AR, Ballantyne CM, Coady SA, Heiss G, Sorlie PD, Catellier D, et al. Coronary heart disease prediction from lipoprotein cholesterol levels, triglycerides, lipoprotein(a), apolipoproteins A-I and B, and HDL density subfractions: The Atherosclerosis Risk in Communities (ARIC) Study. *Circulation* 2001; **104**: 1108–1113.
- Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; **285**: 2486–2497.
- McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. *Ann Intern Med* 2003; **139**: 802–809.
- McLaughlin T, Reaven G, Abbasi F, Lamendola C, Saad M, Waters D, et al. Is there a simple way to identify insulin-resistant individuals at increased risk of cardiovascular disease? *Am J Cardiol* 2005; **96**: 399–404.
- Hannon TS, Bacha F, Lee SJ, Janosky J, Arslanian SA. Use of markers of dyslipidemia to identify overweight youth with insulin resistance. *Pediatr Diabetes* 2006; **7**: 260–266.
- Ridker PM, Rifai N, Cook NR, Bradwin G, Buring JE. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. *JAMA* 2005; **294**: 326–333.
- Chien KL, Hsu HC, Su TC, Chen MF, Lee YT, Hu FB. Apolipoprotein B and non-high density lipoprotein cholesterol and the risk of coronary heart disease in Chinese. *J Lipid Res* 2007; **48**: 2499–2505.
- Ingelsson E, Schaefer EJ, Contois JH, McNamara JR, Sullivan L, Keyes MJ, et al. Clinical utility of different lipid measures for prediction of coronary heart disease in men and women. *JAMA* 2007; **298**: 776–785.
- Ryo M, Nakamura T, Kihara S, Kumada M, Shibasaki S, Takahashi M, et al. Adiponectin as a biomarker of the metabolic syndrome. *Circ J* 2004; **68**: 975–981.
- World Health Organization Western Pacific Region/International Association for the Study of Obesity (IASO)/International Obesity Taskforce (IOTF). The Asia-Pacific perspective: Redefining obesity and its treatment. Melbourne: Health Communications Australia, 2000; 31–33.
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; **28**: 412–419.
- Yoon SJ, Lee HS, Lee SW, Yun JE, Kim SY, Cho ER, et al. The association between adiponectin and diabetes in the Korean population. *Metabolism* 2008; **57**: 853–857.
- Higashiyama A, Okamura T, Ono Y, Watanabe M, Kokubo Y, Okayama A. Risk of smoking and metabolic syndrome for incidence of cardiovascular disease. *Circ J* 2009; **73**: 2258–2263.
- Li C, Ford ES, Meng YX, Mokdad AH, Reaven GM. Does the association of the triglyceride to high-density lipoprotein cholesterol ratio with fasting serum insulin differ by race/ethnicity? *Cardiovasc Diabetol* 2008; **7**: 4.

26. Kannel WB, Vasan RS, Keyes MJ, Sullivan LM, Robins SJ. Usefulness of the triglyceride-high-density lipoprotein versus the cholesterol-high-density lipoprotein ratio for predicting insulin resistance and cardiometabolic risk (from the Framingham Offspring Cohort). *Am J Cardiol* 2008; **101**: 497–501.
27. Walldius G, Jungner I, Holme I, Aastveit AH, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): A prospective study. *Lancet* 2001; **358**: 2026–2033.
28. Lee KH, Sohn JC, Kim BT, Choi BH, Jung SH, Cha CK, et al. Non-HDL cholesterol as a predictive factor for metabolic syndrome in Korean women. *Korean J Obes* 2007; **16**: 102–110 (in Korean).
29. Sumner AE, Finley KB, Genovese DJ, Criqui MH, Boston RC. Fasting triglyceride and the triglyceride-HDL cholesterol ratio are not markers of insulin resistance in African Americans. *Arch Intern Med* 2005; **165**: 1395–1400.