

# Prospective study of alcohol consumption and metabolic syndrome<sup>1-3</sup>

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## ABSTRACT

**Background:** Alcohol consumption is related to the prevalent metabolic syndrome. Few studies have evaluated the effects of alcohol consumption on the development of metabolic syndrome.

**Objective:** We examined the association between alcohol consumption and incident metabolic syndrome.

**Design:** This was a prospective cohort study of 3833 male and female Koreans aged 40-69 y and free of the metabolic syndrome at baseline. Information on alcohol consumption was obtained periodically from interviewer-administered questionnaires. Incident cases of the metabolic syndrome were identified by biennial health examinations during 4 y of follow-up between 2003 and 2006.

**Results:** Compared with nondrinkers, the multivariate relative risk [RR (95% CI)] of the metabolic syndrome for very light drinkers consuming 0.1 to 5 g of alcohol per day (g/d) was 1.06 (0.71, 1.58), that for light drinkers consuming 5.1 to 15 g/d was 1.13 (0.69, 1.83), that for moderate drinkers consuming 15.1 to 30 g/d was 1.25 (0.75, 2.09), and that for heavy drinkers consuming >30 g/d was 1.63 (1.02, 2.62). All individual components of the metabolic syndrome were significantly associated with heavy drinking, particularly among heavy liquor drinkers.

**Conclusions:** Heavy drinking, in particular among liquor drinkers, is associated with an increased risk of the metabolic syndrome by influencing its components. Further data are warranted to clarify the association between drinking minimal alcohol and the metabolic syndrome as well as the beverage-specific association for drinking beer or wine. *Am J Clin Nutr* 2008;87:1455-63.

## INTRODUCTION

The metabolic syndrome is a combination of several clinical features, including central obesity, high blood pressure, elevated concentrations of fasting glucose and triacylglycerols, low concentrations of HDL cholesterol, and insulin resistance (1, 2). The clustering of these features has been speculated to increase the risk of cardiovascular disease because each component is associated with the disease (2). Indeed, recent studies reported that the metabolic syndrome markedly increases cardiovascular morbidity and mortality (3, 4).

Few studies have reported the effects of alcohol drinking on the development of the metabolic syndrome. Several studies have reported an association between alcohol drinking and the prevalent metabolic syndrome, but these unfortunately showed inconsistent findings (5-11). Some reported that the relation is inversely linear (5-8), J-shaped (9), or positively linear (10), whereas another found no relation (11). In addition, the relation

appears to differ by types of alcoholic beverage. Compared with nondrinking, light to moderate drinking of wine and beer is favorable for reducing the prevalence odds ratio of metabolic syndrome (6-8), whereas liquor drinking tends to increase the ratio (6) or has no association with the metabolic syndrome (7, 8). In other studies, information from beverage-specific analyses was unavailable (5, 9-11). Earlier studies on the association between alcohol consumption and the metabolic syndrome are limited in establishing causality because of the cross-sectional design (5-11). To evaluate the effect of alcohol drinking on the development of metabolic syndrome, we prospectively investigated incident metabolic syndrome in relation to alcohol consumption status, including average daily amount consumed, types of alcoholic beverage most consumed, and drinking frequency.

## SUBJECTS AND METHODS

### Study population

The study cohort, an ongoing prospective investigation, is one of the population-based cohorts included in the Korean Genome Epidemiology Study (KoGES), which in the past was called the Korean Health and Genome Study. Information on the design and the study procedures used in the KoGES is available in a previous report (12). At baseline, 5020 male and female Korean citizens participated in a comprehensive health examination and onsite interviews at Korea University Ansan Hospital. We included 5015 participants aged 40-69 y in 2001 and 2002 as members of the study cohort after excluding 5 individuals who did not specify a birth date or who reported 39 y of biological age.

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All participants completed interviewer-administered questionnaires, which included questions on demographic information, medical history and health conditions, family disease history, dietary intake, and lifestyle. Cohort members have been followed biennially by a scheduled site visit. Each participant signed an informed consent form, which was approved by the Human Subjects Review Committee at Korea University Ansan Hospital, before the health examination. In this analysis, we excluded 66 participants who did not complete questions related to alcohol consumption, whose anthropometric measurements were not completed at the health examination, or whose smoking status was not reported. Because the outcome for this study was new cases of the metabolic syndrome, we excluded individuals who were evaluated to have the metabolic syndrome at the baseline health examination. During baseline through follow-up, we also excluded individuals reporting physician-diagnosed cardiovascular disease or cancer as well as patients using any medication for diabetes, hypertension, or dyslipidemia. In addition, we identified individuals with abnormal concentrations of blood albumin and total bilirubin at baseline and excluded them to minimize the effect of potential presence of liver cirrhosis on glucose and lipid metabolism. Thus, 3833 men (51.8%) and women (48.2%) entered the analysis for the first 2-y follow-up, and those who met the inclusion criteria remained in the analysis for a second 2-y follow-up period. During the 4-y period from 2003 to 2006, a follow-up rate of 71% was achieved, resulting in 9985 person-years accrued for the analysis.

### Definition of the metabolic syndrome

We used the diagnostic criteria for the metabolic syndrome proposed by the National Cholesterol Education Program Adult Treatment Panel III (13). According to the criteria, the metabolic syndrome components include 1) central obesity given as waist circumference ( $>102$  cm for men and  $>88$  cm for women), 2) high concentrations of serum triacylglycerols ( $\geq 150$  mg/dL), 3) low concentrations of serum HDL cholesterol ( $<40$  mg/dL for men and  $<50$  mg/dL for women), 4) hypertension (systolic/diastolic pressure  $\geq 130/85$  mm Hg), and 5) high concentrations of fasting glucose ( $\geq 110$  mg/dL). The metabolic syndrome is defined as the presence of 3 or more of these components (13).

### Health examination

A comprehensive health examination, including evaluation of anthropometric indexes, measurement of blood pressure, and collection of biospecimens for assays, was conducted biennially by health professionals who were trained with a standardized protocol. Height (cm) and body weight (kg) were measured to the nearest 0.1 cm or 0.1 kg without shoes, and body mass index (BMI, in  $\text{kg}/\text{m}^2$ ) was calculated. Waist circumference (cm) was measured at the narrowest part between the lower rib and the iliac crest to the nearest 0.1 cm, and the average of 3 repeated measurements was calculated. According to the 1999 World Health Organization Guideline, blood pressure was measured in a sitting position with mercury sphygmomanometers after at least a 5-min period of rest (14). Repeated measurements of blood pressure were performed after about a 30-s interval and recorded to the nearest 2 mm Hg. The average of the measurements was calculated for systolic and diastolic blood pressure.

All participants had at least an 8-h fasting period before the beginning of blood collection. Blood samples were collected and

delivered to the Seoul Clinical Laboratories (Seoul, Korea) for assays of plasma glucose and serum HDL cholesterol, triacylglycerols, and  $\gamma$ -glutamyltransferase concentrations. The laboratory reported the following interassay CVs from routine assays: 2.8% for glucose, 3.8% for HDL cholesterol, 5.2% for triacylglycerols, and 5.8% for  $\gamma$ -glutamyltransferase.

### Alcohol consumption and other exposures

Questionnaire-based interviews were periodically conducted by personnel who are trained every 2 y with a standardized manual. We collected information on alcohol consumption status; demographic characteristics, including age, income, occupation, marital status, and education; and other risk factors, including current and past smoking status, physical activity, and family history of hypertension, diabetes, and dyslipidemia. We also obtained dietary information from a semi-quantitative food-frequency questionnaire that was developed by the Korea Centers for Disease Control and Prevention. Average daily nutrient intakes were calculated on the basis of the food-composition database published by the Rural Development Administration of Korea (15).

Participants were asked whether they had ever consumed alcoholic beverages in their lifetime, whether there was a time in their life when they regularly consumed at least 1 drink of any alcoholic beverage in every month, and whether they drank in the past 30 d. If participants had stopped drinking, they were asked how long they had abstained from alcohol. Participants were also asked to complete a table that inquired about drinking amount and pattern in the past 30 d. Thus, we collected information on average frequency of drinking occasion, amount of 6 types of alcoholic beverage (beer, wine, hard liquor, and 3 types of traditional drinks, including soju, chungju, and makgeolli) consumed for a typical occasion, and the volume of 1 standard drink for each type of alcoholic beverage. Interviewers articulated the volume of 1 standard drink, which is familiar to Koreans. We calculated beverage-specific alcohol consumption in g/d on the basis of the alcohol content (4.5% for beer, 12% for wine, 40% for hard liquor, 22% or 25% for soju, 16% for chungju, and 6% for makgeolli), the frequency of drinking, and the amount consumed. We calculated total alcohol consumption (g/d) by summing up the beverage-specific amount consumed as well as total liquor consumption (g/d) by summing up the alcohol amount from liquor, including hard liquor, soju, and chungju. Among all participants, total alcohol consumption assessed at baseline was strongly correlated with serum concentrations of  $\gamma$ -glutamyltransferase (Spearman correlation coefficient = 0.49,  $P$  value  $< 0.001$ ). Using similar procedures, alcohol consumption was reassessed at the 2-y follow-up.

To obtain information on physical activity, participants were asked to report hours spent in a typical day in sleep and 5 categories of activity intensity (sedentary, very light, light, moderate, and vigorous) after interviewers gave details on activities corresponding to each category. A total metabolic equivalent (MET/h) score was calculated by multiplying hours spent by MET values (1.0 for sleep or sedentary, 1.5 for very light, 2.4 for light, 5.0 for moderate, and 7.5 for vigorous activity), which were determined on the basis of activities given for each category (16).

### Statistical analysis

Alcohol consumption was categorized into 5 groups. Individuals who had consumed  $<1$  drink/mo in their life or who had



abstained in the past 30 d were grouped as nondrinkers. Drinkers, who regularly consumed  $\geq 1$  drink/mo, were further classified into very light (0.1 to 5 g alcohol/d), light (5.1 to 15 g alcohol/d), moderate (15.1 to 30 g alcohol/d), or heavy ( $>30$  g alcohol/d) drinkers on the basis of their average daily consumption in the past 30 d. Across the categories of baseline alcohol consumption, we calculated descriptive statistics for the baseline characteristics of the study participants. For continuous data, the analysis of variance *F* test was used to assess differences in means across the categories. For categorical data, a chi-square test for trend was used to assess a linear trend in proportions across the categories. We also calculated person-years from the date of the baseline health examination until diagnosis of the metabolic syndrome at the follow-up examination, death, or the last date of health examination during the 4-y period, whichever came first.

Alcohol consumption and drinking frequency were updated in further analysis because changes in alcohol drinking over a short period of time can influence the metabolic syndrome components, including HDL cholesterol and blood pressure (17). For other exposures, the baseline data were used in the analysis. Pooled logistic regression analysis was applied to obtain an odds ratio of the metabolic syndrome with its 95% CI (18). Because the incidence of the metabolic syndrome is reasonably low in our data, we considered odds ratios estimates of relative risks (RRs) (19). Using nondrinkers as a reference group, we presented multivariate RRs associated with potential risk factors such as age; sex; BMI; income; occupation; marital status; education; smoking status; physical activity; average daily intake of calories, fat, or dietary fiber; average consumption frequency of red meat, fish, or nuts; and family history of diabetes or hypertension. We further conducted multivariate analyses stratified by sex, body mass index ( $<25$  and  $\geq 25$  kg/m<sup>2</sup>), or types of alcoholic beverage (liquor and nonliquor). Among drinkers, 89% consumed liquor (among these drinkers, 51% drank liquor only), and there were insufficient numbers of drinkers who consumed beer or wine exclusively. Thus, non-liquor-drinkers were defined when their average daily alcohol consumption of beer, wine, and other types of alcoholic beverage except liquor was greater than that of liquor. Liquor drinkers were defined when their average daily alcohol consumption of liquor was greater than that of nonliquor. Lifestyle characteristics including dietary intake, smoking status, and physical activity were compared between liquor drinkers and non-liquor-drinkers. We also analyzed the association between drinking frequency and the metabolic syndrome. Drinking frequency was classified into 3 groups:  $<1$ , 1–2,  $\geq 3$  drinking days/wk. Using  $<1$  drinking day/wk as a reference group, the RRs of the metabolic syndrome were estimated for all drinkers, drinkers consuming  $\leq 30$  g alcohol/d, drinkers consuming  $>30$  g alcohol/d, liquor drinkers, and non-liquor-drinkers. We evaluated the association between alcohol consumption and individual components of the metabolic syndrome. To calculate multivariate relative odds (RO), logistic regression models containing each of the components as a binary dependent variable were fitted to the same data, which were utilized for the association between alcohol consumption and incidence of the metabolic syndrome. We stratified data by liquor drinkers or non-liquor drinkers and estimated the RO of the individual components for drinkers compared with nondrinkers. Statistical significance was set at 0.05 (two-sided). The SAS (SAS 9.1; SAS Institute Inc, Cary, NC) program was used to conduct statistical analyses.

## RESULTS

A follow-up rate of 71% was achieved, and we newly identified 220 cases of the metabolic syndrome during the 4-y follow-up. When we compared the subjects who participated in the follow-up study with those who did not, we found no significant differences in the distribution of alcohol consumption categories.

The characteristics of the study participants are presented in **Table 1**. Except for family history of diabetes or hypertension, significant differences were found in the baseline characteristics across the categories of alcohol consumption. Drinkers were more likely to be working, educated, and current smokers and consumed more fat. Across the categories, there was a trend toward an increase in blood concentrations of  $\gamma$ -glutamyltransferase and the metabolic syndrome components including waist circumference, triacylglycerols, blood pressure, and fasting glucose. Heavy drinkers showed the highest concentrations of HDL cholesterol, but no significant difference was examined among the categories of alcohol consumption.

The association between alcohol consumption and incident metabolic syndrome is shown in **Table 2**. Heavy drinking was associated with a significant 63% increased risk of the metabolic syndrome compared with that in nondrinkers. Although there was a trend toward an increase in the relative risk of the metabolic syndrome according to increasing alcohol consumption, the association was not significant for very light to moderate drinkers (Table 2). According to increasing alcohol consumption, the sex-specific analyses were suggestive of an increased risk of the metabolic syndrome in either sex, albeit the association was not significant (Table 2). In analysis stratified by body mass index, heavy drinking was significantly associated with risk only among overweight persons with a BMI  $\geq 25$  (Table 2). In the beverage-specific analysis, a significant increase in risk was also observed for heavy liquor drinkers, but not for heavy drinkers who preferred nonliquor beverages, including beer, wine, and other types of alcoholic beverage except liquor (Table 2).

We next compared lifestyle characteristics and dietary intake between liquor drinkers and non-liquor-drinkers. Liquor drinkers drank more frequently, consumed red meat and fish more frequently, and were more likely to be smokers than were non-liquor-drinkers (**Table 3**).

Data for the association between drinking frequency and incident metabolic syndrome among drinkers are presented in **Table 4**. No significant association was observed in the analysis for all drinkers or in the amount-specific and beverage-specific analyses (Table 4).

To assess which component contributed to the increased risk of the metabolic syndrome, we evaluated the association between alcohol consumption and the individual metabolic syndrome components (**Table 5**). Compared with nondrinkers, heavy drinkers showed an increase in the relative odds of the 4 components, such as large waist circumference, high triacylglycerols, high blood pressure, and high glucose, after adjustment for potential risk factors (Table 5). Increased relative odds were also observed for high triacylglycerols and high blood pressure among moderate drinkers and for large waist circumference among very light drinkers. A significant inverse association for low HDL cholesterol was observed among all drinkers, showing that alcohol drinking increased HDL cholesterol (Table 5).

TABLE 1

Baseline characteristics and metabolic syndrome components by alcohol consumption

Variables	Drinkers (g/d)					P value <sup>1</sup>
	Nondrinkers	Very light (0.1–5)	Light (5.1–15)	Moderate (15.1–30)	Heavy (>30)	
No. of subjects [n (%)]	1790 (46.7)	671 (17.5)	510 (13.3)	378 (9.9)	484 (12.6)	
Age (y)	48.9 ± 7.6 <sup>2</sup>	47.6 ± 7.1	46.6 ± 6.5	47.3 ± 6.3	46.3 ± 6.2	<0.001
Male (%)	28.7	41.0	76.1	91.5	95.5	<0.001
Alcohol (g/d)						
Total	0	2.0 ± 1.4	9.1 ± 2.9	22.1 ± 3.9	66.3 ± 41.9	<0.001
Liquor	0	1.3 ± 1.3	7.2 ± 3.7	18.9 ± 6.3	56.4 ± 39.8	<0.001
Beer	0	0.6 ± 0.8	1.6 ± 2.5	2.7 ± 4.4	8.9 ± 15.8	<0.001
Wine	0	0.1 ± 0.4	0.2 ± 1.1	0.1 ± 0.5	0.1 ± 0.9	<0.001
Habitual alcohol drinking (%) <sup>3</sup>	0	1.0	4.9	26.2	81.0	<0.001
Low income (%) <sup>4</sup>	16.5	12.6	8.1	7.2	7.2	<0.001
Occupation (%)						
White-collar job	8.3	10.9	20.8	22.5	22.5	<0.001
Blue-collar job	42.8	51.4	63.7	73.8	75.4	<0.001
Keep house	48.7	37.6	15.5	2.7	1.9	<0.001
Married (%)	91.3	93.6	94.3	96.6	96.1	<0.001
Education > 9 y (%)	58.5	64.5	75.1	75.4	71.7	<0.001
Smoking status (%)						
Current smokers	9.3	16.4	36.5	48.7	51.8	<0.001
Former smokers	11.3	15.1	25.9	30.1	32.5	<0.001
BMI (kg/m <sup>2</sup> )	24.1 ± 2.8	24.3 ± 2.8	24.3 ± 2.6	24.6 ± 2.7	24.7 ± 2.6	<0.001
MET-hours/d <sup>5</sup>	23.6 ± 8.8	24.4 ± 8.8	25.0 ± 9.1	24.7 ± 10.5	26.0 ± 10.9	<0.001
Mean daily intakes						
Total energy (kcal/d) <sup>6</sup>	1827 ± 558	1834 ± 461	1903 ± 414	1947 ± 437	1970 ± 441	<0.001
Fat (g/d)	31.0 ± 18.6	32.0 ± 13.9	34.9 ± 14.2	36.6 ± 16.1	38.2 ± 15.8	<0.001
Saturated fat (g/d)	9.5 ± 6.4	9.6 ± 4.5	10.2 ± 4.5	10.9 ± 5.4	11.4 ± 5.5	<0.001
Polyunsaturated fat (g/d)	7.7 ± 4.5	7.8 ± 3.9	8.2 ± 3.2	8.6 ± 3.5	9.2 ± 3.8	<0.001
Dietary fiber (g/d)	6.4 ± 2.7	6.3 ± 2.6	6.3 ± 2.2	6.3 ± 2.2	6.8 ± 2.5	<0.05
Consumption once per week or more (%)						
Red meat intake	61.5	69.0	81.4	82.8	83.3	<0.001
Fish intake	62.6	65.3	70.0	76.2	75.0	<0.001
Nut intake	10.6	11.2	13.1	16.1	18.4	<0.001
Family history of diseases (%)						
Diabetes	13.4	12.1	13.1	12.7	11.8	0.42
Hypertension	17.8	17.3	19.4	17.5	16.3	0.65
Serum $\gamma$ -glutamyltransferase (U/L)	22.7 ± 25.0	25.6 ± 22.4	36.7 ± 39.6	55.7 ± 88.4	71.9 ± 106.5	<0.001
Metabolic syndrome components						
Waist circumference (cm)	77.9 ± 8.0	78.6 ± 8.2	80.7 ± 7.3	82.5 ± 7.2	83.5 ± 6.8	<0.001
Triglycerides (mg/dL)	120.0 ± 71.1	123.7 ± 77.3	140.3 ± 86.4	161.5 ± 92.8	178.3 ± 130.8	<0.001
HDL cholesterol (mg/dL)	50.8 ± 11.5	50.5 ± 11.4	50.1 ± 11.6	49.5 ± 10.2	51.3 ± 11.4	0.13
Systolic blood pressure (mm Hg)	112.4 ± 15.8	111.1 ± 14.9	114.0 ± 14.4	118.0 ± 16.2	119.3 ± 15.5	<0.001
Diastolic blood pressure (mm Hg)	74.4 ± 10.3	74.4 ± 10.4	77.4 ± 10.4	80.9 ± 11.1	81.6 ± 10.9	<0.001
Fasting glucose (mg/dL)	88.6 ± 20.4	87.8 ± 14.3	90.2 ± 16.1	92.6 ± 17.1	96.2 ± 23.0	<0.001

<sup>1</sup> For continuous data, the analysis of variance *F* test was used to assess differences in means across the categories of alcohol consumption. For categorical data, a chi-square test for trend was used to assess a linear trend in proportions across the categories.

<sup>2</sup>  $\bar{x} \pm$  SD (all such values).

<sup>3</sup> Four drinking days per week and more.

<sup>4</sup> Average monthly wage < 10<sup>6</sup> Won, which approximately corresponds to the government-set minimum wage for a family of 3.

<sup>5</sup> Total metabolic equivalent was calculated for daily physical activity.

<sup>6</sup> Calories from alcohol drinking were not included.

Restricting data to beverages preferred, all individual components of the metabolic syndrome were significantly associated with heavy liquor drinking (Table 5). Among non-liquor-drinkers, any amount of alcohol was associated with a favorable increase in HDL-cholesterol concentrations, whereas moderate to heavy drinking was associated with a detrimental increase in triacylglycerols and blood pressure (Table 5).

## DISCUSSION

In this prospective cohort study, we observed a significant increase in the risk of the metabolic syndrome among heavy drinkers after taking into account potential risk factors. In particular, the increased risk associated with heavy drinking was shown among overweight or obese persons as well as

**TABLE 2**  
Relative risks (RR) of the metabolic syndrome in relation to alcohol consumption

	Nondrinkers	Drinkers (g/d)			
		Very light (0.1–5)	Light (5.1–15)	Moderate (15.1–30)	Heavy (>30)
All ( <i>n</i> of observations = 5227)					
No. of cases	85	39	27	27	42
Person-years	4422	1943	1316	1045	1260
Age-adjusted RR (95% CI) <sup>1</sup>	Reference	1.09 (0.74, 1.61)	1.14 (0.73, 1.78)	1.44 (0.92, 2.24)	1.94 (1.32, 2.85)
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.06 (0.71, 1.58)	1.13 (0.69, 1.83)	1.25 (0.75, 2.09)	1.63 (1.02, 2.62)
Stratified analysis by sex					
Men ( <i>n</i> = 2781)					
No. of cases	24	17	21	25	41
Person-years	1307	819	986	944	1217
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.15 (0.60, 2.21)	1.15 (0.61, 2.13)	1.25 (0.68, 2.31)	1.65 (0.94, 2.88)
Women ( <i>n</i> = 2446)					
No. of cases	61	22	6	2	1
Person-years	3115	1123	330	100	43
Multivariate RR (95% CI) <sup>2</sup>	Reference	0.95 (0.56, 1.60)	1.11 (0.45, 2.77)	1.06 (0.24, 4.75)	1.21 (0.15, 10.0)
Stratified analysis by BMI					
BMI < 25 kg/m <sup>2</sup> ( <i>n</i> = 3260)					
No. of cases	35	18	7	16	11
Person-years	2887	1218	843	604	689
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.35 (0.73, 2.49)	0.67 (0.27, 1.65)	2.00 (0.94, 4.24)	1.12 (0.48, 2.60)
BMI ≥ 25 kg/m <sup>2</sup> ( <i>n</i> = 1967)					
No. of cases	50	21	20	11	31
Person-years	1535	725	472	440	570
Multivariate RR (95% CI) <sup>2</sup>	Reference	0.94 (0.54, 1.62)	1.53 (0.83, 2.80)	0.84 (0.39, 1.80)	2.15 (1.18, 3.91)
Stratified analysis by alcoholic beverage					
Liquor drinkers <sup>3</sup> ( <i>n</i> = 2291) and nondrinkers ( <i>n</i> = 2317)					
No. of cases	85	30	26	25	38
Person-years	4422	1250	1070	944	1097
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.22 (0.79, 1.91)	1.35 (0.82, 2.23)	1.28 (0.75, 2.18)	1.70 (1.04, 2.80)
Non-liquor-drinkers <sup>4</sup> ( <i>n</i> = 619) and nondrinkers ( <i>n</i> = 2317)					
No. of cases	85	9	1	2	4
Person-years	4422	693	245	101	163
Multivariate RR (95% CI) <sup>2</sup>	Reference	0.77 (0.37, 1.58)	0.27 (0.04, 2.03)	1.46 (0.33, 6.50)	1.34 (0.43, 4.13)

<sup>1</sup> RR and its 95% CI for the metabolic syndrome were obtained by using logistic regression models.

<sup>2</sup> Data are adjusted for age, sex, BMI, income (wage <10<sup>6</sup> Won/mo, ≥ 10<sup>6</sup> Won/mo), occupation (white-collar, blue-collar, housekeeping), marital status (married, other status), education (<9 y, ≥9 y), smoking status (never smoker, former smoker, current smoker: <20 cigarettes/y, ≥20 cigarettes/y), quartiles of physical activity, quartiles of total energy intake, quartiles of fat intake, quartiles of dietary fiber intake, frequency (<1/mo, 1–3/mo, 1–2/wk, >2/wk) of red meat intake, frequency of fish intake, frequency of nut intake, family history of diabetes (no family history, diagnosis of diabetes in parents or siblings), and family history of hypertension (no family history, diagnosis of hypertension in parents or siblings).

<sup>3</sup> Liquor drinkers are defined when their average daily alcohol consumption of liquor is greater than that of nonliquor (beer, wine, and other types of alcoholic beverage except liquor).

<sup>4</sup> Non-liquor-drinkers are defined when their average daily alcohol consumption of nonliquor is greater than that of liquor.

among liquor drinkers. Among drinkers who preferred beer, wine, and other types of alcoholic beverage except liquor, an insignificant association was observed, which might have been partly due to the small number of cases of metabolic syndrome.

Some earlier epidemiologic studies relating alcohol consumption to the metabolic syndrome have lent data supporting that a minimal amount of drinking has protective effects on the prevalence of the metabolic syndrome compared with non-drinking (5–9). By contrast, Fan et al (10) examined lifetime drinking pattern and found that the prevalence of the metabolic syndrome was directly increased with lifetime drinking

intensity (total drinks/drinking days over lifetime). They also observed that the metabolic syndrome components contributing to the increase are hypertension and elevated concentrations of fasting glucose and triacylglycerols for both men and women and central obesity for women. Thus, they suggested that average moderate drinking over the lifetime does not have favorable effects on the metabolic syndrome (10). Furthermore, some studies found that moderate drinking of liquor tends to increase the prevalence of the metabolic syndrome (6), and >20 drinks per month increases the prevalence of elevated fasting glucose (7), whereas opposite findings were shown for a similar consumption of wine in these studies (6,

TABLE 3

Comparison of baseline characteristics of lifestyle and dietary intake by type of alcoholic beverage

Variables	Type of alcoholic beverage		P value <sup>3</sup>
	Liquor drinkers <sup>1</sup>	Non-liquor-drinkers <sup>2</sup>	
No. of subjects [n (%)]	1647 (81%)	396 (19%)	
Alcohol (g/d)	25.5 ± 34.3 <sup>4</sup>	11.2 ± 20.2	<0.001
Habitual alcohol drinking (%) <sup>5</sup>	27.9	16.2	<0.001
Mean daily intakes			
Total energy (kcal/d) <sup>6</sup>	1913.1 ± 431.5	1868.3 ± 489.0	0.10
Fat (g/d)	35.4 ± 15.1	33.5 ± 14.7	<0.05
Saturated fatty acid (g/d)	10.5 ± 5.0	9.9 ± 4.7	<0.05
Polyunsaturated fatty acid (g/d)	8.5 ± 3.7	7.9 ± 3.6	<0.01
Dietary fiber (g/d)	6.5 ± 2.4	6.2 ± 2.6	0.10
Consumption once per week or more (%)			
Red meat intake	80.2	68.9	<0.001
Fish intake <sup>5</sup>	72.0	65.7	<0.05
Nut intake	14.1	15.2	0.59
Smoking status (%)			
Current smokers	38.5	22.0	<0.001
Former smokers	26.6	15.8	<0.001
MET-h/d <sup>7</sup>	25.0 ± 9.8	25.0 ± 9.5	0.93

<sup>1</sup> Liquor drinkers are defined when their average daily alcohol consumption of liquor is greater than that of nonliquor (beer, wine, and other types of alcoholic beverage except liquor).

<sup>2</sup> Non-liquor-drinkers are defined when their average daily alcohol consumption of nonliquor is greater than that of liquor.

<sup>3</sup> Statistical differences were evaluated by using *t* test for continuous data and Kruskal-Wallis test for categorical data.

<sup>4</sup>  $\bar{x} \pm SD$  (all such values).

<sup>5</sup> Four drinking days per week and more.

<sup>6</sup> Calories from alcohol drinking were not included.

<sup>7</sup> Total metabolic equivalent was calculated for daily physical activity.

7). The different findings by beverage types may be due to drinking behavior such as binge drinking in liquor drinkers (6). In our data for the beverage-specific association, we also observed differences: heavy drinking was significantly associated with an increase in the risk of metabolic syndrome among liquor drinkers but not among non-liquor-drinkers who preferred beer or wine; very light to light drinking tended to increase the risk among liquor drinkers but tended to lower the risk among non-liquor-drinkers. Because this study included a small number of non-liquor-drinkers, however, it is premature to decide at this point whether the effects of alcohol consumption on the metabolic syndrome differ by types of beverage. If there are differences between the effects of liquor and nonliquor drinking, further explorations on factors, such as certain components in a beverage itself or drinking behaviors and lifestyles related to drinking a specific beverage, are needed to clarify beverage-specific effects.

The mechanisms underlying the relation of alcohol drinking with the metabolic syndrome may be explained by the relation with its components. Several studies have reported that alcohol consumption is positively associated with abdominal obesity (20–23). In particular, such an association is more distinct for men (21, 22) and for beer or liquor drinkers (21). A Japanese study observed that moderate and heavy consumption of shochu, which is a Japanese liquor similar to soju in Korea, is significantly associated with an increase in waist-to-hip ratio after adjustment for body mass index, whereas other types of alcoholic beverages are not (23). A meta-analysis of human experimental studies suggested that moderate alcohol drinking is positively

associated with both HDL-cholesterol and triacylglycerol concentrations, but the association did not differ significantly across beverage types (24). Consistent evidence on blood pressure elevated by heavy drinking has been reported, whereas findings regarding light or moderate drinking have shown varied effects on blood pressure, such as beneficial, detrimental, or similar effects compared with abstaining from alcohol (25). Compared with nondrinking, for instance, minimal drinking lowers the risk of hypertension among women (26, 27), but elevates the risk among black (28) or Japanese (29) men. The French DESIR cohort study (17) also observed among men that an increase in alcohol consumption over 3 y is associated with increasing systolic blood pressure without significant changes in other components, including waist circumference, triacylglycerols, and fasting glucose. It has been suggested that 5 to 30 g/d of alcohol may be favorable for type 2 diabetes (30). Observational studies have found an inverse association between alcohol consumption and glycemic control (31, 32), at least in part through enhanced insulin sensitivity (33). However, heavy liquor drinking was shown to increase the risk of type 2 diabetes in men (34) and women (35), whereas similar amounts of beer and wine did not.

Thus, on the basis of these reports, it may be postulated that heavy drinking, in particular liquor drinking, has a detrimental influence on waist circumference, triacylglycerols, blood pressure, and glucose, leading to an increase in metabolic syndrome risk. Our findings support this postulation and further suggest that even moderate liquor drinkers and non-liquor-drinkers need advice on maintaining the normal range of triacylglycerols and

TABLE 4

Relative risks (RR) of the metabolic syndrome according to drinking frequency among drinkers

	Drinking days per week		
	<1	1–2	≥3
All drinkers ( <i>n</i> of observations = 2910)			
No. of cases	33	53	49
Person-years	1649	2136	1778
Age-adjusted RR (95% CI) <sup>1</sup>	Reference	1.27 (0.81, 1.98)	1.42 (0.90, 2.23)
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.22 (0.75, 1.99)	1.35 (0.81, 2.27)
Multivariate RR (95% CI) <sup>3</sup>	Reference	1.16 (0.71, 1.90)	1.10 (0.61, 1.98)
Stratified analysis by alcohol amount			
Alcohol consumption ≤30 g/d ( <i>n</i> = 2247)			
No. of cases	33	47	13
Person-years	1649	2004	650
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.23 (0.74, 2.04)	1.17 (0.57, 1.39)
Multivariate RR (95% CI) <sup>3</sup>	Reference	1.15 (0.68, 1.94)	1.04 (0.49, 2.21)
Alcohol consumption > 30 g/d ( <i>n</i> = 663)			
No. of cases	0	6	36
Person-years	—	132	1128
Multivariate RR (95% CI) <sup>2</sup>	—	Reference	0.74 (0.26, 2.13)
Multivariate RR (95% CI) <sup>3</sup>	—	Reference	0.74 (0.25, 2.14)
Stratified analysis by alcoholic beverage			
Liquor drinkers <sup>4</sup> ( <i>n</i> = 2291)			
No. of cases	27	49	43
Person-years	1125	1781	1456
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.15 (0.68, 1.94)	1.29 (0.73, 2.27)
Multivariate RR (95% CI) <sup>3</sup>	Reference	1.09 (0.64, 1.86)	1.05 (0.55, 2.01)
Non-liquor-drinkers <sup>5</sup> ( <i>n</i> = 619)			
No. of cases	6	4	6
Person-years	524	355	323
Multivariate RR (95% CI) <sup>2</sup>	Reference	1.20 (0.29, 5.00)	2.01 (0.49, 8.25)
Multivariate RR (95% CI) <sup>3</sup>	Reference	1.18 (0.28, 5.01)	1.93 (0.39, 9.64)

<sup>1</sup> RR and its 95% CI for the metabolic syndrome were obtained by using logistic regression models.

<sup>2</sup> Data are adjusted for age, sex, BMI, income (wage <10<sup>6</sup> Won/mo, ≥10<sup>6</sup> Won/mo), occupation (white-collar, blue-collar, housekeeping), marital status (married, other status), education (<9 y, ≥9 y), smoking status (never smoker, former smoker, current smoker: <20 cigarettes/y, ≥20 cigarettes/y), quartiles of physical activity, quartiles of total energy intake, quartiles of fat intake, quartiles of dietary fiber intake, frequency (<1/mo, 1–3/mo, 1–2/wk, >2/wk) of red meat intake, frequency of fish intake, frequency of nut intake, family history of diabetes (no family history, diagnosis of diabetes in parents or siblings), and family history of hypertension (no family history, diagnosis of hypertension in parents or siblings).

<sup>3</sup> Data are further adjusted for the amount of alcohol consumed with other covariates presented above.

<sup>4</sup> Liquor drinkers are defined when their average daily alcohol consumption of liquor is greater than that of nonliquor (beer, wine, and other types of alcoholic beverage except liquor).

<sup>5</sup> Non-liquor-drinkers are defined when their average daily alcohol consumption of nonliquor is greater than that of liquor.

blood pressure to prevent development of the metabolic syndrome.

The present investigation is a sole prospective cohort study to evaluate the association between alcohol consumption and incident metabolic syndrome. Other strengths of our study include the population-based study, the interviewer administration of a questionnaire, and the standardized process of identifying outcome. Our study has potential limitations similar to other studies related to alcohol drinking. For example, drinkers are likely to underreport alcohol consumption, and problem drinkers are less likely to participate in the study. However, these kinds of bias would have minimal effects if they existed in our study, because our society has a tolerant social climate toward alcohol drinking, like the Japanese (29). We cannot rule out that there might be uncontrolled confounding factors, but our analyses included a broad range of potential confounding factors, some of which other studies did not consider. Further investigations for a longer follow-up period as well as for other ethnic groups are warranted.

In addition, the effects of light to moderate drinking on the metabolic syndrome need to be explored for drinkers preferring wine or beer, because our data had insufficient numbers of such drinkers. Further evaluations are needed for female drinking in relation to the metabolic syndrome. In our data, most women abstained from alcohol or rarely drank, and thus several of the cases of the metabolic syndrome among women appeared to be insufficient for stable estimates, leading to the lack of an association.

In summary, our prospective study of a cohort including Koreans aged 40–69 y observed that heavy drinking, in particular heavy liquor drinking, is associated with an increased risk of the metabolic syndrome by influencing its components, including waist circumference, triacylglycerols, blood pressure, and glucose. Further data are warranted to clarify the association between a minimal amount of alcohol consumption and metabolic syndrome risk as well as the beverage-specific association for beer or wine drinking.

TABLE 5

Association between alcohol consumption and the individual metabolic syndrome components

Individual components of the metabolic syndrome as a dependent variable <sup>1</sup>	Nondrinkers	Drinkers (g/d)			
		Very light (0.1–5)	Light (5.1–15)	Moderate (15.1–30)	Heavy (>30)
All ( <i>n</i> of observations = 5227)					
Large waist circumference <sup>1</sup>					
No. of cases/noncases	61/2256	34/975	9/683	4/542	5/658
Multivariate RO (95% CI) <sup>2</sup>	Reference	1.84 (1.08, 3.14)	1.43 (0.57, 3.58)	1.10 (0.30, 4.01)	3.61 (1.09, 12.01)
High triacylglycerol <sup>1</sup>					
No. of cases/noncases	471/1846	202/807	179/513	198/348	283/380
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.88 (0.72, 1.07)	0.97 (0.78, 1.21)	1.31 (1.04, 1.66)	1.60 (1.28, 2.00)
Low HDL cholesterol <sup>1</sup>					
No. of cases/noncases	1244/1073	470/539	233/459	136/410	154/509
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.81 (0.69, 0.95)	0.61 (0.50, 0.75)	0.41 (0.33, 0.52)	0.39 (0.31, 0.49)
High blood pressure <sup>1</sup>					
No. of cases/noncases	311/2006	135/874	124/568	160/386	195/468
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.96 (0.76, 1.20)	1.23 (0.96, 1.59)	2.21 (1.71, 2.86)	2.19 (1.70, 2.82)
High glucose <sup>1</sup>					
No. of cases/noncases	64/2253	25/984	21/671	34/512	58/605
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.81 (0.50, 1.32)	0.85 (0.49, 1.45)	1.57 (0.96, 2.58)	2.37 (1.50, 3.73)
Stratified analysis by alcoholic beverage					
Among liquor drinkers <sup>3</sup> ( <i>n</i> = 2291) and nondrinkers ( <i>n</i> = 2317)					
Large waist circumference <sup>1</sup>					
No. of cases/noncases	61/2256	22/630	6/559	4/491	5/574
Multivariate RO (95% CI) <sup>2</sup>	Reference	2.01 (1.09, 3.71)	1.80 (0.63, 5.14)	1.58 (0.44, 5.72)	4.64 (1.36, 15.87)
High triacylglycerol <sup>1</sup>					
No. of cases/noncases	471/1846	144/508	155/410	181/314	250/329
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.94 (0.75, 1.17)	1.05 (0.83, 1.33)	1.34 (1.05, 1.71)	1.69 (1.34, 2.14)
Low HDL cholesterol <sup>1</sup>					
No. of cases/noncases	1244/1073	315/337	189/376	124/371	133/446
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.89 (0.74, 1.07)	0.61 (0.49, 0.76)	0.41 (0.32, 0.52)	0.38 (0.30, 0.49)
High blood pressure <sup>1</sup>					
No. of cases/noncases	311/2006	98/554	105/460	147/348	176/403
Multivariate RO (95% CI) <sup>2</sup>	Reference	1.03 (0.80, 1.33)	1.26 (0.96, 1.65)	2.24 (1.71, 2.94)	2.32 (1.78, 3.03)
High glucose <sup>1</sup>					
No. of cases/noncases	64/2253	19/633	20/545	33/462	52/527
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.90 (0.53, 1.55)	0.99 (0.57, 1.74)	1.70 (1.02, 2.82)	2.44 (1.51, 3.92)
Among nonliquor drinkers <sup>4</sup> ( <i>n</i> = 619) and nondrinkers ( <i>n</i> = 2317)					
Large waist circumference <sup>1</sup>					
No. of cases/noncases	61/2256	12/345	3/124	0/51	0/84
Multivariate RO (95% CI) <sup>2</sup>	Reference	1.83 (0.78, 4.31)	1.06 (0.19, 5.80)	—	—
High triacylglycerol <sup>1</sup>					
No. of cases/noncases	471/1846	58/299	24/103	17/34	33/51
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.82 (0.60, 1.12)	0.83 (0.51, 1.35)	1.96 (1.03, 3.71)	1.61 (0.99, 2.63)
Low HDL cholesterol <sup>1</sup>					
No. of cases/noncases	1244/1073	155/202	44/83	12/39	21/63
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.68 (0.54, 0.87)	0.62 (0.41, 0.92)	0.46 (0.23, 0.90)	0.46 (0.27, 0.78)
High blood pressure <sup>1</sup>					
No. of cases/noncases	311/2006	37/320	19/108	13/38	19/65
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.85 (0.59, 1.24)	1.12 (0.66, 1.93)	2.07 (1.03, 4.16)	1.52 (0.85, 2.70)
High glucose <sup>1</sup>					
No. of cases/noncases	64/2253	6/351	1/126	1/50	6/78
Multivariate RO (95% CI) <sup>2</sup>	Reference	0.62 (0.26, 1.48)	0.24 (0.03, 1.79)	0.45 (0.06, 3.67)	2.00 (0.76, 5.26)

<sup>1</sup> Models containing each of the metabolic syndrome components, which were large waist circumference (>102 cm for men and >88 cm for women), high triacylglycerol ( $\geq 150$  mg/dL), low HDL cholesterol (<40 mg/dL for men and <50 mg/dL for women), high blood pressure (systolic BP  $\geq 130$  mm Hg or diastolic BP  $\geq 85$  mm Hg), and high glucose (fasting glucose  $\geq 110$  mg/dL), as a binary dependent variable were fitted to the same data for the metabolic syndrome.

<sup>2</sup> Relative odds (RO) and its 95% CI were obtained by using logistic regression models containing age, sex, BMI, income (wage <10<sup>6</sup> Won/mo,  $\geq 10^6$  Won/mo), occupation (white-collar, blue-collar, housekeeping), marital status (married, other status), education (<9 y,  $\geq 9$  y), smoking status (never smoker, former smoker, current smoker: <20 cigarettes/y,  $\geq 20$  cigarettes/y), quartiles of physical activity, quartiles of total energy intake, quartiles of fat intake, quartiles of dietary fiber intake, frequency (<1/mo, 1–3/mo, 1–2/wk, >2/wk) of red meat intake, frequency of fish intake, frequency of nut intake, family history of diabetes (no family history, diagnosis of diabetes in parents or siblings), and family history of hypertension (no family history, diagnosis of hypertension in parents or siblings).

<sup>3</sup> Liquor drinkers are defined when their average daily alcohol consumption of liquor is greater than that of nonliquor (beer, wine, and other types of alcoholic beverage except liquor).

<sup>4</sup> Non-liquor-drinkers are defined when their average daily alcohol consumption of nonliquor is greater than that of liquor.



The contributions of the authors were as follows—IB: provided study inference, conducted the statistical analysis, and wrote the manuscript; CS: designed, initiated, and oversaw the conduct of the study. Both authors contributed to interpreting the results and finalizing the manuscript. CS had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Neither of the authors had a conflict of interest.

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