Original Article

Association between Alcohol Drinking and Metabolic Syndrome in Japanese Male Workers with Diabetes Mellitus

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Aim: Results of previous studies on the relationship between habitual alcohol drinking and metabolic syndrome in a general population are not consistent, and this relationship in patients with diabetes is unknown. The aim of this study was to clarify the relationship of alcohol consumption with metabolic syndrome in patients with diabetes.

Methods: Japanese male workers with diabetes ($n=1960$) were divided into non-, light (<22 g ethanol/day), heavy (≥ 22 and <44 g ethanol/day) and very heavy (≥ 44 g ethanol/day) drinkers. Relationships of alcohol consumption with visceral obesity evaluated by waist circumference, high blood pressure, dyslipidemia (high triglycerides and/or low HDL cholesterol), hyperglycemia, and metabolic syndrome (3 or more of these risk factors by the NCEP-ATP III criteria) were investigated.

Results: Odds ratio vs. nondrinkers for high blood pressure was significantly high in all drinker groups, while odds ratio vs. nondrinkers for low HDL cholesterol was significantly low in all drinker groups. Odds ratio vs. nondrinkers for high triglycerides was significantly low in light drinkers and was significantly high in very heavy drinkers. Odds ratio vs. the nondrinker group for large waist circumference was not significant in any drinker groups. Odds ratio vs. nondrinkers for metabolic syndrome was significantly high in very heavy drinkers but was not significant in light and heavy drinkers.

Conclusion: Excessive alcohol intake is associated with a higher risk for metabolic syndrome through elevations of blood pressure and triglycerides in Japanese male patients with diabetes.

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Key words; Alcohol, Atherosclerosis, Diabetes mellitus, Metabolic syndrome, Risk factors

Introduction

The risk for atherosclerotic diseases is amplified in the presence of metabolic syndrome, a cluster of cardiovascular risk factors including insulin resistance, central obesity, dyslipidemia and hypertension. Correction of an inappropriate lifestyle, such as high calorie intake, low physical activity and smoking, is important for the prevention of metabolic syndrome. Effects of habitual alcohol drinking on the risk for atherosclerotic diseases are known to depend on the

amount of individual alcohol consumption. Incidences of ischemic heart disease and thrombotic stroke are lowered by light-to-moderate drinking through the alcohol-induced increase in high-density lipoprotein (HDL) cholesterol and decrease in blood coagulation activity¹⁻³); however, heavy drinking increases the incidence of hemorrhagic stroke and this effect is mainly explained by alcohol-induced hypertension^{4, 5}). Thus, alcohol influences components of metabolic syndrome, such as hypertension and dyslipidemia. In addition, moderate alcohol consumption has been reported to be associated with a lower incidence of diabetes⁶ and with improvement of insulin resistance in patients with diabetes⁷); however, discrepant results have been obtained from previous studies on the relationship between alcohol drinking and metabolic syndrome in a general population: The relationship has been reported to be inversely linear⁸), J- or U-shaped^{9, 10}),

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positively linear¹¹⁾ and not significant¹²⁾. A recent meta-analysis study using the results of seven previous studies on the relationship between alcohol consumption and metabolic syndrome showed that alcohol consumption of less than 40 g of ethanol per day was associated with a significantly lower incidence of metabolic syndrome in men¹³⁾.

Complication with metabolic syndrome increases the risk for cardiovascular disease also in patients with diabetes¹⁴⁻¹⁶⁾. In individuals with diabetes and without metabolic syndrome, the incidence of cardiovascular disease has been reported not to be different from that in individuals without diabetes and metabolic syndrome¹⁷⁾; however, it remains to be clarified whether and how alcohol drinking influences the risk for metabolic syndrome in patients with diabetes. The purpose of this study was therefore to investigate the relationships of alcohol drinking with metabolic syndrome as well as known risk factors for atherosclerosis in patients with diabetes. Two international sets of criteria have recently been used for the diagnosis of metabolic syndrome. One set is the criteria proposed by the International Diabetes Federation (IDF), in which central obesity, as an essential risk factor, and 2 or more of the other risk factors, such as high blood pressure, dyslipidemia and hyperglycemia, are necessary for diagnosis¹⁸⁾. The other set is the criteria proposed by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III), in which the above 4 risk factors are treated equally and 3 or more of the risk factors are necessary for a diagnosis of metabolic syndrome¹⁹⁾. In Japan, criteria based on those by IDF are generally used for the diagnosis of metabolic syndrome²⁰⁾. In this study, the relationships of alcohol consumption with metabolic syndrome diagnosed by the criteria of IDF and metabolic syndrome diagnosed by the criteria of NCEP-ATP III were investigated separately.

Subjects and methods

Subjects

The subjects were 1960 Japanese male workers aged 30 to 69 years who had received periodic health examinations at workplaces in Yamagata Prefecture in Japan. The data used in this study were collected from April 2008 to March 2009. Subjects with diabetes were defined as those showing high hemoglobin A_{1c} levels ($\geq 6.1\%$), according to the recent criteria for diagnosis of diabetes by the Japan Diabetes Society in 2010, and/or having a history of drug therapy for diabetes. A considerable proportion of the subjects in this study were receiving drug therapy for hypertension

(32.1% of total subjects) or dyslipidemia (15.1% of total subjects), which are known to be complications in patients with diabetes. Thus, those receiving drug therapy for hypertension and/or dyslipidemia were included in the subjects of this study. Subjects who were receiving treatment for any illness were requested to state the diseases in a questionnaire at the health checkup. A cross-sectional study was performed using a local population-based database for the above subjects. This study was approved by the Ethics Committee of Yamagata University School of Medicine.

Average alcohol consumption of each subject per week was reported in questionnaires during the health examinations at each workplace. Since it is difficult to know the correct average alcohol consumption of occasional drinkers, only regular drinkers who drink almost every day were used as drinkers for analysis in this study. Usual weekly alcohol consumption was recorded in terms of the equivalent number of "go", a traditional Japanese unit of sake (rice wine). The amounts of other alcoholic beverages, including beer, wine, whisky and shochu (traditional Japanese distilled spirit), were converted and expressed as units of "go". One "go" contains about 22 g ethanol, and this amount was used to separate heavy drinkers from light drinkers since it is generally accepted that alcohol intake should be reduced to less than 30 ml or 20 - 30 g per day from the viewpoint of prevention of hypertension^{21, 22)}. Average daily alcohol intake (grams of ethanol per day) was then calculated. The subjects were divided into four groups according to ethanol consumption per day (non-drinkers; light drinkers: < 22 g ethanol per day; heavy drinkers: ≥ 22 g and < 44 g ethanol per day; very heavy drinkers: ≥ 44 g ethanol per day). Histories of cigarette smoking and illness were also surveyed by questionnaires.

Measurements

Height and weight were measured with light clothes at the health checkup. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured at the navel level according to the recommendation of the definition of the Japanese Committee for the Diagnostic Criteria of Metabolic Syndrome²⁰⁾. Blood pressure was measured by trained nurses, who belonged to the local health checkup company, with a mercury sphygmomanometer once on the day of the health checkup after each subject had rested quietly in a sitting position. Korotkoff phase V was used to define diastolic pressure. Fasted blood was sampled from each subject, and serum HDL cholesterol and triglycerides were measured by

enzymatic methods using commercial kits. Hemoglobin A_{1c} was determined by the latex cohesion method using a commercial kit (Determiner HbA_{1c}; Kyowa Medex, Tokyo, Japan).

Criteria of metabolic syndrome

The variables of risk factors for atherosclerosis evaluated in this study were waist circumference, blood pressure, HDL cholesterol, triglycerides, and hemoglobin A_{1c}. Two different sets of criteria by IDF¹⁸⁾ and NCEP-ATP III¹⁹⁾ were used separately for the diagnosis of metabolic syndrome. All subjects included in this study had one glycemic risk factor. Metabolic syndrome according to the criteria by IDF was defined as the presence of one or more risk factors, including high blood pressure and dyslipidemia (low HDL cholesterol and/or high triglycerides), in addition to a large waist circumference as an obligatory risk factor. Metabolic syndrome according to the criteria by NCEP-ATP III was defined as the presence of two or more risk factors, including a large waist circumference, high blood pressure and dyslipidemia. Subjects receiving drug therapy for hypertension or dyslipidemia were also included in the above definitions of each risk factor. The criterion for each risk factor was defined as follows: large waist circumference, waist circumference ≥ 85 cm; high blood pressure, systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg; low HDL cholesterol, HDL cholesterol < 40 mg/dl; high triglycerides, triglycerides ≥ 150 mg/dl. In the criteria of metabolic syndrome, dyslipidemia was defined as low HDL cholesterol and/or high triglycerides and was counted not as two separate risk factors but as one risk factor. Subjects with each risk factor included those showing an abnormal level of the risk factor and/or those receiving drug therapy for the risk factor.

Statistical analysis

Statistical analyses were performed using a computer software program (version 16.0 J for Windows; SPSS, Chicago IL, USA). Mean values of each variable in the alcohol groups were compared using analysis of variance followed by Scheffé's F-test. In multivariate analysis, mean values of each variable, calculated after adjustment for additional variables, such as age, BMI, history of smoking and history of drug therapy for hypertension, dyslipidemia or diabetes, were compared among the four alcohol groups using analysis of covariance and then Student's *t*-test after Bonferroni correction. Mean waist circumference was calculated after adjustment for age and a history of smoking. The prevalence of each risk factor in the alcohol groups

was compared using the chi-square test for independence. In logistic regression analysis, the odds ratios of each drinker group vs. the nondrinker group for high blood pressure, low HDL cholesterol, high triglycerides and dyslipidemia were calculated after adjustment for age, BMI and history of smoking. Odds ratios for large waist circumference and metabolic syndrome were calculated after adjustment for age and history of smoking. Probability (*p*) values less than 0.05 were defined as significant.

Results

Univariate analysis of relationships between atherosclerotic risk factors and alcohol intake

Mean levels of each variable related to atherosclerotic risk factors were compared among the alcohol groups (Table 1). Age was significantly higher in light, heavy and very heavy drinkers than in nondrinkers. Percentage of smokers was significantly higher in heavy and very heavy drinkers than in nondrinkers. BMI was significantly lower in light, heavy and very heavy drinkers than in nondrinkers. Waist circumference was significantly smaller in light, heavy and very heavy drinkers than in nondrinkers. Systolic blood pressure was significantly higher in heavy and very heavy drinkers than in nondrinkers, and diastolic blood pressure was significantly higher in very heavy drinkers than in nondrinkers. HDL cholesterol was significantly higher in light, heavy and very heavy drinkers than in nondrinkers. Triglycerides were lower with marginal significance in light drinkers than in nondrinkers and were significantly higher in very high drinkers than in nondrinkers. Hemoglobin A_{1c} was significantly lower in heavy drinkers than in nondrinkers.

Comparison of prevalences of atherosclerotic risk factors and metabolic syndrome among alcohol groups

The prevalences of atherosclerotic risk factors and metabolic syndrome were compared among the alcohol groups (Table 1). Percentage of subjects showing high blood pressure tended to increase with alcohol intake and was significantly higher in heavy and very heavy drinkers than in nondrinkers. Percentage of subjects showing low HDL cholesterol tended to decrease with alcohol intake and was significantly lower in light, heavy and very heavy drinkers than in nondrinkers. Percentage of subjects showing high triglycerides was significantly lower in light drinkers than in nondrinkers and was significantly higher in very heavy drinkers than in nondrinkers. There was no significant

Table 1. Comparison of variables among the nondrinker, light drinker, heavy drinker and very heavy drinker groups of patients with diabetes.

Variable	Overall	Drinker group			
		Non-	Light (< 22 g/day)	Heavy (≥ 22 , < 44 g/day)	Very heavy (≥ 44 g/day)
Number of subjects	1960 (100%)	763 (38.9%)	213 (10.9%)	599 (30.6%)	385 (19.6%)
Age (years)	53.9 ± 7.9	52.0 ± 9.1	$56.2 \pm 6.5^{**}$	$55.4 \pm 6.8^{**}$	$54.2 \pm 6.7^{**}$
Smokers (%)	53.3	48.6	49.3	57.3 ^{**}	58.4 ^{**}
History of therapy for hypertension (%)	32.1	26.6	33.3	37.2 ^{**}	34.5 ^{**}
History of therapy for dyslipidemia (%)	15.1	15.5	16.0	16.4	11.9
History of therapy for diabetes mellitus (%)	49.9	52.0	54.9	48.9	44.4 [*]
Body mass index (kg/m ²)	25.38 ± 4.09	26.39 ± 4.88	$24.97 \pm 3.41^{**}$	$24.58 \pm 3.23^{**}$	$24.85 \pm 3.48^{**}$
Waist circumference (cm)	88.3 ± 10.1	90.1 ± 11.8	$87.3 \pm 8.5^{**}$	$86.7 \pm 8.4^{**}$	$87.8 \pm 9.0^{**}$
Large waist circumference (%)	62.0	64.5	59.2	59.6	62.3
Systolic blood pressure (mmHg)	136.9 ± 17.6	134.3 ± 18.1	135.9 ± 16.2	$138.2 \pm 17.1^{**}$	$140.9 \pm 17.4^{**}$
Diastolic blood pressure (mmHg)	81.3 ± 12.0	80.0 ± 12.5	79.9 ± 10.8	81.7 ± 11.3	$83.9 \pm 12.6^{**}$
High blood pressure (%)	77.6	70.5	76.1	82.6 ^{**}	84.4 ^{**}
HDL cholesterol (mg/dl)	52.6 ± 14.2	47.0 ± 11.4	$53.2 \pm 13.3^{**}$	$56.4 \pm 14.8^{**}$	$57.5 \pm 14.9^{**}$
Low HDL cholesterol (%)	17.1	28.3	14.1 ^{**}	9.7 ^{**}	8.3 ^{**}
Log (triglycerides)	2.166 ± 0.292	2.162 ± 0.271	$2.101 \pm 0.263^{\#}$	2.157 ± 0.307	$2.225 \pm 0.315^{**}$
High triglycerides (%)	47.4	48.5	37.1 ^{**}	44.9	54.8 [*]
Hemoglobin A _{1c} (%)	7.09 ± 1.51	7.25 ± 1.62	7.03 ± 1.48	$6.91 \pm 1.37^{**}$	7.10 ± 1.45
Metabolic syndrome by IDF (%)	58.1	58.8	55.4	57.3	59.5
Metabolic syndrome by NCEP-ATP III (%)	69.3	68.3	64.8	68.4	75.3 [*]

Shown are numbers of subjects, % of drinkers, smokers or subjects receiving drug therapy, means with standard deviations of each variable, and prevalence of each risk factor for atherosclerosis or metabolic syndrome. Light drinkers: < 22 g ethanol/day; heavy drinkers: ≥ 22 - < 44 g ethanol/day; very heavy drinkers: ≥ 44 g ethanol/day. IDF, International Diabetes Federation; NCEP-ATP III, National Cholesterol Education Program's Adult Treatment Panel III. Asterisks denote significant differences from nondrinkers (*, $p < 0.05$; **, $p < 0.01$). A marginally significant difference from nondrinkers: [#], $p = 0.061$.

difference in the percentage of subjects with metabolic syndrome diagnosed by the IDF criteria between each drinker group and the nondrinker group. Percentage of subjects with metabolic syndrome diagnosed by the NCEP-ATP III criteria was significantly higher in very heavy drinkers than in nondrinkers but was not significantly different among nondrinkers, light drinkers and heavy drinkers.

Multivariate analysis of relationships between atherosclerotic risk factors and alcohol intake

Each variable related to atherosclerotic risk factors, except for waist circumference, was compared among the alcohol groups after adjustment for age, smoking history, BMI, and therapy for hypertension, dyslipidemia or diabetes, and only age and smoking history were used for adjustment to compare waist circumference (**Fig. 1**). Waist circumference was significantly smaller in heavy drinkers than in nondrinkers (**Fig. 1A**). Systolic and diastolic blood pressure tended to increase with alcohol intake and was significantly

higher in heavy and very heavy drinkers than in nondrinkers (**Fig. 1B, C**). HDL cholesterol was significantly higher in light, heavy and very heavy drinkers than in nondrinkers (**Fig. 1D**). Log-converted triglycerides was significantly higher in very heavy drinkers than in nondrinkers (**Fig. 1E**). Hemoglobin A_{1c} was significantly lower in heavy drinkers than in nondrinkers (**Fig. 1F**).

Odds ratios of each drinker group vs. the nondrinker group for atherosclerotic risk factors and metabolic syndrome

Relationships of alcohol intake with atherosclerotic risk factors and metabolic syndrome were investigated by logistic regression analysis (**Table 2**). No significant odds ratio vs. the nondrinker group for large waist circumference was found in the light, heavy and very heavy drinker groups. Odds ratio vs. the nondrinker group for high blood pressure tended to be higher with an increase in alcohol intake and was significantly high in the light, heavy and very heavy

Fig. 1.

Multivariate analysis of relationships between alcohol intake and atherosclerotic risk factors in patients with diabetes. Means with standard errors of variables except for waist circumference were calculated after adjustment for age, smoking history, body mass index, and history of drug therapy for hypertension, dyslipidemia or diabetes mellitus. Age and smoking history were adjusted to calculate the mean waist circumference. Means of each variable were compared among non-, light (< 22 g ethanol/day), heavy ($\geq 22 - < 44$ g ethanol/day) and very heavy (≥ 44 g ethanol/day) drinker groups. Asterisks denote significant differences from nondrinkers (*, $p < 0.05$; **, $p < 0.01$).

drinker groups. Odds ratio vs. the nondrinker group for low HDL cholesterol tended to be lower with an increase in alcohol intake and was significantly low in the light, heavy and very heavy drinker groups. Odds ratio vs. the nondrinker group for high triglycerides was significantly low in the light drinker group and was significantly high in the very heavy drinker group. No significant odds ratio vs. the nondrinker group for metabolic syndrome diagnosed by the IDF criteria was found in any drinker groups. Odds ratio vs. the nondrinker group for metabolic syndrome diagnosed by the NCEP-ATP III criteria was significantly high in the very heavy drinker group, while no significant odds ratio vs. the nondrinker group for metabolic syndrome was found in the light and heavy drinker groups.

Discussion

Since metabolic syndrome was defined by international criteria, there have been a considerable number of epidemiological studies on the relationship between alcohol consumption and metabolic syndrome in the past decade; however, the results of previous studies are controversial⁸⁻¹³). Moreover, it is unknown whether and how alcohol consumption affects the risk for metabolic syndrome in patients with diabetes. In this study, an association with a higher risk for metabolic syndrome was found in excessive drinkers (≥ 44 g ethanol/day) compared with nondrinkers in patients with diabetes. Although a previous study using a general population of Japanese demonstrated an association with a lower risk for metabolic syndrome in light-

Table 2. Odds ratio of each drinker group vs. the nondrinker group for each risk factor for atherosclerosis or metabolic syndrome in patients with diabetes.

Risk factor	Drinker group			
	Non-	Light (< 22 g/day)	Heavy (≥ 22 , < 44 g/day)	Very heavy (≥ 44 g/day)
Large waist circumference	1	0.95 (0.69-1.31)	0.95 (0.75-1.19)	1.02 (0.79-1.33)
High blood pressure	1	1.49 (1.02-2.19)*	2.52 (1.90-3.35)**	2.88 (2.05-4.05)**
Low HDL cholesterol	1	0.42 (0.28-0.65)**	0.28 (0.20-0.39)**	0.22 (0.15-0.34)**
High triglycerides	1	0.73 (0.52-1.00)*	1.08 (0.86-1.36)	1.49 (1.15-1.93)**
Dyslipidemia	1	0.65 (0.47-0.90)**	0.87 (0.69-1.09)	1.06 (0.82-1.38)
Metabolic syndrome by IDF	1	1.00 (0.73-1.37)	1.07 (0.86-1.34)	1.13 (0.87-1.46)
Metabolic syndrome by NCEP-ATP III	1	0.91 (0.66-1.26)	1.08 (0.86-1.37)	1.46 (1.10-1.94)**

Odds ratios with 95% confidence intervals in parentheses are shown. Age, history of smoking, body mass index, and history of therapy for hypertension or dyslipidemia were adjusted for calculation of odds ratios for high blood pressure (high systolic and/or diastolic blood pressure), low HDL cholesterol and high triglycerides. Age, history of smoking and body mass index were adjusted for calculation of odds ratios for dyslipidemia (low HDL cholesterol and/or high triglycerides). Age and history of smoking were adjusted for calculation of odds ratios for large waist circumference and metabolic syndrome. Light drinkers: < 22 g ethanol/day; heavy drinkers: ≥ 22 - < 44 g ethanol/day; very heavy drinkers: ≥ 44 g ethanol/day. IDF, International Diabetes Federation; NCEP-ATP III, National Cholesterol Education Program's Adult Treatment Panel III. Significant odds ratios: *, $p < 0.05$; **, $p < 0.01$.

Table 3. Summary of relationships between alcohol intake and risk factors such as large waist circumference, high blood pressure, dyslipidemia (low HDL cholesterol and/or high triglycerides) and metabolic syndrome in patients with diabetes.

Risk factor	Drinker group			
	Nondrinkers	Light drinkers (< 22 g/day)	Heavy drinkers (≥ 22 , < 44 g/day)	Very heavy drinkers (≥ 44 g/day)
Large waist circumference	Reference	No change	Slight decrease*	No change
High blood pressure	Reference	Increase	Increase	Increase
Dyslipidemia	Reference	Decrease	Slight decrease	No change
Low HDL cholesterol	Reference	Decrease	Decrease	Decrease
High triglycerides	Reference	Decrease	No change	Increase
Metabolic syndrome	Reference	No change	No change	Increase

*, mean waist circumference was slightly but significantly smaller in heavy drinkers than in nondrinkers (Figure 1A).

to-moderate drinkers (< 44 g ethanol/day)¹⁰, this association was not found in the present study using patients with diabetes. Therefore, it is thought that light-to-moderate drinking has a beneficial effect on the risk for metabolic syndrome in persons without diabetes but not in persons with diabetes. This study is the first to show the association of alcohol drinking with metabolic syndrome in patients with diabetes. The above difference in the associations of alcohol intake with metabolic syndrome between persons with and without diabetes should be taken into account when alcohol drinking is considered for patients with diabetes.

The relationships between alcohol intake and each risk factor have been summarized in **Table 3**. In light drinkers, the prevalence of high blood pressure

was higher than in nondrinkers, while the prevalence of dyslipidemia was lower than in nondrinkers due to the lower prevalences of low HDL cholesterol and high triglycerides, resulting in a similar prevalence of metabolic syndrome in light drinkers and nondrinkers. In heavy drinkers, the prevalence of high blood pressure was higher than in nondrinkers, while the mean waist circumference was slightly smaller and the prevalence of dyslipidemia was slightly lower than in nondrinkers, resulting in a similar prevalence of metabolic syndrome in heavy drinkers and nondrinkers. In very heavy drinkers, the prevalence of low HDL cholesterol was lower than in nondrinkers, while the prevalence of high triglycerides was higher than in nondrinkers, resulting in a similar prevalence of dyslipidemia in very heavy drinkers and nondrinkers. In very

heavy drinkers, the prevalence of high blood pressure was higher than in nondrinkers, while the prevalences of large waist circumference and dyslipidemia were similar in very heavy drinkers and nondrinkers, resulting in a higher prevalence of metabolic syndrome in very heavy drinkers than in nondrinkers. Therefore, in very heavy drinkers, the increasing effect of alcohol on the prevalence of metabolic syndrome through elevations of blood pressure and triglycerides overcame the decreasing effect of alcohol on the prevalence of metabolic syndrome through elevation of HDL cholesterol. Alcohol-induced hypertension and hypertriglyceridemia are therefore thought to contribute greatly to an increase in the prevalence of metabolic syndrome in very heavy drinkers with diabetes. Regarding anemia as a possible complication in very heavy drinkers, the mean hemoglobin level was slightly but significantly higher in the three drinker groups than in the nondrinker group, and incorporation of the hemoglobin level into variables for logistic regression analysis did not alter the tendencies of the relationship between alcohol intake and metabolic syndrome (data not shown). Thus, it is unlikely that malnutrition complicating excessive drinkers influenced the findings of this study.

In patients with diabetes as well as in the general population, cardiovascular events are predisposed by the presence of metabolic syndrome, which was shown to be associated with excessive alcohol consumption (≥ 44 g ethanol per day) in the present study; therefore, patients with diabetes are recommended to restrict alcohol intake to prevent cerebro- and cardiovascular diseases. On the other hand, a recent meta-analysis study has shown that alcohol consumption of less than 40 g ethanol per day and alcohol consumption of less than 20 g of ethanol per day reduce the incidence of metabolic syndrome in men and women, respectively, in the general population¹³). However, the present study demonstrated that the prevalence of metabolic syndrome in patients with diabetes was not significantly different between nondrinkers and drinkers consuming ethanol of less than 44 g per day. Thus, it is thought that there is no preventive effect of light-to-moderate alcohol drinking against metabolic syndrome for patients with diabetes. Although the prevalences of low HDL cholesterol and high triglycerides were lower in light drinkers than in nondrinkers, these effects were not reflected by a decrease in the prevalence of metabolic syndrome in light drinkers. This may be explained by the findings that the prevalence of hypertension was much higher than the prevalence of dyslipidemia (high triglycerides and/or low HDL cholesterol) (76.1% vs. 49.3% in light drinkers, $p <$

0.01) and that the odds ratio vs. nondrinkers for high blood pressure was significantly high in light drinkers (**Table 2**), resulting in cancellation of the effects of the decreased risk for dyslipidemia and increased risk for hypertension on the prevalence of metabolic syndrome in light drinkers.

Although excessive alcohol intake was suggested to increase the risk for metabolic syndrome diagnosed by the NCEP-ATP III criteria in patients with diabetes, no significant association was found between alcohol consumption and the risk for metabolic syndrome diagnosed by the IDF criteria. A recent study has shown that metabolic syndrome diagnosed by the IDF criteria, including a large waist circumference as an essential risk factor for diagnosis, was not useful for the prediction of cardiovascular disease in patients with diabetes²³). In Japanese men and women with type 2 diabetes, the risk for ischemic heart disease and stroke was not increased in subjects with metabolic syndrome diagnosed by the IDF criteria²⁴). Moreover, a recent prospective study showed no significant associations between a large waist circumference and the risk for cardiovascular disease or stroke in Japanese men²⁵). Thus, the reason for the abovementioned lack of association between metabolic syndrome diagnosed by the IDF criteria and atherosclerotic diseases^{23, 24}) is the inclusion of a large waist circumference as an essential risk factor for the diagnosis of metabolic syndrome. The IDF criteria are less sensitive than the NCEP-ATP III criteria for diagnosing metabolic syndrome, since waist circumference is an essential risk factor for metabolic syndrome in the IDF criteria but is one of the risk factors and is not essential for metabolic syndrome in the NCEP-ATP III criteria. This may be the reason for the lack of a significant association between alcohol intake and metabolic syndrome in very heavy drinkers by the IDF criteria in the present study. Regarding this issue, a recent joint statement by six related international societies also pointed out that waist circumference should not be an obligatory component of metabolic syndrome but will continue to be a useful screening tool²⁶).

In previous studies, the relationships between alcohol consumption and obesity are controversial, and the reason why BMI and waist circumference were greater in the non-alcohol group than in the alcohol drinking groups in the present study (**Table 1**) is not known; however, for the inverse relationship between alcohol intake and body weight, several possible mechanisms, including alteration in energy expenditure, interference with digestion and absorption of nutrients, and increase of sympathetic activity, have been proposed²⁷⁻²⁹).

In subjects with diabetes, the mean hemoglobin A_{1c} level was significantly lower in the heavy drinker group than in the nondrinker group. This finding agrees with the findings of an inverse relationship between alcohol intake and hemoglobin A_{1c} in previous studies using general populations^{30, 31}). However, the amount of alcohol intake is recommended to be less than 20-30 g ethanol per day from the viewpoint of prevention of hypertension²¹), and this amount corresponds to the alcohol intake of light drinkers in the present study. It is needless to say that even light alcohol drinking should not be recommended for patients with diabetes, because drinking could disrupt the control of diabetes by diet therapy, alcohol could acutely induce hypoglycemia in patients with diabetes receiving drug therapy and, in addition, the possibility of future alcohol dependency is always a risk.

One limitation of this study is that the subjects were defined as patients with diabetes from a high hemoglobin A_{1c} level (6.1% or higher) and/or a history of drug therapy for diabetes in a questionnaire at the health checkup. Thus, there is a possibility of the misdiagnosis of diabetes. In addition, information on the type of diabetes was unfortunately not available from the database used in this study. Most of the subjects with diabetes in this study are expected to be classified as type 2 diabetes, since the prevalence of type 2 diabetes among Japanese middle-aged men (mean age of subjects in this study: about 54 years) is speculated to be more than 100-times higher than the prevalence of type 1 diabetes³²). Various factors, such as diet, nutrition, physical activity and socioeconomic status, influence the relationship between alcohol consumption and metabolic syndrome, and information on these factors was not available in the present study. In the database used for the present study, the number of female subjects with diabetes in each drinker group was not large enough for statistical analysis, and thus women were not analyzed in this study. Further studies are therefore needed to clarify the relationship between alcohol consumption and metabolic syndrome in women with diabetes.

In conclusion, excessive drinking (≥ 44 g ethanol per day) is associated with a higher risk for metabolic syndrome through elevations of blood pressure and triglycerides in Japanese male patients with diabetes. Future prospective studies are needed to clarify the causal relationship between alcohol consumption and metabolic syndrome in patients with diabetes.

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