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Original Article

Inverse association of light-to-moderate alcohol drinking with cardiometabolic index in men with diabetes mellitus



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ABSTRACT

Aims: Cardiometabolic index (CMI), calculated as the product of waist-to-height ratio and triglycerides-to-HDL cholesterol ratio, has been proposed as a discriminator of diabetes and has been reported to be associated with progression of atherosclerosis. The purpose of this study was to determine the relationship between alcohol drinking and CMI in men with diabetes.

Methods: The subjects were Japanese male workers aged from 35 to 65 years with diabetes mellitus (n = 1411). The subjects were divided by average daily alcohol consumption (g ethanol/day) into 4 categories of alcohol drinking (nondrinkers; light drinkers, < 22; moderate drinkers, ≥ 22 and < 44; heavy drinkers, ≥ 44). CMI and variables comprising CMI were compared in the nondrinker and each of the drinker groups. Age, habits of smoking and regular exercise, and a present history of medication therapy for diabetes were adjusted in each analysis.

Results: Log-transformed CMI was significantly lower in light and moderate drinkers than in nondrinkers. Waist-to-height ratio was significantly lower in moderate drinkers than in nondrinkers, while log-transformed triglycerides was significantly higher in heavy drinkers than in nondrinkers. HDL cholesterol tended to be higher with an increase of alcohol consumption. Odds ratios with their 95% confidence intervals vs. nondrinkers for high CMI were 0.53 (0.36–0.78) in light drinkers, 0.61 (0.46–0.80) in moderate drinkers, and 0.74 (0.55–1.00) in heavy drinkers.

Conclusions: In men with diabetes, CMI is lower in light-to-moderate drinkers than in nondrinkers, and this results mainly from a positive association between alcohol drinking and HDL cholesterol.

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1. Introduction

Results of periodic health checkups for workers at their workplaces are used for early detection of cardiovascular risk factors including obesity, hypertension, diabetes mellitus, and dyslipidemia. Evaluation of individual cardiometabolic risk and subsequent correction of the risk factors by lifestyle modification and medication therapy are effective for prevention of cardiovascular disease. We have recently proposed cardiometabolic index (CMI) as a new index for discriminating diabetes [1]. CMI is calculated as the product of waist-to-height ratio (WHtR) and triglycerides-to-HDL cholesterol ratio (TG/HDL-C ratio) and has been reported to be associated with the degree of ischemia in the lower extremities of patients with peripheral arterial disease [2],

suggesting that CMI is a useful index to evaluate atherosclerotic progression. For prediction of the risk of coronary heart disease, WHtR has been reported to be a better index than waist circumference alone to detect abdominal obesity [3], and TG-HDL-C ratio has been reported to be a better predictor for myocardial infarction than LDL cholesterol-to-HDL cholesterol ratio [4], a classical atherogenic index [5]. Therefore, CMI is thought to be a reasonable index for predicting overall cardiovascular risk.

Habitual alcohol drinking diversely influences cardiovascular risk depending on the amount of alcohol intake. The incidences of coronary heart disease and ischemic type of stroke have been shown to be lower in light-to-moderate drinkers than in nondrinkers, while heavy drinking has been demonstrated to increase the risks of coronary heart disease and both ischemic and hemorrhagic types of stroke [6,7]. In a general population, alcohol intake has been reported to show a U-shaped relationship with CMI [8]. This finding suggests that cardiometabolic risk is decreased in light-to-moderate drinkers and agrees with the results of the above past epidemiological studies regarding alcohol and cardiovascular disease [6,7].

Abbreviations: ANCOVA, analysis of covariance; CMI, cardiometabolic index; JDS, Japan Diabetes Society; NGSP, National Glycohemoglobin Standardization Program; TG/HDL-C ratio, the ratio of triglycerides to HDL cholesterol; WHtR, the ratio of waist circumference to height.

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Diabetes is a major risk factor for cardiovascular disease. It remains unclear whether habitual alcohol drinking should be allowed for patients with diabetes. Light-to-moderate drinking has been reported to be associated inversely with the risk of cardiovascular disease in patients with diabetes [9,10]. However, it remains to be determined how CMI is modified by alcohol drinking in diabetes patients.

The purpose of this concise study was to elucidate the relationship between alcohol drinking and CMI in male workers with diabetes. Mean CMI levels and percentages of subjects showing high CMI levels were compared in a nondrinker group and groups of subjects who drank different amounts of alcohol.

2. Subjects and methods

2.1. Study design and subjects

A cross-sectional study was performed using a local population-based database. The subjects in the original database of health checkups were Japanese male workers aged from 35 to 65 years who had received periodic health examinations at their workplaces in Yamagata Prefecture in Japan. Subjects who were receiving treatment for any illness were requested to state the names of the diseases in a questionnaire at the health checkup. Subjects with diabetes ($n=1411$; age [mean with standard deviation], 53.4 ± 7.3 years) were extracted from the database. Subjects with diabetes were defined as those showing high hemoglobin A1c levels ($\geq 6.5\%$) according to the criteria for diagnosis of diabetes by the American Diabetes Association [11] and/or having a current history of medication therapy for diabetes. Subjects receiving treatment for dyslipidemia were excluded from the subjects for analysis. This study was approved by the Ethics Committee of Yamagata University School of Medicine. Histories of alcohol consumption, cigarette smoking and regular exercise (almost every day with exercise for 30 min or longer per day) were also surveyed by questionnaires. The subjects were divided into four groups by average cigarette consumption (nonsmokers; light smokers, less than 20 cigarettes per day; heavy smokers, 20 or more and less than 40 cigarettes per day; very heavy smokers, 40 or more cigarettes per day). Average alcohol consumption of each subject per week was reported on the questionnaires.

2.2. Evaluation of alcohol consumption

The frequency of habitual alcohol drinking was asked in the questionnaire as "How frequently do you drink alcohol?". Frequency of weekly alcohol drinking was categorized as "every day" (regular drinkers), "sometimes" (occasional drinkers) and "never" (nondrinkers). Only regular drinkers who answered "every day" were used as drinkers for analyses of the relationships between amount of alcohol consumption and each variable since it was difficult to know the correct average alcohol consumption of occasional drinkers who answered "sometimes". Usual weekly alcohol consumption was recorded in terms of the equivalent number of "go", a traditional Japanese unit of amount 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 of ethanol, and this amount was used to separate moderate-to-heavy drinkers from light drinkers since it is generally accepted that alcohol intake should be reduced to less than 20–30 g ethanol per day from the viewpoint of prevention of hypertension [12]. 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 (nondrinkers; light drinkers: <22 g of ethanol per day; moderate drinkers: ≥ 22

and <44 g of ethanol per day; heavy drinkers, ≥ 44 g of ethanol per day).

2.3. Measurements

Height was measured with the subjects wearing light clothes at the health checkup. Waist circumference was measured at the navel level according to the definition by the Japanese Committee for the Diagnostic Criteria of Metabolic Syndrome. The cut-off value of WHtR used was 0.5 [3]. Fasted blood was sampled from each subject in the morning, and serum triglyceride and HDL cholesterol levels were measured by enzymatic methods using commercial kits, pureauto S TG-N and cholestest N-HDL (Sekisui Medical Co., Ltd, Tokyo, Japan), respectively. The coefficients of variation for the reproducibility of measurement were $\leq 3\%$ for triglycerides and $\leq 5\%$ for HDL cholesterol. Hemoglobin A1c was measured by the NGSP (National Glycohemoglobin Standardization Program)-approved technique using the latex cohesion method with a commercial kit (Determiner HbA1c, Kyowa Medex, Tokyo, Japan). Since the standards of hemoglobin A1c used for measurement are different in the NGSP method and JDS (the Japan Diabetes Society) method, hemoglobin A1c values were calibrated by using a formula proposed by the JDS [13]: hemoglobin A1c (NGSP) (%) = $1.02 \times$ hemoglobin A1c (JDS) (%) + 0.25%. The coefficient of variation for reproducibility of hemoglobin A1c measurement was $\leq 5\%$.

Subjects with high CMI were defined as those showing CMI of ≥ 1.748 , which has been reported to discriminate diabetes best in men [1]. The cut-off values used for hyper-triglyceridemia and hypo-HDL cholesterolemia were 150 mg/dl (\geq) and 40 mg/dl ($<$), respectively.

2.4. Statistical analysis

Statistical analyses were performed using a computer software program (SPSS version 16.0 J for Windows, Chicago IL, USA). Means of each variable with standard deviations and errors or medians of each variable with 25 and 75 percentile values were calculated. Means of each variable were compared among the nondrinker and drinker groups by using analysis of covariance (ANCOVA) followed by Student's *t*-test after Bonferroni correction. Since triglycerides and CMI did not show a normal distribution, they were used after logarithmic transformation in ANCOVA. In logistic regression analysis, odds ratios of each drinker group vs. the nondrinker group for abnormal level of each variable (high CMI, high WHtR, high triglycerides, and low HDL cholesterol) were estimated. Age, habits of smoking and regular exercise, and a history of medication therapy for diabetes were adjusted in ANCOVA and logistic regression analysis. Frequencies of high CMI, high WHtR, high triglycerides, and low HDL cholesterol were compared in the nondrinker group and each of the drinker groups by chi-squared test. All *p* values are two-sided and values of *p* less than 0.05 were considered to indicate statistical significance.

3. Results

3.1. Characteristics of subjects

The mean hemoglobin A1c level with its standard deviation was $7.70 \pm 1.57\%$, and 50.2% of the subjects were receiving medication therapy for diabetes. The percentages of nondrinkers, light drinkers, moderate drinkers and heavy drinkers in the overall subjects were 38.4% ($n=542$), 11.1% ($n=156$), 29.4% ($n=415$) and 21.1% ($n=298$), respectively. The percentages of smokers and subjects having a habit of regular exercise in the overall subjects were 54.9% and 11.1%, respectively. The medians of CMI and

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