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Original Article

Inverse association between excessive alcohol drinking and cardiometabolically healthy status in middle-aged men with and without overweight and obesity

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ABSTRACT

Aims: The aim of this study was to clarify the relationship between drinking and metabolically healthy status in men with normal weight, overweight and obesity.
Methods: The subjects were Japanese men aged from 35 to 60 years (n = 31781) and they were divided by daily amount of drinking (g ethanol) into light (< 22), moderate (≥22 and <44), heavy (≥44 and <66) and very heavy (≥66) drinkers. Metabolically healthy subjects were defined as those without hypertension, dyslipidemia and diabetes.
Results: The percentage of metabolically healthy subjects was much lower in the overweight (BMI ≥25 and <30) and obese (BMI ≥ 30) groups than in the normal weight group (BMI ≥ 18.5 and <25) and was much lower in the obese group than in the overweight group. In each of the normal weight and overweight groups, percentages of metabolically healthy subjects were significantly lower in heavy and very heavy drinkers than in nondrinkers and were marginally significantly higher in light drinkers than in nondrinkers. The above associations between drinking and metabolically healthy status were confirmed by logistic regression analysis. In the obese group, the percentage of metabolically healthy subjects was significantly lower in regular drinkers (including all drinker categories) than in nondrinkers, and metabolically healthy subjects were rare (0.56%) among regular drinkers.
Conclusions: Regardless of absence and presence of overweight or obesity, excessive alcohol drinking is inversely associated with metabolically healthy status and should be avoided for prevention of cardiovascular disease.

1. Introduction

Habitual alcohol drinking has both beneficial and harmful effects on cardiovascular health. The former is explained mainly by the HDL cholesterol-elevating action of alcohol [1,2]. Anti-coagulation actions of alcohol, including inhibition of platelet aggregation [3] and reduction of circulating coagulation factors [4], also contribute to the prevention of thrombotic arterial diseases. On the other hand, blood pressure-elevating action of habitual drinking is mainly involved in its harmful cardiovascular effect [5,6]. In addition, excessive drinking is known to be associated with hypertriglyceridemia [7,8]. Considering both aspects of alcohol effects, light-to-moderate drinking is thought to have a merit for prevention of atherosclerotic diseases including coronary artery disease and ischemic type of stroke [9,10].

The prevalence of metabolic syndrome, a cluster of cardiovascular risk factors including visceral obesity, hypertension, dyslipidemia and diabetes, is influenced by alcohol consumption. In previous meta-analysis studies, light-to-moderate drinking, such as less than 40 g ethanol/day for men and 20 g ethanol/day for women, has been shown to reduce the incidence of metabolic syndrome [11], while heavy drinkers including those with alcohol use disorders showed an increased risk of metabolic syndrome [12,13]. Thus, habitual alcohol drinking shows both beneficial and harmful effects on the risk of metabolic syndrome depending on the amount of alcohol consumption.

Obesity is involved in the pathogenesis of major cardiometabolic risk factors such as hypertension, dyslipidemia and diabetes [14,15]. Significant inverse and positive associations of light and excessive alcohol consumption, respectively, with metabolic syndrome have also been found in men with overweight or obesity [16]. Therefore, habitual alcohol drinking affects the cardiometabolic risk in people with overweight or obesity as well as in people with normal body weight. Moreover, the association

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between obesity and diabetes, a component of metabolic syndrome, has been shown to be weaker in light drinkers than in nondrinkers [17]. Thus, habitual alcohol drinking may modify the impact of obesity on the risk of diabetes.

It was pointed out that a metabolically healthy subgroup of obese individuals must be taken into consideration in both a clinical setting and research work [18]. However, it is still unknown whether metabolically healthy obese individuals are really healthy [19,20]. In a recent prospective study, metabolically healthy obese individuals were shown not to be at increased risk of acute myocardial infarction compared with metabolically healthy individuals with normal weight [21]. However, a meta-analysis of twelve previous studies demonstrated that obese persons were at increased risk for adverse long-term outcomes such as all-cause death and cardiovascular events even in the absence of metabolic abnormalities compared with metabolically healthy individuals with normal weight [22]. Determinants of metabolically healthy obese status are also unclear, particularly regarding dietary factors and lifestyle behaviors [23]. Although there have been some studies in which habitual alcohol drinking was compared in metabolically healthy and unhealthy subjects, the results of those studies were conflicting [24–29] and there has been little information on relationships between different amounts of alcohol consumption and metabolically healthy obesity.

The purpose of this study was therefore to clarify the relationship between habitual drinking and metabolically healthy status and to determine whether or not the relationship was different in those with and without overweight or obesity. Metabolically healthy status was defined as a healthy status without hypertension, dyslipidemia and diabetes [30–32] and was compared among different drinker groups in subjects showing normal weight, overweight or obesity.

2. Subjects and methods

2.1. Subjects

The subjects were Japanese men aged 35–60 years (n = 31781) who had received periodic health checkup examinations at workplaces in Yamagata Prefecture in Japan. This study was approved by the Ethics Committee of Yamagata University School of Medicine (No. 112 from April 2005 to March 2006, approved on March 13, 2006). Histories of alcohol consumption, cigarette smoking, regular exercise (almost every day with exercise for 30 min or longer per day) and illness were surveyed by questionnaires. The subjects were divided by body mass index (BMI, kg/m^2) into normal weight (BMI $\geq$ 18.5 and $<$25), overweight (BMI $\geq$ 25 and $<$30) and obese (BMI $\geq$ 30) groups. Those who showed very low BMI ($<$18.5) and were defined as lean (n = 1231) were excluded from the subjects. The subjects were also divided into four groups by average cigarette consumption (nonsmokers; light smokers, $<$20 cigarettes per day; heavy smokers, $\geq$20 and $<$40 cigarettes per day; very heavy smokers, $\geq$40 cigarettes per day).

2.2. Evaluation of alcohol consumption

Average alcohol consumption of each subject per week was reported on questionnaires. 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 (Fig. 2), 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 [33,34]. Average daily alcohol intake (grams of ethanol per day) was then calculated. The subjects were divided into five groups according to ethanol consumption per day (nondrinkers; light drinkers: $<$22 g of ethanol per day; moderate drinkers: $\geq$22 and $<$44 g of ethanol per day; heavy drinkers, $\geq$44 and $<$66 g of ethanol per day; very heavy drinkers: $\geq$66 g ethanol per day).

2.3. Measurements

Height and body weight were measured with light clothes at the health checkup. Blood pressure was measured by trained nurses, who were part of 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. Hypertension was defined as systolic blood pressure of $\geq$140 mmHg and/or diastolic blood pressure of $\geq$90 mmHg [35]. In addition, subjects who were receiving drug therapy for hypertension were included in the hypertensive group regardless of blood pressure levels. Fasting blood was sampled from each subject, and serum triglycerides, HDL cholesterol and LDL cholesterol were measured by enzymatic methods using commercial kits, pureauto S TG-N, cholestest N-HDL and cholestest LDL (Sekisui Medical Co., Ltd, Tokyo, Japan), respectively. Cut-off values for hyper-triglyceridemia, hypo-HDL cholesterolemia and hyper-LDL cholesterolemia were 150 mg/dl ($\geq$), 40 mg/dl ($<$) and 140 mg/dl ($\geq$), respectively [36]. Dyslipidemia was defined as existence of at least one of the following: hyper-triglyceridemia, hypo-HDL cholesterolemia and hyper-LDL cholesterolemia. Subjects receiving drug therapy for dyslipidemia were included in the dyslipidemia group. Hemoglobin A1c was determined by the latex cohesion method using a commercial kit (Determiner HbA1c, Kyowa Medex, Tokyo, Japan). Hemoglobin A1c values were calibrated by using a formula proposed by the Japan Diabetes Society (JDS) as hemoglobin A1c (National Glycohemoglobin Standardization Program) (%) = 1.02 x hemoglobin A1c (JDS) (%) + 0.25% [37]. Diabetes was defined as hemoglobin A1c $\geq$ 6.5% according to the criteria of the American Diabetes Association [38]. Subjects receiving drug therapy for diabetes were included in the diabetes group. Coefficients of variation for reproducibility of each measurement were $\leq$3% for triglycerides and $\leq$5% for HDL cholesterol, LDL cholesterol and hemoglobin A1c. In most studies, metabolically healthy obese status was defined as the absence of any metabolic disorders including diabetes, dyslipidemia and hypertension in an obese individual [30–32]. Thus, in the present study, metabolically healthy subjects were defined as those without hypertension, dyslipidemia (hyper-triglyceridemia, hypo-HDL cholesterolemia and/or hyper-LDL cholesterolemia) and diabetes according to the above criteria.

2.4. Statistical analysis

Statistical analyses were performed using a computer software program (SPSS version 16.0 J for Windows, Chicago IL, USA). Mean levels of each quantitative variable were compared using analysis

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