Original Article

Excessive Alcohol Intake Increases the Risk of Arterial Stiffening in Men with Normal Blood Pressure

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Excessive alcohol intake is a known atherosclerotic cardiovascular risk factor. However, the relation between excessive alcohol intake and atherosclerotic cardiovascular risk in subjects with normal blood pressure has not been fully elucidated. This cross-sectional study investigated the relationship between alcohol intake and arterial stiffness, as assessed using brachial-ankle pulse wave velocity, in men with normal blood pressure. Middle-aged male workers who were found to have a normal blood pressure during an annual health check-up performed in May–July 2000 ($n = 1,682$) were enrolled in the study. The subjects' laboratory data were analyzed, and information on drinking and smoking habits was obtained by a self-administered questionnaire. The brachial-ankle pulse wave velocity was measured using volume plethysmography. The mean brachial-ankle pulse wave velocities of men with an alcohol intake of 40–59 g/day and ≥ 60 g/day were larger than those of non-drinkers and men with an alcohol intake of < 20 g/day. A multivariate general linear model was used to identify the association between alcohol intake and brachial-ankle pulse wave velocity after controlling for other risk factors using a multivariate analysis. An alcohol intake of more than 60 g of ethanol/day was significantly associated with an elevated brachial-ankle pulse wave velocity, after controlling for conventional atherosclerotic cardiovascular risk factors. In conclusion, the present results suggest that excessive alcohol intake increases the atherosclerotic cardiovascular risk associated with arterial stiffening in men with normal blood pressure. (*Hypertens Res* 2004; 27: 669–673)

Key Words: pulse wave velocity, risk factors, alcohol intake, arterial stiffness, cross-sectional study

Introduction

Excessive alcohol intake is a known cardiovascular risk factor in the general population (1–3). Many studies have reported that a more than moderate alcohol intake elevates blood pressure, and this phenomenon is thought to be an underlying mechanism of the increased cardiovascular risk that is associated with excessive alcohol intake (4, 5). However, excessive alcohol intake has not been definitively determined to be a cardiovascular risk factor among subjects with a normal blood pressure. An evaluation of the association be-

tween excessive alcohol intake and a marker capable of predicting future atherosclerotic cardiovascular events may provide some information about this inconclusive matter. Pulse wave velocity (PWV), which is a measure of arterial stiffness, has been demonstrated to be a clinical predictor of atherosclerotic cardiovascular disease and cardiovascular disease-related mortality that is independent of other conventional atherosclerotic risk factors (6–8).

In the present study, the PWV was measured in a cohort of men with normal blood pressure, and the relation between alcohol intake and PWV was examined after controlling for conventional atherosclerotic risk factors.

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Methods

Design and Study Sample

The present study consisted of a cross-sectional study that was performed at a single large company. Japanese law requires employers to provide annual health check-ups for all employees. Of the 3,094 male workers employed at a construction company in Tokyo, Japan, who underwent a health check-up during the period from May–July 2000, complete information regarding alcohol intake was obtained from 2,282 subjects. Subjects with at least one of the following criteria were excluded from the present study: treatment for hypertension, a systolic blood pressure (SBP) of ≥ 140 mmHg, or a diastolic blood pressure (DBP) of ≥ 90 mmHg ($n = 518$); older than 60 years of age ($n = 34$); a possible diagnosis of arteriosclerosis obliterans, as indicated by an ankle/brachial systolic blood pressure index (ABI) of less than 0.9 ($n = 6$); atrial fibrillation ($n = 2$); treatment for cerebrocardiovascular disease ($n = 27$); a past history of cerebrocardiovascular disease ($n = 12$); or a serum creatinine concentration of >1.5 mg/dl ($n = 1$). Consequently, 1,682 men were available for further analysis. Oral informed consent was obtained from all the participants. The study was approved by the Ethical Guidelines Committee of Tokyo Medical University.

Measurements

Alcohol Intake

Habitual alcohol intake and demographic, behavioral, and clinical information, including past medical history, were assessed using a self-administered questionnaire. Alcohol intake was evaluated using two parameters: average drinking frequency (days/week) and average amount (ml). The average daily alcohol intake (ethanol equivalent [g/day]) was then calculated for each subject, and the subjects were categorized into the following groups: non-drinkers, <20 g/day, 20–39 g/day, 40–59 g/day, and ≥ 60 g/day.

PWV

Brachial-ankle PWV (baPWV) was measured using a volume-plethysmograph (Form ABI/PWV; Colin Co., Ltd., Komaki, Japan) by ten trained specialists. The baPWV was measured after the subjects had rested in a supine position for at least 5 min in a room with a constant room temperature of 20–23°C. The measurement methodology, validity and reproducibility have been previously reported (9, 10). Measurements obtained at the right ankle and right brachium were used for the subsequent analysis.

Blood Pressure

Appendicular blood pressure, heart rate (HR) and ABI were simultaneously measured using the same apparatus under the

Fig. 1. Distribution of baPWV according to alcohol intake in subjects with normal blood pressure. The bars show SD. * $p < 0.05$ vs. non-drinkers, † $p < 0.05$ vs. alcohol intake of <20 g/day.

same conditions as described above.

Laboratory Measurements

Serum creatinine, fasting blood sugar, total cholesterol, and high-density lipoprotein (HDL) cholesterol levels were measured using enzymatic methods (Falco Biosystems Co., Ltd., Tokyo, Japan). All blood samples were obtained in the morning after an overnight fast.

Statistical Analysis

Data were expressed as the mean $\pm$ SD. Inter-group differences were evaluated using a one-way analysis of variance with Bonferroni's adjustment for continuous variables and the χ^2 test for categorical variables. A multivariate general linear model was used to assess the association between alcohol intake and baPWV after controlling for age, SBP, body mass index, smoking status, serum total cholesterol, fasting blood sugar, and HDL cholesterol levels. All analyses were conducted using SPSS software for Windows, version 11.0J (SPSS, Chicago, USA). P values of <0.05 were considered statistically significant.

Results

Figure 1 shows the distribution of baPWV according to the level of alcohol intake. The mean baPWVs in subjects with an alcohol intake of 40–59 g/day and ≥ 60 g/day were larger than those in non-drinkers and subjects with an alcohol intake of <20 g/day. The characteristics of the subjects grouped according to their level of alcohol intake are presented in Table 1. Among the subjects with an alcohol intake

Table 1. Clinical Characteristics of Subjects According to Alcohol Intake

	Non-drinkers	Alcohol intake (g/day)			
		<20	20–39	40–59	≥60
<i>n</i>	365	579	386	271	81
Age (years)	42 ± 9	38 ± 8*	40 ± 9*,†	43 ± 9†	42 ± 9†
BMI	23 ± 3	23 ± 3	23 ± 3	23 ± 3	24 ± 3
Smoking (%)	138 (38)	196 (34)	145 (38)	146 (54)*,†,‡	50 (62)*,†,‡
SBP (mmHg)	120 ± 10	120 ± 9	122 ± 9*,†	124 ± 8*,†	125 ± 8*,†
DBP (mmHg)	74 ± 7	73 ± 7	76 ± 6*,†	77 ± 6*,†	77 ± 6*,†
HR (beats/min)	64 ± 10	62 ± 9*	63 ± 9	64 ± 10*	64 ± 10
TC (mg/dl)	190 ± 26	184 ± 21*	184 ± 21*	186 ± 21	182 ± 21*
HDL (mg/dl)	53 ± 10	56 ± 9*	59 ± 10*,†	59 ± 10*,†	60 ± 10*,†
FBS (mg/dl)	90 ± 10	88 ± 9	89 ± 10	90 ± 10	90 ± 10

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; FBS, fasting blood sugar. * $p < 0.05$ vs. non-drinkers, † $p < 0.05$ vs. less than 20 g/day group, ‡ $p < 0.05$ vs. the 20–39 g/day group.

Table 2. Multivariate Analysis Results for the Relations between Brachial-Ankle Pulse Wave Velocity and Atherosclerotic Cardiovascular Risk Factors, Including High Alcohol Intake

	<i>F</i> value	<i>p</i> value
Alcohol intake ≥60 g/day	5.9	<0.01
Age	234.5	<0.01
Smoking	1.4	ns
BMI	54.6	<0.01
SBP	1,365.4	<0.01
TC	7.6	<0.01
HDL	2.3	ns
FBS	6.6	<0.01
Total: $r^2 = 0.53$		

Smoking, smoking habit; BMI, body mass index; SBP, systolic blood pressure; TC, total cholesterol; HDL, high-density lipoprotein cholesterol; FBS, fasting blood sugar; ns, not significant.

of 40–59 g/day and ≥60 g/day, the blood pressure and number of subjects who smoked were significantly higher than among non-drinkers.

Table 2 shows the relationship between baPWV and high alcohol intake (≥60 g/day) after controlling for known atherosclerotic risk factors using a multivariate analysis. In addition to age, SBP, body mass index, total cholesterol, and fasting blood sugar, an alcohol intake of ≥60 g/day was a significant determinant of baPWV. In the same analysis between baPWV and an alcohol intake of ≥40 g/day, an alcohol intake of ≥40 g/day was not a significant determinant of baPWV.

Discussion

The present study shows that excessive alcohol intake

(40–59 g/day or ≥60 g/day) increased the blood pressure and baPWV in men with normal blood pressure. After controlling for cardiovascular risk factors using a multivariate analysis, excessive alcohol intake (≥60 g/day) continued to be positively related to baPWV in a manner that was independent of conventional atherosclerotic risk factors in men with normal blood pressure.

The precise mechanisms underlying the increased cardiovascular risk in subjects with excessive alcohol intake are uncertain. The elevation in blood pressure, unfavorable effects on lipids profiles or coagulation systems, and psychosocial factors related to excessive alcohol intake are thought to be possible mechanisms (11). PWV, which is a measure of arterial stiffness, is regarded as an independent risk factor for atherosclerotic cardiovascular disease (6–8), and the increased cardiovascular risk associated with excessive alcohol intake may be related to arterial stiffening. However, the number of studies examining the relationship between alcohol intake and PWV is limited. Namekata *et al.* reported that alcohol intake and PWV were not related in men (12). In contrast, Nakanishi *et al.* reported that excessive alcohol intake was associated with a risk of increased PWV in a prospective study (13). Mahmud and Feely demonstrated that while excessive alcohol intake increased the PWV in men, the increase was not significant when corrected for blood pressure (14). Thus, the relationship between these two parameters has not been conclusively determined. Blood pressure is a major determinant of PWV (9), and subjects with hypertension and excessive alcohol intake are naturally at risk for increased arterial stiffness. On the other hand, the PWV has also been shown to be a cardiovascular risk marker in subjects with normal blood pressure (15). In the present study, the baPWV was found to be higher in subjects whose alcohol intake was excessive (40–59 g/day or more than 60 g/day), compared with subjects with lower or no alcohol intake, in a study population with normal blood pressure.

The present study suggests that excessive alcohol intake increases the risk of arterial stiffness even in subjects with normal blood pressure, but the potency of the cardiovascular risk related to this increased risk of arterial stiffness could not be determined.

The precise mechanisms by which excessive alcohol intake affects arterial stiffening have not been clarified. In addition to blood pressure, several studies have reported that conventional atherosclerotic risk factors, such as dyslipidemia or diabetes mellitus, are determinants of arterial stiffening (9, 16, 17). In the present study, excessive alcohol intake was found to be an independent risk factor for arterial stiffening. However, several other factors might affect arterial stiffness. Ethanol stimulates matrix protease activity (18), increases oxidative stress (19), activates NF- κ - β in vascular smooth muscle cells (20), and stimulates sympathetic tone (21). Any or all of these factors may have a direct effect on arterial stiffening.

A J- or U-shaped relation between alcohol intake and atherosclerotic cardiovascular events has been noted (22, 23), and some studies have reported a similar phenomenon between alcohol intake and PWV (24, 25). These previous studies speculated that the cardiovascular risk reduction observed in subjects with light to moderate alcohol intake may be related to the lower degree of arterial stiffness seen in these subjects. However, a significant reduction in the baPWV of subjects with light to moderate alcohol intake was not observed in the present study. All of the subjects in the present study had normal blood pressure. This clinical characteristic might be at least partially related to the absence of a significant decline in baPWV in subjects with light to moderate alcohol intake in the present study. The authors intend to continue studying the J- or U-shaped relation between alcohol intake and arterial stiffness in a study with a large sample size.

The present study has some limitations. Blood pressure, as used to define the degree of cardiovascular risk, is normally determined in a casual office setting (26, 27); in the present study, however, the appendicular blood pressure was determined using an apparatus that measures the baPWV while the subject is in a supine position. A longitudinal study in the same cohort is now underway to clarify the causal association between alcohol intake and arterial stiffening. In addition, alcohol intake was assessed using a self-reporting method. While the underestimation of alcohol intake is a concern with this method, the reliability of self-reporting has been previously reported (28).

In conclusion, the present study revealed a higher degree of arterial stiffening in men with normal blood pressure and excessive alcohol intake than in non-drinkers with normal blood pressure, suggesting that excessive alcohol intake may increase the atherosclerotic cardiovascular risk associated with arterial stiffening in men with normal blood pressure.

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