Alcohol intake and aortic stiffness in young men and women

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Background **Moderate alcohol consumption has been shown to protect against cardiovascular disease. Aortic stiffness can be regarded as a marker of cardiovascular disease risk. Previously we have shown an inverse to J-shaped association between alcohol intake and aortic stiffness in middle-aged and elderly men and postmenopausal women.**

Objective **In the present study we examined whether a relation between alcohol intake and aortic stiffness is already present at a younger age.**

Design **Cross-sectional data of a cohort study in men and women aged 28 years were analysed stratified by gender (240 men and 283 women).**

Measurements **Alcohol intake was derived from a questionnaire and aortic stiffness was assessed by pulse-wave velocity measurement.**

Results **In women an alcoholic beverage intake of $\geq$1 glass/day is associated with a 0.36 m/s (95% confidence interval, −0.58 to −0.14) lower pulse-wave velocity compared with non-drinkers. In men alcohol intake is also inversely related to pulse-wave velocity, but this was not significant. These findings were independent of age, blood pressure and heart rate.**

Conclusions **These findings suggest that moderate intake of alcohol may affect vascular stiffness at an early age, notably in women. These findings may be viewed as compatible with a vascular protective effect of alcohol that expresses well before the occurrence of symptomatic cardiovascular disease.** ***J Hypertens*** **23:731–735 © 2005 Lippincott Williams & Wilkins.**

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Introduction

The relation between alcohol intake and the cardiovascular system seems to be U-shaped, suggesting a higher risk of cardiovascular disease in non-drinkers and heavy alcohol consumers compared with those with moderate alcohol intake [1]. Mechanisms proposed to explain a positive health effect of moderate alcohol consumption include beneficial effects of lipoprotein metabolism [2], haemostasis [3] and inflammatory processes [4] with regard to atherogenesis. In addition, cross-sectional and large prospective studies have shown that moderate alcohol consumption reduces the risk of diabetes mellitus type 2 [5] and increases insulin sensitivity [6].

While cardiovascular protection has been demonstrated in older subjects, it is less clear whether beneficial effects of alcohol intake on the cardiovascular system express already at a younger age when subjects are still free of overt vascular disease. Early vascular evidence of cardiovascular risk may be provided by measurement of arterial characteristics, such as aortic stiffness. Aortic pulse-wave velocity (PWV) is a non-invasive measurement of the distensibility of the aorta, which is reported to be a reliable index of aortic stiffness [7]. An increased aortic stiffness at young adulthood may reflect life-long exposure to risk factors. Increased aortic stiffness has been related to unfavourable levels of risk factors, prevalent cardiovascular disease and atherosclerosis elsewhere in the arterial system. Also, increased arterial stiffness has been shown to predict cardiovascular events [8].

Previously, we reported an inverse to J-shaped association between alcohol intake and aortic stiffness in postmenopausal women [9] and in men aged 40–80 years [10]. In the present study we examined whether such a relation is already present at a younger age.

Methods

Subjects

The Atherosclerosis Risk in Young Adults (ARYA) study comprises two cohorts of young adults, one performed in the city of The Hague and one in the city of Utrecht. Since vascular measurements were not performed in the Hague cohort, this paper is restricted to the Utrecht participants of the ARYA study. The Utrecht cohort includes 750 young adults born between 1 January 1970 and 31 December 1973, who attended secondary school in the city of Utrecht The Netherlands and of whom the original medical records from the Municipal Health Care were available [11]. From 1 October 1999 to 31 December 2000, all participants visited our outdoor clinic twice within a 3-week period. PWV measurements were performed in 524 subjects (46% male). The ARYA study was approved by the Medical Ethics Committee of the University Medical Center Utrecht. All participants gave written informed consent.

Cardiovascular risk factors

During the first visit, anthropometric measurements were performed. Height, weight, and waist–hip circumference were measured with indoor clothes without shoes. A written standardized questionnaire was completed on alcohol intake, smoking, highest education, and contraceptive pill use in women. In the questionnaire, subjects had to select one out of five options to categorize their alcohol intake (0, < 1, 1–2, 3–5 and ≥ 6 glasses/day). Because there were only few subjects in the highest alcohol intake levels, the two highest categories in men and the three highest categories in women were combined. Statistical analyses were performed with four alcohol intake levels for men (0, < 1, 1–2 and ≥ 3 glasses/day) and three alcohol intake levels for women (0, < 1 and ≥ 1 glasses/day).

During the second visit, fasting venous blood samples were drawn. The samples were stored at -20°C until all participants were enrolled into the study. Total cholesterol and high-density lipoprotein (HDL)-cholesterol were determined using an automatic enzymatic procedure (Vitros950 dry-chemistry analyser; Johnson & Johnson, Rochester, New York, USA).

At each visit, blood pressure was measured twice, after 5 min of rest, and at an interval of 5–15 min, in the left brachial artery in a sitting position with an automated device (Dinamap Critikon, Tampa, Florida, USA) without replacing the cuff between the measurements. The mean of two consecutive measurements was used in the analyses. Pulse pressure was defined as systolic blood pressure minus diastolic blood pressure. Mean arterial pressure was calculated as diastolic blood pressure + (1 / 3 × pulse pressure). Unfortunately, the mean arterial pressure was not noted down from the Dinamap, and was therefore estimated. Since this population is of a limited age range, we feel that the calculation of the mean arterial pressure is correct. Only when ages are above 50–60 years may one consider changing the relative weight of pulse pressure in the formula.

Arterial stiffness

Arterial stiffness was non-invasively assessed by measuring the carotid–femoral (aortic) PWV, using an automated device (SphygmoCor device; PWV Medical, Sydney, Australia). Aortic PWV was determined by sequential acquisition of pressure waves from the carotid and femoral arteries by applanation tonometry (Millar Instruments, Houston, Texas, USA). The wave transit time (t) was calculated by the system software, using the R-wave on the simultaneously recorded electrocardiogram as reference frame. The distance travelled by the pulse wave was measured in a straight line to reduce the influence of body contours. The carotid to femoral path length (D) was defined as the distance between the recording sites at the femoral artery to the suprasternal notch minus the distance from the recording site at the carotid artery to the suprasternal notch. PWV was calculated as D/t. The average of 10 successive waveforms was used in the analyses to cover a complete respiratory cycle. The whole procedure was repeated three times per subject and the average PWV value was used for the analysis [11,12].

In order to evaluate the reproducibility of the technique in our research centre, a subset of 25 participants had their PWV re-measured several weeks after their first visit. The absolute mean difference (standard error) in PWV of the repeated measurements between visits was 0.12 m/s (0.45). The intraclass correlation coefficient for repeated measurements was 0.67. Since the repeated measurements were performed on two different occasions, the moderate intraclass correlation coefficient could partially be explained by the variability in blood pressure over time.

Statistical analysis

Data on alcohol consumption were missing in one participant, leaving 523 subjects for analysis. The alcohol intake levels (categorical) were put into a linear regression model as dummy variables with the lowest category as reference.

The association between alcohol consumption and PWV was examined using multivariate linear regression analysis, adjusted for major determinants of PWV; namely age, mean arterial pressure and heart rate (Model A) [13,14].

In addition, Model A was extended with factors that were at least significantly ($P < 0.05$) or that are biologically plausibly related to either PWV or alcohol intake (Model B). This model included waist-to-hip ratio, total cholesterol, HDL-cholesterol, highest education and current smoking.

Table 1 Characteristics of the male study population by reported alcohol consumption

	Alcohol intake			
Variable	None	< 1/day	1–2/day	≥ 2/day
n	31	111	59	39
Age (years)	28.2 (1.1)	28.3 (0.9)	28.2 (1.0)	28.1 (0.9)
Body mass index (kg/m^2)	24.5 (4.6)	25.0 (3.5)	24.4 (3.8)	23.7 (2.7)
Waist-to-hip ratio	0.89 (0.08)	0.90 (0.06)	0.87 (0.06)	0.86 (0.06)
Highest education (%)				
Elementary school	12.9	1.8	1.7	2.6
Secondary school	9.7	20.7	20.3	20.5
Lower/intermediate vocational training	48.4	47.8	25.4	43.6
Higher vocational training/university	29.0	29.7	52.5	33.3
Current smokers (%)	6.5	32.4	44.1	41.0
Total cholesterol (mmol/l)	4.52 (0.71)	5.02 (1.09)	4.84 (0.79)	4.70 (0.74)
HDL-cholesterol (mmol/l)	1.31 (0.35)	1.23 (0.29)	1.37 (0.28)	1.37 (0.28)
Systolic blood pressure (mmHg)	132.4 (16.2)	131.2 (11.3)	129.1 (11.0)	128.2 (12.3)
Diastolic blood pressure (mmHg)	73.1 (9.2)	72.8 (7.1)	71.5 (6.3)	73.0 (6.9)
Mean arterial pressure (mmHg)	92.9 (10.6)	92.2 (7.6)	90.7 (7.3)	91.4 (7.8)
Pulse pressure (mmHg)	59.3 (11.8)	58.5 (9.0)	57.6 (7.7)	55.2 (9.9)
Heart rate (beats/min)	64.5 (7.2)	64.8 (10.7)	61.9 (8.7)	61.1 (8.2)
Pulse wave velocity (m/s)	6.39 (0.82)	6.25 (0.78)	6.28 (0.78)	6.18 (0.64)

Values are expressed as mean (standard deviation) in the case of continuous variables, and as percentages in the case of categorical variables. HDL, high-density lipoprotein.

To validate the self-reported information on alcohol intake, we evaluated the relation of HDL-cholesterol to alcohol intake using multiple linear regression analysis, adjusted for age, mean arterial pressure and heart rate.

Data were analysed using the SAS statistical software package (SAS/STAT Version 8.02; SAS Institute, Cary, North Carolina, USA) [15].

Results

General characteristics of the study are presented by alcohol intake and by gender in Tables 1 and 2. Table 3 presents the relation of alcohol intake to PWV and HDL-cholesterol separately for men and women because the association between alcohol and PWV differed by gender ($P = 0.03$). In both men and women HDL-cholesterol increased with increasing alcohol intake. There was an inverse association between alcohol intake and aortic stiffness in women. An alcoholic beverage intake of ≥ 1 glass/day decreased the PWV by 0.36 m/s (95% confidence interval, −0.58 to −0.14) compared with non-drinkers. In men, alcohol consumption of ≥ 3 glasses/day lowered the PWV by 0.15 m/s (95% confidence interval, −0.51 to 0.20). Additional adjustment for factors that were at least significantly ($P < 0.05$) or that are biologically plausibly related to either PWV or alcohol intake (Table 3, Model B) did not change the magnitude of the relations.

Table 2 Characteristics of the female study population by reported alcohol consumption

	Alcohol intake		
Variable	None	0–1/day	≥ 1/day
n	70	161	52
Age (years)	28.3 (0.9)	28.1 (0.95)	28.4 (0.90)
Body mass index (kg/m^2)	25.7 (5.7)	24.2 (4.2)	23.8 (3.4)
Waist-to-hip ratio	0.82 (0.07)	0.82 (0.06)	0.80 (0.05)
Highest education (%)			
Elementary school	4.3	0.6	1.9
Secondary school	27.1	20.5	17.3
Lower/intermediate vocational training	51.4	34.8	32.7
Higher vocational training/university	17.1	44.1	48.1
Current smokers (%)	18.6	23.6	46.2
Total cholesterol (mmol/l)	4.90 (0.49)	4.87 (0.87)	4.69 (0.73)
HDL-cholesterol (mmol/l)	1.51 (0.34)	1.61 (0.38)	1.59 (0.34)
Systolic blood pressure (mmHg)	119.9 (13.0)	120.6 (11.7)	119.5 (12.4)
Diastolic blood pressure (mmHg)	69.5 (8.4)	71.8 (8.5)	69.6 (7.5)
Mean arterial pressure (mmHg)	86.3 (9.3)	88.0 (9.0)	86.3 (8.6)
Pulse pressure (mmHg)	50.4 (8.5)	48.8 (7.6)	49.9 (8.0)
Heart rate (beats/min)	68.7 (8.7)	65.8 (8.7)	65.1 (8.8)
Pulse wave velocity (m/s)	5.82 (0.69)	5.72 (0.70)	5.47 (0.62)

Values are expressed as mean (standard deviation) in the case of continuous variables, and as percentages in the case of categorical variables. HDL, high-density lipoprotein.

Table 3 Pulse-wave velocity (PWV) and high-density lipoprotein (HDL)-cholesterol in men and women per level of alcohol intake

Alcohol intake level (glasses/day)	*n*	PWV (m/s) (Model A)	PWV (m/s) (Model B)	HDL-cholesterol (mmol/l) (Model A)
Men				
0	31	6.37 (0.13)	6.36 (0.15)	1.32 (0.05)
< 1	111	6.23 (0.07)	6.20 (0.10)	1.24 (0.03)
1–2	59	6.30 (0.10)	6.31 (0.12)	1.36 (0.04)
≥ 3[a]	39	6.22 (0.12)	6.19 (0.14)	1.36 (0.05)*
Women				
0	70	5.85 (0.07)	5.81 (0.10)	1.52 (0.04)
< 1	161	5.70 (0.05)	5.63 (0.09)*	1.61 (0.03)
≥ 1[b]	52	5.49 (0.08)†	5.41 (0.11)‡	1.59 (0.05)

Values are expressed as mean (standard error of the mean). Model A, adjusted for age, mean arterial pressure and heart rate; Model B, adjusted for age, mean arterial pressure, heart rate, waist-to-hip ratio, total cholesterol, HDL-cholesterol, highest education and current smoking. [a]Seventy-nine per cent of the subjects had an alcoholic beverage intake of 3–5 glasses/day. [b]Eighty-five per cent of the subjects had an alcoholic beverage intake of 1–2 glasses/day. *$P < 0.05$. †$P < 0.01$. ‡$P < 0.001$, compared with non-drinkers.

Discussion

These findings provide evidence of an inverse association between alcohol consumption and aortic stiffness in young women. To appreciate the findings, certain aspects of the study need to be addressed. The use of self-reported information on alcohol intake may have introduced misclassification of exposure, specifically those in the heavier drinking groups [16]. However, selective misclassification of heavy drinkers as non-drinkers seems unlikely, because we observed a positive association between alcohol consumption and HDL-cholesterol, a finding that supports the rank-order validity of self-reported alcohol intake. No information was available on alcoholic beverage type consumed, changes in drinking behaviour and drinking pattern. However, type of beverage consumed is not likely to have influenced our findings, since much of the benefit is from alcohol rather than other components of each type of drink [17,18]. In addition, changes in drinking behaviour are probably not relevant at a young age. Drinking pattern might be a factor that has influenced the results. Yet, Mukamal *et al.* [18] recently observed, within categories of frequency of alcohol consumption, similar inversely related risks of myocardial infarction, regardless of the amount of alcohol consumed per drinking day.

We also considered the possibility of confounding of our findings by unmeasured dietary or other lifestyle factors. In order to be a confounder in this analysis, the variable of interest should be related to both alcohol intake and to PWV. In an earlier report, we showed that the main factors related to PWV were age, gender and mean arterial pressure [12]. So, theoretically, only these factors should be considered as potential confounders. However, in our analyses age, mean arterial pressure, heart rate, waist-to-hip ratio, total cholesterol, HDL-cholesterol, highest education and current smoking were controlled for, and thereby we feel that we covered most of the factors that can possibly distort the association studied. Yet, in our study no information on dietary intake was collected. Thus, there might still be some residual confounding through dietary factors, only of those that do not affect the parameters that were already taken into account in the multivariate analyses.

To our knowledge there are only five studies presenting the relation of alcohol consumption on aortic PWV. A cross-sectional study in Japanese-American middle-aged and older men and women reported that the risk for high aortic PWV was lower among current drinkers and ex-drinkers than among non-drinkers [19]. In a follow-up study in middle-aged Japanese men the incidence of aortic stiffness was not related to alcohol intake [20], whereas another longitudinal study in Japanese men suggested that alcohol is an important risk factor for development of aortic stiffness at an intake of more than 16 glasses of alcoholic beverage per week [21]. We recently reported an inverse to J-shaped association between alcohol consumption and aortic PWV in cross-sectional studies among postmenopausal women [9] and among men aged 40–80 years [10].

In young women an alcoholic beverage intake of about 1–2 glasses/day decreased the PWV approximately 7% compared with non-drinkers. This is comparable with the decrease in PWV observed in postmenopausal women with an intake of 10–14 glasses alcoholic beverage per week (8% decrease compared with non-drinkers) [9].

In young men, the inverse relation between alcohol and PWV was less pronounced. There are several possible explanations for the sex difference in strength of association. First, the smaller increase in HDL-cholesterol with increasing alcohol intake in men compared with women might suggest that men were less precise in their recall of alcohol intake. Second, the drinking pattern in men might be unfavourable; namely, binge drinking instead of regular daily consumption. Third, an alternative explanation could be that the effect of atherogenic factors, like smoking and lipids, are more pronounced in young men, in such a way that the influence of alcohol on PWV cannot be observed. Finally, it may be that the association truly does not exist in men, or that the numbers of men in our study, particularly in the non-drinking group, were too

small and the variation in PWV too large for statistical detection of an inverse trend.

The mechanism by which moderate alcohol intake may reduce aortic stiffness is unknown. Alcohol consumption increases HDL-cholesterol [2], with associated increases in paraoxonase activity [2] and cholesterol efflux [22]. These changes might decrease the amount of cholesterol within peripheral cells, and thus increase the flexibility of the vascular wall. However, the relation between alcohol intake and PWV remained when HDL-cholesterol was taken into account, suggesting that our finding could not be fully explained by an increase in HDL-cholesterol. With increasing age the arteries become stiffer due to a decrease in elastin and an increase in collagen and connective tissues in the arterial wall [23]. Alcohol intake might delay or change this process, possibly by an effect on gene expression. Damaging of the vascular wall due to inflammation might also cause arterial stiffness. The observed decrease in the inflammation factor C-reactive protein [4] with moderate alcohol intake could decrease the risk of lesions of the vascular wall and explain the increase in vascular elasticity. Finally, epidemiological studies have shown that moderate alcohol consumption reduces the risk of diabetes mellitus type 2 [5] and increases insulin sensitivity [6]. This effect of alcohol might decrease the formation and cross-linking of glycated collagen in the vascular wall, which is accelerated in hyperglycaemic milieu [24].

Conclusions

Our findings suggest that moderate intake of alcohol may affect vascular stiffness already at an early age, notably in women. These findings may be viewed as compatible with a vascular protective effect of alcohol that expresses well before the first occurrence of symptomatic cardiovascular disease.

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