Moderate alcohol consumption is associated with reduced arterial stiffness in older adults. The Rotterdam Study

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Running head-line Alcohol consumption and arterial stiffness

Abstract

Background. Light to moderate alcohol consumption has been associated with a lower risk of cardiovascular disease. The protective effect of alcohol could involve arterial properties as arterial stiffness and distensibility.

Methods. The relation between alcohol and arterial stiffness was studied within the framework of the Rotterdam Study, a population-based study in individuals aged 55 and older. The present study included 3178 subjects participating in the third examination phase. Arterial stiffness was measured by two different methods, i. e. the carotid-femoral pulse wave velocity and the distensibility coefficient of the common carotid artery. Categories of alcohol consumption were defined as follows; up to 3 glasses alcohol per week, 4-10 glasses per week, 11 to 20 glasses per week, ≥ 21 glasses per week. Linear regression analysis was used to investigate the association between alcohol consumption and measures of arterial stiffness.

Results. In multivariate adjusted models, women drinking 4-10, 11-20 and ≥ 21 glasses of alcoholic beverage per week had a -0.07 (m/s) (0.22 to -0.38), -0.18 (0.12 to -0.49) and 0.12 (0.19 to -0.43) difference in mean pulse wave velocity compared to those drinking 0-3 glasses per week (reference group). Corresponding differences in the carotid distensibility coefficient were 0.68 (10^{-3}/kPa) (1.21 to 0.15), 0.28 (0.82 to -0.25) and 0.36 (0.91 to -0.18). In men, the estimates were not statistically significant, although a similar trend was observed.

Conclusions. Moderate alcohol consumption is associated with lower arterial stiffness in women independently of cardiovascular risk factors and atherosclerosis.

Keywords: Arterial stiffness, older adults, alcohol consumption, risk factors, epidemiology.

Introduction

Light to moderate alcohol consumption seems to have a protective effect on the cardiovascular system. Higher cardiovascular morbidity and mortality have been shown in heavy and non-drinkers compared to moderate drinkers resulting in an U-shaped association (1-3). The mechanism underlying this beneficial effect of moderate alcohol consumption is still incompletely understood. An increase of arterial stiffness, which is one of the characteristics of the aging cardiovascular system (4), and is associated with cardiovascular risk factors as hypertension (5,6) and diabetes mellitus (7), has been considered as possible mechanism. The results obtained in the studies on the relation between alcohol consumption and arterial stiffness, however, are inconsistent. In middle-aged Japanese men alcohol consumption was found to be associated with high aortic stiffness measured as pulse wave velocity (8,9). Conversely, in another study alcohol consumption was shown to be associated with reduced arterial stiffness (10). Recent studies found a J-shaped association between alcohol consumption and arterial stiffness in men aged 40-80 years (11) and an inverse association in healthy postmenopausal women (12). We have investigated the relation between alcohol consumption and arterial stiffness within the framework of the Rotterdam Study, a population-based study in individuals aged 55 and older.

Methods

Population

This study was conducted within the framework of the Rotterdam Study, an ongoing prospective population-based cohort study among subjects aged 55 years and over, living in Ommoord, a suburb of Rotterdam, The Netherlands. The rationale and design of the Rotterdam Study have been described elsewhere (13). The third examination phase took place from 1997 until 1999. During this phase, information on cardiovascular risk factors was

collected, measurements of arterial stiffness and measures atherosclerosis were obtained and alcohol consumption was assessed as part of the interview at the study center. The Medical Ethics Committee of the Erasmus Medical Center approved the study and written consent was obtained from all participants.

Arterial Stiffness

Arterial stiffness was measured by two different methods, i. e. the carotid-femoral pulse wave velocity (PWV) as measure of aortic stiffness and the distensibility coefficient (DC) of the common carotid artery as measure of common carotid arterial stiffness. Both measures were obtained on the same day, in the same room. Subjects were instructed to refrain from smoking and from taking coffee, tea or pain medications on the day of measurements, and from taking alcohol on the day of measurements and the day before.

Carotid-femoral pulse wave velocity

Carotid-femoral pulse wave velocity (PWV) was measured with the subjects in supine position. Blood pressure was measured twice with a sphygmomanometer after five minutes of rest, and the mean was taken as the subject's reading. Mean arterial pressure was calculated by the following formula: diastolic blood pressure + 1/3 (systolic blood pressure-diastolic blood pressure). Carotid-femoral PWV was assessed with an automatic device (Complior, Colson) (14) that assessed the time delay between the rapid upstroke of the feet of simultaneously recorded pulse waves in the carotid and the femoral artery. The distance between the recording sites in the carotid and the femoral artery was measured over the surface of the body with a tape measure. PWV was calculated as the ratio between the distance measured and the foot-to-foot time delay and expressed in meters per second. The average of at least 10 successive measurements, to cover a complete respiratory cycle, was used in the analysis.

Distensibility coefficient of the common carotid artery

Common carotid distensibility was assessed with the subjects in supine position, the head tilted slightly to the controlateral side for the measurement in the common carotid artery. The vessel wall motion of the right common carotid artery was measured by means of a duplex scanner (ATL Ultramark IV, operating frequency 7.5 MHz) connected to a vessel wall movement detector system. The details of this technique have been described elsewhere (15,16). After five minutes of rest, a region at 1.5 cm proximal to the origin of the bulb of the carotid artery was identified using B-mode ultrasound. The displacement of the arterial walls was obtained by processing the radio frequency signals originating from two selected sample volumes positioned over the anterior and posterior walls. The end-diastolic diameter (D), the absolute stroke change in diameter during systole (ΔD), and the relative stroke change in diameter (ΔD/D) were computed as the mean of four cardiac cycles of three successive recordings. Blood pressure was measured twice at the upper arm with a Dinamap automatic blood pressure recorder during the measurement session. The mean was taken as the subjects reading. Pulse pressure (ΔP) was defined as the difference between systolic and diastolic blood pressure. Mean arterial pressure was calculated. The cross-sectional arterial wall distensibility coefficient was calculated according to the following equation: distensibility coefficient = (2 ΔD/D)/ ΔP (10^{-3}/kPa) (17). In a reproducibility study in 47 subjects the intra-class correlation coefficient was 0.80 both for the distensibility coefficient and the carotid-femoral pulse wave velocity.

Alcohol consumption

Alcohol consumption was assessed as part of the interview at the study center. Participants reported the number of alcoholic beverages they consumed weekly. Non- drinkers were asked whether they had been alcohol consumers in the past and if so were considered abstainers. By

adding the number of alcoholic beverages consumed per week, alcohol consumption was divided into 4 categories: 0 to 3, 4 to 10, 11 to 20 and ≥ 21 glasses of alcoholic beverages per week, respectively.

Cardiovascular risk factors

At the research center, blood pressure was measured twice on the right arm using a random-zero sphygmomanometer. Body mass index [weight /height^2] was calculated. Diabetes mellitus was defined as use of anti-diabetic medication and/or a fasting serum glucose level ≥ 7.0 mmol/l (18). Serum total cholesterol and high-density lipoprotein (HDL) cholesterol values were determined by an automated enzymatic procedure (Boehringer Mannheim System). Information on smoking habits was obtained during the interview.

Measure of carotid intima-media thickness

Ultrasonography of both carotid arteries was performed with a 7.5-MHz linear-array transducer and a duplex scanner (ATL UltraMark IV). Common carotid intima-media thickness (IMT) was determined as previously described (19).

Population for analysis

Of the 4024 subjects who underwent the physical examination of the third phase, arterial stiffness as assessed by means of PWV was determined in 3550 subjects whereas common carotid distensibility was measured in 3098 subjects. Missing information on both measures was almost entirely due to logistic reasons. Past drinkers were excluded from the analyses leaving 3178 subjects with data both on alcohol consumption and PWV; data on alcohol consumption and carotid distensibility were available for 2973 subjects.

Statistical Analysis

The association between alcohol consumption and measures of arterial stiffness was investigated by linear regression analysis adjusted for age and performed in men and women separately. Categories of alcohol consumption were included in the model as dummy variables. Subjects consuming up to 3 glasses weekly were chosen as the reference category. Analyses were repeated after adjustment for mean arterial pressure, heart rate, body mass index, diabetes mellitus, smoking habits, total cholesterol and high- density lipoprotein, and, in the last model additionally for measures of carotid IMT. Association are presented with the linear regression coefficient (β) and its 95% confidence interval (95% CI).

Results

Baseline characteristics of the population are shown in table 1. After exclusion of past drinkers, data on both alcohol consumption and PWV were available for 3178 subjects, of these, 57 % was woman. Mean age among men was 71.5±6.4 years, and 72.1±6.8 years among women. In men, 30.5 % of the subjects consumed 0 to 3 glasses alcohol per week, 27.1% consumed 4 to 10 glasses per week, 20.7% consumed 11 to 20 glasses per week and 21.7% consumed ≥ 21 glasses per week. In women, 60% of the subjects consumed 0 to 3 glasses alcohol per week, 21.5% consumed 4 to 10 glasses per week, 13.4% 11 to 20 glasses per week and 5.1% ≥ 21 glasses per week. Mean differences and 95% CI of PWV and carotid distensibility coefficient across categories of alcohol consumption are presented in tables 2 and 3, respectively. Significantly lower measures of PWV were observed in women consuming 11-20 glasses weekly when compared to the reference category, in models adjusted for age, estimates lacked statistical significance after additional adjustment,. In men, data were not statistically significant but a similar trend was observed. Measures of the carotid distensibility coefficient were significantly higher, indicating less stiff arteries, in women

consuming 4-10 glasses alcohol weekly, when compared with the reference category. In men, no association was observed between measures of arterial stiffness and categories of alcohol consumption; the multivariate adjusted mean levels and 95% CI of PWV were 14 (m/s) (13.7-14.3) in subjects drinking up to 3 glasses per week, 13.9 (13.6-14.2) in subjects drinking 4-10 glasses per week, 13.8 (13.5-14.1) in subjects drinking 11 to 20 glasses per week and 14.2 (13.9-14-5) in subjects drinking ≥ 21 glasses per week. Corresponding mean values and 95% CI of carotid distensibility coefficient in the predefined categories were 10.1 (10^{-3}/kPa) (9.7-10.6), 10.3 (9.9-10-7), 10.3 (9.8-10.7) and 10.4 (9.9-10.7), respectively. In women, a significant decrease of PWV was observed in subjects drinking 11-20 glasses per week when compared with the reference category; however estimates lacked statistical significance in fully adjusted models. The multivariate adjusted mean levels and 95% CI of PWV were 13.1 m/s (12.9-13.3) in subjects consuming up to 3 glasses alcohol per week, 13.0 (12.8-13.2) in subjects drinking 4-10 glasses per week, 12.9 (12.7-13.1) in subjects drinking 11 to 20 glasses per week, and 13.0 (12.8-13.2) in subjects drinking ≥ 21 glasses per week. A significant increase of the distensibility coefficient was found in women drinking 4-10 glasses alcohol per week compared to the reference category. Adjustment for cardiovascular risk factors and IMT did not materially change the strength of the association. Mean values of distensibility coefficient in the predefined categories were 9.9 (10^{-3}/kPa) (9.5-10.3), 10.6 (10.2-11.0), 10.2 (9.8-10.6) and 10.3 (9.9-10.7), respectively.

Discussion

In this large population-based study we found that moderate alcohol consumption is associated with reduced arterial stiffness in women. No significant association was observed in men, although a similar trend was observed.

Some aspects of this study need to be discussed. Firstly, the cross-sectional design may limit our ability to infer a causal relationship between measures of arterial stiffness and alcohol consumption. Secondly, information on alcohol intake may have introduced misclassification in exposure; specifically we are afraid of underreporting of the level of alcohol consumption among heavy drinkers (20) affecting our results. Finally, measures on arterial stiffness and data on alcohol consumption were not available for all participants. Because this was primarily due to logistic reasons and therefore random, we believe that this will not have biased the results.

Previous results on the relation between alcohol and arterial stiffness are inconsistent. Longitudinal studies in Japanese men aged 35-59 years found that alcohol consumption was a risk factor for increased aortic stiffness (8,9). Conversely, other studies showed that alcohol consumption was associated with decreased pulse wave velocity in the general population (10) and in patients with diabetes mellitus type 2 (21). Recent studies found a J-shaped association between alcohol consumption and arterial stiffness in men aged 40-80 years (11) and an inverse association in healthy postmenopausal women (12). In the present study, we found that carotid stiffness, measured as distensibility coefficient of the common carotid artery, was reduced in women drinking 4-10 glasses alcohol weekly when compared with women drinking up to 3 glasses per week. The association between pulse wave velocity and alcohol consumption was less consistent. No associations were found in men.

Several cardiovascular risk factors may mediate the association between alcohol consumption and arterial stiffness. Moderate alcohol consumption decreases the risk of

diabetes mellitus type 2 (22) whereas the effects of alcohol consumption on blood pressure have been variously found. Some investigations have found a linear association between alcohol intake and blood pressure (23), other a threshold only above which there is an association (24), and still others a J- or U- shaped association (25) (26). Both diabetes mellitus and hypertension are determinants of arterial stiffness (5-7). Therefore, moderate alcohol consumption might reduce arterial stiffness by interference with the factors responsible for the increase in vascular stiffness, such as diabetes mellitus and hypertension. However, this seems to be unlikely because in fully adjusted models the estimates remained statistically significant. Similarly, an increase in HDL cholesterol (27) which was adjusted for in model cannot completely explain the results obtained.

Although it is known that atherosclerosis may increase arterial stiffness (28) and has an inverse association with moderate alcohol consumption (29), previous studies (8-12) did not evaluate whether the association between alcohol consumption and arterial stiffness was mediated by atherosclerosis. For this reason, we performed analyses with additional adjustment for carotid intima-media thickness, which is an indicator of atherosclerosis. Also in these models, estimates remained unchanged suggesting that the association is independent of atherosclerosis.

Alcohol exposure increases the production of vasoactive substances like nitric oxide, thereby inducing the endothelium-dependent vasodilatation (30,31). Exposure of blood vessels to alcohol can promote nitric oxide generation and subsequent vasodilatation (32,33), but additionally to vasodilatator properties, nitric oxide can convey vasoprotection in several ways. Nitric oxide is a potent inhibitor of platelet aggregation and adhesion to the vascular wall (34,35), protecting against thrombosis but also against the release of platelet-derived growth factors that stimulate smooth muscle proliferation and its production of matrix molecules. Whether such mechanisms are involved needs further investigation.

In conclusion, in this large population-based study of older adults we found a U-shaped association between alcohol consumption and arterial stiffness in women. The association is independent of cardiovascular risk factors and atherosclerosis. In men, the estimates were not statistically significant, although a similar trend was observed.

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343 **Table 1. Characteristics of the study population (n=3178)**

	Men (1367)	Women (1811)
Age (years)	71.5±6.4	72.1±6.8
Body mass index (kg/m^2)	26.3±3.1	27.1±4.2
Systolic blood pressure (mmHg)	135.6±19.1	133.2±19.6
Diastolic blood pressure (mmHg)	73.9±9.5	68.1±9.2
Mean arterial pressure (mmHg)	107.1±12.4	106.4±13.1
Heart rate (bpm)	73.2±14.7	76.6±14.2
Total cholesterol (mmol/l)	5.6±0.9	6.04±0.9
HDL- cholesterol (mmol/l)	1.3±0.3	1.5±0.4
Current smokers (%)	17.3	14.7
Diabetes mellitus (%)	7.3	4.4
Intima media thickness (mm)	0.91±0.15	0.87±0.14
Alcohol intake 0-3 per week (%)	30.5	60
Alcohol intake 4-10 per week (%)	27.1	21.5
Alcohol intake 11-20 per week (%)	20.8	13.4
Alcohol intake ≥ 21 per week (%)	21.6	5.1
Pulse wave velocity (m/s)	13.9±3.1	13.1±2.8
Distensibility coefficient (10^{-3}/kPa)	10.4±4.1	10.3±4.1

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345 Values are expressed as percentage or mean ± standard deviation.

346 * Data on distensibility coefficient and alcohol consumption are available for 2973 subjects.

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Table 2. Regression coefficient and 95% confidence interval describing the change of pulse wave velocity (m/s) per category of alcohol consumption compared with the reference group

	Model 1	Model 2	Model 3
Glasses per week		Men	
0-3 (n= 417)	(reference)	(reference)	(reference)
4-10 (n= 370)	-0.12 (0.33 to -0.57)	-0.04 (0.37 to -0.45)	-0.07 (0.35 to -0.50)
11-20 (n= 283)	-0.10 (0.34 to -0.55)	-0.10 (0.31 to -0.51)	-0.19 (0.24 to -0.62)
≥ 21 (n= 297)	0.38 (0.83 to -0.05)	0.33 (0.76 to -0.09)	0.23 (0.68 to -0.21)
		Women	
0-3 (n= 1087)	(reference)	(reference)	(reference)
4-10 (n= 389)	-0.18 (0.13 to -0.51)	-0.12 (0.16 to -0.42)	-0.07 (0.22 to -0.38)
11-20 (n= 243)	-0.36 (-0.02 to -0.69)*	-0.17 (0.13 to -0.47)	-0.18 (0.12 to -0.49)
≥ 21 (n= 92)	0.31 (0.02 to -0.64)	-0.12 (0.17 to -0.43)	-0.12 (0.19 to -0.43)

Model 1 is adjusted for age.

Model 2 is adjusted for age, mean arterial pressure, heart rate, diabetes mellitus, smoking habits, body mass index, total cholesterol and high density lipoprotein cholesterol.

Model 3 is adjusted for age, mean arterial pressure, heart rate, diabetes mellitus, smoking habits, body mass index, total cholesterol and high density lipoprotein cholesterol and intima media thickness. CI: Confidence interval.

* P= 0.03 compared with the reference category.

Table 3. Regression coefficient and 95% confidence interval describing the change of distensibility coefficient (10^{-3}/kPa) per category of alcohol consumption compared with the reference group

	Model 1	Model 2	Model 3
Glasses per week		Men	
0-3 (n= 370)	(reference)	(reference)	(reference)
4-10 (n= 328)	0.21 (0.86 to -0.43)	0.20 (0.80 to -0.39)	0.19 (0.79 to -0.43)
11-20 (n= 250)	0.31 (0.96 to -0.33)	0.08 (0.68 to -0.51)	0.16 (0.77 to -0.45)
≥ 21(n= 257)	0.57 (1.23 to -0.07)	0.34 (0.96 to -0.27)	0.24 (0.88 to -0.38)
		Women	
0-3 (n= 959)	(reference)	(reference)	(reference)
4-10 (n= 333)	0.84 (1.41 to 0.28)*	0.65 (1.16 to 0.14) †	0.68 (1.21 to 0.15) †
11-20 (n= 212)	0.44 (1.02 to -0.14)	0.23 (0.76 to -0.29)	0.28 (0.82 to -0.25)
≥ 21 (n= 84)	0.46 (1.04 to -0.11)	0.31 (0.84 to -0.21)	0.36 (0.91 to -0.18)

Model 1 is adjusted for age.

Model 2 is adjusted for age, mean arterial pressure, heart rate, diabetes mellitus, smoking habits, body mass index, total cholesterol and high density lipoprotein cholesterol.

Model 3 is adjusted for age, mean arterial pressure, heart rate, diabetes mellitus, smoking habits, body mass index, total cholesterol and high density lipoprotein cholesterol and intima media thickness. CI: Confidence interval.

* P= 0.003 compared with the reference category.

† P= 0.012 compared with the reference category.