Moderate Alcohol Consumption Is Associated With Reduced Arterial Stiffness in Older Adults: The Rotterdam Study

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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 relationship 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 participants in the third examination phase. Arterial stiffness was measured by two different methods, i.e., the carotid–femoral pulse wave velocity and the DC of the common carotid artery. Categories of alcohol consumption were defined as follows: ≤3 glasses of alcohol per week, 4–10 glasses per week, 11–20 glasses per week, and ≥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 (0.22 to −0.38), −0.18 (0.12 to −0.49), and 0.12 (0.19 to −0.43) m/s difference in mean pulse wave velocity compared to those drinking 0–3 glasses per week (reference group). Corresponding differences in the carotid DC were 0.68 (1.21 to 0.15), 0.28 (0.82 to −0.25), and 0.36 (0.91 to −0.18) 10−3/kPa. 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.

METHODS

Population

This study was conducted within the framework of the Rotterdam Study, an ongoing prospective population-based cohort study among persons aged 55 years and older, 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 through 1999. During this phase, information on cardiovascular risk factors was collected, measurements of arterial stiffness and 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 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. Participants were instructed to refrain from alcohol consumption 24 hours prior to the examination.
from smoking and from taking coffee, tea, or pain medications on the day of measurements, and from taking alcohol on the day before and the day of measurements.

**Carotid–femoral PWV.**—Carotid–femoral PWV was measured with the participants in supine position. Blood pressure was measured twice with a sphygmomanometer after 5 minutes of rest, and the mean was taken as the participant’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, Paris, France) (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 was expressed in meters per second. The average of at least 10 successive measurements, to cover a complete respiratory cycle, was used in the analysis.

**DC of the common carotid artery.**—Common carotid distensibility was assessed with the participants 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; Advanced Technology Labs, Bothell, WA) connected to a vessel wall movement detector system. The details of this technique have been described elsewhere (15,16). After 5 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 (∆D), 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 (Critikon Inc., Tampa, FL) during the measurement session. The mean of the two measurements was included in the analyses. Pulse pressure (∆P) was defined as the difference between systolic and diastolic blood pressure. Mean arterial pressure was calculated. The cross-sectional arterial wall DC was calculated according to the following equation: DC = (2 ∆D/D)/∆P (10⁻³/kPa) (17). In a reproducibility study of 47 participants, the intraclass correlation coefficient was 0.80 for both the DC and the carotid–femoral PWV.

**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. Nondrinkers 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: 0–3, 4–10, 11–20, 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/height²) was calculated. Diabetes mellitus was defined as use of antidiabetic 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, Mannheim, Germany). Information on smoking habits was obtained during the interview.

**Measure of Carotid Intima-Media Thickness**

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

**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. Participants drinking ≤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 HDL, and (in the last model) measures of carotid IMT. Associations are presented with the linear regression coefficient (β) and its 95% confidence interval (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 participants, of these, 57% were women. Mean age was
may have introduced misclassification in exposure. Specifically, we are afraid of underreporting 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 relationship 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 PWV in the general population (10) and in patients with type 2 diabetes (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 DC of the common carotid artery, was reduced in women drinking 4–10 glasses of alcohol weekly when compared with women drinking ≤3 glasses per week. The association between PWV 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 type 2 diabetes (22), whereas results on the effects of alcohol consumption on blood pressure have been inconsistent. One investigation found a linear association between alcohol intake and blood pressure (23), another a threshold only above which there is an association (24), and still others a J-shaped or U-shaped association (25,26). Both diabetes mellitus and hypertension are determinants of 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. First, the cross-sectional design may limit our ability to infer a causal relationship between measures of arterial stiffness and alcohol consumption. Second, information on alcohol intake was obtained by self-report and may have introduced misclassification in exposure. Specifically, we are afraid of underreporting 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.

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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 our 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 an 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 such as 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 vasodilator 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.

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.

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

<table>
<thead>
<tr>
<th>No. of Glasses per Week</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3 (n = 417)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>4–10 (n = 370)</td>
<td>−0.12 (0.33 to −0.57)</td>
<td>−0.04 (0.37 to −0.45)</td>
<td>−0.07 (0.35 to −0.50)</td>
</tr>
<tr>
<td>11–20 (n = 283)</td>
<td>−0.10 (0.34 to −0.55)</td>
<td>−0.10 (0.31 to −0.51)</td>
<td>−0.19 (0.24 to −0.62)</td>
</tr>
<tr>
<td>≥21 (n = 297)</td>
<td>0.38 (0.83 to −0.05)</td>
<td>0.33 (0.76 to −0.09)</td>
<td>0.23 (0.68 to −0.21)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
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<tr>
<td>0–3 (n = 1087)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>4–10 (n = 389)</td>
<td>−0.18 (0.13 to −0.51)</td>
<td>−0.12 (0.16 to −0.42)</td>
<td>−0.07 (0.22 to −0.38)</td>
</tr>
<tr>
<td>11–20 (n = 243)</td>
<td>−0.36 (~0.02 to −0.69)*</td>
<td>−0.17 (0.13 to −0.47)</td>
<td>−0.18 (0.12 to −0.49)</td>
</tr>
<tr>
<td>≥21 (n = 92)</td>
<td>0.31 (0.02 to −0.64)</td>
<td>−0.12 (0.17 to −0.43)</td>
<td>−0.12 (0.19 to −0.43)</td>
</tr>
</tbody>
</table>

Notes: 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, high density lipoprotein cholesterol, and intima-media thickness.

*p = .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

<table>
<thead>
<tr>
<th>No. of Glasses per Week</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3 (n = 570)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>4–10 (n = 328)</td>
<td>0.21 (0.86 to −0.43)</td>
<td>0.20 (0.80 to −0.39)</td>
<td>0.19 (0.79 to −0.43)</td>
</tr>
<tr>
<td>11–20 (n = 250)</td>
<td>0.31 (0.96 to −0.33)</td>
<td>0.08 (0.68 to −0.51)</td>
<td>0.16 (0.77 to −0.45)</td>
</tr>
<tr>
<td>≥21 (n = 257)</td>
<td>0.57 (1.23 to −0.07)</td>
<td>0.34 (0.96 to −0.27)</td>
<td>0.24 (0.88 to −0.38)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
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<tr>
<td>0–3 (n = 959)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>4–10 (n = 333)</td>
<td>0.84 (1.41 to 0.28)*</td>
<td>0.65 (1.16 to 0.14)</td>
<td>0.68 (1.21 to 0.15)</td>
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<tr>
<td>11–20 (n = 212)</td>
<td>0.44 (1.02 to −0.14)</td>
<td>0.23 (0.76 to −0.29)</td>
<td>0.28 (0.82 to −0.25)</td>
</tr>
<tr>
<td>≥21 (n = 84)</td>
<td>0.46 (1.04 to −0.11)</td>
<td>0.31 (0.84 to −0.21)</td>
<td>0.36 (0.91 to −0.18)</td>
</tr>
</tbody>
</table>

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

*p = .003 compared with the reference category.

*l = .012 compared with the reference category.
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