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Alcohol Consumption and Risk of Peripheral Arterial Disease

The Rotterdam Study

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Moderate alcohol consumption is associated with a reduced risk of cardiovascular disease. Data on alcohol consumption and atherosclerosis are scarce. To determine the association between alcohol consumption and risk of peripheral arterial disease, the authors carried out a cross-sectional study (1990–1993) in the population-based Rotterdam Study among men and women aged 55 years or over. Data on alcohol consumption and peripheral arterial disease, as measured by the ankle/brachial blood pressure index, were available for 3,975 participants without symptomatic cardiovascular disease. Male drinkers consumed beer, wine, and liquor, while female drinkers consumed predominantly wine and fortified wine types. An inverse relation between moderate alcohol consumption and peripheral arterial disease was found in women but not in men. Because of residual confounding by smoking, analyses were repeated in nonsmokers. In nonsmoking men, odds ratios were 0.86 (95% confidence interval (CI): 0.46, 1.63) for daily alcohol consumption up to and including 10 g, 0.75 (95% CI: 0.37, 1.55) for 11–20 g, and 0.68 (95% CI: 0.35, 1.34) for more than 20 g, compared with nondrinking. In nonsmoking women, corresponding odds ratios were 0.65 (95% CI: 0.48, 0.87), 0.66 (95% CI: 0.42, 1.05), and 0.41 (95% CI: 0.21, 0.77), respectively. In conclusion, an inverse association between alcohol consumption and peripheral arterial disease was found in nonsmoking men and women. *Am J Epidemiol* 2002;155:332–8.

aged; alcohol drinking; alcoholic beverages; atherosclerosis

Alcohol drinking affects the occurrence of ischemic heart disease. The association of alcohol with coronary morbidity and mortality is U or J shaped (1–5). The underlying mechanism of the reduced risk associated with moderate levels of alcohol is not known. One of the potential mechanisms is the effect of alcohol on atherosclerosis (3). The presence of peripheral arterial disease, which is largely asymptomatic, is an indicator of a long-term atherogenic process in the peripheral blood vessels. Peripheral arterial disease is considered present below a certain cutoff point of the ankle/brachial blood pressure index (6), and it is associated with atherosclerotic diseases in other vessel beds (7) and with cardiovascular morbidity and mortality (8–12). Only a few studies have investigated the relation between alcohol consumption and peripheral arterial disease. Among the 1,592 participants of the Edinburgh Artery Study, a positive linear association of alcohol consumption with the ankle/brachial blood pressure index was found in men but not in women (13). The protective effect was attributable to wine drinking in particular, but it was no longer significant after additional adjustment for social class. A recent study in 4,549 American Indian men and women showed a significant inverse association of alcohol consumption with peripheral arterial disease (14). However, the level of alcohol intake and the type of beverages consumed were not taken into account. The prospective Physicians' Health Study demonstrated an inverse association of moderate alcohol use with symptomatic peripheral arterial disease (15), although the range of alcohol intake in the study population was small and this population comprised relatively healthy men. In the Framingham Heart Study an inverse association was found between moderate alcohol consumption and the occurrence of intermittent claudication (16). However, only a small proportion of subjects with peripheral arterial disease were symptomatic. Furthermore, alcohol might have influenced the clinical symptoms of peripheral arterial disease (17).

The population-based Rotterdam Study of 7,983 people aged 55 years or over provides the opportunity to investigate in detail the association of alcohol consumption with peripheral arterial disease. In 3,975 subjects free from cardiovascular disease at baseline, we studied the consumption of different levels and types of alcohol in relation to peripheral arterial disease, taking into account important confounders.

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Abbreviations: CI, confidence interval; OR, odds ratio.

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MATERIALS AND METHODS

The Rotterdam Study

The Rotterdam Study is a prospective study designed to investigate the occurrence and determinants of chronic and disabling cardiovascular, neurogeriatric, locomotor, and ophthalmologic diseases in an aging population. The rationale and design of the study have been described previously (18). The cohort includes 7,983 men and women aged 55 years or over (78 percent of the eligible population), living in a suburb of Rotterdam, the Netherlands. Of these, 879 subjects lived in nursing homes. From August 1990 until June 1993, baseline data were collected during a home interview by a trained research assistant and at two visits to the study center for clinical examination and assessment of diet.

Assessment of alcohol intake and diet

Alcohol consumption was assessed as part of a dietary interview. A trained dietician interviewed the participants at the study center, using a validated, semiquantitative food frequency questionnaire (19). The interview was based on a checklist on which the subjects had indicated the foods and beverages consumed more than once a month during the preceding year. The dietary interviews were performed using a computer program that simultaneously checked the data. Participants reported the number of alcoholic beverages they consumed on a weekly basis, in each of four categories: beer, wine, liquor, and moderately strong alcohol types. The latter category contained predominantly fortified wines, namely, sherry and port. Nondrinkers were considered abstainers. The subjects were asked whether their level of alcohol use had changed during the last 5 years and, if so, whether the amount had increased or decreased. For each of the different beverages, the number of drinks was multiplied by the average amount of ethanol in one drink of the alcoholic beverage. A "drink" was defined as 200 ml of beer that contained 8.0 g of ethanol, 100 ml of wine that contained 10.0 g of ethanol, 50 ml of liquor that contained 14.0 g of ethanol, or 75 ml of moderately strong alcohol types that contained 10.5 g of ethanol. By adding the amounts of ethanol in the four groups, we calculated the total amount of alcohol in grams per day. A validation study that compared the nutrient intake derived from the food frequency questionnaire with that from a 15-day food record showed a correlation coefficient of 0.89 for the intake of alcohol (19). Because most of the moderately strong alcoholic drinks were wine types, this category was combined with the wine category in the analyses. The alcohol consumption was divided into nondrinking, use of ≤10 g, >10–≤20 g, and >20 g/day.

Study interview

Smoking status was assessed, and subjects were categorized as current, former, or never smokers. In ever smokers, we asked for the average number of cigarettes smoked, as well as the number of smoking years. From this information, the number of cigarette pack-years was computed. We used information about the highest attained level of education as an indicator of socioeconomic status. This variable was categorized as low (primary education), intermediate (secondary general or vocational education), and higher (higher vocational education or university). Intermittent claudication was diagnosed according to the criteria of the World Health Organization by means of the Rose questionnaire (20). Information on myocardial infarction and stroke in the subjects' history was obtained by direct questioning and considered positive when confirmed by physicians' records. Data on previous coronary artery bypass graft surgery or percutaneous transluminal coronary angiography were collected during the interview.

Clinical examination

Clinical examinations were performed during a visit at the research center. Height and weight were measured with participants in light clothes and without shoes. Body mass index was calculated as the weight (kg)/height $(m)^2$. Serum total cholesterol was determined by an enzymatic procedure. High density lipoprotein cholesterol was measured similarly after precipitation of the non-high density lipoprotein cholesterol fraction (21). Diabetes mellitus was considered present with current use of antidiabetes medication, or when nonfasting random or postload glucose levels exceeded 11.0 mmol/liter (22, 23).

Blood pressure was measured at the right brachial artery using a random-zero sphygmomanometer with the participant in a sitting position. The mean of two consecutive measurements was used in the analysis. Hypertension was defined as a systolic blood pressure of 160 mmHg or higher, a diastolic blood pressure of 95 mmHg or higher, or current use of antihypertensive drugs for the indication of hypertension. An 8-MHz continuous wave Doppler probe (Huntleigh 500 D; Huntleigh Technology, Bedfordshire, United Kingdom) and a random-zero sphygmomanometer were used to measure the systolic blood pressure level of the posterior tibial artery in both legs (6). The blood pressure was measured once for each leg, with the participant in supine position. The ratio of the ankle systolic blood pressure to the brachial systolic blood pressure, the ankle/brachial blood pressure index, was calculated for each leg. Peripheral arterial disease was considered present when the ankle/brachial index was <0.9 in at least one leg (24).

Population for analysis

Noninstitutionalized participants who visited the study center were eligible for a dietary interview ($n = 6{,}521$). Of these, diet could not be assessed in 271 subjects of the pilot phase and in 122 subjects suspected of dementia. Furthermore, a random group of 481 participants was not interviewed because of logistic reasons. Of the dietary reports, 212 were considered unreliable by the dietician and were excluded. Thus, dietary data were available for 5,435 subjects. Of these 5,435, data on the ankle/brachial blood pressure index were missing for 535 participants. Additionally, subjects with an ankle/brachial blood pressure

index of more than 1.5 ($n = 272$) were excluded because this index usually results from arterial rigidity that prevents compression of the ankle artery. Subjects with complete data on diet and the ankle/brachial blood pressure index ($n = 4,900$) differed from excluded subjects ($n = 1,621$) only in mean age and in diabetes status. The mean age was higher in those excluded because of exclusion of subjects suspected for dementia, while the percentage of diabetes mellitus was higher in subjects excluded because of missing data, probably from nonassessable arteries on both sides. To avoid a spurious association due to a change in alcohol consumption as a result of symptomatic cardiovascular disease, subjects with a history of myocardial infarction, stroke, coronary artery bypass graft surgery, or percutaneous transluminal coronary angiography were excluded from the analysis ($n = 653$). Ultimately, 3,975 subjects were included in the present analysis.

Data analysis

Levels of potential confounders were compared between categories of alcohol consumption, using a general linear model. In this model, age and sex were included as covariates. Risk estimates were obtained for men and women separately. The relation between alcohol consumption and peripheral arterial disease was assessed using logistic regression analysis that adjusted for age. The risk of peripheral arterial disease in each category of alcohol consumption was compared with the risk among nondrinkers. The associations were expressed as odds ratios with 95 percent confidence intervals. A second model additionally adjusted for possible confounding factors, namely, cigarette pack-years, body mass index, and diabetes mellitus. Another model also adjusted for education as a measure of socioeconomic status. The first two logistic models were also conducted after exclusion of subjects who had reduced their alcohol consumption in the last 5 years. Because of potential residual confounding by smoking, we stratified according to smoking status and repeated the logistic regression analysis, adjusting for age and cigarette pack-years. To study the association of drinking (yes/no) specific types of alcohol, we used the two aforementioned logistic regression models but simultaneously took into account the amount of consumption of other types of alcohol. The data were analyzed using SPSS 7.5 for Windows (SPSS, Inc., Chicago, Illinois).

RESULTS

General characteristics of the study population are presented in table 1. Of the participants, 62.5 percent were female. The percentage of drinkers among men (88.5 percent) was higher than that among women (74.7 percent). Furthermore, the average daily amount of alcohol consumed by drinkers was much higher for men than for women (16.4 (standard deviation, 18.8) g and 6.2 (standard deviation, 10.2) g, respectively). The prevalence of peripheral arterial disease was slightly lower in men (13.4 percent) than in women (14.4 percent). Of those with peripheral arterial disease, only a few subjects reported intermittent claudication as assessed by the Rose questionnaire (7.5 percent of male cases, 3.9 percent of female cases). In a general linear model adjusted for sex, the mean level of alcohol intake decreased with an increase in age category (p for trend < 0.001). After

TABLE 1. Baseline characteristics of 3,975 men and women aged 55 years or over without cardiovascular disease, The Rotterdam Study, 1990–1993*

Characteristics	Men (n = 1,489)	Women (n = 2,486)
Age (years)	66.5 (7.2)	67.4 (7.8)
Systolic blood pressure (mmHg)	139 (22)	139 (22)
Diastolic blood pressure (mmHg)	75 (12)	73 (11)
Serum total cholesterol (mmol/liter)	6.3 (1.2)	6.8 (1.2)
Serum high density lipoprotein cholesterol (mmol/liter)	1.23 (0.3)	1.46 (0.4)
Body mass index (kg/m^2)	25.7 (2.8)	26.6 (4.0)
Diabetes mellitus (%)	8.1	8.8
Smoking (%)		
Current	30.1	19.2
Former	61.9	28.6
Never	9.0	52.2
Daily alcohol consumption (%)		
Nondrinker	11.5	25.3
≤10 g	37.3	51.6
>10–≤20 g	19.1	12.7
>20 g	32.1	10.4
Ankle/brachial index	1.11 (0.2)	1.07 (0.2)
Peripheral arterial disease (%)	13.4	14.4
Intermittent claudication (%)	1.4	0.9
Educational level (%)		
Low	20.7	40.4
Intermediate	58.2	52.8
Higher	21.1	6.8

* Values are means (standard deviation) or percentages.

TABLE 2. Consumption of alcoholic beverages in 3,975 men and women without cardiovascular disease, The Rotterdam Study, 1990–1993

	Beverage type					
	Beer		Liquor		Wine and fortified wine	
	Drinkers (%)	Drinks/day* (SD†)	Drinkers (%)	Drinks/day (SD)	Drinkers (%)	Drinks/day (SD)
Men (n = 1,489)	46.6	1.19 (1.7)	40.1	1.20 (1.3)	41.4	0.74 (0.9)
Women (n = 2,486)	5.2	0.48 (0.7)	17.5	0.76 (1.0)	66.4	0.61 (0.8)

* Average number of drinks per day in drinkers.
† SD, standard deviation.

adjustment for age and sex, the level of alcohol intake was associated with cigarette pack-years ($p < 0.001$), diabetes mellitus ($p = 0.12$), and attained level of education ($p = 0.02$) (data not shown). The level of high density lipoprotein cholesterol was significantly higher in male and female drinkers compared with nondrinkers. In addition, women who consumed alcohol were on average older, more often diabetic, more likely smokers, and more highly educated compared with nondrinking women.

Table 2 shows the distribution of consumption of various alcoholic beverages. Among men, beer, liquor, and wines were consumed by almost equal percentages (46.6, 40.1, and 41.4 percent, respectively). The average daily amount consumed by drinkers of the specific beverages was higher for beer and liquor (1.2 drinks) than for wine and fortified wine (0.74 drink). The percentage of women who drank wine and fortified wine was much higher (66.4 percent) than the percentages of women who drank beer and liquor (5.2 and 17.5 percent, respectively). Wine-, beer-, or liquor-drinking women drank less than men who drank the same alcoholic beverages.

Table 3 presents odds ratios of peripheral arterial disease for various levels of alcohol consumption adjusted for age and in multivariate analyses additionally adjusted for cigarette pack-years, body mass index, and diabetes mellitus. In men, there was no inverse association between alcohol consumption and the risk of peripheral arterial disease. In the age-adjusted model, a slightly protective, but statistically nonsignificant association with peripheral arterial disease was observed for men who consumed up to 10 g of alcohol daily compared with nondrinkers (odds ratio (OR) = 0.84, 95 percent confidence interval (CI): 0.51, 1.38). However, this association disappeared in multivariate analysis. In women, a risk reduction of 22–36 percent was observed for alcohol drinkers compared with nondrinkers. This reduced risk among women was significant for daily consumption of up to 10 g of alcohol and in multivariate analysis for up to 20 g of alcohol daily. Additional adjustment for socioeconomic status did not change the results for either sex (data not shown). There was no significant interaction between alcohol consumption and sex (data not shown). Exclusion of subjects who had reduced their alcohol consumption in the last 5 years (190 subjects, 4.0 percent of the women and 6.1 percent of the men) did not affect the associations (data not shown).

Stratified analysis according to smoking status revealed different odds ratios of peripheral arterial disease by category of alcohol consumption in smokers and nonsmokers (table 4). In logistic regression analysis adjusted for age and cigarette pack-years, odds ratios of peripheral arterial disease in increasing categories of alcohol consumption were lower among past and never smokers than among current smokers. In past and never smokers, an inverse association was found between alcohol consumption and peripheral arterial disease. In nonsmoking men, the odds ratios were 0.86 (95 percent CI: 0.46, 1.63) for daily alcohol consumption up to 10 g, 0.75 (95 percent CI: 0.37, 1.55) for 11–20 g, and 0.68 (95 percent CI: 0.35, 1.34) for more than 20 g com-

TABLE 3. Risk of peripheral arterial disease according to level of alcohol consumption among 3,975 men and women without cardiovascular disease, The Rotterdam Study, 1990–1993

Daily alcohol consumption	Cases/controls (no.)	Age-adjusted odds ratio	95% confidence interval	Multivariate-adjusted odds ratio†	95% confidence interval
		Men (n = *1,489*)			
Nondrinker	26/145	1.00	Reference	1.00	Reference
≤10 g	71/485	0.84	0.51, 1.38	0.97	0.58, 1.63
>10–≤20 g	37/247	0.91	0.52, 1.58	1.02	0.57, 1.80
>20 g	65/413	0.97	0.59, 1.61	0.97	0.57, 1.65
		Women (n = *2,486*)			
Nondrinker	122/507	1.00	Reference	1.00	Reference
≤10 g	163/1,119	0.66**	0.51, 0.91	0.70*	0.53, 0.91
>10–≤20 g	39/277	0.69	0.46, 1.02	0.66*	0.43, 1.00
>20 g	34/225	0.78	0.51, 1.19	0.64	0.41, 1.01

* $p < 0.05$; **$p < 0.01$.
† Multivariate analysis: additionally adjusted for cigarette pack-years, body mass index, and diabetes mellitus.

TABLE 4. Risk of peripheral arterial disease by level of alcohol consumption according to smoking status among 3,975 men and women without cardiovascular disease, The Rotterdam Study, 1990–1993

Daily alcohol consumption	Current smokers			Past or never smokers		
	Cases/controls (no.)	Odds ratio	95% confidence interval†	Cases/controls (no.)	Odds ratio	95% confidence interval†
			Men (n = *1,489*)			
Nondrinker	10/42	1.00	Reference	16/103	1.00	Reference
≤10 g	26/125	0.85	0.38, 2.00	45/360	0.86	0.46, 1.63
>10–≤20 g	17/65	1.19	0.49, 2.93	20/182	0.75	0.37, 1.55
>20 g	37/126	1.31	0.59, 2.91	28/287	0.68	0.35, 1.34
			Women (n = *2,486*)			
Nondrinker	22/77	1.00	Reference	100/430	1.00	Reference
≤10 g	33/176	0.75	0.41, 1.39	130/943	0.65*	0.48, 0.87
>10–≤20 g	11/62	0.70	0.32, 1.59	28/215	0.66	0.42, 1.05
>20 g	22/74	1.05	0.53, 2.08	12/151	0.41*	0.21, 0.77

* $p < 0.01$.
† Adjusted for age and cigarette pack-years.

pared with nondrinking (test for trend: $p = 0.21$). In nonsmoking women, corresponding odds ratios were 0.65 (95 percent CI: 0.48, 0.87), 0.66 (95 percent CI: 0.42, 1.05), and 0.41 (95 percent CI: 0.21, 0.77), respectively (test for trend: $p < 0.001$). The lowest odds ratio was found in never smoking women with a daily alcohol consumption of more than 20 g (OR = 0.32, 95 percent CI: 0.11, 0.91). In smoking subjects there was no inverse association between alcohol consumption and peripheral arterial disease.

The risk of peripheral arterial disease associated with the use of the separate alcoholic beverages was computed, adjusted for age and the use of other alcoholic beverages, and in a second model adjusted also for cigarette pack-years, body mass index, and diabetes mellitus. The association was stronger for the consumption of wine and fortified wine than for the consumption of beer or liquor. In women, the risk of peripheral arterial disease associated with the use of wine types was statistically significant (first model: OR = 0.72, 95 percent CI: 0.57, 0.91; second model: OR = 0.74, 95 percent CI: 0.58, 0.95). In men, the odds ratios for wine were 0.81 (95 percent CI: 0.59, 1.13) and 0.88 (95 percent CI: 0.63, 1.24), respectively. The estimates of the risk of peripheral arterial disease associated with beer and liquor consumption for both men and women ranged from 0.86 to 1.14 and were not statistically significant. In logistic regression analysis of data from nonsmokers, no consistent association between an alcoholic beverage and peripheral arterial disease was found, except for wine and fortified wine in women (OR = 0.67, 95 percent CI: 0.51, 0.88). There was no significant inverse association between any type of alcoholic beverage and peripheral arterial disease in current smokers (odds ratios ranging from 0.92 to 1.17).

DISCUSSION

In the large population-based Rotterdam Study, we found an inverse association of alcohol consumption with peripheral arterial disease in women. The association was present already at low levels of alcohol use and was still present for levels of moderate alcohol consumption. In men, there was virtually no association of alcohol intake with peripheral arterial disease. Among nonsmoking subjects, an inverse association was found between alcohol consumption and peripheral arterial disease in both men and women. The largest risk reduction, 59 percent, was found in women who consumed over 20 g of ethanol per day. The strengths of the present study include a large and well-described cohort of elderly men and women, classification of consumption of alcohol and the types of beverages based on a validated food checklist, and a relatively large number of mostly asymptomatic peripheral arterial disease cases (558 subjects).

In the present study, drinking habits were self reported. This might have caused underreporting of alcohol use, especially among heavy drinkers. This is more likely to have occurred for men than for women, since more men were heavy drinkers. Imprecision in the reporting of alcohol consumption would tend to weaken the associations found. Shaper et al. (4) have argued that nondrinkers might not be suitable for use as reference group in an examination of the effects of alcohol on peripheral arterial disease. The group of nondrinkers could be less healthy than expected, because of inclusion of former heavy drinkers and people who have stopped drinking because of ill health, particularly ischemic heart disease. Furthermore, it is probable that lifelong nondrinkers have reasons for being abstainers that introduce other biases and have an adverse risk profile. This is most likely for men, for whom abstaining from alcohol is rather uncommon in society, at least in the age category of our cohort. However, additional exclusion of subjects who had reduced their alcohol consumption in the last 5 years did not change our results. Furthermore, participants with prevalent symptomatic cardiovascular disease were excluded from the analysis. In addition, drinking patterns may influence the risk of cardiovascular diseases (25). In our study, there was no information about the regularity of alcohol consumption.

Using peripheral arterial disease as an indicator of atherosclerosis has the advantage that most subjects with peripheral arterial disease are asymptomatic (6). Thus, spurious associations between alcohol and peripheral arterial disease,

resulting from symptoms that cause a change in alcohol consumption, are not likely to occur. Possible misclassification of peripheral arterial disease cases was probably nondifferential and would only weaken the real associations. In the Rotterdam Study, subjects did not report their physical activity, one of the confounders of the relation between alcohol consumption and peripheral arterial disease. Because measurement of the ankle/brachial blood pressure index was performed only on noninstitutionalized subjects who visited the research center and because participants with dementia were not interviewed about their diet, our subjects were relatively healthy and mobile. They may not be a representative sample of the whole elderly population without prevalent symptomatic cardiovascular disease.

Only a few other studies have investigated the association of alcohol consumption with the presence of peripheral atherosclerosis. Jepson et al. (13) found in the Edinburgh Artery Study a higher ankle/brachial blood pressure index (thus less peripheral arterial disease) in men with high alcohol consumption but no association in women. The ankle/brachial blood pressure index was associated with wine consumption but not with beer or liquor consumption. After additional adjustment for social class the positive associations disappeared, possibly indicating confounding by social class. The findings for women in this study were considered the result of the relatively low consumption of alcohol in this group (median consumption of one drink per week). In the prospective Physicians' Health Study, the relative risk of symptomatic peripheral arterial disease associated with moderate alcohol use was 0.74 in multivariate analysis (15). This cohort comprised subjects who were on average 10 years younger and had a higher average educational level than the men in our study. Furthermore, the overall alcohol consumption was very low in comparison with our study and other studies: 97 percent of the men reported use of less than two drinks a day. The consumption of different types of alcoholic beverages was not taken into account in this study. The Framingham Heart Study found the lowest risk of intermittent claudication at levels of 13–24 g of alcohol per day in men (hazard ratio = 0.67, 95 percent CI: 0.42, 0.99) and 7–12 g in women (hazard ratio = 0.44, 95 percent CI: 0.23, 0.80), compared with nondrinkers (16). Beer and wine especially were negatively associated with the occurrence of intermittent claudication. The study population, although younger than our population, had a distribution of alcohol consumption similar to ours. In this study and the Physicians' Health study, only subjects with an onset of intermittent claudication or peripheral arterial surgery were considered peripheral arterial disease cases. Alcohol may influence the clinical symptoms of peripheral arterial disease by preferentially dilating diseased arteries (16). In a study among American Indians, a study population with fewer cases of peripheral arterial disease than ours, a statistically significant inverse association between alcohol drinking and peripheral arterial disease was found in multiple logistic regression analysis. However, there was no information on the types and amount of alcohol consumed (14).

We found an inverse association between alcohol consumption and peripheral arterial disease for women but not for men. Because of the small range of alcohol intake among women, with only 10 percent consuming over 20 g of alcohol daily, it was not possible to examine the risk of peripheral arterial disease in heavy-drinking women. Although the range of alcohol consumption among men was wider, the odds ratio of peripheral arterial disease was not significantly different from one for any of the alcohol consumption categories compared with nondrinking. Part of the gender difference may be explained by a strong confounding effect of smoking. In nonsmoking subjects, an inverse association between alcohol consumption and peripheral arterial disease was present in both men and women. The inverse association was strongest in never-smoking women. Unfortunately, we were not able to study the association between alcohol consumption and peripheral arterial disease in never-smoking men because of small numbers. In our population, only 8 percent of men had never smoked. The percentage of never-smoking men was higher in the Edinburgh Artery Study (25 percent) and in the Physicians' Health Study (50 percent). The effect of smoking may have been less distorting in these studies. Furthermore, the discrepancy concerning the observed associations for men and women can possibly be explained in part by differences in the distribution of the beverage types consumed. In our study population women consumed mainly wine and fortified wine types, and we found the association to be strongest for these alcoholic beverages. The inverse association of wine consumption and peripheral arterial disease is in concordance with results from the Edinburgh Artery Study (13). Contrary to their results, the associations we found remained after additional adjusting for social class. Although our data for men are not incompatible with an effect of wine, the association was weak and not significant. Furthermore, because of small numbers of cases among beer drinkers and liquor drinkers in women, possible inverse associations between these beverages and peripheral arterial disease cannot be excluded.

An extensive review on alcohol and risk of coronary heart disease concluded that there is strong evidence that beer, liquor, and wine are all three associated with a lower risk of coronary heart disease (26). The review focused primarily on the acute events of coronary atherosclerotic disease, in which clotting and fibrinolysis are also thought to play a major role. We studied the long-term process of atherogenesis, in which the effect of alcoholic beverages on atherosclerosis is more important. Alcohol itself affects hemostasis (27) and affects atherosclerosis through its effect on the lipid profile (28). Possibly additional effects on atherosclerosis may be mediated by substances present only in wines. Wine and fortified wines contain phenolic substances, which have been shown to have antioxidant effects on low-density lipoproteins, thus decelerating atherogenesis (29, 30).

In summary, in this large population-based study moderate alcohol consumption was inversely associated with peripheral arterial disease in women but not in men. Residual confounding by smoking may have influenced the results. Among nonsmokers an inverse association was found between alcohol consumption and peripheral arterial disease in both men and women.

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