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Relation of Alcohol Consumption and Coronary Heart Disease in Hypertensive Male Physicians (From the Physicians Health Study)

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Abstract

Alcohol has diverse effects on the cardiovascular system. Moderate drinking is associated with a reduced risk of cardiovascular disease, and yet increasing amounts of alcohol consumption are known to elevate blood pressure. These opposing effects have led to interest in the effect of moderate alcohol consumption on the risk of coronary heart disease (CHD) in patients with hypertension. To test the hypothesis that moderate alcohol consumption reduces the risk of myocardial infarction (MI) in patients with hypertension, we used data on 5,164 participants in the Physicians' Health Study who were apparently healthy and free of CHD at baseline. Incident MI was ascertained by annual follow-up questionnaires and validated through a review of medical records. Cox proportional hazard model was used to compute multivariable-adjusted hazard ratios with corresponding 95% confidence intervals. Between 1982 and 2008, 623 cases of MI occurred. Compared to subjects consuming <1 drink per week, hazard ratios for MI were 1.05 [95% confidence interval (CI) 0.85–1.28], 0.78 (95% CI 0.64–0.97), and 0.57 (95% CI 0.35–0.95) for alcohol consumption of 1–4, 5–7, and >8 drinks per week adjusted for age, body mass index, smoking, exercise, diabetes, multivitamin use, vegetable intake, breakfast cereal intake, and cholesterol (p for trend <.0022). Similar inferences could be made for the secondary outcomes of angina pectoris and any CHD (which included MI, angina pectoris and prior revascularization). In conclusion, our data demonstrated an inverse relationship between moderate alcohol consumption and CHD in hypertensive men.

Keywords

Alcohol; Coronary Heart Disease; Epidemiology; Hypertension

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Introduction

Only limited data have been published on the association between alcohol consumption and CHD in patients with hypertension[1,2]. Thus, we sought to prospectively evaluate whether alcohol consumption is associated with a reduced risk of myocardial infarction (MI) among hypertensive participants of the Physicians' Health Study (PHS), a large cohort with > 20 years of follow-up. In secondary analyses, we sought to assess the association between moderate alcohol consumption and angina pectoris and any CHD (including MI, angina pectoris, coronary artery bypass surgery, and percutaneous coronary intervention).

Methods

The present study analyzed data from the PHS, a randomized trial used to study low-dose aspirin and β-carotene for the primary prevention of cardiovascular disease and cancer in 22,071 US male physicians without a history of MI at baseline. A description of the PHS has been previously published[3]. For the present study, we included patients with prevalent self-reported hypertension at baseline. Subjects were asked to report their present blood pressure and whether they had ever received drug treatment for hypertension. Prevalent hypertension was defined as a systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or self-reported treatment for hypertension. Of 5236 subjects with prevalent hypertension at baseline, we excluded 72 subjects for missing covariate data, leaving a final sample of 5,164 subjects.

Subject's usual alcohol consumption was self-reported on a standard questionnaire with subjects being asked "How often do you usually consume alcoholic beverages?" Responses included rarely/never, 1–3 times/month, 1 time/week, 2–4 times/week, 5–6 times/week, daily, and ≥ 2 times/day. The response was interpreted as the number of alcoholic drinks consumed during the specified period. A detailed description of alcohol assessment in the PHS has been previously published[3,4].

Ascertainment of outcomes in the PHS has been obtained through yearly questionnaires, and has been previously described[5]. Specifically, a questionnaire was mailed to each participant every 6 months during the first year and annually thereafter. An Endpoint Committee reviewed medical records to confirm the diagnosis of CHD. MI was validated using World Health Organization criteria[6]. Our primary outcome was MI. Secondary outcomes included angina pectoris and total CHD (angina pectoris, MI, coronary artery bypass surgery or percutaneous coronary intervention).

Demographic data was collected at baseline. Information on co-morbid illness has been collected through annual follow-up. Self-reported information on age, physical activity, cigarette smoking, multivitamin use, body mass index, vegetable intake, breakfast cereal consumption, and total cholesterol was obtained at baseline. Each subject gave written informed consent, and the Institutional Review Board at Brigham and Women's Hospital, Boston, Massachusetts approved the study protocol.

We classified each hypertensive subject into categories of alcohol consumption as described above. Subjects who described their alcohol consumption as rarely/never were used as the reference group for all analyses. We calculated person-time of follow-up from baseline until the first occurrence of 1) outcome of interest, 2) death, or 3) censoring date (the date of the receipt of the last follow-up questionnaire, 2008). Within each alcohol category, we calculated the incidence rate by dividing the number of cases of MI by the corresponding person time of follow-up. We used Cox proportional hazards model to compute multivariable-adjusted hazard ratios with corresponding 95% confidence intervals. We assessed confounding by using a 10% change in hazard ratio. Assumptions for the proportional hazards models were tested by

including main effects and product terms of covariates and time factor. These assumptions were met as all p values were >0.05. The initial model adjusted only for age (continuous). The parsimonious model adjusted for age, body mass index (kg/m^2, continuous), smoking (never, past, present), exercise (<1, 1, 2–4, and ≥ 5 times/week) and diabetes (yes/no). The fully adjusted model also controlled for multivitamin use (never, past, present), vegetable consumption (<3, 3–4, 5–6, 7–13, and 14+ servings per day), breakfast cereal intake (0, <1, 2–6, and ≥ 7), randomization arm (aspirin vs. placebo) and treatment for hypercholesterolemia. To explore whether the phenomenon of "sick quitters" might inflate the hazard ratios, we repeated the analysis excluding nondrinkers and using current drinkers of 5–7 drinks per week as the reference group. In secondary analyses, we examined the relationship between alcohol consumption in hypertensive men and both angina pectoris and total CHD. All analyses were completed with the use of SAS, version 9.2 (SAS Institute, Cary, NC). The significance level was set at 0.05.

Results

Among the 5164 participants who reported prevalent hypertension at baseline, the mean age at randomization was 58.1 years; 14.9% of subjects were nondrinkers, and 25.8% of participants reported alcohol consumption of 7 drinks/week, and only 4.3% reported drinking 2+ drinks/day. Table 1 presents baseline characteristics of the study participants according to alcohol consumption. During an average follow-up of 17.9 years, 623 new cases of MI, 1249 cases of angina pectoris, and 1441 cases of total CHD occurred. In the multivariable Cox regression model, alcohol consumption was associated with a lower risk for MI in a dose-dependent manner (p for linear trend 0.0022, Table 2). Repeating the analysis using current drinkers of 5–7 drinks/week as the reference group did not change the relationship between alcohol consumption and risk of MI. In addition, examination of the effect of alcohol consumption on angina pectoris and total CHD demonstrated a similar protective relationship (Table 3).

Discussion

In this cohort of US male physicians, our results confirm the beneficial effect of judicious alcohol use on the risk of MI. Furthermore, our secondary analysis suggests that this benefit extends to all CHD (patients with angina pectoris and prior revascularization in addition to MI). These findings suggest that the effects of moderate alcohol consumption on the cardiovascular system lead to a net benefit. Although alcohol has been shown to increase blood pressure, the relatively modest increase in blood pressure[7,8] is likely countered by the effect of alcohol consumption on insulin sensitivity[9], inflammation[10], high-density lipoprotein cholesterol[11], and platelet aggregation[12] among moderate drinkers. However, it is important to emphasize the reduction in cardiovascular disease with moderate alcohol consumption among hypertensive subjects in no way diminishes the importance of blood pressure control regardless of drinking habits[13].

Previous studies have shown that moderate alcohol consumption decreases the risk of cardiovascular disease in otherwise healthy individuals[14,15] and may confer an advantage in terms of both cardiovascular and overall survival[16,17]. Our findings expand upon this and are consistent with the previously published data suggesting a decreased risk of cardiovascular disease with moderate alcohol consumption even among patients with known hypertension. Earlier work with the PHS cohort suggested an association between light to moderate alcohol consumption among hypertensive men and a reduced risk of total and cardiovascular mortality[2]. In addition, Beulens et al. demonstrated a reduction in the risk of both fatal and nonfatal MI in hypertensive patients with moderate alcohol consumption[1].

Strengths of our study include the large sample size, > 20 years of follow-up, confirmation of CHD via review of medical records, and a large number of covariates to control for confounding. In addition, the fact that CHD diagnoses were self-reported by physicians with confirmation by medical records makes our outcome measures very reliable. This reliability is of particular interest in the case of angina as this endpoint is infrequently used in epidemiological studies given the potential of inaccuracy in self-reported diagnosis, a problem unlikely to occur with physicians. There are certain limitations to our study. The population of the PHS is limited to male physicians who may have somewhat different behaviors than the general population as evidenced by a lower prevalence of smoking, diabetes, and obesity and a higher percentage of regular exercise. These behavior differences and the lack of women in the cohort somewhat limits generalizability and the ability to test for an interaction between gender and the beneficial effects of alcohol. In addition, misclassification bias is possible due to the identification of prevalent hypertension and alcohol consumption by self-report. However, other investigators have reported a good accuracy of self-report of blood pressure in the PHS[18]. Finally, no inference on the association between heavy drinking and CHD in hypertensive subjects can be made as there were a limited number of drinkers of 2+ drinks per day in our sample (n=222 or 4.3%).

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Table 1

Baseline characteristics of 5164 hypertensive male physicians according to alcohol consumption

	Alcohol Consumption			
Characteristics	**<1/week (N=1315)**	**1–4/week (N=1668)**	**5–7/week (N=1959)**	**8+/week (N=222)**
Age (years)	58.1±10.1	56.5±9.8	59.3±9.8	59.8±9.5
Body mass index (kg/m^2)	25.9±3.4	25.6±2.9	25.3±2.9	25.8±3.6
Vegetable Intake (servings/day)	7.9±5.1	8.5±4.9	8.7±4.8	8.3±5.8
Current Multivitamins	23.5%	19.6%	25.7%	27.7%
Current smokers	9.5%	9.7%	13.5%	26.1%
Exercise >1 time per week	63.0%	71.0%	72.3%	60.6%
Diabetes Mellitus	10.1%	4.9%	4.1%	5.9%
Total cholesterol >240 mg/dl or treated	16.4%	16.2%	18.0%	17.5%
Aspirin Arm	49.7%	51.9%	48.8%	50.0%
Breakfast Cereal ≥ 2 servings/week	44.9%	42.3%	39.6%	30.6%

Table 2

Incidence rates and hazard ratios (95% Confidence Intervals) for myocardial infarction according to alcohol consumption

		Hazard Ratio (95% Confidence Intervals)		
Alcohol Consumption (drinks/week)	**Cases**	**Age Adjusted**	**Model 1***	**Model 2†**
<1	172	1.0	1.0	1.0
1–4	223	1.03 (0.84–1.26)	1.08 (0.88–1.32)	1.05 (0.85–1.28)
5–7	211	0.78 (0.64–0.95)	0.81 (0.66–1.00)	0.78 (0.64–0.97)
>8	17	0.62 (0.37–1.02)	0.58 (0.35–0.96)	0.57 (0.35–0.95)
P for linear trend		P=.0021	p=.0046	p=.0022

*Adjusted for age, body mass index, smoking, exercise, and diabetes.

†Adjusted for age, body mass index, smoking, exercise, diabetes, multivitamin use, vegetable intake, breakfast cereal intake, and cholesterol.

Table 3

Hazard ratios (95% Confidence Intervals) for angina pectoris and combined coronary heart disease (myocardial infraction, angina, or revascularization)

	Hazard Ratio (95% Confidence Intervals) for Angina Pectoris			Hazard Ratio (95% Confidence Intervals) for all Coronary Artery Disease		
Alcohol Use (drinks/week)	**Age-Adjusted**	**Model 1***	**Model 2†**	**Age-Adjusted**	**Model 1***	**Model 2†**
<1	1.0	1.0	1.0	1.0	1.0	1.0
1–4	0.92 (0.80–1.06)	0.94 (0.82–1.08)	0.92 (0.80–1.07)	0.95 (0.83–1.08)	0.97 (0.85–1.11)	0.95 (0.83–1.09)
5–7	0.71 (0.62, 0.82)	0.73 (0.63–0.85)	0.71 (0.62–0.83)	0.72 (0.63–0.82)	0.74 (0.65–0.85)	0.72 (0.63–0.83)
>8	0.63 (0.46, 0.88)	0.63 (0.45–0.87)	0.62 (0.44–0.86)	0.65 (0.48–0.88)	0.63 (0.47–0.86)	0.62 (0.45–0.84)
P for trend	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

*Adjusted for age, body mass index, smoking, exercise, and diabetes.

†Adjusted for age, body mass index, smoking, exercise, diabetes, multivitamin use, vegetable intake, breakfast cereal intake, and cholesterol.