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Alcohol Consumption and Heart Failure in Hypertensive US Male Physicians

Luc Djoussé, MDDSc^a and J. Michael Gaziano, MD^{a,b}

a From the Divisions of Aging, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

b From the Divisions of Aging and Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

Abstract

While alcohol drinking raises blood pressure and heavy drinking has been associated with alcoholic cardiomyopathy, little is known about the association between light-to-moderate drinking on the risk of heart failure (HF) among hypertensive subjects. Thus, we prospectively examined the association between light-to-moderate drinking and incident HF in 5,153 hypertensive male physicians who were free of stroke, myocardial infarction, or major cancers at baseline. Alcohol consumption was self-reported and classified as <1, 1–4, 5–7, and 8+ drinks/week. HF was ascertained through follow-up questionnaires and validated using Framingham criteria. The average age was 58 years and about 70% of the participants consumed 1–7 drinks per week. A total of 478 incident HF cases occurred in this cohort during the follow up. Compared to subjects consuming < 1 drink per week, hazard ratios (95% confidence interval) for HF were 0.89 (0.70–1.12), 0.72 (0.57–0.91), and 0.38 (0.20–0.72) for alcohol consumption of 1–4, 5–7, and 8+ drinks/week, respectively, after adjustment for age, body mass index, smoking, randomization's group, use of multivitamins, vegetable consumption, breakfast cereal, exercise, and history of atrial fibrillation (*p* for trend <0.001). Similar results were obtained for HF with and without antecedent myocardial infarction and among subjects without diabetes mellitus. In conclusion, our data suggest that light-to-moderate alcohol consumption is associated with a lower risk of HF among hypertensive male physicians.

Keywords

Alcohol drinking; heart failure; epidemiology; risk factor

Moderate drinking may lower the risk of heart failure (HF) caused by antecedent coronary artery disease. Recent alcohol consumption was not associated with the subsequent risk for HF among patients who had a myocardial infarction^{1,2}. In addition, among post-myocardial infarction patients with left ventricular dysfunction, moderate drinking was not associated with incident HF^{1,2}. In contrast, other investigators have reported an inverse relation between light-to-moderate drinking and HF risk in the general population^{3–6}. No previous study has examined the association between moderate drinking and incident HF among individuals with hypertension. Since moderate alcohol intake could lower the risk of HF (through its beneficial effects on coronary artery disease and neurohormonal changes that might prevent clinical onset of HF^{7–9}) and increase the risk of HF through hypertensive cardiomyopathy, it is important to understand the net benefit if any, of light-to-moderate drinking (≤ 2 drinks per day for men)

among people with hypertension. Thus, we prospectively assessed whether alcohol consumption was associated with a lower risk of incident HF among US male physicians with prevalent hypertension at baseline. In addition, we examined whether alcohol consumption influenced the risk of HF with and without antecedent myocardial infarction in this population.

Materials and Methods

We used data from the Physicians' Health Study (PHS) I, – a randomized trial of aspirin and beta carotene for the primary prevention of cardiovascular disease and cancer among 22,071 US male physicians. Detailed description of the PHS I has been published previously¹⁰. At baseline, subjects were asked a) to report their current blood pressure level (item 13.a of the questionnaire) and b) whether they have ever received drug treatment for hypertension (possible answers were never, past only, or current, item 13.b of the questionnaire). Prevalent hypertension was defined as systolic blood pressure of ≥ 140 mm Hg, diastolic blood pressure of ≥ 90 mm Hg, or positive response to current/past treatment for hypertension. Of the 5,176 subjects with prevalent hypertension at baseline, we excluded 23 subjects with missing data on covariates, leaving a final sample of 5,153 participants for the current analyses. Each participant gave written informed consent and the Institutional review Board at Brigham and Women's Hospital approved the study protocol.

Information about usual alcohol consumption was self-reported on a standard questionnaire. Participants were asked, "How often do you usually consume alcoholic beverages". Possible response categories included "rarely/never", "1–3/month", "1/week", "2–4/week", "5–6/week", "daily", and "2+/day". The response was interpreted as number of alcoholic drinks consumed during the specified period. In addition, similar alcohol questions were repeated on the 84-month follow-up questionnaire.

A questionnaire was mailed to each participant every 6 months during the first year and has been mailed annually thereafter to obtain information on compliance with the intervention and the occurrence of new medical diagnoses including HF. In a pilot study, 66 out of 73 (90%) self-reported HF cases were confirmed using Framingham criteria (details on HF validation in the PHS has been reported previously⁶). Self-reported information on age, height, weight, body mass index, cigarette smoking, physical activity, and prevalent atrial fibrillation, valvular disease, and diabetes mellitus was collected at baseline. In addition, data on selected foods such as fruits and vegetables, breakfast cereals, and history of hypercholesterolemia (defined as reported total cholesterol of ≥ 240 mg/dl or current/past treatments for elevated cholesterol) were obtained at baseline.

We computed person-time of follow up from baseline until the first occurrence of a) HF, b) death, or c) censoring date – date of receipt of last follow-up questionnaire. Within each category of alcohol consumption, we calculated the incidence rate of HF by dividing the number of cases by the corresponding person-time. We used Cox proportional hazard models to compute multivariable adjusted hazard ratios with corresponding 95% confidence intervals using subjects in the lowest category of alcohol consumption as the reference group. We assessed confounding by using 10% change in hazard ratio. Assumptions for the proportional hazard models were tested (by including main effects and product terms of covariates and time factor) and were met (all p values >0.05). The parsimonious model controlled for age (<45 , 45–49, 50–54, 55–59, 60–64, and 65+ years), body mass index (<25 , 25–29.9, and 30 kg/m²), and smoking (never, past, and current smokers). The final multivariable model also controlled for randomization's arm (4 groups), use of multivitamin (never, past, current), breakfast cereal consumption (0, <1 , 2–6, 7+ servings per week), exercise (<1 , 1, 2–4, 5+ times per week), vegetable consumption (<1 , 1, and 2+ servings/day), and history of atrial fibrillation (yes/no). Since alcohol consumption improves insulin sensitivity, we also examined whether

diabetes mellitus was an intermediate factor by adding prevalent diabetes in the multivariable model (we expected attenuation of the hazard ratios if the relationship between alcohol consumption and HF is partially mediated by diabetes mellitus). To explore the fact that sick quitters may inflate the hazard ratios, we repeated these analyses after exclusion of nondrinkers and used current drinkers of 1–4 drinks per week as reference. P value for linear trend was obtained by fitting an ordinal alcohol variable (assigned a value of 1, 2, 3, and 4 from the lowest to the highest category of alcohol, respectively).

In secondary analyses, we examined the association between alcohol consumption and HF with and without antecedent myocardial infarction. Furthermore, we repeated the main analysis while excluding a) subjects with prevalent diabetes, b) individuals with a follow-up time of < 2 years. All analyses were completed using SAS, version 9.1 (SAS Institute, NC). Significance level was set at 0.05.

Results

Among 5,153 PHS participants who reported prevalent hypertension at baseline, the mean age at randomization was 58 ± 10 years (range 40 to 86 years). About 70% of the participants consumed 1–7 drinks per week and only 4% reported consumption of 8+ drinks per week. Table 1 presents baseline characteristics of the study participants. During an average follow up of 18 years, 478 new cases of HF occurred in this cohort. In multivariable Cox regression model, alcohol consumption was associated with a lower risk of HF in a dose-response fashion (p for linear trend < 0.001 , Table 2). Additional adjustment for diabetes mellitus (possible intermediate factor) led to a modest attenuation of the relative risk estimates [hazard ratios (95% confidence interval) of 1.0 (reference), 0.96 (0.76–1.21), 0.78 (0.62–0.99), and 0.40 (0.21–0.76) from the lowest to the highest alcohol category using the fully adjusted model, p for trend 0.002). Excluding subjects with less than 2 years of follow up or excluding subjects with prevalent diabetes mellitus did not alter the results (p for trend < 0.001 and 0.002, respectively). When alcohol was updated at 84-month questionnaire, corresponding hazard ratios (95% confidence interval) were 1.0, 1.05 (0.84–1.31), 0.77 (0.61–0.98), and 0.58 (0.35–0.96), respectively (p for trend 0.008). After exclusion of current non-drinkers, we observed similar relationship among current drinkers (Table 3). Furthermore, in the multivariable adjusted Cox model, alcohol consumption was associated with a lower risk of HF with and without antecedent myocardial infarction (Tables 4 and 5, respectively).

Discussion

In this cohort of hypertensive US male physicians, we found that light-to-moderate alcohol consumption was associated with a lower risk of HF. Furthermore, the inverse relation between light-to-moderate alcohol consumption and HF was observed for HF with and without antecedent myocardial infarction. This is the first study to report an association between light-to-moderate drinking and the risk of HF among hypertensive subjects.

Previous studies have demonstrated that excessive drinking is associated with left ventricular dysfunction^{11,12}, dilated cardiomyopathy^{13,14}, and hypertension^{15,16}. On the other hand, current literature provides evidence supporting beneficial effects of moderate drinking on myocardial infarction and other cardiovascular diseases^{17–19} and mortality²⁰. It is thus possible that some of the HF cases might have been averted through prevention of myocardial infarction by light-to-moderate drinking. However, the fact that we observed an inverse association between alcohol consumption and HF without antecedent myocardial infarction suggests that other biological mechanisms could play a role in the association between alcohol intake and HF.

Earlier reports have shown beneficial effects of moderate alcohol consumption on other risk factors for HF. For example, alcohol consumption has been shown to raise high-density lipoprotein cholesterol²¹; improve insulin sensitivity and lower the risk of diabetes mellitus^{22,23}; lower plasma levels of inflammatory markers²⁴; and raise plasma levels of adiponectin^{25,26}. In experimental studies, adiponectin has been shown to attenuate cardiac hypertrophy in response to pressure overload in adiponectin knockout mice²⁷. These anti-hypertrophic actions of adiponectin are possibly mediated through activation of AMP-activated protein kinase²⁷. Furthermore, alcohol consumption has diuretic effects and has been associated with plasma levels of atrial natriuretic peptide⁹. Such diuretic effect could prevent volume overload and delay onset of signs and symptoms of HF. One or more of these physiologic mechanisms could partially or completely explain the observed association between light-to-moderate alcohol consumption and HF without antecedent myocardial infarction in our study.

Our study has some limitations. First, our sample consists of male physicians who may have different lifestyle factors than the general population, thus limiting the generalizability of our findings. In addition, the lack of data on women limits our ability to make inference on the relation between moderate drinking and HF in hypertensive women or to explore gender-alcohol interaction on HF. Furthermore, identification of subjects with prevalent hypertension was based on self-reported information. However, systolic and diastolic blood pressure measured on a standardized examination have shown a reasonable correlation with self-reported values among physicians (correlation coefficients 0.72 and 0.60 for systolic and diastolic blood pressure, respectively, all $p < 0.0001$)²⁸. Second, because most participants were light-to-moderate drinkers (70% reported consumption of 1–7 drinks/week whereas only 4% reported alcohol consumption of 8+ drinks per week), we could not examine the association between heavy drinking and risk of HF in hypertensive subjects. Third, under reporting of alcohol drinking could have obscured the true association between light-to-moderate drinking and risk of HF. It remains possible that sick quitters may have inflated the observed association as we did not have data to separate lifelong abstainers from former drinkers. However, this is less likely as we showed similar inverse relations between alcohol intake and HF after exclusion of current abstainers. Fourth, we did not have information on drinking patterns, beverage types, or whether alcohol was consumed with meals to examine their influences on the studied association. Fifth, given the observational nature of our data, we can not exclude residual confounding or confounding by unmeasured factors as possible explanation of our findings. Nevertheless, the large sample size, the long-term follow up, the robustness of the data in sensitivity analyses including use of updated alcohol at 84 months from baseline measurements and the standardized and complete follow up in the PHS are major strengths of this study.

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Table 1

Baseline characteristics of 5,153 hypertensive men according to alcohol consumption.

Characteristics	Alcohol consumption (drinks/week)			
	<1 (N=1,312)	1-4 (N=1,661)	5-7 (N=1,958)	8+ (N=222)
Age (years)	58 (10)	56 (10)	59 (10)	60 (10)
Body mass index (kg/m ²)	26 (3)	26 (3)	25 (3)	26 (4)
Vegetable intake (servings/day)	1.1 (0.7)	1.2 (0.7)	1.2 (0.7)	1.2 (0.8)
Smoker				
Never	58%	48%	35%	23%
Past	32%	43%	52%	51%
Current	10%	10%	14%	26%
Atrial fibrillation	1%	1 %	2%	3%
Prevalent diabetes mellitus	10%	5%	4%	6%
Breakfast cereal consumption				
None	31%	33%	39%	53%
7+ servings per week	23%	17%	17%	14%
Exercise (times/week)				
< 1	37%	29%	28%	39%
5+	15%	13%	16%	16%
Current use of multivitamin	23%	20%	26%	28%
Hypercholesterolemia	16%	16%	18%	18%
Aspirin arm	50%	48%	51%	50%

* Means (standard deviation) or percentages

Table 2

Adjusted hazard ratios (95% CI) for heart failure according to alcohol consumption

Alcohol intake (drinks/week)	Cases	Hazard Ratio (95% CI) for heart failure		
		Model 1 [*]	Model 2 [†]	Model 3 [‡]
< 1	135	1.0	1.0	1.0
1–4	156	0.91 (0.73–1.15)	0.89 (0.71–1.13)	0.89 (0.70–1.12)
5–7	177	0.78 (0.62–0.98)	0.75 (0.59–0.94)	0.72 (0.57–0.91)
8+	10	0.46 (0.24–0.87)	0.40 (0.21–0.76)	0.38 (0.20–0.72)
P for linear trend		<0.01	<0.001	<0.001

* Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, and 65+ years).

† Adjusted for age (6 categories as above), body mass (<25, 25–29.9, and 30+ kg/m²), and smoking (never, past, and current smokers).

‡ Adjusted for variables in model 2 plus randomization's arm (4 groups), use of multivitamin (never, past, current), breakfast cereal consumption (0, <1, 2–6, 7+ servings per week), exercise (<1, 1, 2–4, 5+ times per week), vegetable consumption (<1, 1, and 2+ servings/day), and history of atrial fibrillation.

Table 3

Adjusted hazard ratios (95% CI) for heart failure according to alcohol consumption using moderate drinkers as reference

Alcohol intake (drinks/week)	Cases	Hazard Ratio (95% CI) for heart failure		
		Model 1 [*]	Model 2 [†]	Model 3 [‡]
1–4	156	1.0	1.0	1.0
5–7	177	0.85 (0.68–1.05)	0.84 (0.67–1.04)	0.82 (0.65–1.02)
8+	10	0.50 (0.26–0.95)	0.45 (0.24–0.86)	0.44 (0.23–0.84)
P for linear trend		0.02	0.01	<0.01

* Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, and 65+ years).

† Adjusted for age (6 categories as above), body mass (<25, 25–29.9, and 30+ kg/m²), and smoking (never, past, and current smokers).

‡ Adjusted for variables in model 2 plus randomization's arm (4 groups), use of multivitamin (never, past, current), breakfast cereal consumption (0, <1, 2–6, 7+ servings per week), exercise (<1, 1, 2–4, 5+ times per week), vegetable consumption (<1, 1, and 2+ servings/day), and history of atrial fibrillation.

Table 4

Adjusted hazard ratios (95% CI) for heart failure with antecedent myocardial infarction by alcohol consumption

Alcohol intake (drinks/week)	Cases	Hazard Ratio (95% CI) for heart failure		
		Model 1 [*]	Model 2 [†]	Model 3 [‡]
< 1	26	1.0	1.0	1.0
1–4	34	1.01 (0.60–1.68)	0.98 (0.58–1.64)	0.97 (0.58–1.63)
5–7	22	0.51 (0.29–0.90)	0.50 (0.28–0.89)	0.47 (0.26–0.84)
8+	3	§	-	-
P for linear trend		0.02	0.02	0.01

* Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, and 65+ years).

† Adjusted for age (6 categories as above), body mass (<25, 25–29.9, and 30+ kg/m²), and smoking (never, past, and current smokers).

‡ Adjusted for variables in model 2 plus randomization's arm (4 groups), use of multivitamin (never, past, current), breakfast cereal consumption (0, <1, 2–6, 7+ servings per week), exercise (<1, 1, 2–4, 5+ times per week), vegetable consumption (<1, 1, and 2+ servings/day), and history of atrial fibrillation.

§ Insufficient number of cases for stable estimates.

Table 5

Adjusted hazard ratios (95% CI) for heart failure without antecedent myocardial infarction by alcohol consumption

Alcohol intake (drinks/week)	Cases	Hazard Ratio (95% CI) for heart failure		
		Model 1 [*]	Model 2 [†]	Model 3 [‡]
< 1	109	1.0	1.0	1.0
1–4	122	0.89 (0.69–1.15)	0.87 (0.67–1.13)	0.86 (0.66–1.13)
5–7	155	0.84 (0.66–1.08)	0.80 (0.62–1.03)	0.78 (0.60–1.00)
8+	7	0.39 (0.18–0.84)	0.34 (0.16–0.72)	0.32 (0.15–0.70)
P for linear trend		0.03	<0.01	<0.01

* Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, and 65+ years).

† Adjusted for age (6 categories as above), body mass (<25, 25–29.9, and 30+ kg/m²), and smoking (never, past, and current smokers).

‡ Adjusted for variables in model 2 plus randomization's arm (4 groups), use of multivitamin (never, past, current), breakfast cereal consumption (0, <1, 2–6, 7+ servings per week), exercise (<1, 1, 2–4, 5+ times per week), vegetable consumption (<1, 1, and 2+ servings/day), and history of atrial fibrillation.