

Alcohol Consumption and Risk for Congestive Heart Failure in the Framingham Heart Study

Craig R. Walsh, MD; Martin G. Larson, ScD; Jane C. Evans, DSc, MPH; Luc Djousse, MD, MPH; R. Curtis Ellison, MD; Ramachandran S. Vasan, MD; and Daniel Levy, MD

Background: Although excessive alcohol consumption can promote cardiomyopathy, little is known about the association between alcohol consumption and risk for congestive heart failure in the community.

Objective: To determine the relation between alcohol consumption and risk for congestive heart failure in the community.

Design: Community-based, prospective observational study.

Setting: Framingham, Massachusetts.

Participants: Participants in the Framingham Heart Study who were free of congestive heart failure and coronary heart disease.

Measurements: Self-reported alcohol consumption; sex-specific rates of congestive heart failure per 1000 person-years of follow-up by level of alcohol consumption.

Results: In men, 99 cases of congestive heart failure occurred during 26 035 person-years of follow-up. In women, 120 cases of congestive heart failure occurred during 35 563 person-years of follow-up. After adjustment for multiple confounders, risk for con-

gestive heart failure was lower among men at all levels of alcohol consumption compared with men who consumed less than 1 drink/wk. The hazard ratio for congestive heart failure was lowest among men who consumed 8 to 14 drinks/wk (0.41 [95% CI, 0.21 to 0.81]) compared with those who consumed less than 1 drink/wk. In women, the age-adjusted hazard ratio for congestive heart failure was lowest among those who consumed 3 to 7 drinks/wk (0.49 [CI, 0.25 to 0.96]) compared with those who consumed less than 1 drink/wk. However, after adjustment for multiple predictors of congestive heart failure, this association was no longer statistically significant.

Conclusions: In the community, alcohol consumption is not associated with increased risk for congestive heart failure, even among heavy drinkers (≥ 15 drinks/wk in men and ≥ 8 drinks/wk in women). To the contrary, when consumed in moderation, alcohol appears to protect against congestive heart failure.

Ann Intern Med. 2002;136:181-191.

www.annals.org

For author affiliations, current addresses, and contributions, see end of text.

See related article on pp 192-200 and editorial comment on pp 247-249.

Regular, heavy consumption of alcohol is associated with subclinical impairment of left ventricular function (1–3) and occasionally results in overt cardiomyopathy (4). This may be a consequence of direct toxic effects of alcohol or its metabolites (5); coexisting malnutrition (6); associated hypertension (7, 8); increased ventricular mass (9) or, rarely, toxic additives to alcoholic beverages (10). Conversely, moderate alcohol consumption appears to be protective against coronary heart disease (11–14). Myocardial infarction is an important risk factor for congestive heart failure (15–18). By preventing coronary heart disease, moderate alcohol consumption may indirectly protect against congestive heart failure secondary to myocardial infarction. Thus, the relation of alcohol consumption to the risk for congestive heart failure is probably complex, reflecting the interplay of its coronary protective effects and its myocardial toxic effects.

Little is known about the effect of alcohol consumption on the incidence of congestive heart failure in community-based populations. We therefore sought to de-

termine the relation between alcohol consumption and risk for congestive heart failure in participants in the Framingham Heart Study.

METHODS

Study Sample

The Framingham Heart Study is a prospective epidemiologic cohort study established in 1948 to evaluate potential risk factors for coronary heart disease. The original cohort consisted of 5209 residents of Framingham, Massachusetts, 28 to 62 years of age at entry, who have undergone follow-up evaluations every 2 years. In 1971, 5124 additional participants (the offspring of the original participants and their spouses) were enrolled into the Framingham Offspring Study. These participants undergo follow-up evaluations every 4 years. The study design and entry criteria for both cohorts are described elsewhere (19–22).

The study sample was drawn from members of the original cohort who attended examination 12, 15, 17,

20, or 22 (1971 to 1994) and members of the offspring cohort who attended examination 2, 4, or 5 (1979 to 1995). Each of these examinations served as the baseline for subsequent follow-up intervals. Participants with complete information on alcohol consumption at a baseline examination and an examination 6 to 10 years earlier (to identify former drinkers) were eligible for the analysis. All examinations and procedures were approved by the institutional review board of Boston University School of Medicine, and all participants gave informed consent.

Ascertainment of Alcohol Consumption

At examinations 12 through 15 and 17 through 22 of the original cohort and at all examinations of the offspring cohort, participants were asked about the number of 1.5-oz cocktails, 12-oz glasses (or cans) of beer, and 4-oz glasses of wine they consumed in 1 week. Alcohol intake (g/wk) among participants who consumed at least 1 drink/wk was computed by using the following equation: $28.35 + (0.57 + \text{the number of cocktails per week} + 0.44 + \text{the number of beers per week} + 0.40 + \text{the number of glasses of wine per week})$ (23). For each participant, the number of drinks consumed per week was calculated by assuming that each drink contains 13 g of alcohol (24). Men who consumed 15 drinks/wk or more and women who consumed 8 drinks/wk or more were considered to be heavy drinkers in accordance with definitions established by the National Institute of Alcohol Abuse and Alcoholism (25).

Participants who reported consuming less than 1 drink/wk at the index examination were further separated into two groups on the basis of reported alcohol consumption at an examination 6 to 10 years before the index examination. Participants who reported consumption of less than 1 drink/wk at the index examination but more than 1 drink/wk at the previous examination were classified as former drinkers. Participants who reported consumption of less than 1 drink/wk at both examinations were classified as nondrinkers and served as the reference group.

Baseline Measurements

Medical histories and physical examinations were performed for each participant at every clinic visit. Systolic and diastolic blood pressure were measured twice

in the left arm of each participant. The average of the two readings was used for each blood pressure variable. The diagnosis of hypertension was based on a systolic blood pressure of 140 mm Hg or greater, a diastolic blood pressure of 90 mm Hg or greater, or current use of antihypertensive drugs (26). Total and high-density lipoprotein (HDL) cholesterol levels were measured at each examination except examination 17 of the original cohort. For participants attending examination 17, total and HDL cholesterol levels measured at examination 15 were used. Body mass index was calculated as weight in kilograms divided by the square of the height in meters. Participants were separated according to smoking status into nonsmokers, former smokers, and current smokers (those who smoked cigarettes regularly within 1 year of the index examination). The number of cigarettes smoked per day was recorded for current smokers. Diabetes was defined as a nonfasting blood glucose level of 11.1 mmol/L or greater (≥ 200 mg/dL), a fasting blood glucose level of 7.8 mmol/L or greater (≥ 140 mg/dL), or use of insulin or an oral hypoglycemic agent (27). Diagnostic criteria for coronary heart disease (including myocardial infarction, coronary insufficiency, and angina pectoris) are described elsewhere (22). Valvular heart disease was defined as the presence of a systolic murmur louder than II/VI or any diastolic murmur. Electrocardiographic left ventricular hypertrophy was diagnosed if a participant had voltage criteria for left ventricular hypertrophy accompanied by lateral repolarization changes (28).

Outcome Measurements

The primary outcome of interest was incident congestive heart failure. Participants were monitored for the development of congestive heart failure and other cardiovascular events by using routine periodic clinic examinations and surveillance procedures. Information about such events was obtained through medical history, physical examination, and hospitalization records and by communication with personal physicians. All suspected new events were reviewed by a panel of three experienced investigators who evaluated all pertinent medical and hospital records and pathology reports. **Table 1** shows criteria for diagnosis of congestive heart failure. Congestive heart failure was diagnosed if at least two major criteria or one major and two minor criteria were

present. Minor criteria were acceptable only if they could not be attributed to another medical condition (such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or the nephrotic syndrome) (29).

The criteria used to identify participants with congestive heart failure in the Framingham Heart Study compare favorably to other clinically based criteria used to identify persons with congestive heart failure (30) and left ventricular systolic dysfunction (31). Mosterd and colleagues (30) reported that the Framingham Heart Study criteria were 100% sensitive and 78% specific for identifying persons with definite congestive heart failure as determined by clinical assessment by a cardiologist.

Statistical Analysis

Separate analyses were performed for men and women. Because men and women differed markedly in reported alcohol intake, level of alcohol consumption was categorized differently for each sex. Baseline risk factors were computed for each level of alcohol consumption. Age-adjusted and multivariable-adjusted hazard ratios for congestive heart failure were calculated by using Cox proportional hazards regression models (32), with pooled follow-up periods and reported alcohol intake at original cohort examinations 12, 15, 17, 20, and 22 and offspring cohort examinations 2, 4, and 5. Nondrinkers served as the reference group. The following covariates were included in the multivariable-adjusted models: age, smoking (cigarettes/d), body mass index, diabetes, valvular heart disease, HDL cholesterol level, and hypertension. The maximum duration of follow-up was 5 years. For participants attending consecutive examinations that were fewer than 5 years apart (original cohort examinations 15 and 17, and 20 and 22 and offspring examinations 4 and 5), follow-up was censored at the time of the repeated examination (approximately 4 years later). Participants who attended more than one index examination could contribute to multiple observations periods. We used the Anderson–Gill model for multiple failure times (33) to account for the potential for clustering of observations by participant.

Because the effect of alcohol consumption on development of congestive heart failure may be mediated through the effects of alcohol on hypertension or HDL cholesterol level, we performed secondary analyses using multivariable-adjusted models, with and without hypertension status and HDL cholesterol as covariates. To

Table 1. Criteria for Congestive Heart Failure*

Major criteria
Paroxysmal nocturnal dyspnea
Neck-vein distention
Rales
Radiographic cardiomegaly (increasing heart size on chest radiography)
Acute pulmonary edema
S ₃ gallop
Increased central venous pressure (>16 cm H ₂ O at right atrium)
Hepatojugular reflux
Pulmonary edema, visceral congestion, or cardiomegaly at autopsy
Minor criteria
Bilateral ankle edema
Nocturnal cough
Dyspnea on ordinary exertion
Hepatomegaly
Pleural effusion
Decrease in vital capacity by one third from maximum recorded
Tachycardia (heart rate \geq 120 beats/min)

* Congestive heart failure was diagnosed if at least two major criteria or one major and two minor criteria were met.

determine the association between alcohol consumption and risk for congestive heart failure without interceding myocardial infarction, we calculated age-adjusted and multivariable-adjusted hazard ratios, censoring participants at the time of myocardial infarction that occurred during follow-up. To adjust for differences in medical therapy across alcohol consumption categories, models were constructed that adjusted for medications taken at the index examination (aspirin, β -blockers, diuretics, calcium-channel blockers, and angiotensin-converting enzyme inhibitors) in addition to the covariates included in the model used for the primary analysis. For the final model, the proportional hazards assumption was tested and found to be appropriate. Analyses for length-selection biases showed that from the earliest ascertainment of alcohol consumption in the Framingham Study until the period of the current primary analysis, heavy drinkers were not at increased risk for congestive heart failure or death compared with nondrinkers. All statistical analyses were performed by using SAS statistical software (34).

RESULTS

Participants

A total of 3498 men and 4188 women attended at least one baseline examination. We excluded 131 men and 217 women because of missing information on covariates or failure to attend a follow-up examination. An additional 218 men and 245 women were excluded because of missing information on alcohol consumption,

Table 2. Baseline Characteristics in Men, by Level of Alcohol Consumption*

Characteristic	Alcohol Consumption				
	Nondrinkers	Former Drinkers	1–7 Drinks/wk	8–14 Drinks/wk	≥15 Drinks/wk
Age, y	62.7 ± 11.7	60.8 ± 11.7	59.1 ± 11.3	59.6 ± 11.3	58.7 ± 10.7
Body mass index, kg/m ²	27.2 ± 4.3	27.3 ± 4.1	27.3 ± 3.7	27.2 ± 3.6	27.2 ± 3.7
Hypertension, %	50.7	48.6	42.8	47.4	51.8
Medications, %					
Aspirin	36.7	26.4	43.1	38.3	42.2
Diuretics	12.6	15.6	11.9	12.7	15.0
β-Blockers	9.0	8.6	7.2	8.1	9.0
Calcium-channel blockers	6.6	6.4	4.4	3.3	3.3
Angiotensin-converting enzyme inhibitors	10.2	7.7	7.2	8.2	9.1
Total cholesterol level, mmol/L (mg/dL)	5.2 ± 1.0 (202.8 ± 38.2)	5.4 ± 1.0 (208.2 ± 37.9)	5.4 ± 1.0 (210.0 ± 37.3)	5.5 ± 0.9 (211.6 ± 35.7)	5.5 ± 0.9 (214.2 ± 36.3)
HDL cholesterol level, mmol/L (mg/dL)	1.0 ± 0.3 (39.5 ± 10.2)	1.0 ± 0.3 (40.4 ± 10.8)	1.1 ± 0.3 (42.3 ± 10.9)	1.2 ± 0.3 (46.4 ± 12.2)	1.3 ± 0.4 (48.8 ± 13.9)
Diabetes, %	8.6	10.0	7.1	5.6	6.4
Valvular heart disease, %	5.6	4.3	4.4	4.8	4.3
Smoking status, %					
Never	33.1	26.8	29.5	21.8	16.0
Former	47.4	51.1	52.0	54.6	53.0
Current	19.5	22.1	18.5	23.6	31.0
Cigarettes smoked daily, n†	23.8 ± 14.4	25.3 ± 13.8	22.4 ± 11.7	22.2 ± 12.9	26.2 ± 14.2
Alcohol intake, drinks/wk	0	0	3.6 ± 2.1	11.1 ± 2.3	27.3 ± 16.2
Previous alcohol intake, drinks/wk‡	0	8.9 ± 16.1	6.4 ± 7.8	12.5 ± 9.2	23.4 ± 17.6

* Data with the plus/minus sign are the mean ± SD. HDL = high-density lipoprotein.

† Current smokers only.

‡ Reported alcohol consumption at an examination 6 to 10 years before the index examination.

and 353 men and 233 women were excluded because of congestive heart failure or coronary heart disease at baseline, leaving 2796 men and 3493 women for analysis. Tables 2 and 3 show baseline characteristics of men and women, respectively.

Alcohol Consumption and Risk for Congestive Heart Failure

In men, 99 cases of congestive heart failure occurred during 26 035 person-years of follow-up. In women, 120 cases of congestive heart failure occurred during 35 563 person-years of follow up. Table 4 shows the age-adjusted incidence of congestive heart failure in men and women, by level of alcohol consumption.

Among men, risk for congestive heart failure was lower at all levels of alcohol consumption compared with nondrinkers after adjustment for age, smoking, body mass index, diabetes, valvular heart disease, and hypertension (Table 5). The hazard ratio for congestive heart failure was lowest among men who consumed 8 to 14 drinks/wk. Among women, the age-adjusted risk for congestive heart failure was reduced among those who consumed 3 to 7 drinks/wk compared with nondrinkers

(Table 6), but after further adjustment for smoking, body mass index, diabetes, valvular heart disease, and hypertension, the association was only marginally statistically significant ($P = 0.05$). Further adjustment for medications used at the index examination (aspirin, β-blockers, diuretics, angiotensin-converting enzyme inhibitors, and calcium-channel blockers) did not materially change the results of the proportional hazards models (data available from the authors on request).

In secondary analysis, removal of hypertension from the proportional hazards models did not greatly change the observed hazard ratios in both men and women (data not shown). In men, addition of HDL cholesterol to the multivariable-adjusted model attenuated the association between alcohol consumption and risk for congestive heart failure. However, risk for congestive heart failure remained significantly lower in men who consumed 1 to 7 drinks/wk ($P < 0.01$) or 8 to 14 drinks/wk ($P = 0.03$) compared with nondrinkers (Table 5). Risk for congestive heart failure did not significantly differ in former drinkers compared with nondrinkers among men ($P = 0.2$) or women ($P > 0.2$).

Table 3. Baseline Characteristics in Women, by Level of Alcohol Consumption*

Characteristic	Alcohol Consumption				
	Nondrinkers	Former Drinkers	1–2 Drinks/wk	3–7 Drinks/wk	≥8 Drinks/wk
Age, y	65.8 ± 12.4	63.4 ± 12.3	60.2 ± 11.2	59.9 ± 11.6	60.1 ± 10.9
Body mass index, kg/m ²	26.9 ± 5.5	26.5 ± 5.0	26.3 ± 4.9	25.6 ± 4.6	24.9 ± 4.3
Hypertension, %	54.9	49.2	44.2	40.8	47.8
Medications, %					
Aspirin	34.2	27.0	43.3	38.7	43.1
Diuretics	24.8	24.4	19.6	16.6	20.4
β-Blockers	8.7	7.3	6.7	6.4	7.1
Calcium-channel blockers	5.7	3.1	4.2	2.4	4.5
Angiotensin-converting enzyme inhibitors	7.5	5.9	5.1	5.8	6.1
Total cholesterol level, mmol/L (mg/dL)	5.8 ± 1.1 (223.3 ± 42.9)	5.8 ± 1.1 (225.5 ± 41.5)	5.7 ± 1.1 (221.7 ± 42.1)	5.7 ± 1.0 (220.0 ± 40.2)	5.8 ± 1.1 (226.0 ± 42.5)
HDL cholesterol level, mmol/L (mg/dL)	1.3 ± 0.3 (51.3 ± 13.5)	1.4 ± 0.4 (53.2 ± 15.0)	1.4 ± 0.4 (54.6 ± 14.2)	1.5 ± 0.4 (57.9 ± 15.4)	1.6 ± 0.4 (62.5 ± 16.9)
Diabetes, %	9.6	7.4	6.0	7.6	6.6
Valvular heart disease, %	8.1	6.2	4.8	4.7	6.0
Smoking status, %					
Never	60.3	46.1	45.1	36.8	21.6
Former	23.8	33.2	35.2	39.8	41.4
Current	15.9	20.7	19.7	23.4	37.0
Cigarettes smoked daily, n†	19.4 ± 10.5	17.9 ± 11.1	17.6 ± 10.7	18.0 ± 11.3	19.8 ± 11.3
Alcohol intake, drinks/wk	0	0	1.4 ± 0.5	4.9 ± 1.6	14.5 ± 6.8
Previous alcohol intake, drinks/wk‡	0	3.3 ± 5.3	2.5 ± 3.4	6.0 ± 11.5	11.4 ± 8.2

* Data with the plus/minus sign are the mean ± SD. HDL = high-density lipoprotein.

† Current smokers only.

‡ Reported alcohol consumption at an examination 6 to 10 years before the index examination.

Heavy Alcohol Consumption and Risk for Congestive Heart Failure

In our sample, 23% of men consumed 15 drinks/wk or more and 17% of women consumed 8 drinks/wk or more. The risk for congestive heart failure in men who consumed 15 drinks/wk or more was lower

compared with nondrinkers after adjustment for age, smoking, body mass index, diabetes, valvular heart disease, and hypertension (Table 5). Risk for congestive heart failure among women who consumed 8 drinks/wk or more was not increased compared with nondrinkers (Table 6).

Table 4. Age-Adjusted Incidence of Congestive Heart Failure in Men and Women, by Level of Alcohol Consumption

Participants	All-Cause Congestive Heart Failure			Congestive Heart Failure without Preceding Myocardial Infarction		
	Cases	Follow-up	Age-Adjusted Incidence (95% CI)	Cases	Follow-up	Age-Adjusted Incidence (95% CI)
	n	person-years	cases/1000 person-years	n	person-years	cases/1000 person-years
Men						
Nondrinkers	24	2921	6.3 (3.7–8.8)	17	2869	4.7 (2.4–6.9)
Former drinkers	16	3254	4.5 (2.3–6.7)	10	3222	2.9 (1.1–4.7)
1–7 drinks/wk	27	9431	3.0 (1.9–4.1)	18	9341	2.0 (1.0–3.0)
8–14 drinks/wk	13	4450	2.9 (1.3–4.6)	11	4428	2.5 (1.0–4.0)
≥15 drinks/wk	19	5979	3.6 (1.9–5.2)	15	5942	2.9 (1.4–4.4)
Women						
Nondrinkers	44	7733	4.1 (2.8–5.4)	30	7711	2.9 (1.8–4.0)
Former drinkers	29	6181	4.1 (2.6–5.6)	16	6151	2.3 (1.1–3.4)
1–2 drinks/wk	21	8753	2.7 (1.5–3.9)	20	8723	2.6 (1.4–3.7)
3–7 drinks/wk	11	6829	1.9 (0.8–3.1)	8	6815	1.4 (0.4–2.4)
≥8 drinks/wk	15	6067	3.4 (1.6–5.2)	11	6056	2.3 (0.8–3.7)

Table 5. Risk for Congestive Heart Failure in Men, by Level of Alcohol Consumption

Disease	Hazard Ratio (95% CI)				
	Nondrinkers	Former Drinkers	1–7 Drinks/wk	8–14 Drinks/wk	≥15 Drinks/wk
All-cause congestive heart failure					
Age-adjusted model	1.0 (referent)	0.72 (0.38–1.37)	0.48 (0.27–0.83)	0.47 (0.24–0.93)	0.59 (0.32–1.08)
Multivariable-adjusted model 1*	1.0 (referent)	0.63 (0.33–1.20)	0.44 (0.25–0.77)	0.41 (0.21–0.81)	0.53 (0.29–0.97)
Multivariable-adjusted model 2†	1.0 (referent)	0.64 (0.34–1.22)	0.46 (0.27–0.81)	0.47 (0.24–0.94)	0.63 (0.34–1.19)
Congestive heart failure without preceding myocardial infarction					
Age-adjusted model	1.0 (referent)	0.65 (0.30–1.43)	0.45 (0.23–0.89)	0.57 (0.27–1.23)	0.66 (0.33–1.33)
Multivariable-adjusted model 1*	1.0 (referent)	0.54 (0.25–1.20)	0.41 (0.21–0.79)	0.49 (0.23–1.05)	0.59 (0.29–1.20)
Multivariable-adjusted model 2†	1.0 (referent)	0.55 (0.25–1.22)	0.43 (0.22–0.83)	0.56 (0.26–1.22)	0.75 (0.36–1.53)

* Adjusted for age, smoking (number of cigarettes smoked per day), body mass index, diabetes, valvular heart disease, and hypertension.
 † Adjusted for high-density lipoprotein cholesterol level in addition to variables included in model 1.

In men who consumed 42 drinks/wk or more, 3 cases of congestive heart failure occurred during 752 person-years of follow-up. In women who consumed 28 drinks/wk or more, 2 cases of congestive heart failure occurred during 364 person-years of follow-up. After adjustment for age, smoking, body mass index, diabetes, valvular heart disease, and hypertension, the hazard ratio for congestive heart failure was 0.6 (95% CI, 0.2 to 2.1) in men who consumed 42 drinks/wk or more and 2.0 (CI, 0.5 to 8.7) in women who consumed 28 drinks/wk, compared with nondrinkers.

In men, the age-adjusted incidence of death from noncardiovascular causes was 15.4 deaths/1000 person-years (CI, 11.3 to 19.6 deaths/1000 person-years) in nondrinkers and 10.9 deaths/1000 person-years (CI, 8.1 to 13.8 deaths/1000 person-years) in men who consumed 15 drinks/wk or more. In women, the age-adjusted incidence of death from noncardiovascular causes was 9.3 deaths/1000 person-years (CI, 7.3 to 11.2 deaths/1000 person-years) in nondrinkers and 10.0

deaths/1000 person-years (CI, 6.8 to 13.1 deaths/1000 person-years) in women who consumed 8 drinks/wk or more.

Alcohol Consumption and Risk for Congestive Heart Failure without Preceding Myocardial Infarction

During follow-up, 162 myocardial infarctions occurred in men and 102 myocardial infarctions occurred in women. In men, 71 cases of congestive heart failure (72% of all cases) occurred without preceding myocardial infarction during 25 802 person-years. In women, 85 cases of congestive heart failure (71% of all cases) occurred without preceding myocardial infarction during 35 456 person-years. Table 4 shows the age-adjusted incidence of congestive heart failure without preceding myocardial infarction in men and women, by level of alcohol consumption.

Risk for congestive heart failure without preceding myocardial infarction was reduced among men who

Table 6. Risk for Congestive Heart Failure in Women, by Level of Alcohol Consumption

Disease	Hazard Ratio (95% CI)				
	Nondrinkers	Former Drinkers	1–2 Drinks/wk	3–7 Drinks/wk	≥8 Drinks/wk
All-cause congestive heart failure					
Age-adjusted model	1.0 (referent)	1.06 (0.66–1.70)	0.73 (0.43–1.24)	0.49 (0.25–0.96)	0.81 (0.45–1.48)
Multivariable-adjusted model 1*	1.0 (referent)	1.11 (0.69–1.78)	0.77 (0.45–1.30)	0.53 (0.27–1.03)	0.80 (0.44–1.46)
Multivariable-adjusted model 2†	1.0 (referent)	1.15 (0.72–1.86)	0.82 (0.48–1.39)	0.60 (0.31–1.18)	1.04 (0.56–1.92)
Congestive heart failure without preceding myocardial infarction					
Age-adjusted model	1.0 (referent)	0.86 (0.47–1.59)	0.98 (0.55–1.76)	0.51 (0.23–1.11)	0.84 (0.41–1.70)
Multivariable-adjusted model 1*	1.0 (referent)	0.91 (0.50–1.69)	1.07 (0.60–1.90)	0.55 (0.25–1.20)	0.83 (0.41–1.70)
Multivariable-adjusted model 2†	1.0 (referent)	0.95 (0.51–1.75)	1.13 (0.63–2.01)	0.60 (0.27–1.33)	1.02 (0.49–2.10)

* Adjusted for age, smoking (number of cigarettes smoked per day), body mass index, diabetes, valvular heart disease, and hypertension.
 † Adjusted for high-density lipoprotein cholesterol level in addition to variables included in model 1.

consumed 1 to 7 drinks/wk compared with nondrinkers after adjustment for multiple predictors of congestive heart failure, including HDL cholesterol level (Table 5). In women, no association was seen between alcohol consumption and risk for congestive heart failure without preceding myocardial infarction (Table 6). Men and women in the highest categories of alcohol consumption (≥ 15 drinks/wk and ≥ 8 drinks/wk, respectively) had no greater risk for congestive heart failure without preceding myocardial infarction than did nondrinkers.

DISCUSSION

In our community-based sample, risk for congestive heart failure was lower among men at all levels of alcohol consumption compared with nondrinkers, before and after adjustment for multiple predictors of congestive heart failure. The lowest hazard ratio for congestive heart failure was seen in men who consumed 8 to 14 drinks/wk. The observed association between alcohol consumption and risk for congestive heart failure in men was not affected by adjustment for hypertension, but it was mildly attenuated by adjustment for HDL cholesterol. Among women, age-adjusted risk for congestive heart failure was lower among women who consumed 3 to 7 drinks/wk than in nondrinkers. This association remained marginally statistically significant after adjustment for multiple predictors of congestive heart failure. No level of alcohol consumption in men or women was associated with increased risk for congestive heart failure.

Alcohol Consumption and Left Ventricular Function

Case series (1) and case-control studies (2, 3, 35) have found a high prevalence left ventricular dysfunction among asymptomatic persons who consume large quantities of alcohol (>5 drinks/d). In community-based samples that consume less alcohol, cross-sectional studies have demonstrated only modest associations between alcohol consumption and subclinical abnormalities of left ventricular structure and function (9, 36). In the Framingham Heart Study sample, Manolio and colleagues found an association between alcohol consumption and echocardiographic left ventricular mass in men but not women (9). In men, alcohol intake was related to both left ventricular hypertrophy and left ventricular dilation, and this association was independent of systolic blood pressure. Kupari and Koskinen (36) studied the

effects of alcohol consumption on echocardiographic left ventricular function in 93 persons without coronary heart disease who were drawn randomly from the population. Alcohol intake was not associated with left ventricular mass but was associated with increased left ventricular systolic dimension and reduced fractional shortening.

Alcohol Consumption, Coronary Heart Disease, and Congestive Heart Failure

Numerous large, prospective cohort studies have found that moderate alcohol consumption is associated with reduced risk for coronary heart disease and myocardial infarction (11–14). Myocardial infarction, in turn, is an important precursor of congestive heart failure (15–18). Protective effects of moderate alcohol intake against myocardial infarction may offset any potential negative effect of alcohol on ventricular function. Consistent with this hypothesis, Cooper and associates (37) reported that light to moderate alcohol consumption was not associated with increased risk for congestive heart failure progression among patients with ischemic left ventricular systolic dysfunction, but it was associated with a trend toward increased risk for hospitalization for congestive heart failure in patients with nonischemic left ventricular systolic dysfunction. Thus, protective effects of alcohol consumption against coronary heart disease may account for the inverse association between alcohol consumption and congestive heart failure that we observed.

Moderate alcohol consumption increases serum levels of HDL cholesterol (38). High-density lipoprotein cholesterol has been estimated to account for approximately 50% of the protective effect of alcohol against coronary heart disease (39, 40). Adjustment for HDL cholesterol level in our study slightly attenuated the inverse association between moderate alcohol consumption and risk for congestive heart failure in men. This suggests that part of the protective effect of alcohol against congestive heart failure may be related to an alcohol-mediated increase in serum HDL cholesterol levels.

If alcohol consumption protects against congestive heart failure primarily by preventing myocardial infarction, the lower risk for congestive heart failure among drinkers would be expected to result from a lower risk for myocardial infarction. Conversely, risk for conges-

tive heart failure in the absence of myocardial infarction would be expected to be nearly the same among both drinkers and nondrinkers. To test this hypothesis, we repeated our analysis after censoring participants with interim myocardial infarction. We found that risk for congestive heart failure without preceding myocardial infarction was significantly reduced in men in the lowest alcohol intake category (1 to 7 drinks/wk) compared with nondrinkers. Relatively few end points were available for this secondary analysis, and we had limited statistical power. Nonetheless, for men in the highest drinking categories, the risk for congestive heart failure without preceding myocardial infarction was similar to those for all-cause congestive heart failure. Our data are consistent with those of previous reports (41) showing that a lower risk for myocardial infarction among drinkers does not entirely explain the inverse association between moderate alcohol consumption and risk for congestive heart failure.

Heavy Alcohol Consumption and Risk for Congestive Heart Failure

Chronic, excessive alcohol consumption has been proposed as a major cause of cardiomyopathy in industrialized countries, such as the United States (42, 43). In our sample, 23% of men consumed 15 drinks/wk or more and 17% of women consumed 8 drinks/wk or more, levels of alcohol consumption that are considered by the National Institute of Alcohol Abuse and Alcoholism to constitute heavy drinking (25). At this level of alcohol consumption, we observed no increased risk for congestive heart failure compared with nondrinkers. In fact, among men who consumed 15 drinks/wk or more (mean alcohol consumption, 27.3 drinks/wk), the multivariable-adjusted risk for congestive heart failure was significantly reduced compared with nondrinkers (hazard ratio, 0.52 [CI, 0.28 to 0.96]). This was particularly surprising, given that people may underreport alcohol consumption because of the social stigma associated with excessive drinking.

It is possible that alcohol-mediated cardiomyopathy occurs only at higher levels of alcohol consumption than observed in our study sample, or that it may require coexisting malnutrition or genetic predisposition. In addition, because heavy drinkers have increased mortality from cirrhosis, injuries, violence, suicide, and certain

cancers (11), they may die before they clinically manifest alcohol-related cardiomyopathy. However, in our sample, the age-adjusted incidence of death from noncardiovascular causes in participants in the highest categories of alcohol consumption was similar to that in nondrinkers, suggesting that our findings are not a result of an excess of deaths due to alcohol-related illnesses among heavy drinkers.

Alcohol Consumption, Hypertension, and Congestive Heart Failure

Although heavy alcohol consumption is an important cause of hypertension, moderate alcohol consumption appears to have at most a modest effect on blood pressure (8, 44). In our study, controlling for hypertension did not affect the inverse association between moderate alcohol consumption and risk for congestive heart failure, suggesting that alcohol intake at the levels observed in our study contributes little to hypertension-mediated myocardial dysfunction. At higher levels of consumption, protective effects of alcohol against coronary heart disease may be offset by alcohol-related hypertensive heart disease.

Sex Differences in the Association of Alcohol Consumption and Congestive Heart Failure

Among men, drinkers had a lower risk for congestive heart failure than did nondrinkers. Although we observed a reduction in the age-adjusted risk for congestive heart failure among women who consumed 3 to 7 drinks/wk compared with nondrinkers, this association was only marginally statistically significant after adjustment for multiple predictors of congestive heart failure.

Some (45–47) but not all (36) studies have reported sex-related differences in the response of the myocardium to alcohol. Studies of alcoholic persons without overt cardiomyopathy (45, 46) have had conflicting results regarding the differential effects of alcohol on ventricular function in men and women. Wu and colleagues (45) reported that subclinical abnormalities of ventricular systolic function are more common in men than women at comparable levels of alcohol consumption. In contrast, Urbano-Márquez and colleagues (46) reported that women develop ventricular systolic dysfunction at lower levels of alcohol consumption compared with men, and Fernández-Solà and associates (47) found that

women develop alcoholic cardiomyopathy at a lower total lifetime dose of alcohol compared with men.

Data are sparse on sex-specific differences in the association between alcohol consumption and risk for congestive heart failure at the more modest levels of alcohol intake commonly encountered in the community. In our study, the inverse association between alcohol consumption and risk for congestive heart failure was less pronounced in women than men. It is possible that women are susceptible to alcohol-mediated ventricular dysfunction at relatively low levels of alcohol intake, thereby diminishing the potentially protective effects of alcohol against congestive heart failure.

Limitations

First, we relied on self-reporting of alcohol intake, which may result in misclassification of exposure status. Random misclassification would be expected to weaken the observed association of alcohol consumption with risk for congestive heart failure and bias our results toward the null. Alternatively, selective misclassification of heavy drinkers as nondrinkers may account for the increased risk for congestive heart failure seen among participants who reported no alcohol intake. This is unlikely, however, because we observed a positive association between alcohol consumption and HDL cholesterol level in both men and women, a finding that supports the rank-order validity of self-reported alcohol intake. Second, we did not adjust for drinking pattern and beverage type. Alcohol consumption patterns (for example, binge drinking versus regular alcohol consumption) and type of beverage consumed (beer, wine, or spirits) may affect risk for congestive heart failure independently of total alcohol intake. Third, alcoholic cardiomyopathy may occur at a relatively young age. If so, the heaviest drinkers may have developed congestive heart failure before entry into our study. Finally, nondrinkers, who served as the reference group in our study, may include both lifelong abstainers and former drinkers. Former drinkers may be at increased risk for cardiovascular disease relative to mild to moderate drinkers, potentially obscuring deleterious effects of alcohol consumption on risk for congestive heart failure. We attempted to account for this by using as our reference group only participants who reported consuming less than 1 drink/wk at both the index examination and an

examination 6 to 10 years before the index examination. Risk for congestive heart failure in former drinkers did not differ significantly from that in nondrinkers in our study.

Our findings should be interpreted with caution. We excluded persons with congestive heart failure at baseline, and our results therefore do not apply to persons with existing congestive heart failure. In addition, although we found no increase in risk for congestive heart failure among participants in the highest categories of alcohol intake, other studies have shown increased overall mortality due to alcohol-related illnesses among persons reporting similar levels of alcohol consumption (11). Recommendations by health professionals regarding alcohol consumption should take into account the overall health effects of alcohol.

In conclusion, in our community-based sample, alcohol was not associated with increased risk for congestive heart failure among persons with heavy alcohol consumption (≥ 15 drinks/wk in men and ≥ 8 drinks/wk in women) and was associated with a lower risk for congestive heart failure when consumed in moderation. Accounting for the effects of alcohol on risk for myocardial infarction did not entirely explain the apparent protective effects of alcohol against congestive heart failure.

From the National Heart, Lung, and Blood Institute's Framingham Heart Study, National Institutes of Health, Framingham, Massachusetts; Massachusetts General Hospital, Boston University School of Medicine, Beth Israel-Deaconess Medical Center, and Harvard Medical School, Boston, Massachusetts.

Grant Support: By contract N01-HC-38038 from the National Heart, Lung, and Blood Institute and grant AR/AG 41398 from the National Institutes of Health. Dr. Vasani was supported in part by a research career award 1K24 HL04334 from the National Heart, Lung, and Blood Institute.

Requests for Single Reprints: Daniel Levy, MD, Framingham Heart Study, 5 Thurber Street, Framingham, MA 01702.

Current Author Addresses: Drs. Walsh, Larson, Evans, Vasani, and Levy: Framingham Heart Study, 5 Thurber Street, Framingham, MA 01702.

Drs. Djousse and Ellison: Preventive Medicine, Room B-612, Boston University School of Medicine, 715 Albany Street, Boston, MA 02118.

Author Contributions: Conception and design: C.R. Walsh, M.G. Larson, J.C. Evans, D. Levy.

Analysis and interpretation of the data: C.R. Walsh, M.G. Larson, J.C. Evans, R.C. Ellison, R.S. Vasani, D. Levy.
 Drafting of the article: C.R. Walsh, R.C. Ellison, R.S. Vasani, D. Levy.
 Critical revision of the article for important intellectual content: C.R. Walsh, M.G. Larson, L. Djousse, R.C. Ellison, R.S. Vasani, D. Levy.
 Final approval of the article: C.R. Walsh, L. Djousse, R.C. Ellison, R.S. Vasani, D. Levy.
 Statistical expertise: M.G. Larson.
 Collection and assembly of data: L. Djousse.

References

- Bertolet BD, Freund G, Martin CA, Perchalski DL, Williams CM, Pepine CJ. Unrecognized left ventricular dysfunction in an apparently healthy alcohol abuse population. *Drug Alcohol Depend*. 1991;28:113-9. [PMID: 1935563]
- Kupari M, Koskinen P, Suokas A. Left ventricular size, mass and function in relation to the duration and quantity of heavy drinking in alcoholics. *Am J Cardiol*. 1991;67:274-9. [PMID: 1825010]
- Dancy M, Bland JM, Leech G, Gaitonde MK, Maxwell JD. Preclinical left ventricular abnormalities in alcoholics are independent of nutritional status, cirrhosis, and cigarette smoking. *Lancet*. 1985;1:1122-5. [PMID: 2860335]
- Prazak P, Pfisterer M, Osswald S, Buser P, Burkart F. Differences of disease progression in congestive heart failure due to alcoholic as compared to idiopathic dilated cardiomyopathy. *Eur Heart J*. 1996;17:251-7. [PMID: 8732379]
- Patel VB, Corbett JM, Richardson PJ, Dunn MJ, Preedy VR. Chronic effects of alcohol upon protein profiling in ventricular tissue. *Biochem Soc Trans*. 1995;23:461S. [PMID: 8566354]
- Byrne-Quinn E, Fessas C. Beriberi heart disease in London. *Br Med J*. 1969;4:25-8. [PMID: 5822083]
- Gordon T, Kannel WB. Drinking and its relation to smoking, BP, blood lipids, and uric acid. The Framingham study. *Arch Intern Med*. 1983;143:1366-74. [PMID: 6870410]
- Klatsky AL, Friedman GD, Siegelau AB, Gérard MJ. Alcohol consumption and blood pressure Kaiser-Permanente Multiphasic Health Examination data. *N Engl J Med*. 1977;296:1194-200. [PMID: 854058]
- Manolio TA, Levy D, Garrison RJ, Castelli WP, Kannel WB. Relation of alcohol intake to left ventricular mass: The Framingham Study. *J Am Coll Cardiol*. 1991;17:717-21. [PMID: 1825213]
- Alexander CS. Cobalt-beer cardiomyopathy. A clinical and pathologic study of twenty-eight cases. *Am J Med*. 1972;53:395-417. [PMID: 4263183]
- Thun MJ, Peto R, Lopez AD, Monaco JH, Henley SJ, Heath CW Jr, et al. Alcohol consumption and mortality among middle-aged and elderly U.S. adults. *N Engl J Med*. 1997;337:1705-14. [PMID: 9392695]
- Camargo CA Jr, Hennekens CH, Gaziano JM, Glynn RJ, Manson JE, Stampfer MJ. Prospective study of moderate alcohol consumption and mortality in US male physicians. *Arch Intern Med*. 1997;157:79-85. [PMID: 8996044]
- Fuchs CS, Stampfer MJ, Colditz GA, Giovannucci EL, Manson JE, Kawachi I, et al. Alcohol consumption and mortality among women. *N Engl J Med*. 1995;332:1245-50. [PMID: 7708067]
- Friedman LA, Kimball AW. Coronary heart disease mortality and alcohol consumption in Framingham. *Am J Epidemiol*. 1986;124:481-9. [PMID: 3740047]
- Kannel WB, Belanger AJ. Epidemiology of heart failure. *Am Heart J*. 1991;121:951-7. [PMID: 2000773]
- Senni M, Tribouilloy CM, Rodeheffer RJ, Jacobsen SJ, Evans JM, Bailey KR, et al. Congestive heart failure in the community: a study of all incident cases in Olmsted County, Minnesota, in 1991. *Circulation*. 1998;98:2282-9. [PMID: 9826315]
- Eriksson H, Svärdsudd K, Larsson B, Ohlson LO, Tibblin G, Welin L, et al. Risk factors for heart failure in the general population: the study of men born in 1913. *Eur Heart J*. 1989;10:647-56. [PMID: 2788575]
- Remes J, Reunanen A, Aromaa A, Pyörälä K. Incidence of heart failure in eastern Finland: a population-based surveillance study. *Eur Heart J*. 1992;13:588-93. [PMID: 1618198]
- Kannel WB, Feinleib M, McNamara PM, Garrison RJ, Castelli WP. An investigation of coronary heart disease in families. The Framingham offspring study. *Am J Epidemiol*. 1979;110:281-90. [PMID: 474565]
- Feinleib M, Kannel WB, Garrison RJ, McNamara PM, Castelli WP. The Framingham Offspring Study. Design and preliminary data. *Prev Med*. 1975;4:518-25. [PMID: 1208363]
- Gordon T. Some methodological problems in the long-term study of cardiovascular disease: observations on the Framingham Study. *J Chronic Dis*. 1959;10:186-206.
- Dawber TR. An approach to longitudinal studies in a community: the Framingham study. *Ann N Y Acad Sci*. 1963;107:539-56.
- Felson DT, Kiel DP, Anderson JJ, Kannel WB. Alcohol consumption and hip fractures: the Framingham Study. *Am J Epidemiol*. 1988;128:1102-10. [PMID: 3189283]
- U.S. Department of Agriculture, Agricultural Research Service. 1999. USDA Nutrient Database for Standard Reference, Release 13. Available at www.nal.usda.gov/fnic/foodcomp. Accessed 8 January 2001.
- National Institute on Alcohol Abuse and Alcoholism. The Physician's Guide to Helping Patients with Alcohol Problems. Bethesda, MD: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism; 1995. Publication no. NIH 95-3769.
- The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med*. 1997;157:2413-46. [PMID: 9385294]
- Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. National Diabetes Data Group. *Diabetes*. 1979;28:1039-57. [PMID: 510803]
- Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by electrocardiogram. Prevalence, incidence, and mortality in the Framingham study. *Ann Intern Med*. 1969;71:89-105. [PMID: 4239887]
- McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med*. 1971;285:1441-6. [PMID: 5122894]
- Mosterd A, Deckers JW, Hoes AW, Nederpel A, Smeets A, Linker DT, et al. Classification of heart failure in population based research: an assessment of six heart failure scores. *Eur J Epidemiol*. 1997;13:491-502. [PMID: 9258559]
- Marantz PR, Tobin JN, Wassertheil-Smolter S, Steingart RM, Wexler JP, Budner N, et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. *Circulation*. 1988;77:607-12. [PMID: 3342491]
- Cox DR. Regression models and life tables. *Journal of the Royal Statistical Society*. 1972;34:187-220.
- Andersen PK, Gill RD. Cox's regression model for counting processes: a large sample study. *Annals of Statistics*. 1982;10:1100-20.
- SAS Institute Inc. SAS/STAT Software: Changes and Enhancements through Release 6.11. Cary, NC: SAS Institute; 1996:807-84.
- Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E. The effects of alcoholism on skeletal and cardiac muscle. *N Engl J Med*. 1989;320:409-15. [PMID: 2913506]

36. Kupari M, Koskinen P. Relation of left ventricular function to habitual alcohol consumption. *Am J Cardiol.* 1993;72:1418-24. [PMID: 8256737]
37. Cooper HA, Exner DV, Domanski MJ. Light-to-moderate alcohol consumption and prognosis in patients with left ventricular systolic dysfunction. *J Am Coll Cardiol.* 2000;35:1753-9. [PMID: 10841221]
38. Haskell WL, Camargo C Jr, Williams PT, Vranizan KM, Krauss RM, Lindgren FT, et al. The effect of cessation and resumption of moderate alcohol intake on serum high-density-lipoprotein subfractions. A controlled study. *N Engl J Med.* 1984;310:805-10. [PMID: 6366553]
39. Criqui MH, Cowan LD, Tyroler HA, Bangdiwala S, Heiss G, Wallace RB, et al. Lipoproteins as mediators for the effects of alcohol consumption and cigarette smoking on cardiovascular mortality: results from the Lipid Research Clinics Follow-up Study. *Am J Epidemiol.* 1987;126:629-37. [PMID: 3631053]
40. Suh I, Shaten BJ, Cutler JA, Kuller LH. Alcohol use and mortality from coronary heart disease: the role of high-density lipoprotein cholesterol. The Multiple Risk Factor Intervention Trial Research Group. *Ann Intern Med.* 1992;116:881-7. [PMID: 1580443]
41. Abramson JL, Williams SA, Krumholz HM, Vaccarino V. Moderate alcohol consumption and risk of heart failure among older persons. *JAMA.* 2001;285:1971-7. [PMID: 11308433]
42. McKenna CJ, Codd MB, McCann HA, Sugrue DD. Alcohol consumption and idiopathic dilated cardiomyopathy: a case control study. *Am Heart J.* 1998;135:833-7. [PMID: 9588413]
43. Fuster V, Gersh BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL. The natural history of idiopathic dilated cardiomyopathy. *Am J Cardiol.* 1981;47:525-31. [PMID: 7468489]
44. Marmot MG, Elliott P, Shipley MJ, Dyer AR, Ueshima H, Beevers DG, et al. Alcohol and blood pressure: the INTERSALT study. *BMJ.* 1994;308:1263-7. [PMID: 7802765]
45. Wu CF, Sudhaker M, Ghazanfar J, Ahmed SS, Regan TJ. Preclinical cardiomyopathy in chronic alcoholics: a sex difference. *Am Heart J.* 1976;91:281-6. [PMID: 1258724]
46. Urbano-Márquez A, Estruch R, Fernández-Solà J, Nicolás JM, Paré JC, Rubin E. The greater risk of alcoholic cardiomyopathy and myopathy in women compared with men. *JAMA.* 1995;274:149-54. [PMID: 7596003]
47. Fernández-Solà J, Estruch R, Nicolás JM, Paré JC, Sacanella E, Antúnez E, et al. Comparison of alcoholic cardiomyopathy in women versus men. *Am J Cardiol.* 1997;80:481-5. [PMID: 9285662]