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The Association of Alcohol Consumption and Incident Heart Failure

The Cardiovascular Health Study

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OBJECTIVES	We investigated the association between alcohol consumption and incident congestive heart failure (CHF) both overall and after adjusting for incident myocardial infarction (MI).
BACKGROUND	Moderate alcohol consumption has been associated with lower risk of CHF and MI.
METHODS	The Cardiovascular Health study, a prospective cohort study of cardiovascular disease risk factors and outcomes, followed 5,888 subjects ≥ 65 years old for 7 to 10 years. Cox models were used to estimate the adjusted risk of CHF by reported alcohol consumption.
RESULTS	There were 5,595 subjects at baseline at risk for incident CHF with alcohol data and 1,056 events during follow-up. Compared with abstainers, the adjusted risk of CHF was lower among subjects who reported consuming 1 to 6 drinks per week (hazard ratio [HR] 0.82, 95% confidence interval [CI] 0.67 to 1.00, $p = 0.05$) and 7 to 13 drinks per week (HR 0.66, 95% CI 0.47 to 0.91, $p = 0.01$). Time-dependent adjustment for incident MI altered only slightly the association between moderate alcohol consumption and CHF (for 1 to 6 drinks per week, HR 0.84, 95% CI 0.65 to 1.04; for 7 to 13 drinks per week, HR 0.69, 95% CI 0.49 to 0.99). Baseline former drinkers had a higher risk of CHF than abstainers (HR 1.51, $p < 0.01$), but those who quit during the study did not have a higher risk (HR 0.83, 95% CI 0.66 to 1.03).
CONCLUSIONS	Moderate alcohol use is associated with a lower risk of incident CHF among older adults, even after accounting for incident MI and other factors. (J Am Coll Cardiol 2006;48:305–11) © 2006 by the American College of Cardiology Foundation

The association between alcohol consumption and congestive heart failure (CHF) is controversial; heavy alcohol consumption is associated with alcoholic cardiomyopathy (1,2), while moderate alcohol intake may be associated with a lower risk of incident CHF (3,4). Prior cohort studies have suggested that the lower risk of clinical CHF may not be mediated by the lower incidence of myocardial infarction (MI) associated with moderate alcohol consumption, but they have had limited power to examine fully the association between alcohol consumption and CHF while accounting for MI and other risk factors for CHF.

We undertook this study to examine the relationship between alcohol consumption and incident CHF while accounting for incident nonfatal MI and other factors in a

cohort of older adults. To further examine this relationship, we also investigated the effects of prior and recent alcohol cessation on the risk of CHF.

METHODS

Description of cohort. The original CHS (Cardiovascular Health Study) cohort of 5,201 individuals was recruited from 1989 to 1990 using Medicare eligibility lists from Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania. Eligible participants included community dwelling individuals age 65 years and older who were expected to remain within the area for at least 3 years. A second cohort of 687 African Americans was recruited from 1992 to 1993. Subjects were followed prospectively through June 30, 2001. The full design and rationale of the CHS has been described elsewhere (5,6).

Baseline status, laboratory data, exercise, and alcohol consumption. The baseline and annual follow-up examinations included standardized medical history questionnaires, physical examination, and resting electrocardiography. Echocardiography was performed at baseline for the main cohort and in the second year of follow-up for the African American cohort. Participants were classified at baseline for pre-existing cardiovascular disease by hospital

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Abbreviations and Acronyms

CHF	= congestive heart failure
CHS	= Cardiovascular Health Study
CI	= confidence interval
ECG	= electrocardiogram
HR	= hazard ratio
LV	= left ventricle/ventricular
MI	= myocardial infarction

records and physician confirmation (6). Procedures for acquisition of laboratory values, echocardiograms, and regular exercise levels have been described previously (7–10).

Alcohol consumption was classified as in prior publications (11). An alcoholic beverage was defined as a 12-oz beer, a 6-oz glass of wine, or a shot of liquor, and consumption reported as the number of alcoholic beverages reported consumed per week. Baseline consumption was determined at the initial visit, and former drinkers were differentiated from abstainers (never-drinkers). Alcohol consumption was ascertained in a similar manner in follow-up years 2 through 5 and 7 through 9, but was not obtained in follow-up years 1 and 6 for administrative reasons. Years with complete data were used in updated, time-dependent analyses. For these analyses, subjects were classified as abstainers if they did not report any alcohol use during the entire follow-up period, as quitting during the study if they reported alcohol use in a prior exam year but no use in the current year, and as quitting before the study if they were a former drinker at baseline.

Ascertainment of incident CHF and MI. The method of ascertaining incident cardiovascular events in CHS has been described previously (12). Potential events were ascertained by participant report at the time of the event and by field center surveillance semiannually, alternating between annual clinic visits and telephone calls. The CHS Events Committee reviewed all event data, including symptoms, signs, cardiac enzymes, serial electrocardiograms (ECG), and chest X-ray findings. Diagnosis of an incident episode of CHF required the diagnosis of CHF by a physician and confirmation by diagnostic tests or the treatment of CHF, such as new treatment with a diuretic agent, digitalis, or a vasodilator, following a standardized algorithm (12). Events were classified as probable, rather than definite, if data were incomplete or ambiguous. Only definite incident CHF events were included in these analyses; inclusion of probable CHF events did not significantly alter the findings. Incident nonfatal MI was adjudicated by the committee using standardized criteria that included ECG findings and elevated cardiac enzymes gleaned from medical records. A diagnosis of silent MI was made if changes on the annual surveillance ECG met standardized ECG criteria for MI (13). Incident nonfatal MI included both clinical and silent events for these analyses.

Statistical analysis. We compared the distributions of baseline covariates according to alcohol consumption with

analysis of variance for linear variables and chi-square tests for categorical or binary variables.

Two main analyses were conducted on the association between baseline alcohol consumption and CHF: one including all subjects at risk for CHF, and a second that was restricted to subjects without a history of MI at baseline and adjusted for incident nonfatal MI. Cox models were used to estimate the hazard ratios (HRs) associated with alcohol consumption after adjustment for confounding factors. Follow-up ceased at the occurrence of incident CHF, death, or the end of the follow-up period, with incident CHF as the end point of interest; we examined a combined end point of incident CHF and cardiovascular death as a secondary outcome. Nonfatal MI was accounted for in a time-dependent manner. The proportional hazards assumption was evaluated with Schoenfeld residual-based tests globally and for each covariate, with no violations detected (14).

Alcohol consumption may be a marker for better underlying health, and drinkers may have better health status than non-drinkers if patients stopped drinking because of sickness (sick quitter effect) or if only healthier drinkers survived to older age (healthy survivor effect) (15). In addition to segregating former drinkers into a separate group, we performed two additional sensitivity analyses to address potential confounding by health status. First, lagged analyses were performed examining the association between baseline alcohol consumption and events occurring after an imposed delay of 1 to 5 years, so that we included only events that occurred between the conclusion of the delay time and the censor date. Second, a model using annually updated alcohol consumption as a time-dependent variable was performed. Quadratic models with linear and squared terms for alcohol consumption were used to test for non-linear relationships.

Multivariate Cox models included adjustment for age, race, gender, smoking status (current, former, never), education (up to high school vs. vocational school or college), income, marital status (married, widowed, divorced, separated, never married), exercise intensity, diabetes status (normal, impaired fasting glucose, American Diabetes Association-defined diabetes), and body mass index. Sensitivity analyses included additional adjustment for depressive symptoms, pack-years of smoking, echocardiographically defined semiquantitative left ventricular (LV) systolic function and fractional shortening, ECG-defined LV hypertrophy and echocardiographically calculated LV mass (16), use of diuretics, beta-blockers, calcium-channel blockers, digoxin, and vasodilators at baseline, treated hypertension, and blood pressure. Models adjusting for blood pressure used annually obtained average sitting systolic and diastolic pressures as time-dependent covariates. Blood pressure, age, income, body mass index, and exercise intensity were modeled as linear terms; use of body mass index in quintiles did not affect analyses. Participants reported their health status at baseline and yearly during follow-up; the response

Table 1. Characteristics of CHS Participants At Risk for Incident CHF According to Baseline Alcohol Consumption

	Weekly Number of Drinks						p Value*
	None	Former	<1	1–6	7–13	14+	
Number	2,280	487	1,073	972	341	442	
Age (yrs)	73.1	72.6	72.6	72.1	72.9	72.1	<0.01
Women, %	71	40	63	46	43	39	<0.01
African American, %	20	24	12	11	6	9	<0.01
Married, %	63	62	66	72	74	77	<0.01
Current smoker, %	14	9	12	14	11	20	<0.01
Former smoker, %	56	29	42	51	52	60	<0.01
Hypertension, %							
Treated	40	41	35	32	25	38	<0.01
Untreated	14	10	9	9	10	10	0.06
Systolic avg	138	139	136	134	133	139	<0.01
Diastolic avg	71	72	71	71	71	73	0.05
BMI (kg/m ²)	27.2	26.7	26.6	26.4	25.4	25.6	<0.01
Diabetes—ADA	20	27	11	11	8	11	<0.01
Baseline status, %							
MI	11	8	8	8	8	7	0.16
Angina	16	15	15	14	14	10	0.06
Stroke	4	6	3	4	3	3	0.02
TIA	4	3	2	2	2	4	0.12
Claudication	4	2	2	2	0	3	0.01
Baseline LV function, %							
Abnormal LV function, %	3	5	2	3	2	2	0.04
HDL	53	52	54	55	57	62	<0.01
LDL	132	129	131	129	129	127	<0.01
Triglycerides	145	139	140	135	127	131	<0.01
HS or college, %	61	57	78	83	88	85	<0.01
Income >16,000/yr, %	47	49	62	74	75	76	
High exercise, %	6	8	12	15	16	15	<0.01

*The p values derived from analysis of variance for continuous variables and chi-square tests for categorical or binary variables.

ADA = American Diabetes Association; avg = average; BMI = body mass index; CHF = congestive heart failure; CHS = Cardiovascular Health Study; HDL = high-density lipoprotein; HS = high school; LDL = low-density lipoprotein; LV = left ventricular; MI = myocardial infarction; TIA = transient ischemic attack; 16K = \$16,000.00/yr.

was dichotomized into poor-to-fair versus good-to-excellent health.

RESULTS

Of the original 5,888 CHS participants, 275 subjects had prevalent CHF at baseline, leaving 5,613 subjects at risk for incident CHF. Among these, baseline alcohol data were available on 5,595 subjects (Table 1). As expected (11), heavier consumption was more common among those who were white, men, and former smokers. Prevalent cardiovascular disease at the baseline examination was more common among former drinkers, who also tended to have a higher prevalence of abnormal baseline two-dimensional echocardiographic LV function. High-density lipoprotein cholesterol levels were directly related to alcohol consumption.

There were 1,056 events during 49,389 person-years accrued over all consumption categories. A U-shaped relationship was observed in the unadjusted incidence rates (Fig. 1), with the lowest rate of 14 per 1,000 person-years (95% confidence interval [CI] 10 to 19 per 1,000 person-years) occurring among participants who consumed 7 to 13 drinks per week. Both linear and quadratic terms in an unadjusted Cox model were significant ($p < 0.01$ for both).

Adjusted risk of CHF without adjustment for MI. Compared with abstinence, moderate consumption (1 to 6 drinks per week and 7 to 13 drinks per week) was associated with a lower risk of incident CHF after multivariate adjustment (Table 2). Models testing the significance of a quadratic relationship term found the linear term to be significant ($p = 0.04$), but not the quadratic term ($p = 0.18$). In analyses restricted to drinkers, consumption of 7 to 13

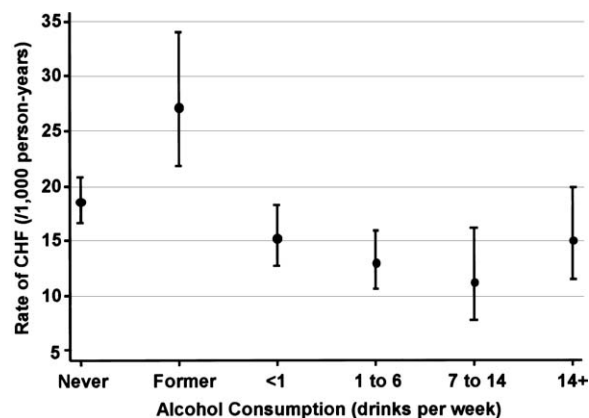


Figure 1. Rate of incident congestive heart failure (CHF) by alcohol consumption category.

Table 2. Hazard Ratios for Incident CHF According to Baseline Alcohol Consumption

Alcohol Intake	All Subjects, Not Adjusted for MI n = 5,595				Subjects Without a Prior MI n = 5,146				Subjects Without CV Disease at Baseline n = 4,368*						
	Person-Yrs	Incident CHF	HR†	95% CI	p Value	Person-Yrs	Incident CHF	HR‡	95% CI	p Value	Person-Yrs	Incident CHF	HR‡	95% CI	p Value
None	19,974	457	1	referent	—	18,809	392	1	referent	—	16,247	302	1	referent	0.001
Former	3,618	136	1.51	1.23-1.85	<0.001	3,332	110	1.58	1.26-1.98	<0.001	2,866	78	1.47	1.13-1.92	0.26
<1	9,760	187	0.90	0.75-1.08	0.27	9,059	153	0.88	0.72-1.08	0.21	7,898	120	0.88	0.70-1.10	0.13
1-6	8,915	156	0.82	0.67-1.00	0.05	8,319	127	0.84	0.67-1.04	0.11	7,246	94	0.82	0.64-1.06	0.13
7-13	3,109	43	0.65	0.47-0.91	0.01	2,931	36	0.69	0.49-0.99	0.04	2,589	29	0.72	0.48-1.08	0.84
14+	4,011	77	0.87	0.67-1.14	0.32	3,782	66	0.94	0.71-1.26	0.70	3,391	51	0.97	0.70-1.33	0.84

*Restricted to subjects without diagnosed cardiovascular (CV) disease at baseline, including angina, MI, stroke, transient ischemic attack, or claudication; †adjusted for age, race, gender, smoking status, education, income, marital status, exercise intensity, diabetes, and body mass index; ‡adjusted for incident non-fatal myocardial infarction (MI) as a time-dependent variable, in addition to the variables in model 1. CHF = congestive heart failure; CI = confidence interval; HR = hazard ratio.

drinks per week was associated with a lower risk of CHF even when compared with intake of <1 drink per week (HR 0.72, 95% CI 0.51 to 1.02, p = 0.06).

When we examined the composite end point of incident CHF or cardiovascular death in the full cohort, the HRs were 0.94 (95% CI 0.82 to 1.08) among consumers of <1 drink per week, 0.84 (95% CI 0.72 to 0.98) among consumers of 1 to 6 drinks per week, 0.70 (95% CI 0.54 to 0.89) among consumers of 7 to 13 drinks per week, and 0.79 (95% CI 0.64 to 0.98) among consumers of 14+ drinks per week.

Adjusted risk of CHF accounting for reduction in MI. There were 5,146 subjects at baseline without a prior MI at risk for CHF, among whom 331 experienced nonfatal MIs and 884 developed incident CHF. The association between alcohol consumption at baseline and risk of CHF remained evident even after adjusting for the effects of nonfatal MI (Table 2). Linear terms for alcohol consumption were significant (p = 0.05), but the quadratic term was not (p = 0.11). No interaction was found between alcohol consumption, incident MI, and risk of CHF (p = 0.83).

Further adjustment for other risk factors. Adjustment for biochemical variables that could mediate or confound the relationship between alcohol consumption and CHF, including high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, and C-reactive protein, altered the results only slightly (HR by category: <1 drink per week, 0.88, 95% CI 0.73 to 1.06; 1 to 6 drinks per week, 0.84, 95% CI 0.69 to 1.03; 7 to 13 drinks per week, 0.66, 95% CI 0.47 to 0.92; 14+ drinks per week, 0.88, 95% CI 0.67 to 1.17). Adjustment for serum creatinine, depressive symptoms, pack-years of smoking, treated hypertension, use of cardiac medications, echocardiographic measures of LV systolic function, or LV hypertrophy by ECG and echocardiographically estimated LV mass also did not significantly change our results. Additional adjustment for blood pressure as time-varying covariate did not influence our results, although intake of 1 to 6 drinks per week was itself inversely associated (HR 0.81; 95% CI 0.68 to 0.97) and intake of 14+ drinks per week positively associated (HR 1.43; 95% CI 1.13 to 1.81) with incident hypertension during follow-up. There was no evidence that the association of alcohol intake and CHF differed by race (white/non-white), gender, apo-e4 genotype, or baseline ejection fraction (normal vs. abnormal and borderline).

Restriction and sensitivity analyses. Analyses of the association between baseline alcohol consumption and CHF restricted to those without angina, MI, stroke, transient ischemic attack, or claudication at baseline (78% of the cohort) produced similar point estimates compared with baseline analyses, although the CIs for current consumers of alcohol crossed 1 in this smaller cohort (Table 2). Interestingly, the association was also roughly similar among participants confirmed to have had a prior MI at baseline, with HRs of 0.78 (95% CI 0.48 to 1.25) among consumers of 1 to 6 drinks per week, 0.44 (95% CI 0.18 to 1.03) among

consumers of 7 to 13 drinks per week, and 0.85 (95% CI 0.44 to 1.65) among consumers of 14+ drinks per week.

Lagged analyses were conducted between baseline consumption and incident CHF occurring after a delay of 1 to 5 years. The number of events and person-years accrued during follow-up decreased with each additional year of delay, with the fifth lag year having 22,508 person-years and 595 events. The same association seen between consumption of 7 to 14 drinks per week and lower risk of CHF was also observed in lagged analyses. This association remained strong even over 5 years of delayed event ascertainment (HRs by category: <1 drink per week, 0.84, 95% CI 0.67 to 1.07; 1 to 6, 0.78, 95% CI 0.60 to 1.01; 7 to 13, 0.58, 95% CI 0.37 to 0.90, $p = 0.02$; 14+, 0.92, 95% CI 0.66 to 1.28).

The sick quitter hypothesis was examined with a time-dependent model using annually collected alcohol consumption data. While those who quit during the study reported baseline consumption ranging through all consumption categories, they tended to be lighter drinkers, consuming on average 1.3 drinks per week. Subjects classified as former drinkers at baseline had an increased risk of CHF compared with non-drinkers (Table 3); however, subjects who quit during the study demonstrated a statistically non-significant trend toward lower rates of CHF. Adjustment for annual self-reported health status did not change estimates, but broadened CIs slightly, so that the association observed among those consuming 1 to 6 drinks per week was marginally significant (HR 0.73, 95% CI 0.53 to 1.02).

DISCUSSION

In this large cohort study of older adults, there was a lower risk of CHF associated with moderate drinking compared with abstinence. This association was relatively unchanged after accounting for incident nonfatal MI, stronger for moderate drinkers than for occasional drinkers, and absent for participants consuming more than 14 drinks per week. The association persisted in analyses that used a lag of up to 5 years or that used annually reported consumption. Adjustment for plausible intermediates or confounders, including high-density lipoprotein cholesterol, C-reactive protein, treated hypertension, blood pressure, and exercise, did not affect the association. Subjects classified at baseline as

former drinkers had a higher risk of CHF than abstainers, but quitting during the study was not associated with an increased risk of incident CHF.

Because MI is an extremely common risk factor for CHF (17–19), and moderate alcohol consumption is associated with reductions in MI and MI-associated mortality (20–22), reductions in risk of MI during follow-up might have been expected to explain the lower rates of CHF observed among moderate drinkers. Moderate drinking has been associated with a lower risk of death from MI among patients with ischemic LV dysfunction in some (23), but not all (24), studies. Although we could not fully differentiate between ischemic and nonischemic causes of CHF, moderate drinking was associated with a lower risk of CHF even after accounting for clinical and silent nonfatal MI and a variety of other risk factors for MI. This implies that some other mechanism may be responsible for the association between moderate alcohol consumption and a lower risk of incident CHF. If the relationship is indeed causal, the association may be through a mechanism not specific to a particular cause of CHF. For example, alcohol consumption has been shown to lower pulmonary artery wedge pressure and reduce afterload (25), cause systemic arterial vasodilatation (26), and improve endothelial function (27–29) in clinical trials.

Alcohol consumption appears to have a complex relationship with incident CHF and other cardiovascular events. While heavy and prolonged drinking leads to cardiomyopathy (1,2), particularly among genetically susceptible individuals (30), emerging evidence suggests that moderate alcohol consumption is not associated with significant cardiotoxicity. Moderate alcohol consumption appears equivalent to abstinence in improving ejection fraction among heavy drinkers with alcoholic cardiomyopathy (31), and moderate alcohol consumption has been associated with lower risk of CHF in prior studies of healthy individuals (3,4). Taken together with our results, these data suggest an inverse association between moderate alcohol consumption and incident CHF that is not entirely mediated through reduction in nonfatal MI.

Study limitations. As in any observational study, confounding by factors unmeasured or poorly measured in our

Table 3. Hazard Ratios for Incident CHF According to Current Alcohol Consumption

Consumption Group	All Subjects, n = 5,595				
	Person-Yrs	Incident CHF	HR*	95% CI	p Value
None	10,746	240	1	referent	
Baseline former	3,217	108	1.36	1.06–1.74	0.02
Quit during study	5,825	120	0.86	0.68–1.09	0.22
<1	5,321	89	0.86	0.67–1.12	0.27
1–6	4,641	61	0.72	0.53–0.97	0.03
7–13	1,998	32	0.80	0.54–1.19	0.27
14+	2,188	31	0.70	0.47–1.06	0.09

*Adjusted for age, race, gender, smoking status, education, income, marital status, exercise intensity, diabetes, and body mass index.

Abbreviations as in Table 2.

study, such as dietary habits, could contribute to biased estimates. However, we adjusted for a variety of physiologic and lifestyle factors related to alcohol consumption, including exercise and cholesterol levels, and still found a similar dose-response relationship to that found in other studies. An unmeasured confounding factor that entirely explained the risk reduction associated with alcohol consumption would need to be strongly associated with both alcohol intake and CHF incidence and not closely related to covariates already included in our models.

Neither coronary angiography nor stress testing was performed routinely in CHS, and coronary artery calcification was measured in 1998 (9 years after the study began) and only in 1 site. Thus, no clear measure of the extent of coronary disease among CHS participants at baseline exists. We performed analyses in a subset of participants with no evidence of angina, MI, or other major cardiovascular disease, with no substantial change in our findings, but it is likely that some differences in extent of subclinical coronary disease exist even in this subset. Although such disease was likely to be subclinical and may not have directly affected alcohol intake, we cannot exclude the possibility that it influenced our findings. Likewise, LV ejection fraction was not quantified in CHS, and, thus, we cannot fully explore its role as a mediator or confounder, although adjustment for semiquantitative ejection fraction and quantitative fractional shortening had no effect on our results.

Although CHS is a population-based cohort study, participants were generally healthy, community-dwelling older adults. As a result, our results cannot be extrapolated to other populations without an appropriate degree of caution.

Relatively few of the CHS participants were heavy drinkers, and the range of alcohol intake was truncated even among the heaviest drinkers. As a result, our ability to define the potentially hazardous effects of truly heavy alcohol consumption was limited. Likewise, binge drinking was not assessed in the CHS, although rates of binge drinking are low among older adults (32).

Conclusions. Alcohol intake does not appear to have cardiotoxic effects among older adults when consumed in moderate doses. While it may exert a general protective effect by favorably altering hemodynamics or influencing other factors that affect either the development or clinical presentation of CHF, the mechanism of the protective association between moderate alcohol consumption and clinical CHF requires further study.

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APPENDIX

A full list of participating CHS investigators and institutions can be found at <http://www.chs-nhlbi.org>.

The Association of Alcohol Consumption and Incident Heart Failure: The Cardiovascular Health Study

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