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Alcohol and Incident Heart Failure Among Middle-Aged and Elderly Men: The Cohort of Swedish Men

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Abstract

Background—Compared with no alcohol consumption, heavy alcohol intake is associated with a higher rate of heart failure (HF) whereas light-to-moderate intake may be associated with a lower rate. However, several prior studies did not exclude former drinkers, who may have changed alcohol consumption in response to diagnosis. This study aimed to investigate the association between alcohol intake and incident HF.

Methods and Results—We conducted a prospective cohort study of 33,760 men 45–79 years old with no HF, diabetes mellitus or myocardial infarction at baseline participating in the Cohort of Swedish Men Study. We excluded former drinkers. At baseline, participants completed a food-frequency questionnaire and reported other characteristics. HF was defined as hospitalization for or death from HF, ascertained by Swedish inpatient and cause-of-death records from January 1, 1998 through December 31, 2011. We constructed Cox proportional hazards models to estimate multivariable-adjusted rate ratios (IRRs). During follow-up, 2916 men were hospitalized for (n=2139) or died (n=777) of incident HF. There was a U-shaped relationship between total alcohol intake and incident HF (p=0.0004). There was a nadir at light-to-moderate alcohol intake: consuming 7 to less than 14 standard drinks per week was associated with a 19% lower multivariable-adjusted rate of HF compared with never drinking (IRR: 0.81, 95% CI: 0.69, 0.96).

Conclusions—In this cohort of Swedish men, there was a U-shaped relationship between alcohol consumption and HF incidence, with a nadir at light-to-moderate intake. Heavy intake did not appear protective.

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None.

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Keywords

alcohol; heart failure; epidemiology; cohort

Epidemiological studies have generally found that, compared to no alcohol intake, light-to-moderate consumption is associated with a lower risk of coronary heart disease morbidity and mortality among adults.^{1, 2} Heavy alcohol intake is associated with a higher rate of HF, likely via alcohol-associated cardiomyopathy,³⁻⁵ but moderate consumption (2 drinks per day for men and 1 drink per day for women) may be associated with a lower rate of incident HF.

Several prospective cohort studies from the US have shown that, compared with non-drinkers, light-to-moderate alcohol consumption is associated with a lower rate of incident HF,⁶⁻¹² with a meta-analysis¹³ reporting that the rate of incident HF is 15% (95% CI: 7%, 22%) lower among those who drink less than 14 drinks per week than among non-drinkers. However, several prior studies did not distinguish between lifelong abstainers and former drinkers^{6-9, 14} who may have quit due to co-morbidities, such as alcoholism or other illness, and may be at higher risk of developing HF. Additionally, only three of these studies assessed the impact of different beverage types.^{6, 10, 12} Therefore, we examined whether incident HF hospitalization or mortality is associated with total alcohol consumption or consumption of beer, wine or spirits among a large population-based cohort of Swedish men followed for up to 14 years.

Methods

Study Population

This study consisted of 33,760 men from the Cohort of Swedish Men (COSM), a prospective study of men living in the Västmanland and Örebro counties in central Sweden. The cohort recruitment, characteristics and study methods have previously been described.¹⁵ Starting in autumn 1997, a questionnaire about demographics, behavioral and anthropometric factors and food and beverage intake was sent to men residing in these counties who were aged 45 to 79 years and 48,850 responded. We excluded participants who did not provide or provided incorrect national identification numbers, who had blank questionnaires, or who had previous diagnosis of cancer (other than non-melanoma skin cancer; n=2944). In addition, we excluded participants with missing or implausible energy intake (>3 standard deviations from the natural log-transformed mean, n=558); missing data on more than half of the food and beverage items (n=4053); missing data on body mass index (BMI; n=1737), or no information on alcohol consumption (n=132). We excluded former drinkers (n=923) since some of these individuals might have stopped drinking in response to underlying health conditions.

In addition to excluding participants with a history of HF (n=869) at baseline, we excluded participants with a history of myocardial infarction (MI) (n=1608) or diabetes mellitus (n=2266) at baseline, since they might have received dietary counseling to change their alcohol intake. HF and MI history were determined via inpatient register linkage; diabetes

history was assessed by self-report and inpatient register linkage. The Regional Ethical Review Board at Karolinska Institute (Stockholm, Sweden) approved the study. Consent was implied by completion and return of the self-administered questionnaire.

Assessment of Alcohol Intake and Diet

In 1997, participants received a 96-item self-administered food frequency questionnaire (FFQ) asking about food and beverage consumption over the past year.¹⁶ Men were asked to report if they never drank alcohol, if they had quit drinking alcohol or if they regularly drink at least some alcohol. For current drinkers, participants reported how frequently they consumed beer (2.8% alcohol), strong beer (4.5% alcohol), wine, fortified wine (>18% alcohol) and liquor (40% alcohol) during the past year. For each type of alcohol, there were nine pre-specified frequency options ranging from never to 3 times per day. In addition, participants reported how many glasses of light beer (1.8% alcohol) they drank per day or per week during the past year.

The nutrient intake from foods and beverages was calculated by multiplying the frequency of consumption by nutrient composition data from the Swedish National Food Administration by age-specific portion sizes determined using weighted diet records. To estimate beverage-specific alcohol intake (g ethanol/d), we multiplied participant-reported frequency of consumption by alcohol composition data and age-specific drink sizes, as previously described in a similar cohort of Swedish women.¹⁷ To estimate total alcohol intake (g/d), we then summed over each type of alcohol. We defined one serving of alcohol as 13 g of alcohol and estimated the average number of standard alcoholic drinks per week. If a current drinker reported information about consumption of at least one, but not all, types of alcohol, we assumed he never drank the alcohol type(s) with missing information, as suggested in prior work.¹⁸

In a validation study of an FFQ similar to that used in COSM,¹⁹ 248 men from the study area randomly selected from the Swedish Population Register completed an FFQ twice one year apart and fourteen 24-hour recall interviews during the year between the first and second FFQ. The Spearman correlation coefficient between the 24-hour recall interviews and the first FFQ estimate of alcohol intake was 0.81.

Assessment of Other Covariates

We used the inpatient register to obtain information on history of MI at baseline, and we classified participants as having diabetes at baseline via either self-report or a diagnosis of diabetes recorded on the inpatient register. We computed total physical activity in metabolic equivalents in hours per day based on questions about occupational physical activity, exercise and sedentary behavior.²⁰ We calculated BMI as weight in kilograms divided by height in meters squared (both self-reported). The questionnaire also included questions about education (less than high school, high school, university), cigarette smoking (current, past, never), marital status (single, married/living with someone, divorced, widower), family history of MI before age 60 (yes, no), history of hypertension (yes, no) and history of high cholesterol (yes, no). We computed a component score for consistency of diet with the Dietary Approaches to Stop Hypertension (DASH) diet, with higher scores indicative of

higher diet quality¹⁶. Men who were in the highest quintile for fruits, vegetables, nuts and legumes, low-fat dairy and whole grains received a score of 5, while those in the lowest quintile received a score of 1; men in the highest quintile for intake of sodium, sweetened beverages and red and processed meats received a score of 1. We calculated the overall DASH score as the sum of the component scores.

Follow-Up and Ascertainment of HF

Participants contributed person-time from January 1, 1998 until the earliest of: December 31, 2011, date of death due to causes other than HF, or date of first HF hospitalization or HF mortality. If a participant died of a non-HF cause, his follow-up time was censored. We followed patients through record linkage to Swedish inpatient and cause-of-death registers. The inpatient register includes >99% of inpatient care in Sweden.²¹ Hospitalization for or death from HF was defined as code 428 from the *International Classification of Diseases, 9th edition* or codes I50 or I11.0 from the *International Classification of Diseases, 10th edition*. We included the first hospitalizations or deaths with HF as the primary or secondary diagnosis and only the first HF event in the register for each individual. Among individuals with HF as a primary diagnosis (first position) in the Swedish inpatient register, 95% had HF confirmed by medical record review using European Society of Cardiology criteria; among individuals with HF as a secondary (second position) diagnosis, 76% had confirmed HF diagnosis.²²

Statistical Analyses

We categorized total alcohol intake as never drinker and into the following categories of standard drinks per week: <0.5, 0.5 to <1, 1 to <7, 7 to <14, 14 to <21 and ≥21. We reported baseline characteristics by category of alcohol intake as mean ± SD or as counts with proportions for continuous and categorical characteristics, respectively. We used Cox proportional hazards models to estimate multivariable-adjusted incidence rate ratios (IRRs) with corresponding 95% confidence intervals (CIs) for the rate of HF incidence among men who consumed alcohol compared to never drinkers. We tested for a quadratic trend by assigning each participant within a category the median drinks per week within that category. We ran a model with this variable and the squared value of this term as continuous predictors and determined the statistical significance of the squared term. We tested for violations of the proportional hazards model by including the product of alcohol intake and the natural log of survival time and did not find evidence of violations.

We chose covariates that we considered to be potential confounders, due to their association with both alcohol intake and with HF occurrence. In the first model, we allowed the baseline rate to vary by age. In the second model, we additionally adjusted for total energy intake (linear term), education (less than high school, high school, university), BMI (linear term), cigarette smoking (current, past, never), marital status (single, married/living with someone, divorced, widower) and component score for consistency with DASH diet (quartiles).¹⁶

In secondary analyses, we evaluated the association between HF incidence and each alcoholic beverage type and mutually adjusted for the two other beverage types. The referent group for each beverage type was non-drinker of that specific beverage. We conducted tests

for quadratic trends to examine the statistical significance of the pattern of association for each alcohol type and HF risk. We carried out several sensitivity analyses. First, we conducted an analysis using Markov chain Monte Carlo-imputed data for BMI (n=1415, 4.0%) and physical activity (n=6907, 19.6%)^{23, 24} and evaluated whether further adjusting for physical activity, family history of MI before age 60, history of hypertension and history of high cholesterol would alter results. Second, we estimated the fully adjusted model of total alcohol intake using a proportional subdistribution hazards model to account for competing risks of non-CHF death.²⁵ Third, we tested whether the association between alcohol consumption and HF differed by self-reported history of hypertension, history of high cholesterol or current smoking using likelihood ratio tests. Fourth, since unrecognized illness may influence alcohol consumption at baseline, we conducted a sensitivity analysis excluding the first 2 years of follow-up. Finally, as some of the cases with HF as secondary diagnosis might have been false positives, we conducted analyses where we defined cases of HF only based on a primary diagnosis. We performed statistical analyses using SAS version 9.3 (Cary, NC) and used the `stcrreg` command in Stata version 12 (Statacorp, College Station, TX) for the competing risks model. For all analyses, two-sided $P < 0.05$ was considered to be statistically significant.

Results

Over 13 years of follow-up of 33,760 men in the study, 2916 were hospitalized for HF for the first time (n=2139) or died of HF (n=777), corresponding to a baseline rate of 67.8 HF cases per 10,000 person-years. Most of the study participants reported drinking 1 to <7 alcoholic drinks per week. Compared with never drinkers, men who reported consuming an average of 7 to <14 drinks per week were on average younger and were more likely to be a current or former smoker and to report history of high cholesterol (Table 1).

There was a statistically significant quadratic trend, supporting a U-shaped relationship between total alcohol intake and HF ($p=0.0004$), with a nadir at light-to-moderate alcohol consumption (Table 2). In the analyses by beverage type, we observed suggestions of U-shaped trends between beverage-specific intake and incident HF (Table 3).

Sensitivity analyses in which we imputed physical activity and BMI and additionally adjusted for hypertension, high cholesterol, family history of MI and imputed physical activity yielded similar results. Accounting for competing risks did not substantially alter the results. In analyses excluding the first two years of follow-up, results did not differ materially. The association between alcohol intake and HF did not differ by self-reported history of hypertension (p -interaction=0.70), smoking status (p -interaction=0.37) or self-reported high cholesterol (p -interaction=0.08). When we defined HF as those cases with a primary diagnosis of HF, the results were similar.

Discussion

In this large prospective cohort study, there was a U-shaped relationship between total alcohol intake and incident HF, with a nadir at light-to-moderate alcohol intake. When we examined the association separately for beer, wine and spirits and mutually adjusted for

other beverage types, we found suggestion of a U-shaped trend for beer, wine and spirits. While wine and spirits no longer appeared protective above 7 drinks per week, beer appeared potentially protective for 7 to 14 drinks per week. This may be due to drinking patterns; non-beer drinkers included a higher proportion of never drinkers than did the non-wine or non-spirit drinkers. Additionally, men in the highest categories of wine (14 drinks per week) or spirits (7 drinks per week) consumed fairly high levels of total alcohol, with medians of 26.9 and 20 standard drinks per week, respectively.

There are several potential mechanisms that may explain how light-to-moderate alcohol intake is associated with a lower rate of HF. Moderate alcohol consumption is associated with a lower rate of MI,²⁶ a key risk factor for HF. In addition, moderate alcohol intake leads to beneficial effects on several coronary artery disease (CAD) risk factors.²⁷ Experimental studies have shown that within weeks, moderate alcohol consumption is associated with increased high-density lipoprotein cholesterol, apolipoprotein A-I and adiponectin and decreased fibrinogen levels.²⁷ Type 2 diabetes mellitus is a major risk factor for heart failure.²⁸ Some observational studies²⁹ have shown that moderate alcohol consumption is associated with a lower risk of type 2 diabetes, and some experimental studies have shown that it lowers insulin levels³⁰ and increases insulin sensitivity.^{30, 31}

Our findings are consistent with many,⁶⁻¹² but not all,¹⁴ of the prior studies showing that moderate alcohol intake is associated with a lower rate of incident HF. For example, in a cohort of people ages 65 years and older,⁶ participants who reported drinking 21–70 ounces of alcohol per day (approximately 1.5–4 drinks) had a 47% lower rate of incident HF compared with non-drinkers (IRR: 0.53, 95% CI: 0.32, 0.88). Some prior studies⁶⁻⁹ did not have information about whether non-drinkers were lifelong abstainers or former drinkers. Therefore, their results may have overestimated the protective benefits of alcohol since some former drinkers might have quit due to co-morbidities, such as alcoholism or other illness. Similar to our study, a recent meta-analysis of alcohol and incident HF also found a non-linear dose-response between alcohol and incident HF¹³.

In one of the studies that examined the association between incident and HF and beer, wine or spirits, the results were similar for all alcoholic beverage types.⁶ In another study, Klatsky and colleagues¹⁰ examined the association between alcohol and HF risk for those with and without known CAD at the time of HF. Among those without known CAD, a higher frequency of wine consumption was associated with a lower rate of HF among men but there was no benefit of a higher frequency of consuming beer or liquor. In our study, there was a suggestion of protective benefit of light intake of all alcohol types.

Our study has several limitations. First, though we adjusted for multiple potential confounders, we cannot rule out the possibility of residual or unmeasured confounding. For instance, we were only able to adjust for smoking status as never, former or current smoker and we did not have information on pack years or years since quitting. However, since smokers tend to drink more alcohol³² and they are at a higher risk of HF,³³ confounding by smoking would make alcohol appear less protective. This is in agreement with our results; light-to-moderate alcohol intake appeared more protective in the model that adjusted for smoking than in the age-adjusted model. Second, we used an FFQ that that is reproducible

and valid¹⁹, but some individuals tend to underreport alcohol consumption³⁴ and heavier drinkers are more likely to underreport drinking than are lighter drinkers. Third, most of the participants reported no or moderate consumption, thereby limiting our ability to assess the impact of heavy consumption of incident heart failure risk. Fourth, though the accuracy of HF diagnosis in Swedish registers has previously been shown to be high,²² these registers only include HF cases that were hospitalized or died, so these findings might not be applicable to less severe cases. Furthermore, these registers do not include information about HF subtype (e.g., systolic or diastolic dysfunction) or etiology.

Our study also has several strengths. Since this is a large, population-based prospective cohort study, concerns about recall bias are minimized. Additionally, we were able to exclude former drinkers who may have altered their alcohol consumption in response to underlying health conditions. Finally, the FFQ includes detailed information on consumption of beer, wine and spirits and is reproducible and valid.¹⁹

In summary, in this large prospective cohort study of middle-aged and elderly Swedish men, there was a U-shaped relationship between alcohol consumption and incident HF. Light-to-moderate, but not heavy, alcohol intake was associated with a lower rate of HF hospitalization or death. Since moderate alcohol consumption also carries potential risks, such as an increased risk of cancer³⁵ and injury,³⁶ public health messages about the potential cardio-protective consequences of alcohol consumption should take into consideration both risks and benefits. Additional work is necessary to examine whether drinking patterns influence the relationship between alcohol consumption and incident HF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Age-Standardized* Baseline Characteristics of 33,760 Participants in the Cohort of Swedish Men by Average Alcohol Intake

	Weekly Number of Drinks						
	Never drinker (n=1396)	<0.5 (n=1538)	0.5 (n=1671)	1-7 (n=18,003)	7-<14 (n=8691)	14-21 (n=1831)	21 (n=630)
Median drinks per week	0	0.3	0.8	3.7	9.3	16.3	25.3
Age (y)	63.0 ± 9.6	60.4 ± 9.5	59.3 ± 9.8	58.2 ± 9.2	57.7 ± 8.7	58.4 ± 9.0	59.7 ± 9.0
Physical activity (MET-h/d)	42.3 ± 5.2	42.5 ± 5.3	42.3 ± 5.1	41.7 ± 4.8	41.1 ± 4.7	40.9 ± 4.9	41.0 ± 5.1
BMI (kg/m ²) [‡]	25.4 ± 3.5	26.1 ± 3.7	25.7 ± 3.3	25.7 ± 3.2	25.5 ± 3.1	25.6 ± 3.1	25.4 ± 3.2
Energy intake (kcal/d)	2950.2 ± 931.0	2752.4 ± 898.2	2724.0 ± 863.2	2663.4 ± 785.5	2774.1 ± 772.4	2954.8 ± 834.0	3304.5 ± 987.9
Cigarette smoking [‡]							
Never	86.2	45.9	46.8	37.7	30.6	25.6	20.1
Past	7.9	30.3	30.1	38.5	44.8	46.9	42.0
Current	5.9	23.8	23.1	23.8	24.6	27.6	37.9
Marital status [‡]							
Single	11.3	11.8	8.3	5.7	4.0	3.6	6.6
Married/living with someone	83.0	77.7	82.2	85.2	87.4	85.6	82.8
Divorced	3.4	7.8	7.0	6.5	5.9	7.3	8.2
Widower	2.4	2.8	2.5	2.6	2.8	3.5	2.4
Education [‡]							
Less than high school	68.2	75.4	73.1	68.6	58.9	53.3	56.0
High school	13.2	10.1	13.9	14.7	18.2	18.8	15.1
University	18.6	14.5	13.0	16.8	23.0	27.9	28.8
Family history of MI before age 60 [‡]	8.9	13.2	12.1	12.4	11.5	12.3	14.4
History of hypertension	16.0	21.0	21.1	19.6	18.7	18.9	20.5
History of high cholesterol	7.1	9.6	13.0	12.3	12.6	12.6	13.2
DASH component score [‡]							
Quartile 1	22.5	27.7	25.0	21.6	20.1	23.8	29.6
Quartile 2	26.5	22.8	25.0	24.6	25.2	24.7	27.2
Quartile 3	25.2	23.0	24.7	26.8	27.9	27.0	26.7

 Weekly Number of Drinks

	Never drinker (n=1396)	<0.5 (n=1538)	0.5 (n=1671)	1-<7 (n=18,003)	7-<14 (n=8691)	14-<21 (n=1831)	21 (n=630)
Quartile 4	25.8	26.5	25.4	27.0	26.8	24.5	16.5

Data are presented as mean \pm SD or %. MET indicates metabolic equivalent of task. DASH indicates Dietary Approaches to Stop Hypertension.

* All values (except for age and median standard drinks per week) are standardized to the age distribution in the study population at baseline.

[†] Missing data on smoking history (n=367), marital status (n=126), education (n=185), family history of MI (n=7882).

[‡] Dietary component score derived from consistency with Dietary Approaches to Stop Hypertension diet (17).

Table 2

Rate Ratios and 95% CIs for Incident HF by Average Baseline Alcohol Consumption among 33,760 Men in the Cohort of Swedish Men

Alcohol Drinks per Week	Cases	Person-Years	Model 1 [*]	Model 2 [†]
Never	192	17,038	1.00 (reference)	1.00 (reference)
<0.5	192	18,821	1.21 (0.99, 1.48)	1.04 (0.85, 1.28)
0.5-<1	157	21,049	0.94 (0.76, 1.17)	0.86 (0.70, 1.07)
1-<7	1532	230,285	0.98 (0.84, 1.14)	0.89 (0.76, 1.04)
7-<14	628	111,970	0.89 (0.76, 1.05)	0.81 (0.69, 0.96)
14-<21	141	23,334	0.91 (0.73, 1.13)	0.81 (0.65, 1.02)
21	74	7710	1.30 (1.00, 1.71)	1.12 (0.85, 1.47)
P for quadratic trend			0.0002	0.0004

Total events = 2916

CI indicates confidence interval.

^{*} Cox proportional hazards model accounting for age.

[†] Additionally adjusted for total energy intake (linear term), education (less than high school, high school, university), body mass index (linear term), dietary component score (quartiles), cigarette smoking (current, past, never), marital status (single, married/living with someone, divorced, widower).

Table 3
Rate Ratios and 95% CIs for Incident HF by Average Baseline Beer, Wine and Spirits Consumption among 33,760 Men in the Cohort of Swedish Men

		Beer			Wine			Spirits			
Drinks/Week	Cases	Person- Years	Rate Ratio (95% CI)	Drinks/ Week	Cases	Person- Years	Rate Ratio (95% CI)	Drinks/ Week	Cases	Person- Years	Rate Ratio (95% CI)
Non beer drinker	352	31,689	1.00 (ref)	Non wine drinker	942	99,975	1.00 (ref)	Non spirits drinker	770	83,708	1.00 (ref)
<0.5	287	36,264	1.02 (0.87, 1.20)	<0.5	728	110,193	0.92 (0.83, 1.03)	<0.5	824	143,347	0.90 (0.81, 1.01)
0.5-1	312	43,735	0.91 (0.78, 1.07)	0.5-1	263	13,257	0.97 (0.84, 1.13)	0.5-1	374	52,895	0.97 (0.84, 1.11)
1-7	1620	263,110	0.90 (0.79, 1.03)	1-7	881	192,636	0.89 (0.80, 1.00)	1-7	891	146,424	0.89 (0.80, 1.01)
7-14	284	47,137	0.87 (0.73, 1.03)	7-14	88	12,693	0.99 (0.79, 1.25)	7*	57	3834	1.27 (0.96, 1.69)
14*	61	8273	0.92 (0.70, 1.22)	14*	14	1454	1.16 (0.68, 1.98)				
p for quadratic trend			0.11				0.09				0.02

CI indicates confidence interval.

Cox proportional hazards model accounting for age and adjusted for total energy intake (linear term), education (less than high school, high school, university), body mass index (linear term), dietary component score (quartiles), cigarette smoking (current, past, never), marital status (single, married/living with someone, divorced, widower). Each model also mutually adjusted for other consumption of other two beverage types.

* Non-drinkers include never consumers of an alcohol and current alcohol drinkers that are not consuming the specific beverage of interest (e.g., beer).

† Among those consuming:

14 standard drinks of beer per week, median weekly standard drinks of total alcohol: 21.2, of beer: 17.3;

14 standard drinks of wine per week, median weekly standard drinks of total alcohol: 26.9, of wine: 16.2;

7 standard drinks of spirits per week, median weekly standard drinks of total alcohol: 20.0, of spirits: 9.6.