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Contrasting association between alcohol consumption and risk of myocardial infarction and heart failure: Two prospective cohorts

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ABSTRACT

Background: The potential cardioprotective effect of light-to-moderate alcohol consumption is disputed, and the association between heavy drinking and heart failure (HF) risk is unclear. We examined the association between alcohol consumption and risk of myocardial infarction (MI) and HF in two prospective cohorts.
Methods: We analyzed data from the Cohort of Swedish Men (40,590 men) and the Swedish Mammography Cohort (34,022 women). Participants were free of ischemic heart disease and HF at baseline. MI and HF cases were ascertained by linkage with the Swedish National Patient Register. Cox proportional hazards regression model was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).
Results: During follow-up (1998–2010), we ascertained 3678 and 1905 cases of MI and HF, respectively, in men and 1500 and 1328 cases of MI and HF, respectively, in women. Alcohol consumption was inversely associated with MI in both men and women (P trend <0.001); compared with light drinkers, the multivariable HRs were 0.70 (95% CI, 0.56–0.87) in men who consumed >28 drinks/week and 0.32 (95% CI, 0.15–0.67) in women who consumed 15–21 drinks/week. Alcohol consumption was not inversely associated with HF risk. However, in men, the risk of HF was higher in never, former, and heavy drinkers (>28 drinks/week; HR = 1.45; 95% CI, 1.09–1.93) compared with light drinkers.
Conclusions: Alcohol consumption has divergent associations with MI and HF, with an inverse association observed for MI but not HF. Heavy drinking was associated with an increased HF risk in men.

1. Introduction

The potential cardioprotective effect of light-to-moderate alcohol consumption is debated. While alcohol consumption has been shown to have beneficial effects on some vascular risk factors (e.g., high-density lipoprotein cholesterol and fibrinogen levels, insulin sensitivity and inflammation) [1–3], it has adverse effects on others (e.g., blood pressure and arrhythmia) [4–6]. Alcohol consumption has often been reported to be inversely associated with ischemic heart disease incidence and mortality [7], whereas controversy exists on the association between alcohol consumption and risk of heart failure (HF). In particular, it is uncertain whether high and heavy alcohol consumption increases HF risk. A meta-analysis of eight prospective studies indicated that light-to-moderate alcohol drinking was inversely associated with risk of HF [8]. High consumption of alcohol was not found to be associated with HF but few studies included heavy drinkers [8]. Besides few heavy drinkers, most previous studies were potentially limited by the use of nondrinkers as the reference group [9–17] and no differentiation was made between lifetime abstainers and former drinkers [9,11,15,18]. This could potentially lead to a spurious inverse association between alcohol consumption and HF in former drinkers, of which some may be sick quitters, and lifetime abstainers differ from current drinkers.

To further evaluate the association between alcohol consumption and incidence of HF, we used data from two population-based prospective cohorts of Swedish men (Cohort of Swedish Men; COSM) and women (Swedish Mammography Cohort; SMC). The objective was to examine whether heavy and former drinkers have a higher risk of HF compared with light drinkers, and to assess whether alcohol consumption has contrasting associations with risk of HF and myocardial infarction (MI).

2. Methods

2.1. Study population

Details about the COSM and SMC studies have been reported previously [19]. Briefly, in the fall of 1997, 48,850 men and 39,227 women from central Sweden answered a questionnaire about diet, alcohol consumption, and other risk factor for diseases. We omitted participants with a missing personal identification number, those who died or had a diagnosis of ischemic heart disease, HF, or cancer before baseline, and those who did not provide information on alcohol consumption (Fig. S1), leaving 40,590 men (aged

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45–79 years) and 34,022 women (aged 49–83 years) for analysis. The Ethical Review Board at Karolinska Institutet in Stockholm, Sweden, approved the study.

2.2. Assessment of alcohol consumption

Participants provided information about their alcohol and food consumption through a food-frequency questionnaire at baseline in 1997. Average alcohol consumption in the past year prior to baseline was assessed with six questions on alcoholic beverages, including class I beer (alcohol by volume, <2.25%), class II beer (2.8–3.5%), class III beer (>3.5%), wine (12%), strong wine (>18%), and liquor. Participants also reported the amount consumed on a single occasion and whether they had never had alcohol or had quit drinking. Weekly alcohol consumption was calculated by multiplying the frequency of consumption of each alcoholic beverage by the amount consumed per occasion. One drink was defined as 12 g alcohol (ethanol). The questionnaire has been validated, and the correlation coefficient was 0.81 for alcohol when comparing estimates from the questionnaire with the mean of fourteen 24-hour recall interviews [20].

2.3. Assessment of covariates

Through the baseline questionnaire, participants provided data on education, family history of myocardial infarction, smoking, weight, height, physical activity, aspirin use, and history of hypertension, hypercholesterolemia, and diabetes. Self-reported history of hypertension and diabetes was complemented with data on diagnosis of these diseases in the Swedish National Patient and Diabetes Registers. Data on atrial fibrillation were acquired from the Swedish National Patient Register.

2.4. Case ascertainment

Incident MI and HF cases were ascertained through record linkage with the Swedish National Patient Register and the Swedish Cause of Death Register. The International Classification of Diseases 10th Revision code I21 was used to define MI and codes I50 and I11.0 were used to define HF. The validity, in terms of specificity, of primary diagnoses of MI in the Swedish Patient Register is 98–100% [21]. The corresponding validity for HF has been reported to be 95% for diagnoses in first position (primary diagnosis), 76% for diagnoses in second position, and 63% for diagnoses in positions 3 to 6 [22]. For each outcome, only the first event for each participant and only events listed as primary diagnosis (to increase specificity) were classified as a case.

2.5. Statistical analysis

Each participant accrued follow-up time from January 1, 1998 until the first of the following; date of primary diagnosis of MI (in analyses of MI) or HF (in analyses of HF), date of death, or December 31, 2010. We categorized men into eight groups according to their alcohol drinking status and number of drinks consumed per week: never (lifetime abstainers), former, and current drinkers of <1 (occasional drinkers; reference group), 1–6, 7–14, 15–21, 22–28, and >28 drinks/week. Because of lower alcohol consumption in women than in men, the two highest categories were collapsed into one category (i.e., highest category >21 drinks/week).

Cox proportional hazards regression models with age as the underlying time scale was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Multivariable models were adjusted for age (as the time scale in all analyses), education (less than high school, high school, or university), family history of myocardial infarction before 60 years of age (yes/no), smoking (never smoker, former smoker and <20 pack-years, former smoker and ≥20 pack-years, current smoker and <20 pack-years, and current smoker and ≥20 pack-years), body mass index (kg/m^2; <25, 25–29.9, or ≥30), walking/bicycling (almost never, <20 min/day, 20–40 min/day, or >40 min/day), exercise (<1 h/week, 1–2 h/week, 3–4 h/week, or ≥5 h/week), use of aspirin (nonuser, <7 tablets/week, or ≥7 tablets/week), and history of hypertension (yes/no), hypercholesterolemia (yes/no), diabetes (yes/no), and atrial fibrillation (yes/no). The multivariable model was also controlled for overall diet using a modified Dietary Approaches to Stop Hypertension diet score, as described previously [23]. For HF, further adjustment for incident MI during follow-up was performed in a second multivariable model.

Tests for trend in current drinkers of alcohol were carried out using the median value for each category as a continuous variable. Analyses were conducted in SAS (version 9.4, SAS Institute, Cary, NC). All statistical tests were two-tailed ($\alpha = 0.05$).

3. Results

Compared with light drinkers of alcohol (<1 drink/week), heavy drinkers (>28 drinks/week in men and >21 drinks/week in women) were younger and less physically active and were more likely to be current smokers and to have a postsecondary education and family history of MI (Table 1). Among men but not women, heavy drinkers were more likely to have a history of hypertension and hypercholesterolemia compared with light drinkers. Former drinkers were more likely to use aspirin regularly and were more likely to have a history of hypertension, diabetes, and atrial fibrillation as well as a family history of MI compared with light drinkers. Among women, the prevalence of hypertension was higher in never and former drinkers than in heavy drinkers.

From January 1998 through December 2010, a total of 3678 MI cases were ascertained among men in the COSM during 471,816 person-years of follow-up and 1500 MI cases were ascertained among women in the SMC during 411,717 person-years of follow-up. HF was diagnosed in 1905 men (481,437 person-years) and 1328 women (414,233 person-years).

The association of alcohol consumption with risk of MI and HF in men and women in the two cohorts is presented in Table 2. Alcohol consumption was statistically significantly inversely associated with risk of MI in both men and women (P for trend <0.001); compared with light drinkers, the multivariable HRs of MI were 0.70 (95% CI, 0.56–0.87) in men who consumed >28 drinks/week and 0.32 (95% CI, 0.15–0.67) in women who consumed 15–21 drinks/week (Table 2). In women, there was indication that the reduction in MI risk was attenuated at heavy alcohol consumption (>21 drinks/week) but the number of heavy drinkers was limited, leading to broad CIs. In women but not in men, former drinkers had an increased risk of MI in the age-adjusted analysis but this association did not persist after adjustment for other risk factors.

Unlike MI, alcohol consumption was not inversely associated with risk of HF, neither before nor after adjustment for incident MI (Table 2). In men, HF risk was higher in never, former, and heavy drinkers (>28 drinks/week) compared with light drinkers after adjustment for other risk factors; the multivariable HRs of HF for never, former, and heavy drinkers were respectively 1.27 (95% CI, 1.02–1.58), 1.36 (95% CI, 1.12–1.66), and 1.45 (95% CI, 1.09–1.93). In women, no increased risk of HF was observed in never, former, or heavy drinkers.

4. Discussion

In these two cohorts of Swedish adults, we observed that alcohol consumption has divergent associations with incidence of MI and HF. In both men and women, alcohol consumption was inversely associated with risk of MI but not HF. In men, heavy drinkers as well as never and former drinkers had a higher risk of HF but not MI compared with light drinkers. There was no association between nondrinking and risk of MI in either men or women.

Our results for alcohol consumption and incidence of MI confirm the findings of a meta-analysis of prospective studies [7]. That meta-analysis showed that alcohol consumption was inversely associated with risk of ischemic heart disease. For ischemic heart disease incidence, all levels of alcohol intake >2.5 g/day had similar degrees of risk reduction and the overall HR for alcohol drinkers compared with nondrinkers was 0.71 (95% CI, 0.66–0.77) [7].

Our findings for HF in men are in agreement with those from a prospective study of 3530 older British men which showed that heavy alcohol consumption (≥35 drinks/week) was associated with an increased risk of HF [24]. In a large prospective cohort study of US adults, alcohol consumption had contrasting association with risk of HF with and without associated coronary artery disease (CAD) [12]. Heavy alcohol consumption (≥42 drinks/week) was associated with an increased risk of HF in individuals without associated CAD but with a lower risk in individuals with associated CAD [12]. The positive association between alcohol consumption and non-CAD-HF was confined to individuals with cardiomyopathy or of unclear preponderant etiology. No other study has, to our knowledge, assessed the association between heavy drinking (≥28 drinks/week) and HF. Heavy drinking may increase the risk of HF through cardiomyopathy, hypertension, and arrhythmia [4–6]. A meta-analysis of eight observational studies showed that an intake of 50 g/day of alcohol (ethanol) was associated with a 57% and 81% higher risk of hypertension in men and women, respectively [4].

The reason why heavy alcohol consumption was associated with an increased risk of HF in men but not in women in the present study is

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