Drinking pattern and mortality in middle-aged men and women

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ABSTRACT

Aims To address the prospective association between alcohol drinking pattern and all-cause mortality.
Setting Denmark.
Participants A total of 26,909 men and 29,626 women aged 55–65 years.
Measurements We obtained risk estimates for all-cause mortality for different levels of quantity and frequency of alcohol intake adjusted for lifestyle factors, including diet.
Findings During follow-up, 1,528 men and 915 women died. For the same average consumption of alcohol, a non-frequent intake implied a higher risk of death than a frequent one.
Conclusions Drinking pattern and not just the total amount of alcohol consumed is important for the association between alcohol intake and mortality. These results suggest that future public guidelines concerning sensible alcohol drinking should include messages about drinking pattern together with quantity of alcohol.

KEYWORDS Alcohol drinking, drinking behaviour, follow-up studies, mortality.

INTRODUCTION

A large number of prospective studies have consistently reported a J-shaped relation between an average measure of alcohol intake and all-cause mortality [1–3]. This characteristic form most probably reflects a beneficial effect on the cardiovascular system of light alcohol intake, and harmful implications, such as liver cirrhosis and cancer, of high consumption. These associations have been addressed mainly without taking drinking pattern into account, with the exception of some recent studies [4–10]. Although these studies differed with regard to type and quality of measures of drinking patterns, results implied consistently the importance of drinking pattern in addition to the total quantity consumed. Most recently it has been suggested that drinking frequency, and not the total amount of alcohol, is the primary determinant of the inverse association between alcohol intake and coronary heart disease [8]. However, it seems unlikely that the cardioprotective benefits would outweigh the detrimental effects of a high alcohol intake, regardless of the drinking pattern. Hence, for public health purposes, a more universal outcome such as mortality from all-causes is relevant, because it constitutes a scientific basis for creating guidelines on sensible drinking.

The aim of the present study is to investigate the association between frequency of drinking episodes for a given level of total alcohol consumption and all-cause mortality. We use data from a large prospective cohort study consisting of middle-aged men and women and have the ability to adjust for related lifestyle factors such as diet and physical activity.
METHODS

During December 1993 to May 1997, 160,725 Danish men and women aged 50–65 years were invited by mail to participate in the population-based study 'Diet, Cancer and Health' [11]. Eligible subjects were born in Denmark and had no previous cancers at the time of inclusion. With the invitation, a detailed 192-item food frequency questionnaire including questions concerning average alcohol intake was enclosed. A first visit to the study clinic was arranged by telephone with subjects who agreed to participate [27,178 men and 29,875 women (35%)]. The food frequency questionnaire was returned during the clinic visit, where another questionnaire concerning life-style and background factors including information on frequency of alcohol intake was completed. A description of the food frequency questionnaire has been published previously [12]. The study was conducted in accordance with the Helsinki Declaration II and was approved by the Ethical Committees for the Copenhagen and the Aarhus municipalities (KF 01–116/96).

Alcohol intake and drinking patterns

In the background questionnaire, subjects reported their usual frequency of alcohol intake in seven possible response categories: never drink alcohol, less than once per month, one to three times per month, once a week, two to four times per week, five to six times per week and daily. In the food frequency questionnaire, participants were asked to state their average quantity (during the last year) of alcohol consumption as the intake of specific amounts of each beverage: light, normal and strong beer (in number of bottles); red, white and fortified wine (in number of glasses); and spirits (in number of drinks). The possible response categories were no alcohol intake, less than one per month, one to three per month, one to three per month, one to two per week, two to four per week, five to six per week, one per day, two to three per day, four to five per day, six to seven per day and eight or more per day. Based on ethanol content in the different beverage types, these categories were converted into number of standard drinks (12 g alcohol) per week and added to yield an average measure of total alcohol intake.

For a given quantity of total alcohol intake, two groups of drinkers were formed to differentiate between individuals drinking little alcohol frequently and individuals consuming a larger quantity of alcohol more rarely. Frequent drinkers were defined as individuals who consumed alcohol at least 2 days per week and non-frequent drinkers were defined as subjects who used to drink alcohol less often. Abstainers were defined as subjects who, in both questionnaires, reported never to drink.

For women, total alcohol intake was categorized into five levels (none, less than one, one to six, seven to 13 and more than 13 drinks per week) and for men, total alcohol intake was categorized into six levels (none, less than one, one to six, seven to 13, 14–20 and more than 20 drinks per week).

Education

In the life-style questionnaire, education was estimated from length of basic schooling as 7 years or less, 8–10 years or 11 years and longer.

Smoking habits

Subjects reported if they were never-smokers, ex-smokers or current-smokers. Current smokers reported number of daily cigarettes, cheroots, cigars and pipes. Assuming one cigarette to be equivalent to 1 g, one cheroot or one pipe to 3 g and one cigar to 5 g tobacco, total amount of smoking was calculated. Two variables were constructed, one indicating smoking status (never, ex, current) and one indicating amount of smoking (0 for never and ex-smokers, and 1–14 g per day, 15–24 g per day or more than 24 g per day for current smokers).

Body mass index

The participants’ height and weight were measured in light clothes and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m) and modelled as linear splines after log-transformation with knots at 18.5, 25, and 30 kg/m². These limits were set in accordance with guidelines from the World Health Organization [13].

Physical activity

Subjects reported if they were physically active during leisure time, including undertaking sports, housework, gardening, taking walks and bicycling. For each activity, a dichotomized variable was computed with the cut-point defined as performing or not performing the activity in question.

Diet

Indicators of a healthy diet among the participants were chosen from the food frequency questionnaire. For intake of fish, cooked vegetables, salad and fruit, respectively, the intake was dichotomized as high or low. The cut-points were defined as close as possible to the 10th percentile of the sex-specific distribution (fish, once a month or less; vegetables, twice per month or less; salad, once a month or less; and fruit, once a week or less). The participants also indicated which type of fat used mainly for cooking.
and two groups were formed: the participants in one group who used mainly olive oil and those in another group who used mainly other types of fat for cooking. Use of fat spread on bread was used as a measure of saturated fat intake because one-third of saturated fat intake in Denmark is consumed as spread on bread. Two groups were formed, users and non-users of fat spread on bread.

Diseases before baseline

Information on the participants’ health status when entering the study cohort was obtained from the population-based Danish Patient Register, which keeps records of all somatic hospitalizations in Denmark since 1977. The diagnoses are classified according to the World Health Organization’s International Classification of Diseases, 8th revision (ICD-8). By linking the study cohort to this register, information on the participants’ health status from 1977 to baseline (1993–97) was obtained. Dichotomized variables were constructed for stroke (ICD-8 codes: 430–438), acute myocardial infarction (ICD-8 code: 410), angina pectoris (ICD-8 codes: 411 and 413), other cardiovascular diseases (ICD-8 codes: 390–409, 412, 414–429 and 439–458) and other diagnoses implying diseases with a chronic character. The latter includes infectious, endocrinological, nervous system, chronic lung, gastrointestinal, alcohol-related, urological and musculoskeletal diseases (ICD-8 codes: 40–46, 79–83, 93–95, 240–289, 340–358, 490–493, 530–537, 560–573, 577, 580–584 and 710–738).

Follow-up

Vital status of the study population sample was followed until 20 February 2003 by using the unique person identification number in the Civil Registration System. The observation time for each participant was the period from enrolment into the study (December 1993 to May 1997) until 20 February 2003, death (n = 2443), emigration (n = 255) or disappearance (n = 4), whichever came first.

Statistical analysis

Subjects with incomplete information on alcohol intake (n = 104) or on any of the potential confounders (n = 240) were excluded from the analyses. A few subjects had reported conflicting answers between their average total alcohol intake and the frequency of alcohol intake, and as it was difficult to categorize such subjects they were excluded from the analyses (n = 174). A total of 56 535 subjects were eligible for this study.

Pearson’s correlation coefficient was calculated to examine the magnitude of correlation between drinking frequency and amount of drinking. Risk estimates were computed by means of Cox proportional hazard regression models [14] (SAS/STAT program software). Age was used as the time axis to ensure that the estimation procedure was based on comparisons of individuals at the same age. The analyses were corrected for delayed entry, such that individuals were considered at risk only from the age at entry into the study cohort. In one model (Fig. 1), the frequency of drinking was categorized into two levels (subjects consuming alcohol at least 2 days per week and subjects consuming alcohol less often) for each level of total alcohol intake. In another model (Table 1a,b), the frequency of drinking was categorized into four levels (once per week or less, two to four times per week, five to six times per week and daily drinking) for every level of total alcohol intake. For each model, all combinations of frequency and level of total alcohol intake were entered simultaneously. Having had a diagnosis of a disease before baseline, school education, smoking, BMI, intake of fish, fruit, salad and vegetables, use of olive oil in cooking and of fat on bread were included as covariates in the adjusted model. All analyses were performed for each sex separately. The assumption of proportional hazards in the Cox model was tested for each covariate by evaluating the parallelism of the stratified survival curves graphically and by constructing time-dependent variables for the covariates in question and testing these for statistical significance. No violations were detected. Analyses were repeated after exclusion of subjects with a disease before baseline.

We used the Wald test to examine the joint hypothesis of differences in the hazard ratio for mortality between non-frequent and frequent drinkers for a weekly alcohol intake of more than one drink per week.

RESULTS

Among men who reported to consume any alcohol, 21 083 did so at least twice per week while 4450 drank alcohol less frequently (Table 2a). Among alcohol-consuming women, 16 659 were frequent drinkers and 8103 were non-frequent drinkers (Table 2b). Among both men and women, the median alcohol consumption was higher among frequent drinkers for each category of total alcohol intake than among the corresponding non-frequent drinkers. Overall, drinking frequency was correlated moderately to amount of drinking [Pearson’s correlation coefficient = 0.70 (women) and 0.63 (men)]. Among both men and women, non-frequent drinkers generally had a lower educational level, were more often smokers, more often obese and eating fewer vegetables and fruit than frequent drinkers.

During a mean follow-up of 6.8 years, 1528 men and 915 women died. The adjusted hazard ratios for non-frequent and frequent drinkers according to total alcohol...
Table 1

Adjusted hazard ratios* of all-cause mortality (95% confidence limits) according to quantity and frequency of alcohol intake.

<table>
<thead>
<tr>
<th>Alcohol intake, drinks per week</th>
<th>Frequency of alcohol intake</th>
<th>Abstainers</th>
<th>Once per week or less</th>
<th>2–4 times per week</th>
<th>5–6 times per week</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td></td>
<td>1.31</td>
<td>(0.96–1.78)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Less than one</td>
<td></td>
<td>1.00</td>
<td>(reference)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>1–6</td>
<td></td>
<td>0.61</td>
<td>(0.47–0.79)</td>
<td>0.74</td>
<td>0.91</td>
<td>0.84</td>
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<tr>
<td>7–13</td>
<td></td>
<td>0.61</td>
<td>(0.42–0.90)</td>
<td>0.56</td>
<td>0.51</td>
<td>0.63</td>
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<td>14–20</td>
<td></td>
<td>1.11</td>
<td>(0.62–2.00)</td>
<td>0.61</td>
<td>0.52</td>
<td>0.67</td>
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<tr>
<td>21+</td>
<td></td>
<td>1.25</td>
<td>(0.70–2.24)</td>
<td>1.03</td>
<td>0.68</td>
<td>0.84</td>
</tr>
<tr>
<td>(b) Women</td>
<td></td>
<td>1.62</td>
<td>(1.19–2.19)</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>0</td>
<td></td>
<td>1.00</td>
<td>(reference)</td>
<td>–</td>
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<tr>
<td>Less than one</td>
<td></td>
<td>1.05</td>
<td>(0.85–1.30)</td>
<td>0.90</td>
<td>0.72</td>
<td>0.83</td>
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<tr>
<td>1–6</td>
<td></td>
<td>1.30</td>
<td>(0.85–2.01)</td>
<td>0.94</td>
<td>0.84</td>
<td>0.90</td>
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<tr>
<td>7–13</td>
<td></td>
<td>2.19</td>
<td>(1.15–4.17)</td>
<td>1.06</td>
<td>1.03</td>
<td>1.31</td>
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</table>

*Adjusted for education, smoking, BMI, physical activity, diet and diseases before baseline.

Figure 1

Hazard ratios (age-adjusted estimates are represented by broken lines and fully adjusted† estimates by full lines) for all-cause mortality according to quantity and frequency of alcohol intake in men and women‡. († frequent = at least 2 drinking days per week, non-frequent = less than 2 drinking days per week.

†Adjusted for education, smoking, BMI, physical activity, diet and diseases before baseline;
‡reference category is drinkers of less than one but more than zero drinks per week.

*p = value less than 0.05 compared to reference category.
intake compared with non-drinkers (drinkers of more than zero but less than one drink per week) were estimated (Fig. 1). The hazard ratios of mortality were higher among non-frequent drinkers than among frequent drinkers for a weekly alcohol intake of more than one drink per week \[ P = 0.03 \text{ (men)} \] and \[ P = 0.05 \text{ (women)} \] using the Wald test. Among non-frequent drinking men, the hazard ratios were 0.61 (95% CI, 0.47–0.79), 0.61 (95% CI, 0.42–0.90), 1.11 (95% CI, 0.62–2.00) and 1.25 (95% CI, 0.70–2.24) for subjects drinking one to six, seven to 13, 14–20 and more than 20 weekly drinks, respectively. Correspondingly, the hazard ratios among frequent drinking men were 0.76 (95% CI, 0.58–0.99), 0.57 (95% CI, 0.44–0.72), 0.61 (95% CI, 0.47–0.80) and 0.83 (95% CI, 0.66–1.04). Among non-frequent drinking women, the hazard ratios were 1.05 (95% CI, 0.85–1.30), 1.31 (95% CI, 0.85–2.01) and 2.19 (95% CI, 1.15–4.17) for subjects drinking one to six, seven to 13 and more than 13 weekly drinks, respectively. Correspondingly, the hazard ratios among frequent drinking women were 0.89 (95% CI, 0.69–1.14), 0.91 (95% CI, 0.72–1.16) and 1.20 (95% CI, 0.96–1.51).

The mortality rate ratios for different combinations of quantity and frequency of alcohol intake were also estimated (Table 1a,b). For men, the lowest risk estimates was for drinking seven to 13 drinks per week distributed 5–6 days per week (0.51 95% CI: 0.36–0.73) and for drinking 14–21 drinks per week distributed on 5–6 days per week (0.52 95% CI 0.35–0.76) (Table 2a). The highest hazard ratios were obtained among men drinking on 1 day per week or more rarely; for this category the hazard ratio was 1.11 (95% CI: 0.62–2.00) for drinking 14–20 drinks per week and 1.25 (95% CI: 0.70–2.24) for drinking more than 20 drinks per week. The hazard ratio for drinking totally 21 or more drinks per week distributed on 7 days per week was 0.84 (95% CI: 0.66–1.06). For women, the lowest risk estimate was for drinking one to six drinks per week distributed on 7 days per week was 0.84 (95% CI: 0.66–1.06). For women, the lowest risk estimate was for drinking one to six drinks per week distributed on 7 days per week was 0.84 (95% CI: 0.66–1.06). For women, the lowest risk estimate was for drinking one to six drinks per week distributed on 7 days per week was 0.84 (95% CI: 0.66–1.06).
per week and 2.19 (95% CI: 1.15–4.17) for drinking more than 13 drinks per week. The hazard ratio for drinking 14 or more drinks per week distributed on 7 days per week was 1.31 (95% CI: 1.02–1.68). Risk estimates of subjects without diseases before baseline did not differ from the estimates for all subjects (data not shown).

The following covariates were associated independently and positively with mortality for men: having a diagnosis of acute myocardial infarction, angina, other cardiovascular diseases or any chronic disease before baseline, not performing any physical activity, smoking, not eating fruit and salad, not using olive oil for cooking, having a BMI < 18 kg/m² and having school education for less than 11 years. For women, having had a diagnosis of acute myocardial infarction or any chronic disease before baseline, not performing any physical activity, smoking, not eating salad and having a BMI < 18 kg/m² were independently and positively associated with mortality.

**DISCUSSION**

We found that drinking pattern influenced the relation between alcohol intake and all-cause mortality. For the same average consumption of alcohol, a non-frequent intake implied a higher risk of death than a frequent one. However, frequent heavy drinking (>20 drinks per week for men and >13 drinks per week for women) also implied an increased risk of death compared to light drinking. Our study population consisted of middle-aged men and women. This age group constitutes a high-risk population for heart diseases and it is therefore qualified for investigating how the deleterious effects of alcohol are balanced against the protecting effect, according to drinking frequency and amount of intake.

The follow-up period in this study was 6.8 years, which is a shorter period than that seen in most other epidemiological studies. This means that the information on alcohol intake given by the participants at baseline probably describes more accurately the actual behaviour of the subjects at follow-up in the present study. The combination of this relatively short follow-up period, the large number of participants and a large variation in frequency and amount of alcohol intake allows us to estimate the hazard ratios for non-frequent and frequent drinkers separately.

The finding that the association between alcohol intake and mortality depends upon drinking pattern has been suggested previously [4–7]. Although other measures of drinking patterns were used, results imply consistently a hazardous effect of drinking alcohol in large amounts per occasion. Most of these studies did not assess drinking pattern over the whole spectrum of total alcohol intake and it was difficult to differentiate between the influence from total alcohol intake and drinking pattern. We avoided the term ‘binge drinking’, which in most studies is defined as drinking a minimum number of drinks per occasion, such as six or 13 [6,7], because the participants were not asked directly about occasional heavy drinking and we can therefore not comment on this with the present data. The drinking pattern in the present study was constructed by combining information on average quantity with usual drinking frequency, as has been performed in some other studies [8,10].

In the present study, covariates were distributed unequally in the two groups of drinkers for most factors and the more ‘unhealthy’ pattern was observed consistently among the non-frequent drinkers (Table 1). Also, Kesse et al. showed that dietary habits are unequally distributed on different categories of alcohol intake [15]. This underlines the importance of a thorough confounder control when addressing alcohol intake and drinking pattern as independent variables. We held information on smoking habits, physical activity, BMI, diet and school education, which provided the possibility to adjust for these potential confounders. To adjust for diet, five presumed indicators of a healthy diet were chosen: intake of fruit, vegetables, saturated fat, plant oil and fish. Adjusting for diet and physical activity reduced the difference in hazard ratios between frequent and non-frequent drinkers and hence the importance of drinking pattern. Possible confounders of our results are social factors, as high volumes of alcohol per occasion have been shown to be associated with negative social circumstances [16]. In the present study, adjustment was made for education, which is expected to correlate strongly with social status. However, more detailed information on other social factors was not accounted for.

Among light drinkers there was little difference in hazard ratios between non-frequent and frequent drinkers. Consequently, the reduced risk of death in light drinkers compared with abstainers seems to depend less on drinking pattern than suggested previously [9]. The beneficial effect of a light alcohol intake on cardiovascular disease has several plausible biological mechanisms, including an increase of serum high-density lipoprotein (HDL) [17], inhibition of platelet production, activation and aggregation [18,19] and increased fibrinolysis [20,21]. The influence of drinking pattern on these mediators has been studied in interventions with moderate to heavy drinkers, where there were no differences in lipid profile or fibrinolysis between weekend and daily drinkers [22,23]. In contrast, non-frequent drinkers had a higher degree of coronary occlusion and a decreased HDL to low-density lipoprotein ratio compared with drinkers with a more regular drinking pattern [24]. The question is whether the latter finding applies to individuals with a light to moderate alcohol intake, especially as another study has shown
that most light drinkers rarely drink daily and that most daily drinkers are not light drinkers [25].

We used information on mortality from the Civil Registration System, which is updated to 2003. In the future, it will be interesting to include information on cause-specific deaths, but because the follow-up time in the registries containing this information is much shorter than for the Civil Registration System, it is not yet possible.

The non-frequent drinking pattern compared to frequent drinking involves higher alcohol concentrations in the gastrointestinal tract and in the blood as the non-frequent drinkers consume more alcohol per drinking occasion than do frequent drinkers. This could lead to an enhancement of the harmful effects of alcohol, including alcoholic liver disease and upper gastrointestinal cancers. Wetterling et al. have investigated drinking patterns among alcoholics and found that the occurrence of alcohol-related disorders were more common among subjects with frequent inebriation compared with more continuous drinkers with similar life-time alcohol intake [26]. To our knowledge, the association between drinking pattern and neoplasms in the gastrointestinal tract has not been investigated. Occasional drinking of high concentrations of alcohol is probably also stronger when associated with accidents and suicide, due to increased risk-taking behaviours.

In conclusion, we found that frequency of drinking for moderate and high consumption of alcohol influenced the association between alcohol intake and mortality. At these levels, mortality was higher among non-frequent drinkers compared with frequent drinkers.

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