



Alcohol consumption and mortality from aortic disease among Japanese men: The Japan Collaborative Cohort study



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ABSTRACT

Background and aims: Only a few population-based prospective studies have examined the association between alcohol consumption and abdominal aortic aneurysm, and the results are inconsistent. Moreover, no evidence exists for aortic dissection. We examined the effect of alcohol consumption on risk of mortality from aortic diseases.

Methods: A total of 34,720 men from the Japan Collaborative Cohort study, aged 40–79 years, without history of cardiovascular disease and cancer at baseline 1988 and 1990 were followed up until the end of 2009 for their mortality and its underlying cause. Hazard ratios of mortality from aortic diseases were estimated according to alcohol consumption categories of never-drinkers, ex-drinkers, regular drinkers of ≤ 30 g, and > 30 g ethanol per day.

Results: During the median 17.9-year follow-up period, 45 men died of aortic dissection and 41 men died of abdominal aortic aneurysm. Light to moderate drinkers of ≤ 30 g ethanol per day had lower risk of mortality from total aortic disease and aortic dissection compared to never-drinkers. The respective multivariable hazard ratios (95% confidence intervals) were 0.46 (0.28–0.76) for total aortic disease and 0.16 (0.05–0.50) for aortic dissection. Heavy drinkers of > 30 g ethanol per day did not have reduced risk of mortality from total aortic disease, albeit had risk variation between aortic dissection and abdominal aortic aneurysm.

Conclusions: Light to moderate alcohol consumption was associated with reduced mortality from aortic disease among Japanese men.

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1. Introduction

Light to moderate alcohol consumption has a protective effect against the development of cardiovascular diseases such as ischemic stroke and coronary artery disease [1]. However, previous observational studies reported inconsistent results with positive [2], inverse [3], and U-shaped [4] relationships between alcohol consumption and the risk of abdominal aortic aneurysm. To our knowledge, there is no prospective evidence on the risk of

abdominal aortic aneurysm among nonwhite populations or on the risk of aortic dissection in either whites or nonwhites. We examine the association of alcohol consumption with mortality from aortic disease among male participants in a large population-based cohort study.

Although the etiologies of aortic diseases remain unclear, advancing age, smoking, and hypertension are reported risk factors for both aortic aneurysm and dissection [2,4–6]. Thoracic aortic aneurysm and aortic dissection are characterized by minimal plaque formation [7,8], whereas abdominal aortic aneurysm is usually comorbid with severe atherosclerosis [6,9]. Chronic alcohol consumption raises blood pressure [10], while light to moderate alcohol consumption reduces atherosclerosis formation [11]. Therefore, the effect of alcohol consumption on aortic dissection

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and abdominal aortic aneurysm may be different.

2. Materials and methods

The Japan Collaborative Cohort (JACC) Study is a population-based cohort study with baseline survey conducted from 1988 to 1990 in 45 areas in Japan. Details of the study have been described elsewhere [12–14]. In total, 110,585 eligible participants (46,395 men and 64,190 women) aged 40–79 years were registered in the study. Baseline information was collected by a self-administered questionnaire. Additionally, about 5 years after the baseline survey, an interim survey regarding lifestyle changes was conducted in 31 areas. Informed consent was obtained before administration of the questionnaire from most participants in written or verbal form. In some communities, informed consent was obtained from the local community leader based on the guidelines of the Council of International Organizations of Medical Science [15]. The present study was approved by the ethics committees of Nagoya University and Osaka University.

Of the 46,395 male participants, we excluded 2574 men because of a history of cancer, stroke, or myocardial infarction and 9101 men because of missing information regarding drinking habits. In total, 34,720 men were included in this study. We limited our analysis to male participants because the proportion of current drinkers was 15% among female participants and the number of deaths from aortic disease among them was small ($n = 6$).

Date of mortality and its underlying cause were followed up on the death certificate annually or biennially by inquiring to the Ministry of Internal Affairs and Communication of Japan. Moving-outs from the study area were followed in collaboration with local governments in each area. In most of the areas, the subjects' mortality was followed up until the end of 2009, with the exceptions of 4 areas until 1999, 4 areas until 2003, and 2 areas until 2008. The underlying cause of death was recorded using the International Classification of Diseases version 10 (ICD 10). Aortic dissection corresponds to ICD-10 code I710, and aortic aneurysm corresponds to I711 to I719.

Baseline information collected by self-administrated questionnaire included alcohol drinking status and its consumption; demographic characteristics; histories of hypertension, diabetes mellitus, and other chronic disease; and lifestyle factors such as smoking, diet, sports, and walking habit.

Drinking status was inquired to classify participants into never-, ex-, and regular drinkers. Alcohol consumption was estimated from frequency (occasions per week), beverage type, and average amount on one occasion for regular drinkers. Beverage type was asked by a multiple choice question with items of sake (filtrate of fermented rice), shochu (beverage distilled from fermented barley, potatoes, buckwheat, or rice), beer, whisky, or wine. The daily amount of alcohol consumption (g per day) was calculated as the product of the frequency (occasion per week) and amount per occasion divided by seven.

2.1. Statistical analysis

The subjects were classified into four groups according to their drinking status and amount of alcohol consumption (never-drinkers, ex-drinkers, and current drinkers who consume ≤ 30 and > 30 g ethanol per day). Ex-drinkers were those who had had drinking habit but quit until the baseline survey. The age-adjusted mean value and prevalence of risk factors for each category were calculated by a general linear model. The p value for trend was derived from linear regression for continuous variables and logistic regression for prevalence. Hazard ratios of mortality from aortic diseases were estimated with reference to never-drinkers using a

Cox proportional hazard model. Covariates in the model were age at baseline (continuous), history of hypertension and diabetes mellitus (yes or no), smoking status (nonsmokers, ex-smokers, and <20 and ≥ 20 cigarettes per day), body mass index (quintile). Proportions of missing information were 4.4% for body mass index, 9.6% for history of hypertension, 11.6% for history of diabetes mellitus, and 0% for smoking habit. Those with missing data in the covariates were kept in the analyses by assigning them a value for missing category. Because the number of events per variable in the Cox proportional hazards model should not exceed 7 or 10 for stable estimation [16], we performed multivariable analyses by adding each covariate one by one.

The beverage-specific association between alcohol consumption and mortality from total aortic disease was examined for Japanese traditional alcohol beverage sake and shochu, which accounted for 35% of the beverage consumed in the study population.

Changes in the alcohol consumption were assessed according to the result of baseline and the 5-year interim survey. Proportions of respondents in the same category, the adjacent category, and the reversal category was calculated. The adjacent category consists of those reported themselves as never drinker at baseline and regular drinker with ≤ 30 g ethanol per day at the interim surveys; regular drinker with ≤ 30 g per day at baseline and never drinker or regular drinker of >30 g per day at the interim surveys; and regular drinker of >30 g per day at baseline and regular drinker of ≤ 30 g per day at the interim surveys. The reversal category consists of those reported never drinker at baseline but regular drinker of >30 g per day at the interim survey, and regular drinker of >30 g per day at baseline but never drinker at the interim survey. The former drinker category was excluded in the definition of these drinking habit change because of they may refrain from alcohol because of their ill health condition.

All statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC). Two-tailed p values of <0.05 were considered statistically significant.

3. Results

Current drinkers were younger, more hypertensive, and heavier smokers than never-drinkers. Ex-drinkers were older, more hypertensive, lighter smokers, and more likely to have a history of diabetes mellitus than never drinkers and current drinkers (Table 1).

During the follow-up of 530,542 person-years, we documented 117 deaths from aortic disease: 45 aortic dissections, 24 thoracic aortic aneurysms, 41 abdominal aortic aneurysms, 3 thoracoabdominal aortic aneurysms, and 4 aortic aneurysms of an unspecified site. The crude mortality rate of total aortic disease was 22 per 100,000 person-years.

Light to moderate alcohol consumption (≤ 30 g ethanol per day) was associated with reduced risk of mortality from total aortic disease and aortic dissection with multivariable hazard ratios (95% confidence interval [CI]) of 0.46 (0.28–0.76) and 0.16 (0.05–0.50), respectively (Table 2). Heavy drinkers of >30 g ethanol per day did not have lower risk of mortality from total aortic disease, although they tended to have lower risk of mortality from abdominal aortic aneurysm but not from aortic dissection (Table 2). The adjustments for each covariate showed similar results to the age-adjusted and multivariable models (Supplementary Table 1).

History of hypertension was associated with increased mortality from aortic dissection with multivariable hazard ratio (95% CI) of 4.18 (2.21–7.89), but not with abdominal aortic aneurysm with multivariable hazard ratio of 1.47 (0.70–3.11). The multivariable hazard ratios (95% CI) of mortality from thoracic aortic disease (aortic dissection or thoracic aortic aneurysm) were 0.34

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