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Alcohol consumption and risk of stroke and coronary heart disease among Japanese women: The Japan Public Health Center-based prospective study

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ABSTRACT

Objective. The study aims to examine the association between a wide range of alcohol consumption and risk of stroke and coronary heart disease.

Methods. The Japan Public Health Center-based prospective study was initiated in 1990 in Cohort I and in 1993 in Cohort II, with follow-up until 2009. The sample consisted of 47,100 women aged 40–69 years.

Results. During an average of 16.7-years, the incidence of 1846 strokes and 292 coronary heart diseases was observed. Heavy drinking (≥300 g ethanol/week) was associated with increased risk of total stroke. The multivariable hazard ratios for heavy versus occasional drinkers were 2.19 (95% confidence interval: 1.45–3.30) for total stroke, 2.25 (1.29–3.91) for hemorrhagic stroke, 2.24 (1.05–4.76) for intraparenchymal hemorrhage, 2.26 (1.01–5.09) for subarachnoid hemorrhage and 2.04 (1.09–3.82) for ischemic stroke. In the exposure-updated analysis, the positive association between heavy drinking and risks of total stroke, hemorrhagic stroke and intraparenchymal hemorrhage became more evident. Light drinking (<150 g ethanol/week) was not associated with risk of ischemic stroke. There was also no association between alcohol consumption and risk of coronary heart disease.

Conclusion. Heavy drinking was associated with increased risk of hemorrhagic and ischemic strokes among Japanese women.

Introduction

According to meta-analyses, women who were heavy drinkers (>60 g ethanol/day) had four-times higher risk of total stroke (Reynolds et al., 2003), while those who were light-to-moderate drinkers had reduced risk of coronary heart disease (CHD) compared with non-drinkers (Hvidtfeldt et al., 2010). As for subtypes of stroke, the Nurses' Health Study with a four-year follow-up showed that light-to-moderate alcohol consumption was associated with reduced risk of ischemic stroke and increased risk of subarachnoid hemorrhage compared with non-drinkers (Stampfer et al., 1988). Another study with a 26-year follow-up showed reduced risk of total stroke for light (0.1–4.9 g ethanol/day) and moderate (5.0–14.9 g ethanol/day) drinkers, but there was no excess risk of total, hemorrhagic or ischemic stroke for heavy drinkers (30–45 g ethanol/day) (Jimenez et al., 2012).

However, it is uncertain whether these associations are similar to what is observed among Asian women with a smaller body size than American and European women. Moreover, there is little data regarding the effect of alcohol consumption on risk of CHD among Japanese women probably due to the low CHD incidence (Kitamura et al., 2008) and prevalence of female drinkers (Ikehara et al., 2008).

Therefore, the present study examined the association between a wide range of alcohol consumption and risk of stroke, stroke subtypes and CHD among Japanese women in a large prospective cohort.

Methods

Materials and methods

The Japan Public Health Center-based prospective study (JPHC study) started the first cohort aged 40–59 years in 1990 (Cohort I) and the second

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cohort aged 40–69 years in 1993 (Cohort II) within eleven PHC areas. The details of the study design were described elsewhere (Tsugane and Sobue, 2001). The present study was approved by the Ethical Review Committee of the National Cancer Center and Osaka University.

Baseline and follow-up surveys

A self-reported baseline questionnaire was distributed to all registered, non-institutionalized residents in 1990 for Cohort I and in 1993–1994 for Cohort II. The questionnaire included information on demographic characteristics, medical history, drinking habits and other lifestyles. Of a total of 116,896 residents, 95,405 residents responded to the questionnaire (81.6%) and were included in the study cohort (Tsugane and Sobue, 2001).

Subjects in Cohort I were asked about frequency of alcohol consumption: almost never, 1–3 days/month, 1–2 days/week, 3–4 days/week, 5–6 days/week, or every day. Subjects who drank at least once a week were also asked about type of beverage and average daily consumption. Subjects in Cohort II were asked about their current drinking status: never-, former-, or current drinkers. Former (without specifying the duration for drinking cessation) and current drinkers were further asked about average frequency (1–3 days/month, 1–2 days/week, 3–4 days/week, or almost every day), type of beverage and average daily consumption. At 5-year follow-up surveys of Cohorts I and II, alcohol consumption was assessed by 6 frequency categories (almost never, 1–3 days/month, 1–2 days/week, 3–4 days/week, 5–6 days/week, or every day) and subjects who drank at least once a month were asked about type of beverage and average daily consumption.

We assigned a score to each category of current frequency as follows: 1.5 for 1–2 days/week, 3.5 for 3–4 days/week, 5.5 for 5–6 days/week, and 7.0 for every day in Cohort I, 0.5 for 1–3 days/month, 1.5 for 1–2 days/week, 3.5 for 3–4 days/week, 5.5 for 5–6 days/week, and 6 for almost every day in Cohort II and 0.5 for 1–3 days/month, 1.5 for 1–2 days/week, 3.5 for 3–4 days/week, 5.5 for 5–6 days/week, and 7.0 for every day in the 5-year follow-up surveys. Alcohol consumption was then quantified in grams of ethanol based on the following equivalents: 180 ml *sake* as 23 g ethanol, 180 ml *shochu* and *awamori* as 36 g ethanol, 30 ml whiskey or brandy as 10 g ethanol, 60 ml wine as 6 g ethanol and 633 ml beer as 23 g ethanol. Weekly ethanol intake was assessed by multiplying the quantity by the score. Alcohol consumption was classified into 6 categories: non-drinkers (never or former drinkers), occasional drinkers (1–3 days/month), and 1–74, 75–149, 150–299 or ≥300 g ethanol/week intake. The validity of these quantity–frequency (QF) measures (Dawson, 2003) was examined in subsamples by comparing them to those determined by four 7-day diet records (DRs). The Spearman rank correlation coefficients between the QF- and DR-derived ethanol consumptions among women were 0.44 (n = 107) in Cohort I (Tsubono et al., 2003) and 0.40 (n = 178) in Cohort II (Otani et al., 2003) for the baseline survey. The reproducibility of alcohol consumption was 0.66 in Cohort I between 1990 and 1995 (5-year interval) and 0.63 in Cohort II between 1993 and 1997 (4-year interval) (Tsubono et al., 2003).

Among 49,001 women aged 40–69 years who provided adequate self-reported data on their alcohol consumption at baseline, we excluded subjects who reported a history of stroke, myocardial infarction (MI), angina pectoris, or cancer (n = 1901). A total of 47,100 women were included in the present analysis.

Ascertainment of stroke and CHD and classification of stroke subtypes

A total of 64 hospitals were registered within the sampling area of the JPHC cohort for the surveillance of stroke and CHD. All were major hospitals capable of treating patients with acute and chronic cardiovascular disease. All medical records of strokes and CHDs were reviewed by hospital physicians, public health center physicians, or research physicians who were blinded to the information at baseline and at 5-year follow-up, using a standard format of registry. Incidences of stroke and CHD were registered during the follow-up period.

Strokes were defined according to the criteria of the National Survey of Stroke (Walker et al., 1981), which requires a constellation of neurological deficits of sudden or rapid onset lasting at least 24 h or until death. For each subtype of stroke, i.e., intraparenchymal hemorrhage, subarachnoid hemorrhage and ischemic stroke, a definitive diagnosis was established based on computed tomography, magnetic resonance images or autopsy findings. Hemorrhagic stroke included the cases of intraparenchymal hemorrhage and subarachnoid hemorrhage.

To complete the surveillance for fatal stroke and CHD, we also conducted a systematic search for death certificates. All deaths resulting from stroke (*International Classification of Diseases*, 10th Revision [ICD-10] I60–I69), CHD, or acute heart failure (I21–23, I46 and I50) that were listed on the death certificate but had not been registered were reviewed. When medical records were unavailable (death certificate information only), these fatal strokes were registered as probable strokes.

MI was defined according to the criteria from the Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) Project (Tunstall-Pedoe et al., 1994), which requires positive findings from electrocardiogram, cardiac enzymes, and/or autopsy. In cases where clinical findings were suggestive of MI in the absence of such a workup, a probable diagnosis was made. Deaths that occurred within 1-h from the onset of undiagnosed events were regarded as sudden cardiac deaths.

Total stroke was comprised of both confirmed and probable cases of stroke, while CHD was comprised of confirmed and probable cases of MI and sudden cardiac death. Changes in residential status were identified through the residential registry in each area. Subjects who moved from their original residential areas were treated as censored at that time.

Statistical analysis

Statistical analyses were based on incidence rates of stroke or CHD during an average of 16.7-years of follow-up. For each woman, individual months of follow-up were calculated from January 1, 1990 for Cohort I and from 1993 for Cohort II, to the first endpoint, whether it was death, emigration, or January 1, 2010.

Analysis of covariance and chi-square tests were used to compare age-adjusted mean values and proportions of cardiovascular risk factors, respectively. Tests for linear trends of covariates across alcohol consumption categories were tested by using the median values of alcohol consumption in each category among regular drinkers. Hazard ratios (HRs) with 95% confidence intervals (CIs) for total stroke, hemorrhagic stroke, ischemic stroke and CHD were calculated with reference to the risk for occasional drinkers according to alcohol consumption categories at baseline in the first analysis. Estimates of HRs were adjusted for age at baseline and other potential confounding factors including smoking status (never, past, current), body mass index (sex-specific quintiles), history of diabetes (yes/no), sports at leisure time (<1 day/month, 1–3 days/month, ≥1 day/week), flushing after drinking alcohol (yes/no), perceived mental stress (low, moderate, high), menopausal status (premenopausal, natural, or induced postmenopausal), and area of residence (9 PHC areas). We adjusted further for history of hypertension in another model. Tests for trends were conducted using the median value of each alcohol consumption category among regular drinkers. We also analyzed the effect of more recent alcohol consumption on each endpoint using the data of the 5-year follow-up questionnaire survey in the second analysis (84.0% of the baseline participants were available). In that analysis, we used the updated data of confounding factors except for history of hypertension (not available in the 5-year follow-up questionnaire), flushing after drinking alcohol and area of residence (regarded as constant), but we continued to use the baseline data for the subjects who had had information on alcohol consumption at baseline only or who experienced stroke, CHD, death or lost to follow-up during the 5-year follow-up.

Additionally, to assess the effect modification by selected risk factors, we conducted the analysis stratified by age (aged 40–55 years and 56 or older), history of hypertension (yes/no), and smoking status (never or past and current) using data at baseline. Statistical interactions were checked by using cross-product terms of these factors and alcohol consumption (continuous) in the multivariate-adjusted Cox proportional hazards regression model. The median value of alcohol consumption among occasional drinkers in Cohort II was substituted into those in Cohort I because alcohol consumption could not be calculated among occasional drinkers in Cohort I. All statistical analyses conducted were two-tailed and were calculated using SAS (version 9.3). p-Values of <0.05 were regarded as statistically significant.

Results

Table 1 shows the age-adjusted mean values and prevalence of baseline characteristics according to categories of alcohol consumption. Heavy drinkers of ≥300 g ethanol/week were more likely to