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Association of alcohol consumption and aortic calcification in healthy men aged 40–49 years for the ERA JUMP Study

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ABSTRACT

Background and aims: Several studies have reported a significant inverse association of light to moderate alcohol consumption with coronary heart disease (CHD). However, studies assessing the relationship between alcohol consumption and atherosclerosis have reported inconsistent results. The current study was conducted to determine the relationship between alcohol consumption and aortic calcification.

Methods: We addressed the research question using data from the population-based ERA-JUMP Study, comprising of 1006 healthy men aged 40–49 years, without clinical cardiovascular diseases, from four race/ethnicities: 301 Whites, 103 African American, 292 Japanese American, and 310 Japanese in Japan. Aortic calcification was assessed by electron-beam computed tomography and quantified using the Agatston method. Alcohol consumption was categorized into four groups: 0 (non-drinkers), ≤1 (light drinkers), >1 to ≤3 (moderate drinkers) and >3 drinks per day (heavy drinkers) (1 drink = 12.5 g of ethanol). Tobit conditional regression and ordinal logistic regression were used to investigate the association of alcohol consumption with aortic calcification after adjusting for cardiovascular risk factors and potential confounders.

Results: The study participants consisted of 25.6% nondrinkers, 35.3% light drinkers, 23.5% moderate drinkers, and 15.6% heavy drinkers. Heavy drinkers [Tobit ratio (95% CI) = 2.34 (1.10, 4.97); odds ratio (95% CI) = 1.67 (1.11, 2.52)] had significantly higher expected aortic calcification score compared to nondrinkers, after adjusting for socio-demographic and confounding variables. There was no significant interaction between alcohol consumption and race/ethnicity on aortic calcification.

Conclusions: Our findings suggest that heavy alcohol consumption may be an independent risk factor for atherosclerosis.

1. Introduction

Although a J-shaped association has been very well established between alcohol consumption and coronary heart disease (CHD) [1], with light to moderate drinkers showing a reduced risk compared to both heavy drinkers and nondrinkers, the underlying

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pathophysiological mechanisms remain to be elucidated. Plausible mechanisms for the protective effect of moderate alcohol consumption on CHD include: increase in high-density lipoprotein cholesterol (HDL-C), lower inflammation, anticoagulant effect (inhibition of the fibrinolytic system), improved endothelial function, and a reduced risk of type 2 diabetes mellitus [2–5]. Studies assessing the relationship between alcohol use and atherosclerosis (the major underlying cause of CHD [6]) reported conflicting results: no significant association [7,8], a U or J-shaped association [9–12], and a dose-response association [13–15]. The reason for these inconsistent results is not clear. To investigate the relationship between alcohol and atherosclerosis may help clarify the mechanisms underlying the association between alcohol and CHD.

Aortic calcification, a reliable and validated biomarker of atherosclerosis, is independently associated with cardiovascular morbidity and mortality [16,17] and has a high specificity for detection of severe coronary atherosclerosis [18]. Aortic calcification is a less commonly used measure of atherosclerosis compared to coronary artery calcification (CAC) which is a well-established biomarker of coronary atherosclerosis. Some studies have reported that aortic calcification may be a better measure of atherosclerosis than CAC because it is more prevalent, has an earlier onset [19], has a better association with cardiovascular risk factors [16,20,21], and seems to add prognostic information of atherosclerotic burden beyond CAC [16,20]. However, unlike CAC, studies examining the relationship between alcohol consumption and aortic calcification are scarce [10,13,19]. Moreover, the available results are inconsistent partly because of variability in studied populations, aortic segment examined, imaging modalities, and scoring method used, which avert an unbiased comparison across different populations [13,19,22].

Our objective is to determine the relationship between alcohol consumption and aortic calcification measured in asymptomatic men aged 40–49 years, using data from the ERA-JUMP Study (the Electron Beam Computed Tomography (**E**BCT), **r**isk factor **a**ssessment among **J**apanese and the United States (**U**S) **m**en in the **p**ost-World-War-II birth cohort). Based on our previous finding of a J-shaped association between alcohol consumption and CAC among Japanese in Japan [23], as well as following the notion of a J-shaped association between alcohol consumption and CHD, we hypothesized that light to moderate alcohol consumption would have an inverse association, and heavy alcohol consumption would have a positive association with aortic calcification. To our knowledge, this is the first population-based study exploring the association of alcohol consumption and aortic calcification among asymptomatic middle-aged men across different races/ethnicities, from various countries, in a standardized manner.

2. Materials and methods

2.1. Study population

The details of the study protocol have been described previously [24]. Briefly, during 2002–2006, a population-based sample of 1033 men aged 40–49 years, with no clinical cardiovascular diseases (CVD) or other severe illnesses, was obtained from 3 centers: 310 White and 107 Black from Pittsburgh, Pennsylvania, US; 303 Japanese American from Honolulu, Hawaii, US; and 313 Japanese from Kusatsu City, Shiga, Japan [24,25]. The study protocol followed 'the 1975 Declaration of Helsinki ethical guidelines'. The Institutional Review Boards of University of Pittsburgh, Pittsburgh, US; Kuakini Medical Center, Honolulu, Hawaii, US; Shiga University of Medical Science, Otsu, Japan approved the study. Written informed consent was obtained from all participants. We excluded participants with missing data for aortic calcification (n = 27). Our final sample size was 1006, with 301 US White, 103 US Black, 292 Japanese American, and 310 Japanese in Japan.

2.2. Risk factor assessment

All participants underwent a physical examination, completed a lifestyle questionnaire, and a laboratory, as described previously [24,25]. Data collection procedures were standardized across all centers. Body weight and height were measured while the participant was wearing light clothing without shoes. Body Mass Index (BMI) was calculated as weight (kg) divided by the square of the height (m^2). Blood pressure and heart rate were measured after the participant emptied his bladder and sat quietly for 5 min. Blood pressure was measured twice on the right arm with an automated sphygmomanometer (BP-8800, Colin Medical Technology, Komaki, Japan) using an appropriately sized cuff; average of the two measurements was used. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or use of antihypertensive medications [26]. Participants were considered smokers if they reported current use of cigarettes or had stopped smoking within the past 30 days. Pack-years of smoking were calculated as years of smoking multiplied by the number of cigarettes per day divided by 20. Use of medications (antihypertensive, antidiabetic, and lipid-lowering) was reported as 'yes/no'. Meat intake was defined as individuals who ate beef, pork, or sausage ≥2 times per week. Physical activity related to the current job was self-reported and categorized into sedentary, light, medium, and heavy physical activity [27].

Venipuncture was performed early in the clinic visit after a 12-h fast. Blood samples were stored at −70 °C and shipped on dry ice from all the centers to the University of Pittsburgh. Serum lipids were determined using the protocol standardized by the Centers for Disease Control and Prevention, including total cholesterol, HDL-C, and triglycerides [28]. Low-density lipoprotein cholesterol (LDL-C) was estimated by the Friedewald equation [29]. When the value of triglycerides exceeded 4.52 mmol/l (400 mg/dl), LDL-C was measured directly using an automated spectrophotometric assay [LDL Direct Liquid Select (Equal Diagnostics, Exton US)]. Serum glucose was determined by using hexokinase-glucose-6-phosphate-dehydrogenase enzymatic assay. Diabetes was defined as individuals with fasting glucose ≥7.0 mmol/l or use of medications for diabetes [30]. C-reactive protein (CRP) was determined using a calorimetric-competitive-enzyme-linked-immuno-sorbent assay, and fibrinogen was determined using an automated-clot-rate assay (Diagnostica Stago, Parsippany, U.S.)

2.3. Alcohol consumption assessment

The drinking habits of each subject were assessed by a validated self-administered questionnaire [31]. Alcohol consumption was assessed by asking whether the participant drank beer, wine, liquor, sake (Japanese rice wine), or other alcoholic beverages. Alcoholic status of the study participants was decided as never drinker (lifetime abstainers), former drinkers, and current drinkers. Among current drinkers, alcohol consumption per day was estimated assuming that the concentration of alcohol was 5% for beer, 12% for wine, 40% for liquor, and 16% for sake. Current alcohol drinkers were further categorized into three groups: 'light drinkers' (≤1 drink), 'moderate drinkers' (>1 to ≤3 drinks), and 'heavy drinkers' (>3 drinks) per day, with one drink, equaled to 12.5 g of alcohol [32] [which is approximately equivalent to 350 ml (12 oz) of regular beer, 150 ml (one glass) of wine, 45 ml of distilled spirits, and 110 ml of sake]. Former alcohol drinkers were combined with never drinkers (lifetime abstainers) and were together considered as 'nondrinkers.'