Nutrition 32 (2016) 637–644

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Meta-analysis

Alcohol consumption and risk of coronary artery disease: A dose-response meta-analysis of prospective studies

Yang Yang M.D., Dong-Chen Liu M.D., Qi-Ming Wang Ph.D., Qing-Qing Long M.D., Shan Zhao M.D., Zhen Zhang M.D., Yao Ma M.D., Ze-Mu Wang Ph.D., Lei-Lei Chen M.D., Ph.D., Lian-Sheng Wang M.D., Ph.D. *

Department of Cardiology, the First Affiliated Hospital of Nanjing Medical University, Nanjing, China

ARTICLE INFO

Article history:
Received 8 July 2015
Accepted 29 November 2015

Keywords:
Coronary artery disease
Alcohol consumption
Meta-analysis
Prospective studies

ABSTRACT

Objectives: To investigate and quantify the potential dose-response association between alcohol consumption and risk of coronary artery disease (CAD).

Methods: We searched the PubMed database from inception to March 2015 and reviewed the reference list of relevant articles to identify prospective studies assessing the association between alcohol consumption and risk of CAD. Study-specific relative risk (RR) estimates were combined using a random-effects model. Publication bias was estimated using Begg's funnel plot and Egger's regression asymmetry test. The meta-analysis included 18 prospective studies, with a total of 214 340 participants and 7756 CAD cases. The pooled adjusted RRs were 0.62 (95% confidence interval [CI] 0.56–0.68) for highest alcohol consumption amount versus lowest amount. Begg's and Egger's regression tests provided no evidence of substantial publication bias ($P = 0.762$ for Begg's test and 0.172 for Egger's test).

Results: In a dose response analysis, we observed a nonlinear association between alcohol consumption and risk of CAD (P for nonlinearity <0.00). Compared with non-drinkers, the RRs (95% CI) of CAD across levels of alcohol consumption were 0.75 (0.70–0.80) for 12 g/d, 0.70 (0.66–0.75) for 24 g/d, 0.69 (0.64–0.75) for 36 g/d, 0.70 (0.64–0.77) for 60 g/d, 0.74 (0.67–0.83) for 90 g/d, and 0.83 (0.67–1.04) for 135 g/d.

Conclusions: Alcohol consumption in moderation is associated with a reduced risk of CAD with 36 grams/d of alcohol conferring a lower risk than other levels.

Introduction

Coronary artery disease (CAD) is now a severe public health problem, affecting millions of people in both developed and developing countries. CAD is the major cause of death in developed countries [1], accounting for up to 40% of all fatal events [2]. In low and middle income countries, the incidence of cardiovascular disease has significantly increased. By 2020, the disease is expected to be the leading cause of morbidity and mortality in most developing countries [3]. Increased CAD risk is associated with increased atherosclerosis, which is more frequent in patients with chronic kidney disease, especially the dialysis ones, than in the general population [4]. CAD is by far the most common initiating cause of heart failure (in ~70% of patients), which makes things even worse [5].

Alcohol is one of the most widely consumed beverages in the world and is the fifth leading reason for death and disability accounting for 4% of life years lost due to disease [6]. Disease burden and disability are closely associated with the volume of alcohol consumption [7]. Consumption of alcohol is believed to have potential health benefits, such as antiinflammatory effect on atherosclerosis [8], increases in high-density lipoprotein cholesterol (HDL-C) [9], inhibitory effects on platelet aggregation [9], influence on antioxidant capacity and insulin sensitivity, thus restraining atherosclerosis [10,11]. Nevertheless, it can also have

Yang Yang and Dong-Chen Liu contributed equally to this work. This work was supported by grants from the National Natural Science Foundation of China (No 81270255), the Project Funded by the Science and Technological Innovation Group of Jiangsu Higher Education Institution "Qing-Lan Project" (JX2161015030). The authors state no conflict of interests.

* Corresponding author. Tel./fax: 0086-25-83724440.
E-mail address: Drlswang@njmu.edu.cn (L.-S. Wang).

http://dx.doi.org/10.1016/j.nut.2015.11.013
0899-9007/

harmful effects. Alcohol use is associated with a worse hematological picture of total cholesterol, low-density lipoprotein cholesterol (LDL-C) levels, and systolic blood pressure [12].

The association between alcohol consumption and the risk of CAD is of great importance because of the popularity of alcohol and the huge burden caused by CAD. The role of alcohol in the risk of CAD is well established, and has been assessed in a large number of observational epidemiologic studies or meta-analyses [12–16]. Though all demonstrated a U-shaped or J-shaped association between alcohol intake and CAD such that both non-drinkers and heavy drinkers appear to have higher morbidity rates than light and moderate drinkers, few studies have been designed to quantitatively assess the amount of alcohol, rather than qualitatively studying levels of alcohol consumption (e.g., "heavy" versus "low"). Thus, we aimed to better quantify the association between alcohol consumption and the risk of CAD through a comprehensive systematic literature review and dose-response meta-analysis that can intuitively reflect the relationship between alcohol consumption and risk of CAD.

Materials and methods

Literature search and selection

We identified potentially relevant articles regardless of language by a computerized search of the PubMed database from inception to April 2015. The following search terms were used: "coronary artery disease", "coronary heart disease", "cardiovascular disease", "myocardial infarction" (MI), "ischemic heart disease" (IHD), "CAD", "IHD combined with alcohol consumption", "drink", "drinking", and "ethanol". The reference lists of pertinent articles were reviewed to identify additional studies. Two investigators independently reviewed all identified studies. Eligibility criteria for inclusion in the present meta-analysis were: (1) the study was prospective design; (2) the exposure was alcohol consumption; (3) the outcome was total CAD incidence (including MI, CAD, nonstroke cardiovascular disease, and other coronary events); (4) the population was free from CAD at baseline; and (5) relative risks (RRs) with 95% confidence intervals (CIs), adjusted for at least age, were reported. If a study reported more than one set of RR estimates, we used the maximally adjusted RRs. We considered sex-specific estimates in cases where a study reported data separately for men and women.

Data extraction

From each study, we extracted the first author's last name, country in which the study was performed, duration of follow-up, sex and age, method of alcohol consumption assessment, total numbers of cases and participants, and person-years in every exposure category, the most fully adjusted RRs with corresponding 95% CIs for each category of alcohol consumption and covariates adjusted for in the analysis. If there was disagreement between the two investigators about eligibility of the data, it was resolved by consensus with a third reviewer.

Statistical methods

We standardized alcohol consumption across studies using a common scale, i.e., alcoholic g/d to pool the study-specific RRs. When a study reported alcohol consumption in drinks/week, we converted the intake into g/d assuming that one drink contains 12 g of alcohol. For each study, we assigned the median or mean alcohol consumption for the category to each corresponding RR. When the median or mean consumption was not reported, we assigned the midpoint of the upper and lower boundaries in each category as the median consumption. If the upper boundary for the highest category was not provided, the midpoint of the category was set at 1.5 times the lower boundary. When the lowest category was open-ended, we set the lower boundary to zero. If the number of cases and person-years were not available, we used the relative risks comparing the highest versus lowest categories of alcohol intake to obtain a summary estimate.

The heterogeneity among studies was estimated by the Cochran Q test and I^2 statistic. Heterogeneity was confirmed with a significance level of $P \leq 0.10$. The I^2 statistic describes the percentage of total variation in point estimates that can be attributed to heterogeneity. For the I^2 metric, we considered low, moderate, and high I^2 values to be 25%, 50%, and 75%, respectively. We used a fixed effect model (Mantel-Haenszel method) when heterogeneity was negligible and a random effect model (DerSimonian and Laird method) when heterogeneity was significant. Publication bias was evaluated using Begg's funnel plot [17] and Egger's regression asymmetry test [18].

To evaluate the dose-response association between alcohol consumption and risk of CAD, a 2-stage random-effects dose-response meta-analysis, taking into account the between-study heterogeneity, was performed proposed by Orsini

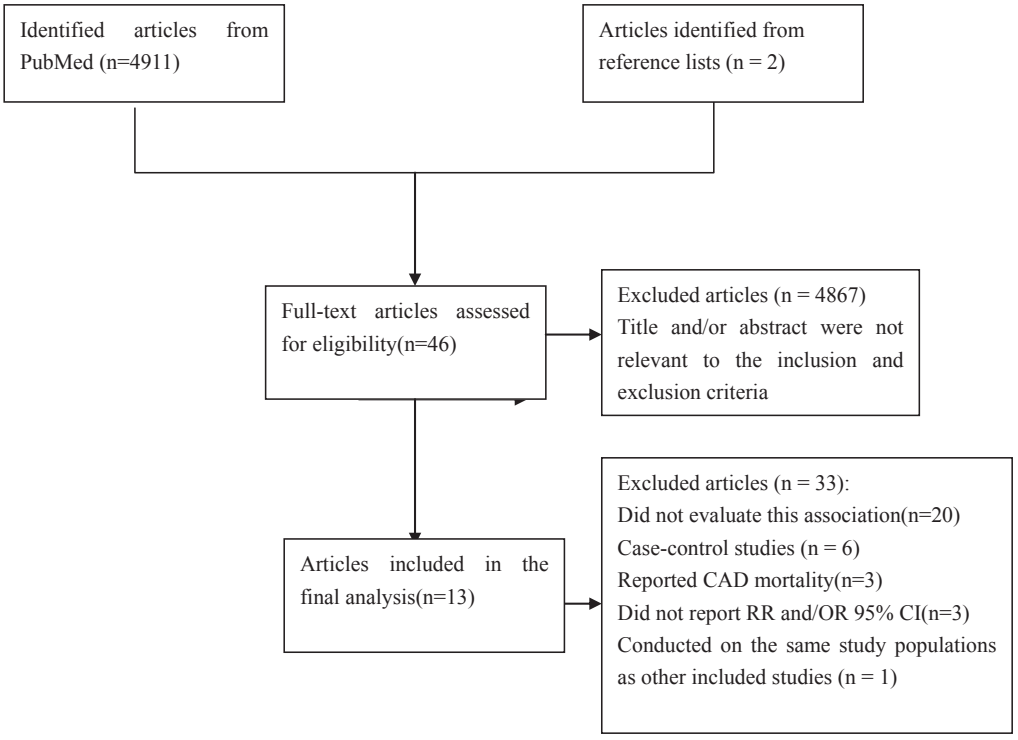

Fig. 1. Flow chart of study selection.