

Association Between Alcohol Consumption and Risk of Cardiovascular Disease and All-Cause Mortality in Patients With Hypertension: A Meta-Analysis of Prospective Cohort Studies

Chao Huang, BS; Jian Zhan, MPH; Yu-Jian Liu, MPH; De-Jia Li, PhD;
Su-Qing Wang, PhD; and Qi-Qiang He, PhD

Abstract

Objective: To conduct a meta-analysis summarizing the risk of cardiovascular disease (CVD) and all-cause mortality (ACM) in relation to alcohol consumption in patients with hypertension, focusing on clarifying dose-response associations.

Patients and Methods: PubMed and EMBASE were searched for eligible prospective cohort studies from December 3, 1949, through January 18, 2014. The semi-parameter method and dose-response analysis were used.

Results: Nine studies (11 cohorts) were included in the meta-analysis. Compared with the lowest alcohol level (abstainers/occasional drinkers), the pooled relative risk (RR) was 0.72 (95% CI, 0.68-0.77) for the third highest category (median, 10 g/d), 0.81 (95% CI, 0.71-0.93) for the second highest category (median, 20 g/d), and 0.60 (95% CI, 0.54-0.67) for the highest category (median, 30 g/d). A J-shaped relationship between alcohol use and ACM was observed, and the nadir (RR, 0.82; 95% CI, 0.76-0.88) was found to be at a dose of 8 to 10 g of alcohol consumption per day.

Conclusion: Findings of this meta-analysis suggest that low-to-moderate alcohol consumption was inversely significantly associated with the risk of CVD and ACM in patients with hypertension.

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Alcohol drinking is very common all over the world. Excessive alcohol consumption has a deleterious effect on health. It has been estimated that alcohol is responsible for 3.8% of global deaths and 4.6% of global disability-adjusted life-years worldwide.¹ However, several studies have suggested that regular light-moderate alcohol intake is inversely associated with cardiovascular disease (CVD) and all-cause mortality (ACM) in the healthy population.²⁻⁵ Similarly, patients with hypertension also seem to benefit from low levels of alcohol intake.^{6,7} The latest US hypertension guideline advises that alcohol intake should not exceed 2 drinks per day among men and 1 drink per day among women.⁸ Recommendations from the European Society of Hypertension and the European Society of Cardiology also suggest moderate alcohol consumption in subjects with hypertension.⁹

Although there is evidence that alcohol elevates blood pressure in a dose-dependent

way^{5,10} and the relationship between stroke and alcohol consumption is J-shaped,¹¹ guidelines about alcohol consumption are most likely to be grounded on the consensus of experts rather than substantial scientific evidence, because no evidence-based studies were cited in any of them.^{8,9} It remains unclear whether patients with hypertension should be advised to drink small amounts or cut down or abstain completely from alcohol. Considering that patients with hypertension are at a higher risk of cardiovascular events than healthy people, we, therefore, conducted a meta-analysis to clarify the quantitative associations between alcohol consumption and the risk of CVD and ACM among populations with hypertension.

METHODS

Search Strategy and Inclusion Criteria

PubMed and EMBASE were searched for prospective cohort studies that evaluated the



From the School of Public Health (C.H., J.Z., Y.-J.L., D.-J.L., S.-Q.W., Q.-Q.H.) and Global Health Institute (D.-J.L., S.-Q.W., Q.-Q.H.), Wuhan University, Wuhan, P. R. China.

association between alcohol consumption and the risk of ACM or CVD in patients with hypertension from December 3, 1949, to January 18, 2014. The search terms included the following key words: “alcohol OR ethanol OR beer OR wine OR spirits,” “stroke OR cerebral infarction OR brain infarction OR coronary heart disease OR intracerebral hemorrhage OR brain hemorrhage OR ([cerebrovascular OR cardiovascular OR CVD OR coronary OR stroke] AND [disease OR incidence OR survival OR morbidity OR fatal OR fatality OR mortality OR mortalities OR death]) OR all-cause mortality OR total mortality,” and “hypertension OR hypertensive OR hypertensives OR blood pressure.” We limited the search to studies on humans and published in English. Contents of bibliographies from retrieved articles including original articles, reviews, and other article types were searched for additional studies of interest.

We included studies in this meta-analysis if they met the following criteria: (1) prospective cohort studies; (2) the exposure was alcohol consumption, including alcohol, wine, beer, and spirits; (3) the outcomes were ACM and CVD events, the latter including mortality and incidence of CVD, coronary heart disease (CHD), stroke, and heart failure; and (4) quantitative data were available on the relationship between alcohol consumption and the risk of ACM or CVD in patients with hypertension, including risk estimates with 95% CIs or sufficient data to calculate these statistics. In cases of duplicate publication by the same authors, the study with the longest follow-up was included. [Supplemental Figure 1](#) (available online at <http://www.mayoclinicproceedings.org>) shows a flowchart of the publication screening in this article.

Data Extraction and Quality Assessment

Two investigators (H.C. and Z.J.) independently performed the literature search and extracted all data; any disagreements were resolved by consensus. The following information was recorded from each study: authors, country and study designation, sex, outcome, number of cases and participants/person-years of follow-up, multivariate-adjusted risk estimates (relative risks [RRs] or hazard ratios, but hereinafter formalized with the generic term RRs^{12,13}) and corresponding 95% CIs,

alcohol consumption categories, follow-up period, age range, and confounders. If the reference group was not the lowest alcohol consumption category or the multivariate-adjusted risk estimates were not available in the study, unadjusted crude risk estimates were calculated using original data.

The study quality was evaluated using an assessment scale for observational studies modified from previous studies.¹⁴ The total score ranges from 0 to 10 points, with a higher score indicating higher quality.

Statistical Analyses

Because the studies reported alcohol consumption in diverse measuring units, we transferred the exposure data into a uniform measurement of grams of ethanol per day (g/d) for the purpose of pooling estimates across studies. If a study did not provide data on the ethanol content of a drink or a unit, the average alcohol consumption was assumed to be 12 g per drink in studies conducted in the United States, 10 g per unit in Europe,¹⁵ and 11.5 g per drink in Japan.¹⁶ The median dose of each alcohol category was extracted and recalculated if not ready-provided for the purpose. For closed exposure interval, the median of the range was computed. If the lower bound for the lowest category was not provided, half of the upper bound of that category was taken as the median dose. For the highest open-ended exposure levels, the corresponding dose was assigned as the summation of the lower limit and three-quarters of the preceding category range.¹⁷

The semi-parametric method used in this analysis was modified from Ding et al.¹⁸ Four alcohol consumption groups were created, namely, the lowest, the third highest (median alcohol consumption, 10 g/d; range, 5.1-15 g/d), the second highest (median alcohol consumption, 20 g/d; range, 15.1-25 g/d), and the highest (median alcohol consumption, 30 g/d; range, 25.1-65 g/d). Abstainers/occasional drinkers, the lowest category, were considered as the reference group. For each included study, the lowest alcohol consumption categories were arranged to the lowest groups, and the highest to the highest. For other exposure categories in the study, they were arranged to either the second or the third highest group, depending on whether the median consumptions fell into the

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