Wine, Beer, and Spirits
Are They Really Horses of a Different Color?

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The study of alcohol and its effects on health has a long history, ranging from anecdotal accounts in biblical times to more recent rigorous studies of populations with hundreds of thousands of participants. The largest studies suggest that men and women who drink 1 to 2 drinks per day on average have lower total mortality rates, reflected in lower incidence of coronary heart disease, diabetes, and in some populations, ischemic stroke. The clear benefit of moderate alcohol consumption on risk of coronary disease has been documented in almost 100 studies. The early hypothesis that the apparent benefit might be explained by inclusion of sicker individuals among the nondrinkers ("sick quitter effect") has been decisively refuted in studies that excluded those with poor health at baseline or included only lifelong nondrinkers in the comparison group. Although no randomized trials with clinical end points have been conducted, further evidence for a causal link between moderate alcohol consumption and lower risk of coronary disease derives from genetic and metabolic studies. The finding of a strong interaction between alcohol intake and a common polymorphism in the gene for alcohol dehydrogenase strongly supports causality because such a result cannot plausibly be attributed to confounding factors (that is, the polymorphism can be considered as distributed at random with regard to other lifestyle practices like diet and exercise). Our understanding of the beneficial metabolic changes caused by alcohol consumption and the importance of genetic predisposition to these changes has advanced tremendously in recent years. With the general acceptance of the benefits of moderate alcohol consumption and the documented hazards of heavy consumption, research priorities of epidemiologic studies have shifted to the study of possible differential health effects of beverage choice and drinking patterns.

In this issue of Circulation, Di Castelnuovo et al provide a quantitative summary of population studies that have reported for wine and beer the beverage-specific risk estimates for cardiovascular disease. The authors report a strong and statistically significant benefit for both beer and wine at levels of moderate consumption, but they find a stronger inverse association for wine (32% risk reduction) than beer (22%). Several reviews, including our own, found the benefits of wine to be about the same as those of beer or spirits; thus, we concluded that it was unlikely that any one beverage was substantially more beneficial. It is therefore helpful to examine their results in more detail and to explore the importance of potential biases, if any, that may have influenced the findings.

The ethanol content in a serving of wine is similar to that in a serving of beer, and results from metabolic studies suggest that the effects of these beverages on lipid and hemostatic factors are similar. Thus, if this apparent difference in beverage-specific relative risks is true, then components in wine other than ethanol must confer substantial additional benefit. Several antioxidants and other compounds have been identified in red wine, but the incremental benefits of these compounds on biomarkers predictive of coronary heart disease have not been established. An alternative explanation might be that beer and wine have the same physiological effect, but differences in the risk factor patterns among beer and wine drinkers might create the appearance of a difference in coronary heart disease risk.

Table 2 in the article by Di Castelnuovo et al is instructive for further examination of their results because it outlines the important influences of individual study characteristics. Although the authors reported little difference between prospective and retrospective studies, when they excluded the 3 studies that did not simultaneously adjust for different types of alcoholic beverages (the most unbiased method to control for confounding), there was no meaningful difference in the relative risk (RR) of cardiovascular disease between wine drinkers (25%) and beer drinkers (23%) compared with abstainers. Again, in the dose-response analyses presented in Figures 2 and 5, the inverse association for beer would be very similar to that of wine if a few small studies were not included. These differences may be due to chance, but they do illustrate how susceptible results from meta-analyses are to a few potentially biased studies.

An additional pitfall of meta-analyses is that important covariates may not be treated equally across studies. Therefore, pooling RRs from studies that do not equally account for risk factors, such as dose of smoking or dietary pattern, can exaggerate or mask differences. This becomes especially complex for alcoholic beverage consumption because the direction of potentially important confounders, such as a prudent diet, can be completely opposite as a result of the cultural norms of the population under study. For example, in a large Danish study, fruit and vegetable consumption was strongly associated with wine intake, whereas in the recent
report from the French component of the European Prospective Investigation into Cancer and nutrition (EPIC) study,\\(^{12}\) drinkers of wine consumed fewer servings of fruits and vegetables. Even within the same country, the direction of confounding can differ. Contrary to the results from the EPIC study, in a separate population from France, wine consumption was associated with a better lifestyle profile; after controlling for diet and social class, the differential beneficial effects of wine over beer were eliminated.\\(^{13}\) Although individual studies vary, studies typically have found that wine drinkers tend to have a healthier lifestyle profile than do beer drinkers. Without careful control for such confounders across all studies, it is not possible to interpret the biases that may occur by pooling such estimates.

The growing number of studies addressing drinking patterns and preferences in recent years\\(^{11,14–16}\) should provide better insight into the importance of specific alcoholic beverages. Regardless of the population or the distribution of beverage consumption, however, residual confounding by diet, physical activity, behavioral characteristics, or even psychological parameters needs to be carefully addressed. In previous trials of alcohol, no important differences in lipids or hemostatic parameters have been reported across beverage types.\\(^{17}\) However, these trials have limitations. Few have monitored participants for periods longer than 4 weeks, and most are conducted on young (20- to 40-year-old), lean participants who may benefit the least from moderate ethanol consumption. To test the difference between the health effects of beverage preference, a trial may need to last for 1 to 2 years and measure risk factors, such as change in lipids, insulin sensitivity, hemostatic parameters, and oxidation status, and more complex markers of cardiovascular disease, such as change in intima-media thickness or carotid plaques. Even more creative approaches may be required because the power to detect small differences between beverages, if they exist at all, will be limited. Until such results are available, the interpretation of purported differences in the health effects of beverage type should be viewed cautiously.

References


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