Is There a Causal Relationship Between the Amount of Alcohol Consumption and Stroke Risk?

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In a review of the topic, Gorelick noted that alcohol consumption has been recognized as a possible risk factor for stroke for over 3 centuries.1 Subsequent studies find that the association between drinking alcohol and stroke risk is not straightforward. Literature on the subject is complicated by nonstandardized definitions of alcohol consumption, varying study designs, inadequate sample sizes, differing inception cohorts, as well as case-ascertainment and other potential biases. It is therefore not surprising that a systematic literature review revealed that individual studies report inconsistent relationships between the overall amount of alcohol use and stroke (although most show an association between recent use and increased stroke risk).2 However, the weight of available evidence indicates that light to moderate drinking is associated with a protective effect, whereas heavy consumption is associated with an increased risk of stroke (a so-called “J-shaped” or “U-shaped” relationship).3–6 This relationship is supported by a meta-analysis that identified 35 relevant cohort or case-control studies published between 1966 and April, 2002, which found that, as compared with abstention, consumption of less than 12 g (≈1 drink) of alcohol per day is associated with a 20% reduction in both ischemic (relative risk [RR]=0.80, 95% CI, 0.67 to 0.96) and total stroke (RR=0.83, 95% CI, 0.75 to 0.91), whereas >6 drinks per day is associated with increased risks of both ischemic (RR=1.69, 95% CI, 1.34 to 2.15) and total stroke (RR=1.64, 95% CI, 1.39 to 1.93).7

Consistent with the overall results of previous studies as reflected in the meta-analysis, the Northern Manhattan Stroke Study (NOMASS) investigators found that, after adjusting for age, sex, race-ethnicity, hypertension, diabetes, atrial fibrillation, HDL-cholesterol, and current smoking, reported recent (over the prior year) moderate alcohol use (≥1 drink per month to ≤2 drinks per day) was independently associated with reduced risks of ischemic stroke (adjusted hazard ratio [HR]=0.67, 95% CI, 0.46 to 0.99), all strokes (adjusted HR=0.68, 95% CI, 0.47 to 0.98), and ischemic stroke, myocardial infarction, or vascular death combined (adjusted HR=0.74, 95% CI, 0.59 to 0.94) as compared with those who reported not drinking.8 The estimate changed minimally with further adjustment for lifetime smoking history, body mass index, waist-hip ratio, coronary artery disease, low-density lipoprotein cholesterol, homocysteine level, and leucocyte count.

It needs to be recognized that all population-based cohort studies have inherent limitations. This is true even for the carefully conducted NOMASS analysis. In this study, inception cohort biases were minimized by identification of subjects without stroke at baseline through random-digit dialing (using both published and unpublished phone numbers).9 This methodology obviously excludes persons who could not be contacted by telephone. Although the overall response rate was high (68%), this means that responses were not available (because of refusal of informed consent or other reasons) for almost 1/3 of potential subjects.8 The amount of alcohol consumption was based on in-person interviews and provided estimates that had both high test-retest reliability and significant concurrent validity (based on the level of agreement between different questionnaires).3 However, these estimates are still based on patient or proxy report, which may be subject to a variety of biases. Relatively few participants reported being heavy consumers of alcohol, limiting the evaluation of the relative impact of higher levels of intake on stroke risk.

Perhaps the most important caveat is that epidemiological studies can provide evidence of statistical associations, but cannot prove causal relationships. To illustrate this type of problem, one need only consider the experience with postmenopausal hormone replacement therapy, where observational studies suggested a protective effect of estrogens on cardiovascular risk,10 but prospective randomized trials subsequently showed that hormone replacement therapy could cause harm.11 The demonstration of a causal, protective relationship between moderate drinking and stroke might be incorrectly inferred from the title of this NOMASS report, “Moderate alcohol consumption reduces risk of ischemic stroke.” The analysis provides further support for this association, but not causality.

Based on its association with an increased risk of stroke and for a variety of other health-related reasons, heavy drinkers should continue to be advised to reduce or eliminate their consumption of alcohol. As previously pointed out by the NOMASS investigators, “...no study has shown a benefit of recommending alcohol consumption to those who do not drink,”12 but there is no evidence of increased stroke risk and possible benefit for those who consume alcohol in moderation. Much work remains to be done to better understand the effects of alcohol on the cerebro- and cardiovascular systems.12
References


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