Critique 112: Relation of alcohol intake to risk of dying from cancer — 23 May 2013

Authors' Abstract

Background: Epidemiological studies have suggested an inconsistent relationship between alcohol drinking and risk of all cancer mortality. As far as we know, no meta-analysis has been conducted to explore this issue.

Patients and Methods: We carried out a PubMed search to find relevant articles published before April 2012 in English. Categorical and dose-response meta-analyses were conducted to identify the impact of alcohol drinking on all cancer mortality. Potential sources of heterogeneity were detected by meta-regression and stratification analyses. Sensitivity and cumulative meta-analyses were also carried out.

Results: Eighteen independent cohort studies met the inclusion criteria. Compared with non/occasional drinkers, the pooled relative risks (RRs) were 0.91 [95% confidence interval (CI) 0.89-0.94] for light, 1.02 (95% CI 0.99-1.06) for moderate, and 1.31 (95% CI 1.23-1.39) for heavy drinkers. Former drinkers presented a higher risk (RR = 1.32, 95% CI 1.15-1.50) than current drinkers (RR = 1.06, 95% CI 0.98-1.16). There was a J-shaped relationship between all cancer mortality and alcohol consumption in males but not in females.

Conclusions: This meta-analysis confirms the health hazards of heavy drinking (≥50 g/day) and benefits of light drinking (≤12.5 g/day). Large-sample, well-designed, prospective epidemiological studies, especially on heavy drinking among women, should be developed in future.

Forum Comments

There have been many papers relating alcohol intake to specific types of cancer. It is clear that heavy drinking is associated with an increase in the risk of most upper aero-digestive cancers (e.g., cancer of the mouth, pharynx, larynx), and even moderate drinking has been associated with a slight increase in the risk of breast cancer. On the other hand, the risk of thyroid cancer, lymphoma, renal cancer, and certain other cancers has been shown to be lower among moderate drinkers than among abstainers.

There have been few studies describing the relation between varying levels of alcohol consumption and the total risk of cancer. The present paper presents a meta-analysis relating alcohol intake to all cancer mortality, with data on more than 48,000 cancer deaths reported in 18 prospective cohort studies.

Surprisingly, the analyses demonstrated a J-shaped curve for alcohol and cancer. Light drinkers showed a statistically significant 9% lower risk, moderate drinkers showed no effect, and heavier drinkers showed a 32% increased risk of all cancer mortality.

Specific comments by Forum reviewers: Forum member Waterhouse found some troubling inconsistences in the paper. For example, in one place the risk of cancer for males, comparing non/occasional and "light" drinkers (≤ 12.5 g/day), is reported as a risk ratio (RR) of 0.91 (95% CI 0.87-0.94), while in a separate figure the risk is shown as essentially 1.0 with the 95% CI extending above 1 (suggesting lack of statistical significance). Further, in several

places in the text the authors refer to "borderline increased risk" when the calculated RR = 1.00: such a RR indicates no difference between the reference category and light drinkers. Reviewer Svilaas agreed that this meta-analysis has several weaknesses, mainly through a lack of studies with uniform inclusion criteria and purposes.

Reviewer Skovenborg commented: "This meta-analysis of alcohol drinking and cancer mortality is basically a state-of-the-art meta-analysis with strengths and weaknesses depending on the quality of the studies retrieved for the meta-analysis. For example, the cumulative time, frequency, and pattern of alcohol drinking were not analysed comprehensively in the present study due to insufficient data. However, considering that the International Agency for Research on Cancer (IARC) has confirmed alcohol as a Group 1 carcinogen for humans, the results of the meta-analysis are remarkable: a J-shaped relationship between alcohol consumption and cancer mortality."

Skovenborg continued: "Non/occasional drinkers were regarded as the reference group (which may be appropriate); however, subjects consuming 12.6–49.9 g/day were considered to be 'moderate' drinkers. However, this range of alcohol intake is equivalent to 1 – 4 drinks per day, with 4 drinks/day usually not being considered as 'moderate.'" Forum reviewer Finkel stated that he hopes that future studies (and meta-analyses) will focus more on how drinking *patterns* influence cancer risk, rather than having to focus just on the reported average amounts of alcohol consumed.

While realizing that the authors were limited by the published data from previous studies, Forum member Lanzmann-Petithory was disappointed that the authors were not able to differentiate the effects of beer, wine, and spirits on cancer mortality. Wine is a fermented fruit juice, and fruits are considered as protective against cancer. While alcohol is a carcinogen, the polyphenols and other substances in wine may have a different effect on cancer risk than alcohol. If there is a field where the differentiation of alcoholic beverages is essential, it is in relation to cancer.

Reviewer Ellison was surprised to see that the analyses indicated a significant overall *decrease* in the risk of total cancer for light drinkers. Further, in subgroup analyses, very similar decreases in risk were seen regardless of the degree of adjustment for confounders, among both men and women, for subjects from both population -based and occupation-specific cohorts, and when comparing results by categories of ethnicity. Still, he believed that residual confounding cannot be ruled out as a partial cause for the estimated reduced risk of cancer mortality among light drinkers. And there is the possibility that mistakes in classifying cause of death (e.g., defining a death as due to cancer when it may have been due to cardiovascular disease) may have contributed to such a result.

On the other hand, it is especially important that the only significant *increase* in risk in cancer mortality (among the almost 50,000 deaths reported in this meta-analysis) was for consumers of 50 grams or more of alcohol. This suggests strongly that the overall risk of cancer mortality related to alcohol consumption is primarily (perhaps almost exclusively) from heavier drinking. Certainly, the findings from this study do *not* support the premise that "any amount of alcohol increases the risk of dying from cancer."

Forum Summary

This paper presents a meta-analysis that related alcohol consumption to all-cancer mortality; it was based on almost 50,000 deaths reported in the literature from prospective cohort studies. Forum reviewers had some concerns about the conclusions of the paper, based on some discrepancies in the text, the lack of data on drinking pattern, no beverage-specific results, etc. Nevertheless, as expected, the reported average consumption of 50 or more grams of

alcohol per day (equivalent to 4 or more typical drinks each day) was associated with an estimated 32% increased risk of dying from cancer.

However, there was *no* increase in the estimated risk of cancer death for subjects classified as "moderate" drinkers (defined by the authors using a wide range of intake: 12.6 to 49.9 grams/day, the equivalent of up to approximately 4 or more typical drinks). Further, Forum members were surprised that a slight but statistically significant *decrease* in cancer mortality risk was seen for "light" drinkers (those reporting an average of ≤ 12.5 grams/day, or about one typical drink). Forum members appreciated that misclassification of cause of death or residual confounding could have contributed to this latter result.

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The following members of the International Scientific Forum on Alcohol Research made contributions to this critique:

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