

Letters to the Editor**Wine Consumption and Epithelial Ovarian Cancer**

To the Editors: We read with interest the article by Webb et al. (1) in which the authors showed a statistically significant trend toward lower risk of epithelial ovarian cancer with increasing wine consumption in a large case-control study of Australian women. They did not observe any association between consumption of beer or sherry/liquor and ovarian cancer risk.

We examined the relationship between consumption of specific alcoholic beverages, including wine, beer, and liquor, and risk of epithelial ovarian cancer using data from the Swedish Mammography Cohort, a population-based prospective study of 61,084 women ages 38 to 76 years at enrollment in 1987 to 1990. Information on consumption of alcoholic beverages was obtained through a mailed food frequency questionnaire. The Pearson correlation coefficients for the responses to the questionnaire for consumption of wine, beer, and liquor compared with four 1-week diet records (validation study among a subsample of 129 women from the cohort) were 0.8, 0.7, and 0.5, respectively. We used Cox proportional hazards models to estimate multivariate rate ratios (RR) and 95% confidence intervals (95% CI) while adjusting for age, body mass index, educational level, parity, oral contraceptive use, and intakes of energy and lactose (consumption of wine, beer, and liquor was mutually adjusted).

During a mean follow-up of 13.5 years (from March 1987 through June 2003), 266 incident cases of invasive epithelial ovarian cancer were diagnosed. Overall, wine consumption was not associated with risk of ovarian cancer. The multivariate RRs of ovarian cancer according to wine consumption (no consumption, <1 glass/wk, and ≥ 1 glass/wk) were 1.00 (reference), 1.00 (95% CI, 0.74-1.37), and 0.98 (95% CI, 0.65-1.47). Our ability to assess the role of higher wine consumption was limited because only a few women in our study regularly consumed wine (only 16% of women reported ≥ 1 glass/wk; $n = 39$ cases). We observed a statistically significant positive association of beer consumption with ovarian cancer risk ($P_{\text{trend}} = 0.04$). The multivariate RRs across increasing categories of beer consumption (no consumption, <1 glass/wk, and ≥ 1 glass/wk) were 1.00 (reference), 1.07 (95% CI, 0.75-1.52), and 1.35 (95% CI, 1.00-1.81). The association persisted after adjusting for alcohol (ethanol) consumption (RR, 1.38; 95% CI, 0.95-2.01 for the highest versus the lowest category), indicating that the observed increased risk with beer was not attributed to its alcohol content. Beer contains *N*-nitroso compounds, which are carcinogenic in animals (2). We found no association between liquor consumption and ovarian cancer risk.

We reported recently that alcohol consumption was positively associated with risk of ovarian cancer among women with a low dietary folate intake but not among women with a high folate intake (3). Therefore, we

considered the association of wine consumption with ovarian cancer risk among women with a high folate intake (i.e., ≥ 178 $\mu\text{g}/\text{d}$; corresponding to the median value for the cohort). Among these women, the multivariate RR of ovarian cancer was 0.94 (95% CI, 0.61-1.43) for <1 glass/wk of wine and 0.54 (95% CI, 0.27-1.09) for ≥ 1 glass/wk of wine ($P_{\text{trend}} = 0.13$) compared with no wine consumption. In an analysis controlling for alcohol consumption, the corresponding multivariate RRs were 0.76 (95% CI, 0.42-1.36) and 0.37 (95% CI, 0.15-0.93), respectively ($P_{\text{trend}} = 0.04$). This finding suggests that the observed inverse association with wine consumption is not due to its alcohol content. Wine is abundant in various antioxidants and also contains resveratrol, a phytoestrogen with anticarcinogenic properties (4).

In conclusion, our results corroborate and extend those of Webb et al. (1), suggesting that light-to-moderate wine consumption might reduce the risk of epithelial ovarian cancer. However, a benefit of wine consumption may require an adequate folate intake. The apparent increased risk of ovarian cancer associated with beer consumption warrants further study.

Susanna C. Larsson
Alicja Wolk
Division of Nutritional Epidemiology,
National Institute of Environmental Medicine,
Karolinska Institutet,
Stockholm, Sweden

References

1. Webb PM, Purdie DM, Bain CJ, Green AC. Alcohol, wine, and risk of epithelial ovarian cancer. *Cancer Epidemiol Biomarkers Prev* 2004; 13:592-9.
2. Lijinsky W. *N*-nitroso compounds in the diet. *Mutat Res* 1999; 443:129-38.
3. Larsson SC, Giovannucci E, Wolk A. Dietary folate intake and incidence of ovarian cancer: the Swedish Mammography Cohort. *J Natl Cancer Inst* 2004;96:396-402.
4. Jang M, Cai L, Udeani GO, et al. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. *Science* 1997; 275:218-20.

In Response: We thank Drs. Larsson and Wolk for their response to our article and were very interested to learn that they also saw an apparently strong protective effect of wine, but not other alcoholic beverages, on ovarian cancer risk although this was only for women with higher folate intake (1). Unlike the Swedish group, we did not see an appreciable effect for beer consumption.

Unfortunately, we were not able to evaluate folate intake in our study population and thus could not assess the potential interaction between folate and wine

consumption. Based on data from the Australian National Nutrition Survey, mean dietary folate intake among women ages 15 to 49 years was 229 $\mu\text{g}/\text{d}$ in 1995, and 67% of women had an intake $>200 \mu\text{g}/\text{d}$, the recommended level (2). Women in our study (3) were recruited in the early 1990s, but folate intake did not seem to change appreciably between 1983 and 1995 (2); thus, the 1995 data give an indication of folate intake in our study population. There was no folate fortification of foods in Australia at this time. It seems likely therefore that average dietary folate intake in our study population may have been higher than in the Swedish cohort (median, 178 $\mu\text{g}/\text{d}$), possibly reflecting the year-round availability of fresh fruit and vegetables in Australia compared with a temperate climate such as Sweden. This difference could potentially explain our finding of an overall reduction in risk of ovarian cancer with moderate wine intake regardless of folate status. Wine consumption was also higher among the Australian women, with 6.5% of cases reporting drinking ≥ 1 glass/d compared

with 16% drinking ≥ 1 glass/wk in the Swedish cohort. We look forward to seeing further data evaluating the relations among folate, wine and beer intake, and risk of ovarian cancer.

Penelope M. Webb
David M. Purdie
Christopher J. Bain
Adèle C. Green

References

1. Larsson SC, Wolk A. RE Alcohol, wine and risk of ovarian cancer. *Cancer Epidemiol Biomarkers Prev*. In press 2004.
2. Abraham B, Webb K. Interim evaluation of the voluntary folate fortification policy. Australian Food and Nutrition Monitoring Unit. Canberra: Commonwealth Department of Health and Aged Care; 2001.
3. Webb PM, Purdie DM, Bain CJ, Green AC. Alcohol, wine and risk of epithelial ovarian cancer. *Cancer Epidemiol Biomarkers Prev* 2004; 13:592–9.