“FOCUS ON” session:

**Nutrition and antioxidants
in vascular disease
and thrombosis**

A meta-analysis of studies on wine and beer and cardiovascular disease

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Abstract

Many epidemiologic studies have evaluated whether different alcoholic beverages protect against cardiovascular disease. We performed a meta-analysis of 26 studies on relationship between wine or beer consumption and vascular risk.

General variance-based method and fitting models were applied to pooled data derived from 26 studies that gave quantitative estimation of the vascular risk associated with either beverage consumption. From 13 studies involving 209,418 persons, the relative risk of vascular disease associated with wine intake was 0.68 (95% CI: 0.59-0.77) relative to nondrinkers. There was strong evidence from 10 studies involving 176,042 persons to support a J-shaped relationship between different amounts of wine intake and vascular risk. A statistically significant inverse association was found up to a daily intake of 150 ml of wine. The overall relative risk of moderate beer consumption, which was measured in 15 studies involving 208,036 persons, was 0.78 (95% CI: 0.70-0.86). However, no significant relationship between different amounts of beer intake and vascular risk was found after meta-analyzing 7 studies involving 136,382 persons.

These findings show evidence of a significant inverse association between light to moderate wine consump-

tion and vascular risk. A similar, although smaller association was also apparent in beer consumption studies. The latter finding, however, is difficult to interpret because no meaningful relationship could be found between different amounts of beer intake and vascular risk.

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Studies of alcohol and its effects on health have a long history, ranging from anecdotal accounts in biblical times to more recent rigorous studies of populations with hundreds of thousands of participants (1). 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. With the general acceptance of the benefits of moderate alcohol consumption and the documented hazards of heavy consumption, research priorities of epidemiological studies have shifted to the study of possible differential health effects of beverage choice and drinking patterns (1).

We have recently provided a quantitative summary of population studies that have reported for wine and beer the beverage-specific risk estimates for cardiovascular disease (2).

Table 1. Overall and subgroup analysis using studies included in a " Drinkers versus non-drinkers " meta-analysis (From ref. 2)

SUBGROUP	WINE			BEER		
	N	RR	99% CI	N	RR	99% CI
OVERALL	13	0.68	0.59-0.77*	15	0.78	0.70-0.86*
Type of cohort						
prospective studies	5	0.64	0.50-0.83*	8	0.79	0.67-0.94*
case-control studies	8	0.71	0.56-0.90*	7	0.74	0.57-0.96*
Type of event						
Coronary heart disease	11	0.71	0.59-0.85	13	0.79	0.68-0.91
Cerebrovascular disease	2	0.43	0.24-0.78	2	0.67	0.41-1.10
Non-fatal vascular events	8	0.71	0.56-0.90	7	0.74	0.57-0.96
Cardiovascular mortality	2	0.49	0.34-0.70	3	0.76	0.55-1.05
Gender effect						
Only males	6	0.87	0.68-1.12	6	0.82	0.68-0.99
Both gender	7	0.53	0.42-0.68	9	0.72	0.58-0.90
Adjustment for different types of alcoholic beverages						
Not adjusted	3	0.53	0.39-0.73	4	0.79	0.62-1.01
Adjusted	10	0.75	0.61-0.93	11	0.77	0.65-0.92
Adjustment for indicators of social class level						
Not adjusted	3	0.78	0.56-1.08	3	0.68	0.41-1.14
Adjusted	10	0.64	0.52-0.79	12	0.78	0.68-0.91
Other						
No light or occasional drinkers in the reference group	10	0.73	0.59-0.91	11	0.80	0.66-0.97
No ex-drinkers in the reference group	5	0.61	0.47-0.79	5	0.77	0.63-0.94
With the same reference group both for wine and beer	9	0.62	0.50-0.77	9	0.72	0.59-0.88

*95% Confidence interval

Evidence obtained from this meta-analysis indicates an average significant reduction of 32% of overall vascular risk associated with drinking wine (Table). Not only were non-fatal vascular endpoints significantly reduced in wine drinkers, but also cardiovascular mortality. In studies with only males, the protection offered by wine was surprisingly small (13%) and not significant, in contrast with studies enrolling both genders (47%). Whether women are more susceptible to the benefit of wine or they more likely drink lower amounts taking its maximal advantage remain to be established. In relation to the reported association between moderate alcohol consumption and increased risk of breast cancer (3) our finding suggests that the overall effect of moderate wine intake on women health may actually be favorable. In agreement with the relation between alcohol intake and all-cause mortality previously reported, (4-5) we observed a J-shaped relationship between wine intake and vascular risk, suggesting that light to moderate wine drinkers (up to 200 ml/day on average) have lower vascular risk than either heavier drinkers or non-drinkers.

Beer drinking was also found to be associated with a reduced risk of vascular events, though at an extent lower than that observed with wine (22%). A significant inverse association was still apparent when CHD was only considered, but -at variance with wine- it did not reach statistical significance when CVD events or cardiovascular mortality were separately evaluated, likely due to the small number of available studies. Risk reduction connected with beer drinking was smaller but, at variance with wine, still significant in studies where only males were included. This suggests that women might be particularly "responsive" to alcohol itself rather than to non-alcoholic components of these beverages. The most important difference between wine and beer consumption was however observed in the meta-analysis of studies reporting trend analysis. In contrast with wine, indeed, the fitted models failed to show any significant relationship between different amounts of beer intake and vascular risk, even when different subgroups were analyzed. Thus, the inverse association between beer consumption and vascular risk should be interpreted with caution.

Previous reviews (1, 4) found the benefits of wine to be about the same as those of beer or spirits, and concluded that it was unlikely that any one beverage was substantially more beneficial. When we 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 indeed no meaningful difference in the relative risk (RR) of cardiovascular disease between wine drinkers (25%) and beer drinkers (23%) compared with abstainers. However, the relative 10% overall difference between RR of wine versus beer drinkers were unchanged in studies that assessed both wine and beer drinking versus the same reference group. The potential confounding effect of combined drinking of different type of alcoholic beverages in the same population was excluded by pooling data from studies that had taken this issue into consideration. Errors in reporting beer intake might have contributed

to our failure to draw any statistically significant “dose-response” curve from studies on this beverage. Irregular (binge) drinkers possibly frequent in cohorts of beer drinkers, might have obscured a possible dose-dependent risk reduction in regular beer drinkers.

In conclusion, association does not prove cause and effect, but the presence of a “dose-response” relation in wine meta-analysis, although of a complex, J-shaped type, is of importance. Definite proof could only be obtained by large long-term intervention trials. Such trials however appear to be unfeasible for several reasons, including ethical concern. The evidence for the benefit connected with wine or beer consumption should therefore critically include molecular and cell biology, animal and observational epidemiological studies and their meta-analysis (6).

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