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Alcohol and mortality: if you drink, do not forget fruits and vegetables

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Abstract: Moderate amounts of alcohol may have cardioprotective effects. Several studies reported a higher protection by the consumption of wine. The favorable effects of wine have been attributed to different polyphenol compounds, among others. However, these biochemical compounds are also found in other beverages. In view of the present evidence, there is no "right" or "wrong" drink, only a "right" and "wrong" drinking behavior regarding absolute amounts, drinking frequency, and accompanying lifestyle and eating pattern

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cal intervention, this study also seems to counter the arguments of people who oppose the use of sodium restriction to control blood pressure, i.e., that the large epidemiologic studies and meta-analyses of clinical trials are statistically invalid such that their demonstrations of an association can not be trusted. The fact that it worked in all of the subgroups studied suggests that a widespread application in the general population is warranted.

The question that remains to be answered is whether or not this approach will translate well to the general population. Because the DASH diet and its low-sodium version were well tolerated in this study (as evidenced by the low dropout rate), there is hope that the people who adopt this approach could continue it. If they can continue to comply without the intense oversight that generally accompanies a clinical intervention trial, there is evidence from studies of sodium restriction⁶ that the dietary approach will likely continue to be successful. Still, this remains to be shown. As they design studies to evaluate this issue, the DASH study group might be wise to pay attention to the results of the nine National Cancer Institute-funded "5-A-Day" interventions aimed at increasing the consumption of fruits and vegetables in various groups within the U.S. general population.⁷ Collectively, these studies show that one of the keys to successful dietary change is directed nutritional education through channels that provide a strong social support network (e.g., churches, schools, social organizations, and workplaces). Another area that they might consider for future follow-up is to determine whether DASH or DASH-sodium could be coupled with drug therapy to more effectively treat severe hypertension. This idea has precedent in the work of Siani et al.,⁸ who showed that a diet high in potassium (reached through increased fruit and vegetable

consumption) could reduce the amount and number of medications that one needs to control hypertension. Regardless of the future directions of the DASH research group, their work provides a strong argument in favor of nonpharmacologic alternatives (such as diet) to control high blood pressure.

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Alcohol and Mortality: If You Drink, Do Not Forget Fruits and Vegetables

Moderate amounts of alcohol may have cardioprotective effects. Several studies reported a higher protection by the consumption of wine. The favorable effects of wine have been attributed to different polyphenolic compounds, among others. However, these biochemical compounds are also found in other beverages. In view of the present evidence, there is no "right" or "wrong" drink, only a "right" and "wrong" drinking behavior regarding absolute amounts, drinking fre-

quency, and accompanying lifestyle and eating pattern.

Alcoholic beverages including wine have a long tradition as potential remedies and modulators of morbidity and mortality.¹ Despite the many epidemiologic and experimental studies regarding the cardioprotective effect of alcohol, the role of alcohol itself, the type of beverage, and drinking pattern remain controversial. Several studies reported an inverse relationship between the consumption of wine² and coronary artery disease risk; however, such a relationship was not found for beer³ or liquor^{4,5} consumption. On the other hand, in the Canada Health Survey, light-to-moderate beer drinkers had a lower morbidity than

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expected.⁵ Contrary to the latter studies, several meta-analyses and studies concluded that the alcohol-related protection is independent of the type of alcohol.⁶⁻¹⁰ In view of the potential protective effect of alcohol consumption, it is of general interest to clarify the question whether different alcoholic beverages elicit different effects on mortality.

In a recent pooled prospective cohort study, the relation between consumption of different types of alcoholic beverages and death from all causes, cancer, and coronary artery disease was published.¹¹ In this study, data from three different population samples were pooled and a total of 13,064 men and 11,459 women were included in the final analysis. The different study samples were initiated and recruited between 1964 and 1976 and all participants were followed up until 1995. At the baseline evaluation, total alcohol intake as well as alcohol intake according to beverage type was assessed. In addition, other lifestyle factors such as smoking habits, education level, leisure time physical activity, and body mass index were assessed, and the statistical analysis was adjusted for these parameters. Despite the large population and rather long follow-up, less than 1% of the participants were lost to follow-up.

The analysis revealed a J-shaped curve for mortality and total alcohol consumption, as well as consumption of alcohol from wine.¹¹ The consumption of one to seven drinks per week (1 drink defined as 12 g of alcohol) produced a lower relative risk (RR) for all-cause mortality (RR 0.82; 95% confidence interval [CI], 0.76–0.88) compared with nondrinkers. The intake of more than 35 drinks per week was associated with a nonsignificantly increased RR for all-cause mortality (RR 1.10; 95% CI, 0.95–1.26). Total alcohol intake was inversely related to coronary artery disease death, and positively related to death from cancer. Light beer consumption (i.e., 1–7 drinks of beer/week) had a small but significant effect on all-cause mortality (RR 0.90; CI 95%, 0.83–0.97) and on coronary artery disease risk (RR 0.78; 95% CI, 0.67–0.91). Light to moderate intake of wine seemed to have favorable effects on the RR for all-cause mortality. Light alcohol consumers avoiding wine had an RR for all-cause mortality of 0.90 (95% CI, 0.82–0.99); however, light consumers drinking wine had a considerably lower all-cause mortality risk. Compared with light drinkers who avoided wine, those consuming 30% or less of their total alcohol in the form of wine had an RR for all-cause mortality of 0.67 (95% CI, 0.53–0.84); the RR for those consuming more than 30% of their alcohol intake in the form of wine was 0.83 (95% CI, 0.74–0.93). The difference between these two strata of wine consumers was not significantly different ($P = 0.15$). Wine drinkers showed a significantly lower all-cause mortality risk than non-wine drinkers at all levels of consumption ($P < 0.001$). Cancer risk increased with increasing alcohol intake. Independent of the level of alcohol intake, non-wine drinkers had

a higher cancer risk than wine drinkers. The consumption of small quantities of spirits had no significant effect on all-cause mortality risk or coronary artery disease. Higher quantities of spirit consumption led to an increase in RR for death from all causes, coronary artery disease, and cancer.

The data from this Danish study offer additional support for beneficial effects of light to moderate wine and beer consumption on all-cause mortality. Despite these positive results, the data from the present study have to be interpreted and implemented with caution.

An important question in studies involving alcoholic beverages and disease risk is whether the effect is due to alcohol per se or if it is alcoholic beverage-specific. Although it has been reported that the effect of alcohol on risk of death including coronary artery disease risk is independent of the type of beverage,⁷ several cross-sectional studies found only an inverse relationship between red wine consumption and the incidence of coronary artery disease,¹²⁻¹⁴ and no protective effect was found for other alcoholic beverages, i.e., beer and spirits. The favorable effects of wine have been attributed to its polyphenolic compounds such as flavonols, catechins, resveratrol, or anthocyanins.¹⁵⁻¹⁸ In several epidemiologic studies, cardioprotective effects of flavonoids from dietary sources other than red wine have been observed.¹⁹⁻²¹ Most plant foods contain phenolic substances and the dietary intake of phenolic substances, depending on the composition of the diet, may be several hundreds of milligrams per day.^{15,22} It is often wrongly assumed that polyphenolic compounds are found in red wine but not in beer or other alcoholic beverages.¹¹ As a function of the production process of alcoholic beverages, flavonoids are also found in beer. Indeed, beer may even be a more important source of flavonoids than certain red wines, although the variability of the content of phenolic acids in selected beers is very high.¹⁵ More than 60 different phenolic compounds have been identified in beer.¹⁵ The concentration of phenolic acids in commercial beer depends mainly on the extent of their extraction during mashing. The concentration of polyphenols decreases owing to protein precipitation, especially during the processes of fermentation¹⁵ and filtration. As a general rule, it can be said that beer with turbidity usually has higher polyphenol content.

Because polyphenolic compounds elicit a bitter taste and astringency, they are usually eliminated or at least reduced during food processing.²³ Modern beer processing includes several filtration steps to eliminate turbidity, which leads to removal of most of the polyphenolic compounds.¹⁵ A highly processed beer is therefore a negligible source of flavonoids for the reasons stated above. If a beer contains flavonoids, they seem to be bioavailable;²⁴ however, whether the bioavailability is different from the bioavailability of red wine flavonoids is not known. The content of polyphenolics in red wine also show much vari-

ability as a function of many different factors such as the type of grape, origin, processing, and storage. Despite the polyphenol content of red wine, to what extent these polyphenolics are bioavailable is still controversial. In a recent paper, it was concluded that red wine is actually a poor source of bioavailable flavonols for humans.²⁵ In the study by Gronbaek et al.¹¹ the consumption of one to seven drinks per week was associated with a favorable risk reduction, which would imply that the consumption of 1 drink per week would result in a favorable risk reduction. The flavonol content of one glass of red wine would be negligible and hardly elicit a pharmacologic effect leading to a measurable cardioprotective effect. Although red wine represents a potential source of polyphenolic compounds, other dietary sources such as tea, fruits, and vegetables represent quantitatively more important sources.^{15,21} Accordingly, data about favorable effects of wine polyphenolics must be interpreted with caution.²⁶ This suggests that other mechanisms are responsible for the cardioprotective effects of red wine.

Alcohol may elicit a cardioprotective effect through other mechanisms such as antithrombotic effects,²⁷⁻²⁹ effects on glucose tolerance,³⁰ increased high-density lipoproteins (HDL),³¹ inhibition of low-density lipoprotein oxidation,³² specific lipid effects such as cholesterol metabolism,³³ ischemic preconditioning,³⁴ or sedative effects.³⁵ Despite many different proposed mechanisms, it remains unclear by which mechanism alcohol exerts its protective effect. In addition, neither ethanol nor red wine polyphenols affect mature atherosclerosis in an apolipoprotein E-deficient mice model.³⁶

The drinking pattern in the present study differs from most other countries because most participants drank moderately or heavily on the weekends, and lightly during the week.¹¹ It has been reported that the pattern of drinking in relation to food intake may explain some of the cardioprotective effects of alcohol in the form of wine. The Mediterranean lifestyle is characterized by consumption of wine with the main meals^{37,38} and it seems that alcohol may modulate postprandial metabolism favorably.²⁷

The mean age of the study population was greater than 50 years, more than 50% were smokers, the majority (approximately two-thirds) were physically inactive, and the mean body mass index (BMI, kg/m²) was ≥ 25 .¹¹ These baseline characteristics reveal a rather high prevalence of the well known cardiovascular risk factors. Accordingly, it is not surprising that alcohol elicits a reduction in the relative risk of death because earlier studies showed that the protective effects of alcohol are especially seen in older subjects with multiple cardiovascular risk factors.^{39,40} This suggests that alcohol modulates the deleterious effects of some cardiovascular risk factors favorably.

There is controversy regarding whether differences exist in the modulation of all-cause mortality and coronary artery disease risk as a function of the beverage type. It is

established, however, that there is a J-shaped relationship between all-cause mortality and alcohol intake.⁴¹⁻⁴⁵ It is also very controversial as to where the nadir of the curve lies, i.e., at which consumption level is the lowest mortality risk seen. The heterogeneity of subjects in epidemiologic studies reflects the heterogeneity of the metabolic effects of alcohol in one individual compared with another. Recently, it was shown that cardiovascular risk might be modulated differently by alcohol as a function of the genetic make-up of alcohol dehydrogenase (ADH).⁴⁶ Hines et al.⁴⁶ reported that subjects homozygous for the slow-oxidizing ADH (ADH3) do have higher HDL cholesterol levels and a substantially decreased risk of myocardial infarction. The cardioprotective effect of the ADH3 polymorphism is caused by the slower rate of alcohol clearance, which is also associated with higher levels of HDL cholesterol.⁴⁶ The amount of alcohol that provides the minimum risk for coronary artery disease varies considerably from one individual to the other according to the genetic make up of the alcohol metabolizing enzymes. Similarly, the level of alcohol consumption with the least all-cause mortality varies largely from one country to the other.⁴¹ Based on several studies, the pooled estimates of the nadir of alcohol intake (i.e., the level of alcohol consumption at which mortality is lowest) is 7.7 units of alcohol per week for U.S. men (95% CI, 6.4-9.1).⁴¹ The corresponding number for U.S. women is 2.9 units/week (95% CI, 2.0-4.0); for U.K. men it is 12.9 units/week (95% CI, 10.8-15.1).⁴¹ These data do show the large variability of the amount of alcohol needed for beneficial and/or adverse effects. These data show that it may be very deleterious to formulate recommendations of alcohol consumption for cardioprotection.

Although alcohol represents an important modulator of cardiovascular risk, the effects may be largely due to characteristics of the consumer and less to chemicals associated with a certain type of beverage and/or the alcohol per se. There is insufficient evidence for a public health recommendation and justification of alcohol in any form for cardioprotection owing to the lack of large-scale prospective clinical trials, as discussed in a recent advisory statement of the American Heart Association.⁴⁷ There is no "right" or "wrong" drink, therefore, but only a "right" or "wrong" amount and frequency of alcohol consumption.⁴⁸ It seems that if you ingest moderate amounts of wine (and probably any other alcoholic beverage), doing so *in combination* with a diet rich in fruits and vegetables would be a prudent way to elicit cardioprotective effects.

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