Wine, Beer, and Mortality in Middle-aged Men From Eastern France

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Objective: To evaluate prospectively the health risk of wine and beer drinking in middle-aged men in the area of Nancy, France.

Design: Prospective cohort study.


Main Outcome Measures: Education, professional and leisure activities, and smoking and drinking habits were evaluated using a questionnaire. Blood pressure and mean corpuscular volume and γ-glutamyltransferase, glucose, and serum cholesterol levels were routinely measured, and electrocardiography was routinely performed. We recorded mortality from all causes and specific causes during a 12- to 18-year follow-up across categories of baseline alcohol consumption.

Results: Of the subjects, 28% drank beer, 61% drank wine but no beer, and 11% were abstainers; there was not much difference between social classes. During the follow-up, 3617 subjects died. The relative risk of death was estimated by the Cox proportional hazards model using nondrinkers as the reference and adjusting for 4 or 5 covariables. Moderate intake of both wine and beer was associated with lower relative risk for cardiovascular diseases; the risk was more significant with the intake of wine. For all-cause mortality, only daily wine intake (22-32 g of alcohol) was associated with a lower risk (0.67; 95% confidence interval, 0.58-0.77; P < .001) due to a lower incidence of cardiovascular diseases, cancers, violent deaths, and other causes.

Conclusion: In eastern France, moderately drinking only wine was associated with a lower all-cause mortality, although drinking both wine and beer reduced the risk of cardiovascular death.

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The conclusion of a recent meta-analysis1 on drinking and mortality was that the results were “inconsistent with the belief that daily consumption of a few glasses of wine has salutary effects.” To conclude whether wine may have salutary effects, its influence on all-cause mortality should be precisely evaluated. Recent prospective studies2-6 observed that a moderate intake of alcohol was associated with a lower overall death rate. However, only 2 of these studies determined the respective role of the different alcohols. In Shanghai, China,7 the consumption of wine, mostly rice wine, was not more beneficial than that of beer or spirits. By contrast, in Denmark6 only the moderate intake of wine (grape wine) could lower mortality from cardiovascular and other causes. Grape wine appears to be the main alcoholic beverage that contains antioxidant phenolic substances, which are known to inhibit oxidation of low-density lipoprotein7 and affect platelet functions.8 Among these substances, resveratrol may even inhibit the 3 main stages of carcinogenesis.9

We reported recently10 that all-cause mortality in middle-aged men from eastern France who consumed mostly wine (1-3 drinks per day) was 20% to 30% lower compared with abstainers. In that study, because specific causes of mortality were available for only 1529 men, the number was not sufficient to determine whether beer drinking offered similar protection to wine drinking. The aim of the present study of the same cohort with 2 more years’ follow-up and, this time, 3617 deaths, for which we obtained permission to use death certificates, was to evaluate whether beer drinking would have effects similar to wine drinking on all causes and specific causes of mortality.

RESULTS

The abstainers, who only occasionally drank, had significantly lower levels
PARTICIPANTS AND METHODS

We used data from 36,250 men, aged 40 to 60 years, born in France, who underwent medical examinations at the Centre de Médecine Préventive, Vandoeuvre-les-Nancy, France, between January 1, 1978, and December 31, 1983. As described previously,10 the examination is a free routine extensive health appraisal offered by the regional Caisse Nationale d’Assurance Maladie des Travaillleurs Salariés to 93% of the families in the area. The sample represents a cross section of active men in the area as confirmed by a survey of the Institut National des Statistiques et des Études Démographiques. The examination includes a comprehensive questionnaire on current and past medical history, education, professional and leisure activities, smoking habits, and amount and type of alcoholic beverages consumed. The questionnaire on drinks included 6 different beverage categories, of which 3 were alcoholic: wine, beer, and aperitifs and liqueurs. The categories of consumption for wine and beer were never or occasionally; less than 250 mL; 250 to 500 mL; 0.5 to 1 L; 1 to 2 L; 2 to 3 L; and more than 3 L. The categories of weekly consumption for aperitifs and liqueurs were rarely or never; 1 to 2; 3 to 5; 6 to 9; and 10 or more drinks. For the conversion to grams of alcohol, we assumed that 1 L of wine contained 88 g of alcohol; 1 L of beer, 44 g; and 1 glass of spirits, 15 g. Thus, 120 mL of wine and 240 mL of beer contain 10.5 g of alcohol.

To determine whether the drinking habits changed with time, a random subsample of 8350 men was evaluated twice, 5 to 6 years apart.10 The correlation coefficient between the 2 evaluations was 0.61 (95% confidence interval [CI], 0.60-0.62) despite a decrease in the mean intake of alcohol (48.0-41.1 g/d) during that period. That decrease was concurrent with the 12.3% decrease in alcohol consumption between 1978 and 1984 in France.11

As already reported,10 the medical examination comprised an electrocardiogram, thoracic x-ray films, and determination of weight, height, blood pressure, and numerous variables in blood and urine samples. In the present study,

(Tables 1) of mean corpuscular volume and γ-glutamyltransferase compared with wine and beer drinkers. The percentage of abstainers who were smokers was also lower. In addition, they had a tendency to have lower blood pressure and serum cholesterol and glucose levels. There were significant (P<.001) increasing trends in values for mean corpuscular volume, γ-glutamyltransferase, blood pressure, serum cholesterol, and glucose with higher intakes of alcohol. Thus, except for engaging in more sedentary activities, the abstainers were the healthiest group.

Among the alcohol drinkers, we considered at first 3 categories: the wine drinkers who did not drink any beer (22,093 subjects and 2080 deaths); the beer drinkers whose consumption of alcohol was more than 40% beer (2466 subjects and 334 deaths); and the beer and wine drinkers (7673 subjects and 811 deaths).

As summarized in the Figure, after adjusting for age, smoking, education, and BMI, only those who drank only wine daily, and did so in moderation (1-54 g of alcohol), had a significantly (P<.02 to .001) lower all-cause mortality compared with abstainers. The RR of mortality in the wine and beer drinkers was between that of the 2 other groups. Nevertheless, heavy drinking (≥131 g/d) in the 3 groups was associated with a significantly (P<.01 to .001) increased risk of death.

Because of the small number of subjects (2466) whose consumption of alcohol was more than 40% beer, in further analysis, all subjects drinking beer were considered beer drinkers (10,139; Table 1) even if 86% of the subjects had also consumed some wine. In all subsequent analyses (Tables 2, 3, and 4), those 10,139 beer drinkers were compared with the 22,093 wine drinkers who did not have any beer. All-cause mortality (Table 2), after adjusting for age, smoking, education, and BMI, was lower by 20% (P<.02) to 33% (P<.001) for those who drank wine daily (as much as 54 g of alcohol) compared with abstainers. For all cancers, there was also a lower mortality (10%-22%) in wine drinkers, which was significant only for a daily intake of 22 to 32 g of alcohol (P<.05).

In the moderate beer drinkers, after adjusting for the same factors (Table 2), there was no significant lower mortality from all causes and cancer. The high intake of both beer and wine increased the risk of death from all causes and cancer, especially if the daily intake was more than 131 g of alcohol (P<.001).

In wine drinkers, after adjusting for age, smoking, education, BMI, and physical activity, mortality from CHD (Table 3) was lower by 45% (P<.003) to 48% (P<.003) for a daily intake of 22 to 54 g of alcohol. At that level of wine intake, mortality from CVD was reduced by 39% (P<.001) to 40% (P<.001).

In beer drinkers (Table 3), adjusting for the same factors, mortality from CHD and CVD was also lower by 42% (P<.02) and 32% (P<.02), respectively, but only

Table 1. Baseline Characteristics of Abstainers and Wine and Beer Drinkers*

<table>
<thead>
<tr>
<th>Subjects</th>
<th>No. of Men</th>
<th>Age, y</th>
<th>BMI, kg/m²</th>
<th>Abnormal ECG, %</th>
<th>MCV, cµ</th>
<th>GGT, U/L</th>
<th>Systolic BP, mm Hg</th>
<th>Serum Cholesterol, mmol/L (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstainers</td>
<td>4018</td>
<td>48.90 ± 5.67</td>
<td>25.45 ± 3.50</td>
<td>6.31 ± 3.45</td>
<td>90.67 ± 4.47</td>
<td>34.42 ± 35.45</td>
<td>133.89 ± 17.93</td>
<td>5.93 ± 1.12 (229 ± 43)</td>
</tr>
<tr>
<td>Wine drinkers</td>
<td>22,093</td>
<td>49.22 ± 5.74</td>
<td>25.90 ± 3.30</td>
<td>6.40 ± 3.50</td>
<td>92.41 ± 4.61</td>
<td>50.86 ± 56.91</td>
<td>136.66 ± 17.99</td>
<td>6.22 ± 1.12 (241 ± 43)</td>
</tr>
<tr>
<td>Beer drinkers</td>
<td>10,139</td>
<td>48.02 ± 5.68</td>
<td>25.54 ± 3.38</td>
<td>5.79 ± 3.34</td>
<td>93.37 ± 4.89</td>
<td>64.74 ± 74.36</td>
<td>137.20 ± 18.22</td>
<td>6.29 ± 1.16 (243 ± 45)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SD unless otherwise indicated. Wine drinkers did not drink beer. Most of the beer drinkers also had wine. Abstainers occasionally drank alcohol. BMI indicates body mass index; ECG, electrocardiogram; MCV, mean corpuscular volume; GGT, γ-glutamyltransferase; and BP, blood pressure.
we tested the serum cholesterol and γ-glutamyltransferase levels, as tested in the previous study, and also mean corpuscular volume and glucose levels to confirm that the abstainers were really nondrinkers with fewer risk factors.

The vital status of the subjects was determined 12 to 18 years after their first visit to the center, yielding 515 600 person-years of follow-up through 1995. The vital status was supplied by the Institut National des Statistiques et des Etudes Démographiques. After permission was granted by the Commission Nationale de l’Informatique et des Libertés, the causes of death according to the death certificates were obtained through the Institut National pour la Santé et la Recherche Médicale (Service Commun 8), Le Vesinay, France, for all subjects. The cause of death was classified according to the International Classification of Diseases, Ninth Revision. In the present article, the causes of death were all cardiovascular diseases (CVDs) (codes 390-459), coronary heart disease (CHD), including sudden death (codes 410-414), all cancers (codes 140-209), cirrhosis (code 571), and unnatural death (codes 800-999). Other causes were the sum of the causes of death not listed above.

We calculated relative risk (RR) estimates as the ratio of incidence density of death in different categories of alcohol intake to the incidence density among abstainers. We used the Cox proportional hazards model to estimate the RR, adjusting for age, education (high school graduate or no high school), cigarette smoking (currently, formerly, or never), and body mass index (BMI), which is calculated as the weight in kilograms divided by the square of the height in meters. Analyses of mortality from CHD and CVD were also adjusted for physical activity. As suggested by Camargo et al, the RR was not adjusted for predictors of mortality affected by alcohol consumption, such as blood pressure and serum cholesterol levels, because they may not be confounders but effects of exposure. The RR is presented with 95% CIs, and P values are 2-sided. Finally, the proportionality of the model was confirmed by fitting the model using 3 alcohol strata and plotting the log (−log [survival]) curves. The 3 curves were nearly parallel for each covariable included in the model.

### COMMENT

We found that French men who consumed 2 to 5 drinks of wine per day had a significant 29% to 33% reduction in overall mortality relative to abstainers, a finding previously reported in a much smaller sample of the same cohort. The association we observed could not be explained by confounding factors, such as age, cigarette smoking, BMI, or level of education. By contrast, in the beer drinkers there was no reduction in the overall death rate, a finding similar to that of Gronbaek et al.

In the wine drinkers, the lower all-cause mortality was associated with a significant reduction in mortality from CHD (45%-48%) and CVD (39%-40%). In the beer drinkers (3-9 drinks per day) a reduction in the mortality from CHD (23%-42%) and CVD (26%-32%) was also noted. The somewhat less consistent effect of drinking fewer than 5 drinks per day of beer on mortality from CHD and CVD compared with drinking the same amount

<table>
<thead>
<tr>
<th>Glucose, mmol/L (mg/dL)</th>
<th>Smokers, %</th>
<th>Sedentary, %</th>
</tr>
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<tbody>
<tr>
<td>5.74 ± 0.95 (222 ± 37)</td>
<td>33.35 ± 47.15</td>
<td>17.59 ± 38.00</td>
</tr>
<tr>
<td>5.87 ± 0.86 (227 ± 33)</td>
<td>41.02 ± 49.19</td>
<td>12.43 ± 33.00</td>
</tr>
<tr>
<td>5.99 ± 0.92 (227 ± 36)</td>
<td>49.32 ± 49.99</td>
<td>13.66 ± 34.33</td>
</tr>
</tbody>
</table>

Adjusted relative risk of death from all causes in relation to the intake of alcohol and type of beverage. The beer drinkers (2466 subjects and 334 deaths) were consuming at least 40% of alcohol as beer. The beer and wine drinkers (7673 subjects and 811 deaths) consumed less than 40% of alcohol as beer. The wine drinkers (22 093 subjects and 2080 deaths) did not drink any beer. The abstainers occasionally drank alcohol (4018 subjects and 392 deaths). Evaluated by the Cox proportional hazards model, adjusted for age, smoking, education, and body mass index (calculated as weight in kilograms divided by the square of the height in meters). The fitted curves are from polynomial regression models. The asterisk indicates P < .02; dagger, P < .001; double dagger, P < .01. 

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of wine may be due to the small number of events in beer drinkers.

The lower mortality from CHD and CVD with a moderate intake of alcohol is consistent with results of numerous studies reported by Rimm et al.\textsuperscript{13} By contrast, we observed a reduction in overall mortality only with wine drinking. The main explanation could be that only wine drinking was associated with a significantly lower death rate from cancer (by 20%-22%) and other causes (by 28%-42%) for 1 to 3 drinks per day.

Could bias explain the associations we observed between wine drinking and mortality? A possibility is that the nondrinkers were an unsuitable group for comparison as emphasized by Shaper et al.\textsuperscript{14,15} The nondrinkers

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|c|}
\hline
Alcohol Intake, g/d & All Causes & Cancer & All Causes & Cancer & All Causes & Cancer \\
\hline

\begin{tabular}{|c|c|c|c|}
\hline
No. & RR (95\% CI) & P & No. & RR (95\% CI) & P \\
\hline
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\end{tabular}
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\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|c|}
\hline
Alcohol Intake, g/d & CHD & CVDs & CHD & CVDs & CHD & CVDs \\
\hline

\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
No. & RR (95\% CI) & P & No. & RR (95\% CI) & P & No. & RR (95\% CI) & P \\
\hline
\end{tabular}

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\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
Alcohol Intake, g/d & Wine & Beer & Wine & Beer & Wine & Beer \\
\hline

\begin{tabular}{|c|c|c|c|}
\hline
No. & RR (95\% CI) & P & No. & RR (95\% CI) & P \\
\hline
\end{tabular}

\hline
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\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
Alcohol Intake, g/d & Wine & Beer & Wine & Beer & Wine & Beer \\
\hline

\begin{tabular}{|c|c|c|c|}
\hline
No. & RR (95\% CI) & P & No. & RR (95\% CI) & P \\
\hline
\end{tabular}

\hline
\end{tabular}
\end{table}

*CI indicates confidence interval, which was evaluated by the Cox proportional hazards model, adjusted for age, smoking, education, and body mass index; ellipses, not applicable; and abstainers, subjects who occasionally drank alcohol.
included the real controls, such as lifelong abstainers and ex-drinkers who may have a high rate of cardiovascular-related disorders. In the study\textsuperscript{19, 15} of men from England, Wales, and Scotland, moderate drinkers had a 34% reduction in RR of death due to CHD but only a nonsignificant 13% reduction in death due to CVD and no reduction in death due to all causes. In 1980, 67% of alcohol consumed in England was in the form of beer\textsuperscript{11}; therefore, the subjects of that study\textsuperscript{15} were probably consuming mostly beer.

In our study, the abstainers (occasionally drinking) were not likely to be predisposed to CHD, since the percentage of electrocardiogram abnormalities was similar to that of the wine drinkers. In addition, they had the lowest blood pressure, serum cholesterol levels, and glycemia and the lowest incidence of smoking, suggesting that they were healthier than drinkers. In addition, as reported previously,\textsuperscript{18} when we excluded the men who died within 24 months of screening and could have been sick at enrollment, the relationship between alcohol intake and mortality was not modified. However, our finding is that the lower all-cause mortality of moderate drinkers was apparently not due to sick controls but to the consumption of wine. By contrast, in beer drinkers, there was no reduction in all-cause mortality, which is similar to the study of Shaper et al.,\textsuperscript{15} in which the subjects were most likely consuming more than 40% of alcohol as beer, just as our beer drinkers.

Additional possible bias could come from the collected data. Our evaluation of the intake of alcohol using the results of a questionnaire that the subjects knew would remain confidential appears to be reasonably reliable as shown by a second evaluation, 5 to 6 years later. The information on mortality was supplied by the official government-run Institut National des Statistiques et des Études, which is not unreliable. Concerning the causes of death that were supplied and verified by the Institut National pour la Santé et la Recherche Médicale, there were possibly some misclassifications. Nevertheless, in our previous smaller study,\textsuperscript{10} the causes of death were obtained primarily from attending physicians on the basis of medical records. Still, the association between the intake of wine and cause-specific mortality was identical to that observed in the present study, which used only death certificates.

The lower risk of cancer by drinking only 2 to 3 glasses of wine, but not beer, is concordant with a recent report\textsuperscript{10} that showed that contrary to drinking beer and spirits, a moderate intake of wine does not increase the risk of cancer of the upper digestive tract. In 1933 in London, England, Stocks and Karn\textsuperscript{17} showed that daily drinking of beer but not wine markedly increased the risk of cancer. These studies suggested that alcohol intake predisposes subjects to certain cancers but that wine contains additional substances that may impede the eventual carcinogenic effects of alcohol. Such a substance seems to be resveratrol, a phenolic compound contained in wine, that inhibits the 3 main stages of carcinogenesis, in addition to its antioxidant and antiplatelet effects.\textsuperscript{9}

Another possibility is that beer contains specific carcinogenic substances in addition to alcohol. Those substances may be nitrosamines,\textsuperscript{18} which, until 1990, were in most of the beers analyzed in Europe and the United States at a level of 2 to 10 µg/L.\textsuperscript{19} Nowadays, concentrations of nitrosamines may be about 0.4 µg/L. Since our subjects have been drinking beer with a high content of nitrosamines for most of their lives, consuming beer with the present levels of nitrosamines may not have the same predisposing effect for cancer. If nitrosamines are responsible for the carcinogenic effect of beer, it will be only in the next decade that a change will be observed in the association between beer drinking and cancers. Nevertheless, heavy drinking of any alcoholic beverage with or without nitrosamines or resveratrol increases the risk of cancer by 100% as observed in the present study in heavy wine drinkers.

We also noted that for 1 to 5 drinks, the risk of violent death was 51% lower in wine drinkers than in those who drank beer, concordant with the recent report\textsuperscript{20} that beer and spirits, but not wine, are related to homicide and assault rates. Finally, we found, as did other investigators,\textsuperscript{2} that moderate drinking was associated with a lower risk of death from other causes, significant only with wine drinking, possibly owing to a small number of events in the subjects who drank a moderate amount of beer. However, 86% of beer drinkers consumed wine. Since the Figure shows that when wine consumption replaces part of the beer consumption, the risk of death from all causes is decreased, further studies seem to be required to completely disentangle the respective health effects of drinking wine and beer.

**CONCLUSIONS**

An important bias in our study, in terms of public health, is that young adults were not included. Thus, our results apply only to middle-aged men. In the case of middle-aged men from eastern France, a moderate daily intake of wine (22-32 g of alcohol) was associated with a lower risk of death due to CVDs (40%), cancer (22%), other causes (42%), and all causes (33%). A moderate intake of alcohol from beer (at least with the beer consumed in eastern France during the second half of this century) was also associated with a lower risk of death from CVDs but not from cancer and all causes, despite the consumption of some wine in 86% of beer drinkers.

Similar health effects of wine drinking have been reported in Denmark.\textsuperscript{6} It remains to be determined whether the protective effect of a moderate intake of alcoholic beverages on the risk of death from all causes observed in the United States\textsuperscript{2, 3} and the United Kingdom\textsuperscript{1} is due to alcohol or specifically to wine.

Nevertheless, because of the potential health hazards of any alcoholic beverage, our results suggesting that a few glasses of wine may have salutary effects should not be interpreted as an incentive to drink. As advised by the 1995 US dietary guidelines for Americans, “If you drink alcoholic beverages, do so in moderation, with meals and when consumption does not put you or others at risk.”\textsuperscript{21}
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