Moderate wine drinkers have lower hypertension-related mortality: a prospective cohort study in French men

Serge C Renaud, René Guéguen, Pascale Conard, Dominique Lanzmann-Petithory, Jean-Marc Orgogozo, and Olivier Henry

ABSTRACT

Background: For a given blood pressure, the risk of death from coronary artery disease is much higher in northern Europe and the United States than in Mediterranean countries.

Objective: In this prospective cohort study, we tested the hypothesis that regular wine drinking reduces the hypertension-related risk of death.

Design: We used data from 36,583 healthy middle-aged men who had normal results on an electrocardiogram and were not taking drugs for cardiovascular disease risk factors. The subjects underwent a comprehensive health appraisal at the Center for Preventive Medicine between 1 January 1978 and 31 December 1985. Mortality from all causes and from specific causes during a 13–21-y follow-up was recorded.

Results: In a Cox model adjusted for 6 confounding variables, moderate wine drinkers (those who consumed 60 g alcohol/d and no beer) with systolic blood pressure (SBP) of 158, 139, or 116 mm Hg had significantly lower risks of death from all causes by 23%, 27%, and 37%, respectively, than did abstainers. Even for the highest quartile of blood pressure, moderate wine drinkers were protected from all-cause mortality. No significant reduction in all-cause mortality in relation to SBP was observed in other drinkers (those who consumed >60 g alcohol/d or who consumed beer and wine).

Conclusion: A moderate intake of wine is associated with a lower risk of mortality from all causes in persons with hypertension.

KEY WORDS Mortality, hypertension, alcohol, wine

INTRODUCTION

A moderate, regular intake of alcoholic beverages is associated with a lower risk of death from coronary artery disease (CAD) (1) and all causes (2–4). However, consumption of alcohol (5), including wine (6), increases blood pressure, a main risk factor for CAD and all-cause mortality (7).

For a given blood pressure, the risk of mortality from CAD is higher by a factor of 3 in northern Europe and the United States than in Mediterranean Europe (8). Mediterranean countries are known for their regular wine intake. We thus investigated whether consumption of wine or other types of alcohol lowers the risk of death associated with hypertension. We studied a cohort of men from eastern France (4) 13 to 21 y after blood pressure measurements had been made. We examined mortality from all causes and from cardiovascular diseases in drinkers of wine and other alcohol and in abstainers for different levels of systolic (SBP) and diastolic (DBP) blood pressure.

SUBJECTS AND METHODS

Study population

From January 1978 to December 1985, 43,450 men born in Europe and aged 40–60 y came to the Center of Preventive Medicine for a health examination, as in previous studies (4, 9). It has been postulated that some of the nondrinkers were sick and had stopped drinking because of their sickness (10). That source of bias was at least partly eliminated in the present study by excluding from analysis the subjects who at baseline were at high risk of CAD. The group excluded comprised 1923 subjects with an abnormal electrocardiogram result, 1388 subjects receiving antihypertensive therapy, 451 subjects being treated for hyperglycemia, 1117 subjects being treated for hyperlipemia, 469 subjects being treated for arrhythmia, and 1204 subjects being treated for stable angina. Finally, 315 subjects were excluded for having incomplete data. In the present study, we compared abstainers, wine drinkers, and other drinkers, for a total of 36,583 healthy men at baseline and 4203 deaths.

The Ethical Committee of the Nancy Preventive Medicine Center approved the research. Each man gave his informed consent to participate in the study at the time of his first visit to the center.

Methods

As described elsewhere (9), the examination was a free, routine, extensive health appraisal offered by the regional social security office to 95% of the population in the area. The sample was a cross-section of 375,140 active men (aged 30–59 y old). The examination included a comprehensive questionnaire on 

1 From the Hospital Emile Roux, Limeil-Brévannes, France (SCR, DL-P, and OH); the Center for Preventive Medicine, Vandoeuvre-Les-Nancy, France (RG and PC); and the University Hospital, Neurology Service, Bordeaux, France (J-MO)
2 Supported by the French Ministry of Agriculture and the European Institute for Wine and Health, Montpellier, France.
3 Address reprint requests to SC Renaud and D Lanzmann-Petithory, Hôpital Emile Roux, Pavillon Buisson Jacob, 94456 Limeil-Brévannes, France. E-mail: serge.renaud@erx.ap-hop-paris.fr and dominique.lanzmann@erx.ap-hop-paris.fr.

Received September 26, 2002.
Accepted for publication March 2, 2004.

current and past medical history, education, professional and leisure-time activities, smoking habits, and amount and type of alcoholic beverages consumed. The medical examination included an electrocardiogram, chest X-ray, measurement of weight, height, blood pressure (supine position, left arm, after 5 min of rest), and many blood and urine tests. SBP and DBP were included in the present study.

Alcohol assessment

The questionnaire on drinking included 6 different beverage categories of which 3 were alcoholic—wine, beer, and aperitifs—as previously reported (9). For the conversion to grams of alcohol, we assumed that 1 bottle of wine contains 88 g alcohol; 1 bottle of beer, 44 g; and 1 glass of spirits, 15 g. Thus, one drink of wine (120 mL) contains 10.5 g alcohol, which is comparable with one drink of beer (240 mL). The reproducibility of the alcohol intake evaluation was examined in previous studies (9). As shown in Table 1, the alcohol drinkers were separated into 1) wine drinkers, who did not drink any beer, and 2) other drinkers, who consumed both beer and wine.

Vital status assessment

The vital status of the subjects was determined 13–21 y after their first visit to the center, yielding 546 904 person-years of follow-up through December 1998. Vital status was supplied by a government organization, the Institut National des Statistiques et des Études Démographiques.

Permission was granted by the Commission Nationale de l’Informatique et des Libertés to record cause of death. The cause of death as given on the reevaluated death certificate was obtained through INSERM (Service Commun no. 8). Cause of death was classified according to the International Classification of Diseases, 9th revision. In the present study, in addition to all causes, we used death from cardiovascular diseases (codes 390 to 459 and 798), including all sudden deaths. In France, sudden death is not necessarily included in cardiac death, as reported in the Monica Project (11).

Data analysis

The explanatory variables were compared across groups of drinkers and nondrinkers by using analysis of variance and chi-square tests. Post hoc pairwise comparisons of means were made by using Tukey’s Studentized range method and Scheffe’s method. Similar comparisons for proportions used the partitioning method recommended by Fleiss for $m \times 2$ contingency tables. We calculated relative risk (RR) estimates as the ratio of the incidence density of death for different values of blood pressure to the incidence density among abstainers. We used the Cox proportional hazards model to estimate the RR of death. It was adjusted for the following 6 variables: age (2 y/category), education (high school graduate compared with no high school), cigarette smoking [never, formerly, or currently (1–10, 10–19, or $\geq$20 cigarettes/d)], physical activity (sedentary, some exercise, or vigorous exercise $\geq$1 time/wk), serum cholesterol ($<5.2, 5.2$ to $<5.9, 5.9$ to $<7.1, 7.1$ to $<7.1, 7.1$ to $\geq7.1$ mmol/L), and body mass index (in kg/m$^2$: $<23, 23$ to $<24.8, 24.8$ to $<26.4, 26.4$ to $<28.4, 28.4$).

RRs were evaluated with 95% CIs, and $P$ values are two-sided. The PROPORTIONALITY of the model was tested through a stratification on each covariate and by checking a constant difference between strata on the log (-log) survivor function. The statistical software package used to analyze the data was BMDP, version 7 (distributed by Statistical Solutions Limited, Cork, Ireland).

RESULTS

The baseline characteristics of the study subjects are summarized in Table 2. The abstainers had significantly lower mean corpuscular volumes and gamma glutamyl transferase activity than did the wine drinkers and other drinkers ($P < 0.01$). The abstainers also had significantly lower SBP and DBP, had lower concentrations of serum cholesterol and glucose, and included a lower percentage of smokers ($P < 0.01$). Thus, on the basis of these characteristics, except for a lower level of physical activity, the abstainers may have been the healthiest group.

An overall test for interactions on all-cause mortality between level of alcohol intake and SBP was significant ($P = 0.004$), with significant main effects of alcohol ($P = 0.018$) and of SBP ($P < 0.0001$) (Table 3). After adjustment for 6 covariates (age, cholesterol, education, body mass index, cigarette smoking, and physical activity), only wine drinkers with moderate intakes ($<60$ g alcohol/d) had a smaller risk of all-cause mortality than did abstainers in the first, third, and fourth quartiles of blood pressure. In the highest quartile of blood pressure, only moderate wine drinkers had a lower risk of death than did abstainers. The nonmoderate drinkers (those who consumed $\geq 60$ g alcohol/d) had a higher risk regardless of the type of alcohol consumed. When the Cox model was adjusted for only 2 covariates (age and smoking) instead of 6, the results were not much different (Table 3).

The overall test for interaction between alcohol and DBP was not significant for total mortality but main effects of DBP and alcohol were highly significant ($P < 0.0001$). The RR of death compared with the first quartile of DBP (mean of 67 mm Hg) was 1.065 (95% CI: 0.981, 1.156) for DBP of 79 mm Hg, 1.190 (95% CI: 1.019, 1.298) for DBP of 88 mm Hg, and 1.596 (95% CI: 0.981, 1.298) for DBP of 102.7 ± 15.2.

### Table 1

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Subjects</th>
<th>Deaths</th>
<th>Death rate $^*$</th>
<th>Wine intake</th>
<th>Beer intake</th>
<th>Aperitif intake</th>
<th>Total alcohol intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wine drinkers of &lt;60 g/d $^2$</td>
<td>16 304</td>
<td>1373</td>
<td>8.42</td>
<td>74.8</td>
<td>0</td>
<td>25.2</td>
<td>31.48 ± 16.9$^3$</td>
</tr>
<tr>
<td>Wine drinkers of $\geq$60 g/d</td>
<td>5924</td>
<td>876</td>
<td>14.78</td>
<td>95.3</td>
<td>0</td>
<td>4.7</td>
<td>102.7 ± 31.2</td>
</tr>
<tr>
<td>Other drinkers of &lt;60 g/day</td>
<td>4588</td>
<td>467</td>
<td>10.17</td>
<td>46.5</td>
<td>44.5</td>
<td>9.0</td>
<td>41.0 ± 15.2</td>
</tr>
<tr>
<td>Other drinkers of $\geq$60 g/day</td>
<td>5930</td>
<td>971</td>
<td>16.37</td>
<td>67.5</td>
<td>25.7</td>
<td>6.8</td>
<td>105.3 ± 39.4</td>
</tr>
</tbody>
</table>

$^*$ There was a significant difference between the 4 groups, $P < 0.000001$.

$^2$ Moderate drinkers.

$^3$ SD (all such values).
1.448, 1.758) for DBP of 101 mm Hg. In a Cox model adjusted for age and smoking, the RR of death compared with that in abstainers was 0.739 (95% CI: 0.662, 0.824) for moderate wine drinkers, 1.132 (95% CI: 1.008, 1.271) for wine drinkers of ≥60 g/d, 0.925 (95% CI: 0.810, 1.055) for moderate other drinkers, and 1.183 (95% CI: 1.053, 1.329) for other drinkers of ≥60 g/d.

We also looked at cardiovascular disease mortality, for which the effects of blood pressure and alcohol were significant but no significant interaction between alcohol and blood pressure was found. The main effects of SBP and alcohol were highly significant, $P < 0.0001$ for SBP and $P < 0.0305$ for alcohol. The RR of death compared with the first quartile of SBP (mean of 116 mm Hg) was 1.565 (95% CI: 1.236, 1.984) for SBP of 129 mm Hg, 1.871 (95% CI: 1.477, 2.369) for SBP of 139 mm Hg, and 2.590 (95% CI: 2.073, 3.237) for SBP of 158 mm Hg. In a Cox model adjusted for age and smoking, the RR of death compared with that in abstainers was 0.755 (95% CI: 0.591, 0.965) for moderate wine drinkers, 0.971 (95% CI: 0.748, 1.261) for wine drinkers of ≥60 g/d, 0.853 (95% CI: 0.631, 1.153) for moderate other drinkers, and 0.951 (95% CI: 0.729, 1.241) for other drinkers of ≥60 g/d.

### DISCUSSION

In these middle-aged men, the risk of death differed among abstainers, wine drinkers, and other drinkers for a given level of blood pressure. In the highest quartile of SBP (158 mm Hg) and thus among those with the highest risk of death, only moderate wine drinkers had a lower risk of all-cause mortality than did abstainers. No reduction in risk was observed at higher intakes of wine or in drinkers of wine and other alcohols. Only a moderate intake of wine was associated with a lower risk of death from all causes, as was observed in studies not related to blood pressure (4). However, compared with cardiovascular disease death, the relative risk of death from all causes was lowest at more SBP levels by up to 37%.

The mechanisms of the protective effect of wine on cardiovascular and all-cause mortality may not be similar. For cardiovascular death, wine may have a specific effect yet to be explained that protects against the noxious effect associated with high blood pressure. The present results are consistent with the observation that for a given blood pressure, the absolute risk of death from CAD in northern Europe and the United States is lower.

### TABLE 3

Adjusted relative risk (RR) of death from all causes by quartile of systolic blood pressure in relation to alcohol intake

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Quartile 1: 116 ± 5.96 mm Hg</th>
<th>Quartile 2: 129 ± 2.32 mm Hg</th>
<th>Quartile 3: 139 ± 2.47 mm Hg</th>
<th>Quartile 4: 158 ± 12.72 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>RR (95% CI)</td>
<td>P</td>
<td>n</td>
</tr>
<tr>
<td>Abstainers</td>
<td>0</td>
<td>126</td>
<td>Reference</td>
<td>—</td>
</tr>
<tr>
<td>Minimally adjusted</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wine drinkers of &lt;60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wine drinkers ≥60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other drinkers of &lt;60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other drinkers of ≥60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fully adjusted</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wine drinkers of &lt;60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wine drinkers ≥60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other drinkers of &lt;60 g/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Cox proportional hazards model adjusted for age and smoking.

$^b$ Cox proportional hazards model adjusted for age, cholesterol, education, BMI, cigarette smoking, and physical activity.
much higher than in wine-drinking Mediterranean countries (8). Thus, the lower death rate from CAD, but also from all causes, observed in Mediterranean countries in relation to hypertension may be due, at least in part, to regular wine consumption.

Our results may also be concordant with the observation that in wine-drinking hypertensive subjects, the risk of death from stroke is lower than that in nondrinkers (12). Because hypertension is a strong risk factor for heart failure, our results also seem of interest in relation to the reported protective effect of alcohol consumption on the risk of heart failure (13).

In the present study, only a moderate intake of wine was associated with protective effects on cardiovascular and all-cause mortality. However, this finding should be confirmed in further studies in which the intake of other alcoholic beverages is not contaminated by an intake of wine.

Concerning all-cause mortality in relation to hypertension, only wine was related to a lower risk in the women studied by Palmer et al (12). These results are also concordant with previous work showing that only wine, at moderate intakes, is associated with a significantly lower death rate from all causes (4, 14). Thus, the protective effect of wine may be related to its content of phenolic substances, such as resveratrol, which is shown to lower blood pressure in stroke-prone hypertensive rats (15). Nevertheless, it has to be determined whether it is the polyphenols that are associated with the lower risk of death related to hypertension.

The possible effect of wine on the risk of mortality in persons with hypertension does not exclude additional beneficial effects of foodstuffs consumed in Mediterranean countries. These dietary habits markedly lower the mortality rate from cardiovascular diseases and all causes without changing blood pressure (16). However, it should not be concluded that the possible protective effect on mortality observed in wine drinkers is explained by their dietary habits, as suggested recently in Denmark (17). In Mediterranean countries such as Italy and France, it has been reported that the dietary habits of wine drinkers are not healthier than those of abstinence (18, 19). In addition, in our cohort from eastern France, the largest consumers of wine were workers (9), not the higher social classes as in Great Britain or Denmark.

We previously defined the "French paradox" as a low mortality rate from CAD despite risk factors similar to those in the United Kingdom and the United States (20). We have postulated that this paradox may be attributable in part to wine consumption. The results of the present study, which show that wine drinking may be associated with a lower risk of all-cause mortality in persons with hypertension, support the hypothesis that the French paradox is partly explained by the consumption of wine.

Up to now, alcohol consumption (5) [even of wine (6)] was known to increase blood pressure. It was concluded that at intakes >30 g/d, alcohol in increments of 10 g/d increases SBP by 1–2 mm Hg (21). In the present study, the mean difference in SBP between wine drinkers and abstainers was 2.2 mm Hg. That increment may be associated with a higher risk of death but is small compared with the reduced risk of all-cause mortality observed here (23–37%).

The present study has limitations. The French are the highest consumers of wine in the world. That large intake should not be duplicated in other countries, especially because only a moderate intake was associated with a lower risk of death. In terms of public health, a bias was that young adults were not included in the present study. Therefore, the present results apply only to men of middle age. Intakes of alcohol by women are much lower than those of men, and in our cohort, mortality in women occurred later in life. For these reasons, the effect of alcohol on mortality in women will be examined and reported separately.

In conclusion, the beneficial effect of moderate wine intake on the risk of all-cause mortality in persons with hypertension has now been observed in France in addition to Great Britain (12). These findings may have important implications for hypertensive middle-aged and elderly patients who are already moderate wine drinkers. This habit may lower these patients’ risk of death, especially that from all causes, which has not improved even with recent antihypertensive drugs (22). Concordant with this hypothesis are results suggesting a specific effect of wine drinking on protection from ischemic stroke in aged subjects (23).

REFERENCES