Alcohol Consumption and Risk of Intermittent Claudication in the Framingham Heart Study

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Background—Intermittent claudication (IC) is associated with an increased risk of cardiovascular disease morbidity and mortality. The relation of alcohol consumption to the risk of IC remains controversial. The purpose of this study was to assess the relation of alcohol consumption and type of beverage to the development of IC among participants in the Framingham Heart Study.

Methods and Results—Alcohol consumption was categorized as 0, 1 to 6, 7 to 12, 13 to 24, and ≥25 g/d. During a mean follow-up of 6.8 years, 414 subjects developed IC. From the lowest to the highest category of alcohol intake, the age-standardized incidence rates of IC were 5.3, 4.1, 4.2, 3.2, and 4.6 cases/1000 person-years for men and 3.4, 2.5, 1.5, 1.9, and 2.5, respectively, for women. A multivariate Cox regression model demonstrated an inverse relation, with the lowest IC risk at levels of 13 to 24 g/d for men and 7 to 12 g/d for women compared with nondrinkers; the hazard ratio (95% CI) was 0.67 (0.42 to 0.99) for men and 0.44 (0.23 to 0.80) for women. This protective effect was seen mostly with wine and beer consumption.

Conclusions—Our data are consistent with a protective effect of moderate alcohol consumption on IC risk, with lowest risk observed in men consuming 13 to 24 g/d (1 to 2 drinks/d) and in women consuming 7 to 12 g/d (0.5 to 1 drink/d).

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Key Words: alcohol ■ smoking ■ peripheral vascular disease

Intermittent claudication (IC) is a clinical manifestation of peripheral arterial disease and a predictor of myocardial infarction and stroke. IC is associated with a 2- to 4-fold increased risk of cardiovascular morbidity and mortality and with increased healthcare costs in the United States. Previous studies have identified cigarette smoking, diabetes mellitus, older age, and elevated blood pressure as major risk factors for IC. The relation of alcohol consumption to the development of IC remains controversial. Weak and inconsistent inverse relations have been reported, as well as positive associations between alcohol and risk of IC. In the Physicians’ Health Study, alcohol consumption was associated with a 26% reduction of IC risk. Few studies have assessed the effects of different types of alcohol on the risk of IC. The purpose of this study was to assess the relation of total alcohol consumption to IC among participants in the Framingham Heart Study and to determine whether this relation differed by type of alcoholic beverage.

Methods
The Framingham Heart Study is a population-based cohort study that began in 1948 in Framingham, Mass. The original cohort included 5209 subjects aged 28 to 62 years at the first examination. In 1971, 3124 offspring (and their spouses) of the original cohort (referred to as the offspring cohort) were entered into a prospective cohort study. Detailed descriptions of the Framingham Heart Study have been published previously. Informed consent was obtained from study participants, and the study protocol was approved by the Institutional Review Board of the Boston Medical Center.

Assessment of Alcohol Consumption
Data on alcohol were collected at examinations 2, 7, 12 through 15, and 17 and at all subsequent examinations for the original cohort and at all examinations for the offspring cohort by use of a standardized questionnaire. At every qualifying visit, subjects were asked if they had consumed alcohol in the past 12 months. If yes, the average weekly number of drinks consumed during the past 12 months for spirits, beer, and wine was recorded. For this study, a drink was defined as 360 mL of beer containing 12.6 g of alcohol, 120 mL of wine containing 13.2 g of alcohol, or 45 mL of 80-proof spirits containing 15 g of alcohol. At each examination, total alcohol was computed as the sum of the beverage-specific alcohol contents of beer, wine, and spirits. The alcohol content of a “typical drink” at the time of examinations 2 and 7 was different from that of drinks consumed later in that the typical glass or bottle of beer at the time was 240 mL (rather than 360 mL), the typical wine was fortified wine with higher alcohol content than table wine, and the usual serving size of spirits was larger than it was later. Therefore,
alcohol consumption data from these 2 examinations were adjusted, as follows: 1 drink of wine, beer, and spirits in examination 2 or 7 is equivalent to 1.68 drinks of wine, 0.91 drinks of beer, and 1.75 drinks of spirits, respectively, in subsequent examinations. Because alcohol is lighter than water, we used 1 mL of alcohol as equivalent to 0.886 g to convert alcohol to grams. These analyses are limited to subjects with nonmissing data on alcohol consumption.

Outcome

During each examination, subjects were queried about exertional leg discomfort and about cramping in the calf related to steepness of incline and rapidity of walking or that forced the subject to stop walking. Any subject with possible or definite IC was interviewed independently by a second physician. A detailed description of IC criteria has been published previously.4 A review panel of 3 physicians made the final diagnostic determination of presence or absence of IC.

Other Variables

Smoking information was assessed through questionnaire. Pack-years of cigarettes smoked was calculated by multiplying the number of cigarettes smoked per day by the duration of smoking in years divided by 20. Resting blood pressure was measured twice by a physician according to a standard protocol. Diabetes mellitus was defined as a history of diabetes mellitus or current treatment with hypoglycemic medication. Prevalent coronary heart disease (CHD) was ascertained by a standard protocol described previously.14,19 Total cholesterol was measured at examinations 1 through 11, 13 through 15, 20, 22, and 23 for the original cohort and at all examinations for the offspring cohort. HDL cholesterol was measured at examinations 11, 15, 20, 22, and 23 for the original cohort and at all examinations for the offspring cohort. Total cholesterol was measured by a manual Abell-Kendall procedure20; HDL was measured by a heparin–manganese chloride procedure according to the protocol adopted by the Lipid Research Clinics21 (examinations 11 and 15 for the original cohort and 1 and 2 for the offspring cohort) or by the dextran-Mg2+ method22 (from examinations 20 and 3 onward in the original and offspring cohorts, respectively).

Statistical Methods

We conducted sex-specific analyses because men smoked more cigarettes and generally consumed larger amounts of alcohol than women did. Because alcohol consumption and/or the number of cigarettes smoked per day changed over time, a pooling method was used to update alcohol consumption and other covariates obtained at baseline were updated at examinations 7, 12, 17, and 22 for the original cohort and at examinations 2 and 4 for the offspring cohort. Each person-examination and its 8-year follow-up period were considered as 1 observation in the data analysis.23 Given the 10-year-interval between examinations in the offspring cohort, the 4-year-interval between examinations in the offspring cohort, and the 8-year-interval within which the risk of IC was assessed, each subject could contribute to several observations in the analyses if he/she was free of IC at the time of alcohol update. Of the 19 293 observations with alcohol data, 954 were deleted because of missing information on pack-years of cigarettes smoked. The final data set consisted of 18 339 observations. We combined the 2 cohorts for 2 reasons. First, the sex-specific relations of alcohol to IC were similar in both cohorts: from the lowest to the highest category of alcohol consumption, multivariate adjusted hazard ratios among women were 0.77, 0.43, 0.37, and 0.67 and 0.75, 0.45, 0.38, and 0.70 for the offspring and original cohorts, respectively, compared with nondrinkers; for men, corresponding hazard ratios were 0.98, 0.94, 0.74, and 0.69 and 1.00, 0.92, 0.78, and 0.71, respectively, for the offspring and original cohorts. Second, the sex-specific results between the 2 cohorts were similar when the follow-up in the original cohort was begun at examination 12, which corresponds to the inception period of the offspring cohort (results not shown).

Using the total alcohol intake at the beginning of each follow-up period, we created the following categories of alcohol intake: 0, 1 to 6, 7 to 12, 13 to 24, and ≥25 g/d and 4 indicator variables. These cutoff points were chosen because we assumed that a drink is ~12 g of ethanol, and we wanted to evaluate the alcohol-IC relation specifically using easily understandable cut points, such as “up to a half drink per day” or “a half to 1 drink per day.” In addition, we were particularly interested in the alcohol-IC relation in alcohol consumption ranges commonly referred to as “light-to-moderate drinking.”

Person-time of follow-up (pooled examinations each with 8-year follow-up) was calculated as the time from the beginning of each follow-up period to the occurrence of either (1) IC, (2) loss to follow-up, (3) 8 years of follow-up, or (4) December 1995. Using the direct standardization method, we calculated the age-adjusted incidence rates of IC using the sex-specific age distribution of the total population. Within each sex, we fitted a Cox model to estimate the association of alcohol with IC, adjusting for age (5-year categories), diabetes mellitus (yes/no), pack-years of cigarettes smoked, smoking status (never, former, and current smokers), systolic blood pressure, and prevalence of CHD (yes/no). Assumptions for the proportional hazard models were met. To further explore confounding by smoking, we conducted additional analyses stratified by smoking status (never-smokers, former smokers, and current smokers). Similarly, we assessed the effects of age, diabetes mellitus, and prevalent CHD on the alcohol-IC association using stratification; we did not have sufficient numbers of IC cases among subjects with diabetes mellitus to perform a separate analysis.

We also assessed the association of beverage-specific alcohol with IC. For these analyses, each beverage was categorized as 0, 1 to 7, or ≥8 drinks/wk. We used drinks/wk because we were interested in the nonalcoholic components of a drink that might affect the risk of IC. Because sex-specific results were similar, we combined both sexes to gain statistical power. The effects of each beverage were adjusted for the other 2 beverages. We performed additional analyses restricted to 13 406 observations with data on total and HDL cholesterol to explore whether the alcohol-IC association was mediated through lipid effects.

Results

Of the 18 339 observations free of IC at baseline, 8012 were in men and 10 327 were in women with mean age (SD) of 49.0 (13.5) and 51.2 (14.5) years, respectively. During a mean follow-up of 6.8 years, 229 men and 185 women developed IC. Table 1 shows the baseline characteristics of the study sample: alcohol consumption was associated with cigarette smoking and lower prevalence of CHD in both sexes; nondrinkers were older than drinkers; and men had higher rates of prevalent CHD and were more likely to be former or current smokers than women. From the lowest to the highest category of alcohol intake, the age-adjusted incidence rates of IC were 5.27, 4.09, 4.18, 3.20, and 4.56 cases/1000 person-years for men and 3.40, 2.52, 1.50, 1.91, and 2.48 for women (Table 2).

Compared with nondrinkers, the multivariate adjusted hazard ratios showed an inverse relation of alcohol to IC in both sexes, with the lowest IC risk at an alcohol level of 13 to 24 g/d (~1 to 2 drinks/d) among men and 7 to 12 g/d (~0.5 to 1 drink/d) among women; at these intake levels, the risk of IC was 33% and 56% lower than that of nondrinking men and women, respectively (Table 2). When stratified by age, the trend was suggestive of an inverse relation of alcohol to IC, mostly below the age of 65 years among men and across all ages among women (data not shown). An inverse relation was seen among...
never, former, and current smokers (Table 3). There was an interaction between smoking and alcohol: drinking was associated with greater IC rate reduction among smokers than nonsmokers (rate difference of 6.7 versus 0.23 for men and 2.96 versus 1.93 for women, Table 4). The inverse relation persisted when the analysis was restricted to subjects without diabetes and subjects with or without prevalent CHD at baseline (data not shown). There were too few subjects with diabetes at baseline to allow subgroup analysis. There was only a moderate attenuation of the point estimates when additional adjustment was made for

### TABLE 1. Characteristics at Beginning of 8-Year Follow-Up According to Total Alcohol Intake

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>0</th>
<th>1–6</th>
<th>7–12</th>
<th>13–24</th>
<th>≥25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n*</td>
<td>1498</td>
<td>1581</td>
<td>1039</td>
<td>1429</td>
<td>2465</td>
</tr>
<tr>
<td>Ethanol, g/d</td>
<td>0.0 ± 0.34</td>
<td>1.6</td>
<td>0.8</td>
<td>5.7</td>
<td>9.8</td>
</tr>
<tr>
<td>Age, y</td>
<td>52.4 ± 14.9</td>
<td>48.4 ± 13.7</td>
<td>46.6 ± 13.2</td>
<td>47.2 ± 13.3</td>
<td>49.2 ± 12.8</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>128.7 ± 18.5</td>
<td>128.4 ± 16.7</td>
<td>126.5 ± 15.9</td>
<td>128.0 ± 17.1</td>
<td>131.9 ± 17.9</td>
</tr>
<tr>
<td>Prevalent diabetes, %</td>
<td>6.1</td>
<td>4.2</td>
<td>3.6</td>
<td>2.8</td>
<td>3.6</td>
</tr>
<tr>
<td>Prevalent CHD, %</td>
<td>10.2</td>
<td>12.5</td>
<td>14.7</td>
<td>16.9</td>
<td>19.2</td>
</tr>
<tr>
<td>Never-smokers, %</td>
<td>38.8</td>
<td>39.1</td>
<td>32.9</td>
<td>28.8</td>
<td>19.2</td>
</tr>
<tr>
<td>Former smokers, %</td>
<td>31.4</td>
<td>26.8</td>
<td>31.7</td>
<td>33.1</td>
<td>33.2</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>29.8</td>
<td>34.2</td>
<td>35.4</td>
<td>38.1</td>
<td>47.6</td>
</tr>
<tr>
<td>Cigarettes/d†</td>
<td>24.0 ± 12.8</td>
<td>22.5 ± 11.8</td>
<td>21.6 ± 11.7</td>
<td>22.2 ± 11.7</td>
<td>25.5 ± 13.5</td>
</tr>
<tr>
<td>Women, n*</td>
<td>3480</td>
<td>3377</td>
<td>1304</td>
<td>1155</td>
<td>1011</td>
</tr>
<tr>
<td>Ethanol, g/d</td>
<td>0.0 ± 0.30</td>
<td>1.5</td>
<td>0.8</td>
<td>5.7</td>
<td>9.8</td>
</tr>
<tr>
<td>Age, y</td>
<td>55.1 ± 15.4</td>
<td>48.7 ± 13.8</td>
<td>48.0 ± 13.8</td>
<td>49.9 ± 13.5</td>
<td>51.9 ± 12.3</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>130.9 ± 22.6</td>
<td>127.7 ± 20.5</td>
<td>124.1 ± 21.0</td>
<td>127.5 ± 21.8</td>
<td>130.9 ± 21.5</td>
</tr>
<tr>
<td>Prevalent diabetes, %</td>
<td>5.1</td>
<td>3.1</td>
<td>3.4</td>
<td>4.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Prevalent CHD, %</td>
<td>5.9</td>
<td>3.1</td>
<td>1.6</td>
<td>1.6</td>
<td>2.0</td>
</tr>
<tr>
<td>Never-smokers, %</td>
<td>62.2</td>
<td>49.3</td>
<td>39.6</td>
<td>34.4</td>
<td>24.3</td>
</tr>
<tr>
<td>Former smokers, %</td>
<td>15.8</td>
<td>19.9</td>
<td>23.2</td>
<td>28.2</td>
<td>22.4</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>22.0</td>
<td>30.8</td>
<td>37.2</td>
<td>37.4</td>
<td>53.3</td>
</tr>
<tr>
<td>Cigarettes/d†</td>
<td>18.0 ± 10.7</td>
<td>16.9 ± 10.7</td>
<td>17.4 ± 11.0</td>
<td>17.8 ± 11.8</td>
<td>20.3 ± 11.7</td>
</tr>
</tbody>
</table>

*Rate of IC per 1000 person-years standardized to the sex-specific age distribution of the total sample.
†Number of cigarettes smoked per day among current smokers.

### TABLE 2. Risk of IC According to Sex and Total Alcohol Intake

<table>
<thead>
<tr>
<th>Alcohol, g/d</th>
<th>Cases/8-Year Person-Examinations</th>
<th>Rates*</th>
<th>Age-Adjusted HR 95% CI</th>
<th>Multivariate-Adjusted HR† 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>55/9421</td>
<td>5.27</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1–6</td>
<td>44/10 797</td>
<td>4.09</td>
<td>0.87 (0.58–1.30)</td>
<td>0.94 (0.63–1.40)</td>
</tr>
<tr>
<td>7–12</td>
<td>24/7014</td>
<td>4.18</td>
<td>0.86 (0.52–1.38)</td>
<td>0.88 (0.54–1.43)</td>
</tr>
<tr>
<td>13–24</td>
<td>28/9717</td>
<td>3.20</td>
<td>0.71 (0.44–1.11)</td>
<td>0.67 (0.42–0.99)</td>
</tr>
<tr>
<td>≥25</td>
<td>78/17 329</td>
<td>4.56</td>
<td>0.94 (0.67–1.34)</td>
<td>0.70 (0.49–0.98)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>90/22 962</td>
<td>3.40</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1–6</td>
<td>51/23 672</td>
<td>2.52</td>
<td>0.75 (0.53–1.06)</td>
<td>0.74 (0.52–1.05)</td>
</tr>
<tr>
<td>7–12</td>
<td>11/8984</td>
<td>1.50</td>
<td>0.45 (0.24–0.85)</td>
<td>0.44 (0.23–0.80)</td>
</tr>
<tr>
<td>13–24</td>
<td>15/8049</td>
<td>1.91</td>
<td>0.62 (0.35–1.07)</td>
<td>0.51 (0.29–0.90)</td>
</tr>
<tr>
<td>≥25</td>
<td>18/7313</td>
<td>2.48</td>
<td>0.77 (0.46–1.28)</td>
<td>0.52 (0.30–0.86)</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio.
*Rate of IC per 1000 person-years standardized to the sex-specific age distribution of the total sample.
†Adjusted for age (5-year category), diabetes mellitus, history of CHD, systolic blood pressure, smoking status (never, former, and current smokers), and pack-years of cigarettes smoked.
HDL cholesterol (Table 5). The inverse relation was seen primarily with beer and wine (Table 6).

### Discussion

IC is associated with considerable morbidity and cardiovascular mortality.²⁻⁴ Moderate alcohol consumption has been associated with a reduced risk of CHD and all-cause mortality.²⁴⁻²⁷ The present study demonstrated an inverse relation between alcohol consumption and IC risk, with the lowest risk observed at a consumption level of 13 to 24 g/d for men and 7 to 12 g/d for women. The alcohol-IC relation was seen primarily with wine and beer consumption. This inverse relation was independent of major predictors of IC. We also demonstrated a smoking-alcohol interaction in both sexes.

Limited data are available on the effects of alcohol on IC. Most of the few observational studies that have evaluated this relation have yielded weak and inconsistent results.⁹⁻¹² The lack of sufficient power and incomplete adjustment for confounding by smoking may have contributed to these inconsistencies. Gofin et al¹¹ reported a null finding in a study with 25 cases of IC in which smoking was dichotomized (yes/no). However, in a prospective study design, Camargo et al¹³ showed that moderate alcohol consumption was associated with decreased risk of peripheral arterial disease. Although limited to men, those findings are consistent with our results. Little information is available on the effects of type of alcoholic beverage on IC. In a cross-sectional study, ankle brachial pressure index was related to wine consumption but not to beer or spirits consumption in men.¹⁰

Our findings have potential limitations. First, alcohol consumption in this study was self-reported. Although we used trained interviewers and a standardized questionnaire, study participants may have underestimated their usual alcohol intake. Because such underestimation is more likely to attenuate the true effect measure, this bias would not explain these findings. Second, we were not able to distinguish binge drinkers from regular drinkers, or ex-drinkers (who may have quit before the baseline examination because of an illness) from never-drinkers. Because we would expect the lowest IC risk among regular moderate drinkers compared with binge drinkers, a potential bias introduced by lack of adjustment for binge drinking would bring the hazard ratio toward the null and would not explain our results. Third, loss to follow-up and missing data may not have been at random and could have biased the findings. Although the proportionality of hazards was met, we do not know whether the assumed model matched the true data. Fourth, confounding by unmeasured variables (eg, dietary factors and exercise) and/or misclassification of IC cases might have been an issue in this study despite the standard criteria for case ascertainment. The consistency of the results in both sexes and both cohorts, as well as the known physiological mechanisms of alcohol, makes chance unlikely as the cause of our findings. Finally, the fact that our participants did not consume large amounts of alcohol on average and were almost all white limits the generalizability of our findings. The large sample size, with a wide age range and similar numbers of men and women, is an important strength of the present study. Another strength of the present study is that to the best of our knowledge, no

![Table 3](http://circ.ahajournals.org/content/123/16/3095.full)

Table 3: Adjusted Hazard Ratios (95% CI) for IC According to Total Alcohol Intake and Smoking Status

<table>
<thead>
<tr>
<th>Total Alcohol, Drinks/wk</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never-smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7/3586</td>
<td>1.0</td>
</tr>
<tr>
<td>1–7</td>
<td>13/6403</td>
<td>1.58 (0.61–4.01)</td>
</tr>
<tr>
<td>≥8</td>
<td>8/5798</td>
<td>0.90 (0.32–2.50)</td>
</tr>
<tr>
<td>Former smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>13/2800</td>
<td>1.0</td>
</tr>
<tr>
<td>1–7</td>
<td>17/4777</td>
<td>0.94 (0.45–1.94)</td>
</tr>
<tr>
<td>≥8</td>
<td>45/8688</td>
<td>1.22 (0.65–2.28)</td>
</tr>
<tr>
<td>Current smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>35/3061</td>
<td>1.0</td>
</tr>
<tr>
<td>1–7</td>
<td>38/6648</td>
<td>0.70 (0.44–1.12)</td>
</tr>
<tr>
<td>≥8</td>
<td>53/12582</td>
<td>0.41 (0.27–0.64)</td>
</tr>
</tbody>
</table>

*Adjusted for age (5-year category), diabetes mellitus, history of CHD, systolic blood pressure, and pack-years of smoking. PY indicates person-years of follow-up.

![Table 4](http://circ.ahajournals.org/content/123/16/3095.full)

Table 4: Crude Incidence Rates of IC (Cases/1000 Person-Years) by Sex, Alcohol, and Smoking

<table>
<thead>
<tr>
<th>Alcohol drinking</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>No</td>
<td>11.43</td>
<td>1.95</td>
</tr>
<tr>
<td>Yes</td>
<td>4.73</td>
<td>1.72</td>
</tr>
<tr>
<td>Rate difference</td>
<td>6.7</td>
<td>0.23</td>
</tr>
</tbody>
</table>

*Restricted to never-smokers and current smokers.
previous study has examined the association between beverage-specific alcohol and IC.

Several mechanisms for an inverse relation of alcohol to IC have been proposed. Alcohol raises HDL cholesterol.\textsuperscript{13,28–30} HDL plays an important role in LDL transport from the bloodstream to the liver, where it is degraded.\textsuperscript{31} Oxidized LDL is a key element in the pathophysiology of atherosclerosis.\textsuperscript{32} Fowkes et al.\textsuperscript{33} reported an inverse association between HDL and IC. We demonstrated that adjustment for HDL only moderately attenuated the point estimates, indicating that the observed association is largely mediated through other mechanisms. In addition, alcohol intake may prevent thrombogenesis or improve fibrinolysis through its favorable influence on fibrinogen,\textsuperscript{34} plasminogen activator inhibitor type-1,\textsuperscript{35,36} factor VII,\textsuperscript{35} and lowering of platelet aggregation.\textsuperscript{37–39} Alcohol might also reduce the risk of IC through direct peripheral vascular effects.\textsuperscript{40} Nonalcoholic components may contribute to IC risk reduction for wine and beer, because beer and wine contain polyphenols with antioxidant properties; phenolic compounds may delay the onset of atherosclerosis by preventing oxidation of LDL.\textsuperscript{41} Phytoalexin, an antifungal compound found in grape skin (found in higher concentration in red wine), may raise HDL and reduce platelet aggregation.\textsuperscript{10}

In conclusion, this study shows an inverse relation between alcohol consumption and IC in both sexes, with the greatest risk reduction at consumption levels of 12 to 24 g/d (\textasciitilde 1 to 2 drinks/d) for men and 7 to 12 g/d (\textasciitilde 0.5 to 1 drink/d) for women. Further studies are needed to confirm the levels of alcohol associated with greatest IC risk reduction.

Acknowledgments

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References


\begin{table}[h]
\centering
\caption{Hazard Ratios (95\% CI) for IC With and Without Adjustment for Total and HDL Cholesterol\textsuperscript{*}}
\begin{tabular}{lcccc}
\hline
Alcohol, g/d & Case/PY & Model 1 & Model 1 + Total Cholesterol & Model 1 + HDL Cholesterol & Model 1 + Total Cholesterol + HDL Cholesterol \\
\hline
\multicolumn{6}{c}{Men} \\
0 & 34/6696 & 1 & 1 & 1 & 1 \\
1–6 & 24/7656 & 0.91 (0.54–1.55) & 0.91 (0.53–1.54) & 0.93 (0.55–1.57) & 0.92 (0.54–1.56) \\
7–12 & 15/5444 & 0.92 (0.49–1.70) & 0.88 (0.47–1.63) & 0.95 (0.51–1.77) & 0.90 (0.49–1.67) \\
13–24 & 18/7792 & 0.66 (0.37–1.18) & 0.64 (0.36–1.15) & 0.74 (0.41–1.34) & 0.72 (0.40–1.29) \\
\geq 25 & 46/12166 & 0.77 (0.49–1.23) & 0.70 (0.44–1.12) & 0.89 (0.56–1.43) & 0.81 (0.50–1.30) \\
\multicolumn{6}{c}{Women} \\
0 & 49/13832 & 1 & 1 & 1 & 1 \\
1–6 & 32/2422 & 0.83 (0.52–1.31) & 0.85 (0.54–1.35) & 0.88 (0.55–1.39) & 0.91 (0.57–1.44) \\
7–12 & 8/6926 & 0.80 (0.23–1.07) & 0.53 (0.24–1.14) & 0.57 (0.26–1.21) & 0.60 (0.28–1.28) \\
13–24 & 13/6112 & 0.69 (0.37–1.29) & 0.71 (0.38–1.34) & 0.84 (0.44–1.57) & 0.86 (0.46–1.62) \\
\geq 25 & 11/4452 & 0.58 (0.29–1.14) & 0.57 (0.29–1.13) & 0.79 (0.39–1.59) & 0.78 (0.39–1.56) \\
\hline
\end{tabular}
\textsuperscript{*}Results in this table are restricted to subjects with data on HDL and total cholesterol; model 1 controls for age (5-year category), diabetes mellitus, history of CHD, systolic blood pressure, smoking status (never, former, and current smokers), and pack-years of smoking. PY indicates person-years of follow-up.
\end{table}

\begin{table}[h]
\centering
\caption{Rates of IC According to Type of Beverage}
\begin{tabular}{lcccc}
\hline
Beverage & Cases/PY & Hazard Ratio (95\% CI) & \\
\hline
Wine, drinks/wk & & & \\
0 & 295/72 962 & 1.0 & \\
1–7 & 103/45 566 & 0.81 (0.64–1.03) & \\
\geq 8 & 16/6854 & 0.64 (0.38–1.07) & \\
\textit{P} for trend & & 0.013 & \\
Beer, drinks/wk & & & \\
0 & 294/78 571 & 1.0 & \\
1–7 & 70/30 676 & 0.69 (0.52–0.91) & \\
\geq 8 & 50/16 135 & 0.60 (0.43–0.83) & \\
\textit{P} for trend & & 0.0005 & \\
Spirits, drinks/wk & & & \\
0 & 195/55 639 & 1.0 & \\
1–7 & 138/52 692 & 0.88 (0.69–1.10) & \\
\geq 8 & 81/17 050 & 0.89 (0.68–1.18) & \\
\textit{P} for trend & & 0.30 & \\
\hline
\end{tabular}
\textsuperscript{PY indicates person-years of follow-up. Hazard ratio (95\% CI) adjusted for sex, age (5-year category), diabetes mellitus, systolic blood pressure, prevalent CHD, smoking (pack-years and smoking status [never, former, and current smokers]), and other types of beverages (the effect measures of wine are adjusted for beer and spirits; the effect measures for beer are adjusted for wine and spirits, and the point estimates for spirits are adjusted for wine and beer).}
\end{table}


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