Original Contribution

Smoking, Hypertension, Alcohol Consumption, and Risk of Abdominal Aortic Aneurysm in Men

Daniel R. Wong1,2, Walter C. Willett1,3,4, and Eric B. Rimm1,3,4

1 Department of Nutrition, Harvard School of Public Health, Boston, MA.
2 Division of Cardiac Surgery, Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, Nova Scotia, Canada.
3 Department of Epidemiology, Harvard School of Public Health, Boston, MA.
4 The Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA.

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Despite the known protective association between moderate alcohol consumption and ischemic heart disease, little is known about the effects of alcohol consumption on abdominal aortic aneurysms (AAA). The authors analyzed prospective, biennially updated data for a cohort of 39,352 US men from 1986 to 2002. The association of incident AAA diagnosis with alcohol consumption in grams per day was assessed at baseline and by using alcohol consumption data updated every 4 years, controlling for previously reported cardiovascular risk factors. During 576,374 person-years of follow-up, 376 newly diagnosed cases of AAA were demonstrated. After adjustment for other risk factors for AAA, including smoking, hypertension, and body mass index, alcohol consumption at baseline was independently associated with AAA diagnosis ($p$ for trend $= 0.03$), with a maximum hazard ratio of 1.21 (95% confidence interval: 0.78, 1.87) for $\geq 30.0$ g/day (approximately $\geq 2$ standard drinks) of daily alcohol consumption. This association was stronger when the updated alcohol consumption data were assessed rather than simply baseline exposure ($p$ for trend $= 0.02$); the hazard ratio for the highest level of intake ($\geq 30.0$ g/day) was 1.65 (95% confidence interval: 1.03, 2.64). Small numbers limited analyses by beverage type, but liquor demonstrated the strongest positive association with AAA.

alcoholic beverages; aorta; aortic aneurysm; ethanol; risk factors; smoking

Abbreviations: AAA, abdominal aortic aneurysms; CI, confidence interval; METs, metabolic equivalents.
molecular mechanisms. We sought to elucidate the association of alcohol consumption and other lifestyle and health characteristics with risk of AAA in a large prospective cohort of men.

MATERIALS AND METHODS

The Health Professionals Follow-up Study includes a prospective cohort of 51,529 US men aged 40–75 years at inception in 1986. Ethics approval was obtained from the institutional review board. Participants completed an initial mailed questionnaire on lifestyle and medical history and subsequently sent biennial follow-up questionnaires, with a detailed food frequency questionnaire included every 4 years. Subjects who did not provide complete dietary or alcohol information at baseline were excluded, leaving 49,818 eligible men. We then excluded 4,461 subjects with a history of myocardial infarction, angina, coronary artery bypass grafting surgery, stroke, or transient ischemic attack; 76 men with problematic covariate data; and 5,875 baseline nondrinkers who had stopped drinking alcohol during the previous 10 years. We excluded the latter group to reduce bias related to “sick quitters” in the nondrinker category. Excluded also were 49 subjects with thoracic aneurysms and five with known nondegenerative aneurysm etiology (such as due to Marfan syndrome, and mycotic and traumatic aneurysms). A total of 39,352 men were included in these analyses.

Medical and lifestyle exposures were assessed from self-reports every 2 years. Smoking was categorized into five groups (never, former, current 1–14 cigarettes/day, current 15–24 cigarettes/day, and current ≥25 cigarettes/day). To reduce any residual confounding that might remain, former smokers were then further subdivided according to time since cessation of smoking (<10 years, ≥10 years, and unknown). Age at initiation of smoking was initially studied, but this variable was not independently associated with AAA diagnoses after adjustment for smoking categories and hence subsequently was excluded from analysis. Level of physical activity was assessed based on self-reported weekly duration of a variety of exercises and activities. Metabolic equivalents (METs) were calculated for each, were summed, and then were categorized into five groups (0.1–5.9 METs/week, 6.0–13.7 METs/week, 13.8–24.2 METs/week, 24.3–40.8 METs/week, and ≥40.9 METs/week). One MET is defined as a standard metabolic resting rate of energy expenditure, such as while sitting quietly (approximately 3.5 ml of oxygen uptake per kilogram of body weight per minute, or 1 kcal per kilogram of body weight per hour) (19).

Alcohol consumption was determined from a semiquantitative food frequency questionnaire in which respondents were asked to mark their “average use during the past year” of “beer (1 glass, bottle, can),” “red wine (4-ounce (120 ml) glass),” “white wine (4-ounce glass),” and “liquor, e.g., whiskey, gin, etc. (1 drink or shot).” Frequency of consumption was reported as never or less than once per month, 1–3 per month, 1 per week, 2–4 per week, 5–6 per week, 1 per day, 2–3 per day, 4–5 per day, and ≥6 per day. The alcohol content was assigned as 12.8 g for beer, 11.0 g for wine, and 14.0 g for liquor (20). Average alcohol consumption was calculated as the sum of all beverages reported on each food frequency questionnaire (i.e., 1986, 1990, 1994, and 1998). Light beer (with 11.3 g of alcohol) was added starting in 1994. Daily alcohol consumption in grams was categorized into six groups: none, 0.1–4.9, 5.0–9.9, 10.0–14.9, 15.0–29.9, and ≥30.0; a highest level of ≥50.0 g was collapsed into the ≥30.0-g group because of small numbers in that category. Self-reported alcohol consumption was validated by using dietary records for a subset of subjects, with correlation coefficients ranging from 0.83 to 0.86 for 1986 and 1987, respectively (21). To reduce bias from changes in alcohol consumption related to newly diagnosed angina, myocardial infarction, coronary artery bypass grafting, transient ischemic attack, or stroke, participants were excluded from further follow-up when these conditions preceded AAA. For the same reason, updating of alcohol consumption and other lifestyle characteristics was also stopped after a diagnosis of hypertension, hypercholesterolemia, and diabetes during follow-up.

We confirmed self-reported diagnoses of aortic aneurysm with medical records. An aneurysm was confirmed if it was greater than 3 cm in luminal diameter, or required surgical or endovascular intervention treatment, or resulted in death. Deaths were confirmed when reported by families, postal officials, or the National Death Index, with a combined follow-up of better than 98 percent (22).

Person-years of follow-up time was calculated from the date of return of the 1986 questionnaire to the date of aneurysm diagnosis or January 31, 2002. We calculated cumulative incidence and relative risks, adjusted for age in 5-year categories and smoking in seven categories. Cox proportional hazards multivariable modeling was used to calculate relative risks, controlling for age, smoking status, quintiles of body mass index, physical activity, and presence or absence of self-reported hypertension, diabetes mellitus, and hypercholesterolemia. For the updated analyses, we excluded AAA diagnosis when preceded by a diagnosis of myocardial infarction, angina, coronary artery bypass grafting surgery, stroke, or transient ischemic attack. In the analysis of beverage types, linear tests for trend for all four beverage types were included simultaneously in one model.

RESULTS

Baseline characteristics

At baseline, higher alcohol consumption was positively associated with hypertension, hypercholesterolemia, smoking, and total caloric intake (table 1). The prevalence of diabetes was higher among nondrinkers than among light or moderate drinkers.

Atherosclerotic risk factors

We confirmed the diagnosis of 376 cases of AAA during follow-up, for a total incidence of 65 per 100,000 person-years. The period of follow-up totaled 576,374 person-years. Strong positive associations with AAA were noted
for age and smoking (table 2). Compared with never smokers, men who currently smoked ≥25 cigarettes per day had a 15-fold increased risk of aortic aneurysm. Even among former smokers, the risk remained elevated, particularly for those who ceased smoking within 10 years. These findings persisted even after multivariable adjustment for other risk factors. Hypertension and body mass index were also significantly associated with AAA. Hypercholesterolemia, diabetes, and physical activity were not associated with AAA after adjusting for other risk factors at baseline. In the updated analysis, which excluded AAA preceded by a diagnosis of angina, myocardial infarction, coronary artery bypass grafting, stroke, or transient ischemic attack, 315 cases remained. Similar associations for smoking and hypertension were noted, but no longer for body mass index (not shown). In this analysis, we found an inverse association between diabetes and AAA (hazard ratio = 0.55, 95 percent confidence interval (CI): 0.33, 0.93).

Alcohol consumption

In age-adjusted analyses, we found a strong positive trend between alcohol consumption and AAA (p < 0.0001) (table 3). After control for smoking and other covariates, a modest positive association remained (p = 0.03). Compared with nondrinkers, men who consumed ≥30 g/day had a hazard ratio of 1.21 (95 percent CI: 0.78, 1.87) for AAA.

In the updated analysis, which took into account changes in alcohol consumption over time, similar but stronger findings were observed (table 4). The highest level of alcohol consumption (≥30.0 g/day) was now associated with a hazard ratio of 1.65 (95 percent CI: 1.03, 2.64) for AAA. When the putative intermediary covariate, hypertension, was added to the model, this association was attenuated. Hypercholesterolemia added to the model did not appreciably attenuate the association. Similarly, adjustment at baseline for hypertension, but not hypercholesterolemia, attenuated the relation (p for trend = 0.06, not shown).

Beverage type

In an analysis of beverage type, liquor was positively associated with risk of AAA (p for trend = 0.009; hazard ratio for ≥15 g/day = 1.55, 95 percent CI: 1.09, 2.20). Beer, red wine, or white wine was not significantly associated with risk, although fewer men consumed ≥15.0 g of alcohol from these beverages daily (not shown).

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**TABLE 1. Baseline characteristics of US men according to alcohol consumption, 1986**

<table>
<thead>
<tr>
<th>Average daily alcohol consumption (g/day) at baseline (1986)</th>
<th>0</th>
<th>0.1–4.9</th>
<th>5.0–9.9</th>
<th>10.0–14.9</th>
<th>15.0–29.9</th>
<th>≥30.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>4,649</td>
<td>10,907</td>
<td>6,603</td>
<td>5,784</td>
<td>6,025</td>
<td>5,384</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>53.2</td>
<td>53.2</td>
<td>53.2</td>
<td>53.4</td>
<td>53.5</td>
<td>53.7</td>
</tr>
<tr>
<td>Mean body mass index†</td>
<td>25.6</td>
<td>25.3</td>
<td>25.4</td>
<td>25.3</td>
<td>25.3</td>
<td>25.6</td>
</tr>
<tr>
<td>% with risk factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>17.3</td>
<td>18.0</td>
<td>18.5</td>
<td>17.8</td>
<td>20.3</td>
<td>24.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.7</td>
<td>2.4</td>
<td>1.7</td>
<td>1.6</td>
<td>1.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>8.6</td>
<td>10.5</td>
<td>10.1</td>
<td>10.8</td>
<td>10.3</td>
<td>11.4</td>
</tr>
<tr>
<td>Current smoking</td>
<td>4.3</td>
<td>7.5</td>
<td>8.2</td>
<td>9.5</td>
<td>9.3</td>
<td>20.0</td>
</tr>
<tr>
<td>Physical activity (METs†/week)</td>
<td>17.5</td>
<td>20.5</td>
<td>22.9</td>
<td>23.1</td>
<td>24.2</td>
<td>21.0</td>
</tr>
<tr>
<td>Mean daily consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total calories (kcal)</td>
<td>1,952</td>
<td>1,928</td>
<td>1,962</td>
<td>1,967</td>
<td>2,082</td>
<td>2,228</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
<td>25.8</td>
<td>25.1</td>
<td>24.9</td>
<td>24.6</td>
<td>24.0</td>
<td>22.4</td>
</tr>
<tr>
<td>Monounsaturated fat (g)</td>
<td>28.5</td>
<td>27.7</td>
<td>27.7</td>
<td>27.5</td>
<td>27.0</td>
<td>24.9</td>
</tr>
<tr>
<td>Polyunsaturated fat (g)</td>
<td>13.4</td>
<td>13.4</td>
<td>13.4</td>
<td>13.4</td>
<td>13.3</td>
<td>12.0</td>
</tr>
<tr>
<td>Trans fat (g)</td>
<td>3.1</td>
<td>2.9</td>
<td>2.9</td>
<td>2.8</td>
<td>2.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Folate (mcg)</td>
<td>460</td>
<td>486</td>
<td>488</td>
<td>481</td>
<td>482</td>
<td>441</td>
</tr>
<tr>
<td>Beer (g)</td>
<td>0.0</td>
<td>0.6</td>
<td>2.4</td>
<td>4.3</td>
<td>5.9</td>
<td>16.5</td>
</tr>
<tr>
<td>Red wine (g)</td>
<td>0.0</td>
<td>0.4</td>
<td>0.8</td>
<td>1.3</td>
<td>2.6</td>
<td>3.3</td>
</tr>
<tr>
<td>White wine (g)</td>
<td>0.0</td>
<td>0.7</td>
<td>1.5</td>
<td>2.4</td>
<td>4.1</td>
<td>4.8</td>
</tr>
<tr>
<td>Liquor (g)</td>
<td>0.0</td>
<td>0.5</td>
<td>2.4</td>
<td>4.3</td>
<td>7.4</td>
<td>22.0</td>
</tr>
<tr>
<td>Total alcohol (g)</td>
<td>0.0</td>
<td>2.5</td>
<td>7.3</td>
<td>12.5</td>
<td>20.1</td>
<td>46.1</td>
</tr>
</tbody>
</table>

* Except for age, all variables were adjusted for age by direct standardization to the cohort of 39,352 men free from cardiovascular disease.
† Weight (kg) divided by height squared (m²).
‡ METs, metabolic equivalents.
DISCUSSION

Aortic aneurysms account for an important burden of cardiovascular death and morbidity, especially among men aged 50 years or older. The associations between several traditional risk factors for atherosclerotic disease, including smoking and hypertension, have been identified in the literature (5–9). We were able to confirm and expand these findings in a large cohort of men with prospectively collected, updated follow-up over 16 years. Specifically, we found strong positive associations with age and smoking. For smoking, we found a dose-response association with a 15-fold increase in risk for men who smoked ≥25 cigarettes a day. Hypertension and body mass index were also related to incidence of AAA. The importance of body mass index is underscored by recent reports of the increasing prevalence of overweight and obesity (23). Interestingly, we also found an inverse association with diabetes in updated analyses—an unexplained finding that others too have reported.

We further explored the impact of alcohol consumption on AAA risk to determine whether a J-shaped curve exists, as it does with other cardiovascular disease endpoints (10). We demonstrated an increased risk of aneurysm with the...
highest levels of alcohol consumption—two drinks or more daily (≥30.0 g/day). This association was stronger when we used the updated alcohol assessment measured every 4 years during follow-up. The highest category of alcohol consumption was associated with a 65 percent increase in risk (hazard ratio = 1.65, 95 percent CI: 1.03, 2.64). The positive

### TABLE 3. Hazard ratios for aortic aneurysm according to baseline average daily alcohol consumption among US men, 1986

<table>
<thead>
<tr>
<th>Baseline average alcohol consumption (g/day)</th>
<th>Cases (no.)</th>
<th>Person-years (no.)</th>
<th>HR*, †</th>
<th>95% CI</th>
<th>HR§</th>
<th>95% CI</th>
<th>Multivariable HR¶</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>29</td>
<td>68,494</td>
<td>1.00</td>
<td>0.71, 1.68</td>
<td>1.00</td>
<td>0.53, 1.29</td>
<td>1.00</td>
<td>0.83</td>
</tr>
<tr>
<td>0.1–4.9</td>
<td>74</td>
<td>160,551</td>
<td>1.09</td>
<td>0.91, 2.21</td>
<td>1.01</td>
<td>0.64, 1.62</td>
<td>1.02</td>
<td>0.83</td>
</tr>
<tr>
<td>5.0–9.9</td>
<td>58</td>
<td>97,134</td>
<td>1.41</td>
<td>0.84, 2.08</td>
<td>0.79</td>
<td>0.53, 1.35</td>
<td>1.41</td>
<td>1.02</td>
</tr>
<tr>
<td>10.0–14.9</td>
<td>53</td>
<td>84,655</td>
<td>1.32</td>
<td>1.00, 2.41</td>
<td>1.01</td>
<td>0.61, 1.53</td>
<td>1.32</td>
<td>1.02</td>
</tr>
<tr>
<td>15.0–29.9</td>
<td>62</td>
<td>88,820</td>
<td>1.55</td>
<td>1.00, 2.41</td>
<td>1.01</td>
<td>0.61, 1.53</td>
<td>1.55</td>
<td>1.02</td>
</tr>
<tr>
<td>≥30.0</td>
<td>100</td>
<td>76,720</td>
<td>2.52</td>
<td>1.66, 3.82</td>
<td>1.01</td>
<td>0.78, 1.87</td>
<td>2.52</td>
<td>1.02</td>
</tr>
</tbody>
</table>

* HR, hazard ratio; CI, confidence interval. † Adjusted for age. ‡ Mantel-Haenszel chi-square test. § Adjusted for age and smoking. ¶ Risk factors in the model: age, smoking, diabetes, body mass index, and physical activity. # Linear trend across increasing categories of alcohol consumption using the midpoint of consumption of each category as a continuous variable.

### TABLE 4. Hazard ratios for aortic aneurysm according to updated average daily alcohol consumption among US men, 1986–2002

<table>
<thead>
<tr>
<th>Updated average alcohol consumption (g/day)</th>
<th>Cases (n = 315) (no.)</th>
<th>Person-years (no.)</th>
<th>Basic models</th>
<th>HR*, †</th>
<th>95% CI</th>
<th>HR§</th>
<th>95% CI</th>
<th>Multivariable HR¶</th>
<th>95% CI</th>
<th>Basic models with intermediary variables</th>
<th>Multivariable HR**</th>
<th>95% CI</th>
<th>Multivariable HR††</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>25</td>
<td>80,523</td>
<td>1.00</td>
<td>0.87, 2.19</td>
<td>0.72, 1.85</td>
<td>1.00</td>
<td>0.75, 1.93</td>
<td>1.20</td>
<td>0.73, 1.87</td>
<td>1.00</td>
<td>0.73, 1.87</td>
<td>0.75, 1.92</td>
<td>1.17</td>
<td>0.73, 1.87</td>
</tr>
<tr>
<td>0.1–4.9</td>
<td>66</td>
<td>156,732</td>
<td>1.38</td>
<td>0.97, 2.58</td>
<td>0.81, 2.15</td>
<td>1.20</td>
<td>0.80, 2.08</td>
<td>1.32</td>
<td>0.76, 2.08</td>
<td>1.20</td>
<td>0.76, 2.08</td>
<td>0.80, 2.17</td>
<td>1.26</td>
<td>0.68, 1.87</td>
</tr>
<tr>
<td>5.0–9.9</td>
<td>45</td>
<td>93,991</td>
<td>1.58</td>
<td>0.97, 2.60</td>
<td>0.81, 2.15</td>
<td>1.20</td>
<td>0.80, 2.08</td>
<td>1.32</td>
<td>0.76, 2.08</td>
<td>1.20</td>
<td>0.76, 2.08</td>
<td>0.80, 2.17</td>
<td>1.26</td>
<td>0.68, 1.87</td>
</tr>
<tr>
<td>10.0–14.9</td>
<td>44</td>
<td>82,711</td>
<td>1.59</td>
<td>1.19, 3.06</td>
<td>0.72, 1.97</td>
<td>1.20</td>
<td>0.80, 2.08</td>
<td>1.32</td>
<td>0.76, 2.08</td>
<td>1.20</td>
<td>0.76, 2.08</td>
<td>0.80, 2.17</td>
<td>1.26</td>
<td>0.68, 1.87</td>
</tr>
<tr>
<td>15.0–29.9</td>
<td>54</td>
<td>87,665</td>
<td>1.91</td>
<td>1.19, 3.06</td>
<td>0.72, 1.97</td>
<td>1.20</td>
<td>0.80, 2.08</td>
<td>1.32</td>
<td>0.76, 2.08</td>
<td>1.20</td>
<td>0.76, 2.08</td>
<td>0.80, 2.17</td>
<td>1.26</td>
<td>0.68, 1.87</td>
</tr>
<tr>
<td>≥30.0</td>
<td>81</td>
<td>74,681</td>
<td>2.97</td>
<td>1.90, 4.66</td>
<td>0.91, 2.41</td>
<td>1.20</td>
<td>0.87, 2.30</td>
<td>1.41</td>
<td>0.87, 2.30</td>
<td>1.20</td>
<td>0.87, 2.30</td>
<td>0.86, 2.29</td>
<td>1.32</td>
<td>0.81, 2.16</td>
</tr>
</tbody>
</table>

* HR, hazard ratio; CI, confidence interval. † Adjusted for age. ‡ Mantel-Haenszel chi-square test. § Adjusted for age and smoking. ¶ Risk factors in the model: age, smoking, diabetes, body mass index, and physical activity. # Linear trend across increasing categories of alcohol consumption using the midpoint of consumption of each category as a continuous variable. ** Risk factors in the model: age, smoking, diabetes, hypercholesterolemia, body mass index, and physical activity. †† Risk factors in the model: age, smoking, diabetes, hypertension, body mass index, and physical activity.

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The effect of alcohol on aneurysms may be mediated through its known ability to raise blood pressure at higher levels of consumption (17, 18). Controlling for hypertension attenuated the association with alcohol in our results, which is consistent with hypertension acting as an intermediary mechanism. On the other hand, the salutary effects of alcohol in raising high density lipoprotein cholesterol may be of less consequence in aneurysmal disease, especially where only a modest association with hypercholesterolemia was found in this cohort.

The association of alcohol with cardiovascular diseases may follow an occlusive versus nonocclusive (aneurysmal, other) pattern. Similar to the lower risk of coronary heart disease, an inverse association with peripheral vascular disease of the lower extremities was reported by Camargo et al. (24), with moderate drinking conveying an adjusted risk reduction of 0.74. The risk of ischemic stroke also appears to be reduced with alcohol consumption (25–27). Conversely, high levels of alcohol consumption have been linked to cardiomyopathy and hemorrhagic stroke (28, 29). The increased risk of hemorrhagic stroke is particularly intriguing because of the known pathophysiology involving rupture of cerebral aneurysms, which has been linked to heavy alcohol consumption (30).

The distinct associations of alcohol with occlusive and aneurysmal disease may be related to underlying mechanical, inflammatory, or genetic factors, and alcohol may act differentially in these two domains. Proteolytic degradation of connective tissue in the aorta by matrix metalloproteinases is one important mechanism relevant to AAA formation (31). Long-term alcohol consumption in rats resulted in increased matrix metalloproteinase-2 activity and disruption of aortic elastic fibers (32). Matrix metalloproteinases have also been up-regulated in other models, including in human breast cancer cells in response to alcohol exposure (33, 34). Furthermore, enhanced vascular reactivity to vasoconstrictor agents such as phenylephrine, which may be mediated by thromboxane and enhanced calcium influx (35), and reduced aortic relaxation with acetylcholine has also been demonstrated in alcohol-treated rats (36). Other evidence of altered antioxidant and nitric oxide levels with alcohol has been reported (37), and these and other factors may be responsible for inducing hypertension with increased wall stress as well as structural and biomechanical changes in the aorta. Indeed, greater yield point elongation of the abdominal aorta was demonstrated in alcohol-treated rats (38). Finally, evidence of a differential response to moderate (9 percent of calories) versus high (18 percent of calories) alcohol doses in vascular relaxation mediated by nitric oxide has been shown in rat models, with moderate alcohol consumption increasing relaxation by 26 percent and higher levels of intake impairing maximum vascular relaxation by 22 percent (39). Recall that moderate intake was associated in epidemiologic studies with protection in occlusive disease states, whereas high levels of consumption were linked to increased risk of hemorrhagic stroke and aneurysms.

We found that the influence of alcohol was apparent when assessing baseline consumption, consistent with the known chronicity of degenerative aneurysmal change. Analyses of most recent (updated) intake suggested a moderately stronger association, which highlights the importance of reassessing exposure to improve the precision of estimates. To minimize misclassification due to changes in drinking patterns after illness, we stopped updating after incident diagnoses of hypertension, diabetes, and hypercholesterolemia and also excluded patients who developed cardiovascular endpoints (angina, myocardial infarction, coronary artery bypass grafting, stroke, and transient ischemic attack) during follow-up.

The Health Professionals Follow-up Study cohort provides a large group of men in which to study aortic aneurysms. Because they are health professionals, they may tend to have a greater awareness of medical issues than the general public, which may translate into a higher likelihood of diagnosis before clinical symptoms manifest. In addition, the frequency and length of follow-up, including repeated assessment of detailed food frequency questionnaires and other risk factors, makes this cohort ideal for assessing lifestyle and nutritional exposures on chronic diseases.

The most important limitation of this study is the self-reported nature of both exposures and outcomes. In this cohort, stringent efforts were made to validate exposures (including alcohol) and to verify outcomes with medical records. Nevertheless, bias might be possible, whereby other alcohol-related diagnoses may result in increased medical contact and testing, predisposing to a higher likelihood of aneurysm diagnosis. On the other hand, it is also possible that alcoholism may have been a barrier to health care access. In general, though, we think that this group of generally middle- and upper-class health care professionals would have consistent and adequate medical care. When we repeated the analysis by including only those men who reported that they had sought basic medical care (a physical examination for either screening or unspecified symptoms) during the prior 2 years since the last questionnaire, the results were not substantively different given the much reduced sample size (161 cases; hazard ratio for \( \geq 30 \) g/day drinkers = 2.34, 95 percent CI: 1.07, 5.12; \( p \) for trend = 0.02).

The largely silent nature of aortic aneurysmal disease means that some aneurysms will likely remain undiagnosed in this study compared with ultrasound screening studies. In this cohort, a proportion of subjects discontinued drinking over the course of the study follow-up, which may have been prompted by other health-related effects of alcohol, possibly prior to the diagnosis of aortic aneurysm among cases. This factor would lead to misclassification in updated analyses if the presence of an aneurysm was not as yet detected. To mitigate this phenomenon in our analysis, we did not update alcohol or other lifestyle characteristics after new diagnoses of hypertension, hypercholesterolemia, or diabetes, and we further excluded subjects during follow-up with previous diagnoses of cardiovascular outcomes. When the updated analyses were repeated without stopping updating in this manner, no association between alcohol and AAA was found. Similarly, if patients with prior cardiovascular comorbidity at baseline were not excluded from the analyses, the association was no longer evident (\( p = 0.36 \)).
We were not able to restrict our analyses to patients with larger aneurysms (≥5 cm) for two reasons: the number of subjects with aneurysms ≥5 cm at initial diagnosis was too small (168 cases) to model stably; and, if patients were followed beyond their initial diagnosis until aneurysms were ≥5 cm, there would be a significant risk of bias among patients who changed their diet and lifestyle after initial diagnosis. Finally, the results of this study are limited to men, in whom aortic aneurysm is more prevalent. Whether this association is present in women is not known to have been studied.

To our knowledge, this report is the first to demonstrate an association between alcohol consumption and aortic aneurysm. We found a positive trend with the highest risk among men who consumed ≥30 g/day of alcohol. In the clinical context, among patients with or at risk of aortic aneurysm, the benefits of alcohol consumption must be carefully considered. Low alcohol consumption did not appear to be harmful or beneficial regarding aneurysms, and its use may be based on other considerations, including the salutary effect on high density lipoprotein cholesterol and coronary disease. Nevertheless, in this study, higher alcohol consumption (≥2 drinks per day) increased the risk of aortic aneurysmal disease in men without preexisting cardiovascular disease. This finding is also consistent with the recent recommendations against higher levels of alcohol consumption by the American Heart Association Science Advisory for hypertensive patients (40). Future studies of alcohol and cardiovascular disease may benefit from including AAA as an endpoint of interest. In addition, more research to examine the importance of alcohol on a variety of cardiovascular endpoints, including aortic aneurysm, is warranted to further elaborate these associations and the pathophysiologic mechanisms.

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