Alcohol Consumption and Carotid Atherosclerosis in the Lausanne Stroke Registry

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We evaluated the association between alcohol consumption and carotid atherosclerosis in 261 consecutive patients >50 years old admitted to our community-based primary-care center with first ischemic stroke; their characteristics were entered into a computerized data bank (Lausanne Stroke Registry). Reported regular alcohol consumption was compared with the presence and severity of internal carotid artery disease as assessed by duplex scanning with spectral analysis of the Doppler signal and real-time B-mode imaging at the level of the carotid bifurcation. We found an inverse linear relation between light-to-moderate alcohol intake (<4 standard drinks/day) and severity of internal carotid artery stenosis. No conclusion could be drawn for heavier drinkers because there were too few. A logistic regression model showed that hypertension, cigarette smoking, and age in men and diabetes mellitus and cigarette smoking in women strongly counterbalanced the potential benefit of alcohol consumption. Although regular alcohol drinking cannot be advocated on the basis of our findings, light-to-moderate consumption of alcohol is the first factor to be inversely associated with extracranial carotid atherosclerosis in symptomatic patients with cerebrovascular disease. (Stroke 1990;21:715–720)

Although the issue is still controversial, there is some evidence from ecologic, case-control, cohort, autopsy, and clinical studies that alcohol consumption may be an independent factor protecting against ischemic heart disease at moderate levels yet promoting coronary atherosclerosis at high levels (U-shaped response).1–6 With moderate alcohol consumption (<4 standard drinks/day), the relative risk for coronary heart disease has been estimated to be 0.4–0.7.6 Similarly, a recent case-control study of 230 patients with stroke admitted to a district-based hospital suggested that the relative risk for stroke may decrease to 0.5 in light drinkers (10–90 g/wk) compared with nondrinkers, whereas heavy drinkers (≥300 g/wk) may have a fourfold increase in risk.7 On the other hand, some authors have suggested that acute alcohol ingestion is a risk factor for ischemic stroke,8,9 although it is possible that acute alcohol ingestion does not act independent of other risk factors.10 The mechanisms by which alcohol may protect against stroke when consumption is moderate but promote stroke with acute binge drinking remain unclear. We examined alcohol consumption in consecutive patients with carotid-territory ischemic stroke who were admitted to our community-based primary-care center over 2 years, and we analyzed alcohol consumption and other risk factors with reference to the presence and severity of carotid atherosclerosis on duplex ultrasonography.

Subjects and Methods

We studied all patients >50 years of age who were admitted to our center from December 1985 to December 1987 with a diagnosis of first ischemic stroke (cerebral infarction) in the carotid territory (cerebral hemisphere). These patients were part of the Lausanne Stroke Registry,11 in which all patients with first stroke (cerebral infarction or cerebral hemorrhage) admitted since 1982 have been prospectively coded and entered into a computerized data bank. The Centre Hospitalier Universitaire Vaudois is the only public hospital (the sole hospital with acute stroke care facilities) in the Lausanne area and serves approximately 300,000 people. All patients with suspected stroke undergo a standard protocol of investigation: brain computed tomography (CT) with and without contrast (except in those with known allergy to the contrast media), Doppler ultrasonography with frequency spectrum analysis, 12-lead electrocardiography (ECG), and standard blood and urine tests. Cerebral angiography, two-dimensional echocardiography, and 24-hour ECG monitoring are performed in selected patients. The coding forms comprise 42 items, including age, sex, hypertension (blood pressure of >160/90 mm Hg at least twice before the stroke), diabetes mellitus (fasting blood
glucose concentration of >6 mmol/l and glucosuria known before the stroke), current or former use of oral contraceptives, cigarette smoking, hypercholesterolemia (fasting level of >6.5 mmol/l), and associated cardiovascular and other diseases. Cerebral infarction is diagnosed when CT shows a hypodense area corresponding to the clinical signs and symptoms or when CT excludes a hemorrhage or a nonvascular lesion.

The 261 patients included in the present study underwent selective ultrasonography of the carotid bifurcation using duplex scanning with spectral analysis of the Doppler signal (Dopscan, Carolina Medical Electronics, Inc., King, North Carolina) and real-time B-mode imaging (compact real-time imager with a MHz probe, Diasonics, Milpitas, California) of the extracranial carotid arteries. The patients were examined in the supine position, and the distal common carotid arteries and the proximal internal carotid arteries (ICAs) were examined in the lateral and transverse views. On real-time B-mode images, the degree of maximal stenosis was estimated as a percentage of the lumen diameter at the nearest adjacent nonstenosed segment. These findings were correlated in all 261 patients with the Doppler signal spectral analysis and in 96 patients with angiographic findings (Seldinger technique). The ICA lesions were classified by severity (class 1, no visible lesion; class 2, 0–25% stenosis; class 3, 26–50% stenosis; class 4, 51–75% stenosis; class 5, 76–99% stenosis; and class 6, total occlusion) by an investigator blinded to the patient’s alcohol consumption. We defined a carotid score (ranging from 2 to 12) as the sum of the classes of the ipsilateral and contralateral ICAs. The patients and their closest relatives were asked about the number of weekdays on which the patient drank wine, beer, hard liquor, and other alcoholic beverages and about the amount ingested on each day. These questions were asked among other usual questions while taking the medical history, without using a standard questionnaire. Alcohol consumption was estimated from the regular intake during the 2 years before the stroke as grams of pure alcohol per week. We considered a standard drink to contain 10 g alcohol. One standard drink per day corresponds to 70 g alcohol/wk or 1 unit of alcohol consumption. Nondrinkers consumed no alcohol. Light drinkers consumed up to 2 units of alcohol, moderate drinkers had 2–4 units, and heavy drinkers averaged >4 units.

Alcohol consumption of patients with various lesion severities were compared using the \( \chi^2 \) test and the nonparametric Kruskal-Wallis test. A logistic regression model was fitted using GLIM software to predict the presence or absence of stenosis considering alcohol consumption and the dichotomous variables age (patients below the median age were considered to be 60 years old and those above the median age to be 75 years old), hypertension, diabetes mellitus, cigarette smoking, and hypercholesterolemia. This model allowed evaluation of the risk of stenosis after adjusting for confounding factors.

Results

We included 261 patients, 169 men (mean±SEM age 65±8 years) and 92 women (mean±SEM age 67±9.5 years); all were white. There were 141 patients with hypertension, 39 with diabetes mellitus, 114 who currently smoked cigarettes (mean±SEM 22±14/day), 42 with hypercholesterolemia, 69 with known ischemic heart disease, and 22 with atrial fibrillation. Seventy patients had suffered transient ischemic attacks before their stroke (ipsilateral in two thirds). CT showed the cerebral infarct in 233 patients; the infarct involved the superficial middle cerebral artery (MCA) territory in 45%, the deep MCA territory in 36%, the superficial and deep MCA territories in 9%, the anterior cerebral artery territory in 3%, and the watershed territory in the remaining 7%.

Ultrasonograms of the ICA ipsilateral to the infarct showed class 1 stenosis in 66 patients, class 2 stenosis in 109, class 3 stenosis in 19, class 4 stenosis in seven, class 5 stenosis in 12, and class 6 stenosis in the remaining 48. Ultrasonograms of the contralateral ICA showed class 1 stenosis in 96 patients, class 2 stenosis in 137, class 3 stenosis in 15, class 4 stenosis in seven, class 5 stenosis in four, and class 6 stenosis in the remaining two.

Among the 261 patients, 94 reported consumption of no alcohol. Among the 167 alcohol drinkers, 31 reported consuming ≤1 unit, 55 reported consuming 1–2 units, 48 reported consuming 2–3 units, and the remaining 33 reported consuming >3 units. For the 167 alcohol drinkers, mean±SEM alcohol consumption was 102.7±7.7 (median 80) g/wk.

The relation between alcohol consumption and ICA lesion severity is summarized in Table 1 and Figure 1. Drinkers had less severe ipsilateral ICA lesions than nondrinkers, but the difference was significant only for men (\( \chi^2=31.3, df=3, p<0.001 \); for women \( \chi^2=4.6, df=3, p<0.02 \); Figure 1 top [bar graph]). When the carotid score (both ipsilateral and contralateral ICAs) was considered, this difference was significant for both men (\( \chi^2=31.3, df=3, p<0.001 \)) and women (\( \chi^2=6.8, df=3, p<0.05 \); Figure 1 bottom [bar graph]). Alcohol consumption in grams per week decreased while ipsilateral ICA lesion severity increased (Kruskal-Wallis one-way analysis of variance: for men, \( p<0.0001 \) and for women, \( p<0.001 \); Figure 1 top [upper graph]). This remained true when the carotid score was considered (for men, \( p<0.001 \) and for women, \( p<0.02 \); Figure 1 bottom [upper graph]). When the patients were grouped according to alcohol consumption in units, this inverse relation was still observed, for both the ipsilateral (significant for men and women) and the contralateral (significant for men only) ICAs (Table 1).

The inverse relation between ICA lesion severity and alcohol consumption was linear for light and moderate drinkers. For heavy drinkers, no correlation was found because only 10 patients reported...
drinking >4 standard drinks/day. However, these 10 patients had no or only minimal ICA atherosclerosis (for the ipsilateral ICA seven patients had class 1 stenosis, two had class 2 stenosis, and the other had class 3 stenosis; for the contralateral ICA eight patients had class 1 stenosis and the other two had class 2 stenosis). All four patients who drank >6 standard drinks/day had no ICA stenosis.

We analyzed the distributions of the recognized cardiovascular risk factors hypertension, diabetes mellitus, cigarette smoking, and hypercholesterolemia with reference to alcohol consumption groups and mean alcohol intake (Table 2). There was no significant association between these risk factors and alcohol consumption. No association between alcohol consumption and presumed cardioembolic or lacunar etiology of stroke was found either (data not shown).

As risk factors differed between the sexes, the logistic regression model was fitted separately for men and women using data from all 169 men but only 66 women. Because both cigarette smoking and diabetes mellitus affected carotid atherosclerosis so strongly in women that other effects were very hard to detect, we excluded data from 26 women who were either diabetic or smoked (among the 16 smokers excluded 15 had carotid atherosclerosis). Factors not in the model did not contribute significantly to the fit (except smoking and diabetes for women). For men, the equation is \( \ln(P/Q) = -1.88 + 0.070 \times \text{age} + 1.98 \times \text{hypertension} \times \text{smoking} - 0.73 \times \text{units alcohol} \), with standard errors of 0.50 for the intercept, 0.29 for age, 0.67 for the interaction term, and 0.18 for alcohol consumption. For women, the equation is \( \ln(P/Q) = -5.82 + 0.089 \times \text{age} + \left(0.87 \times \text{hypertension}\right) - 0.56 \times \text{units alcohol} \), with standard errors of 1.13 for the intercept, 0.032 for age, 0.34 for hypertension, and 0.26 for alcohol consumption. For both equations, \( \ln \) = natural logarithm, \( P \) = probability of ICA lesion of severity classes 2–6, and \( Q = 1 - P \).

Table 3 shows that for the younger men, alcohol consumption significantly decreased the probability of having carotid atherosclerosis; this effect was strongest in younger men who did not smoke and were not hypertensive. Although alcohol consumption decreased the probability of carotid atherosclerosis in older men, the effect was barely perceptible as the predicted probability in those with hypertension who smoked but drank >3 units of alcohol was ≈90%. For nondiabetic and nonsmoking women, an effect of alcohol consumption was found only in the absence of hypertension; in women with hypertension, the hypertension–alcohol consumption association increased the probability of carotid atherosclerosis. However, this finding should be considered with caution as the number of observed cases was small.

**Discussion**

Our results show an inverse relation between light-to-moderate alcohol consumption and the severity of ICA stenosis in patients >50 years of age with cerebral infarction. This negative association was strongest for younger men without hypertension who did not smoke (relative risk of having an ICA lesion 0.77 with 1–2 units alcohol consumed, 0.38 of ≥3 units). The inverse relation was less marked for older men, for those with hypertension, and those who smoke, probably because of the strong effect of these factors on carotid artery disease. The negative correlation between carotid atherosclerosis and alcohol consumption was also weaker for women, mainly because the strong association of carotid artery disease with smoking and diabetes mellitus limited our assessment of other factors in this rather small population.

The negative association between alcohol consumption and carotid atherosclerosis was linear in that the effect of 4 units was stronger than that of fewer units, which was still better than consumption of no alcohol. In studies of coronary heart disease, a J- or U-shaped curve has usually been suggested. Because of the very few heavy drinkers in our study
population, our results are limited to light and moderate drinkers (<4 units).

Another way of looking at our results is to speculate that alcohol combines with minor atheroma to cause stroke, whereas without alcohol severe atheroma alone explained the occurrence of stroke. However, the high alcohol intake that has been associated with the occurrence of stroke7-9 was rather uncommon among our patients; the majority reported a regular intake of <4 standard drinks/day.

**Table 2. Alcohol Consumption and Cardiovascular Risk Factors for 261 Patients With First Ischemic Stroke**

<table>
<thead>
<tr>
<th>Alcohol consumption (units)</th>
<th>Hypertension</th>
<th>Diabetes mellitus</th>
<th>Cigarette smoking</th>
<th>Hypercholesterolemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>94 (+) 51 (-) 43 (+) 16 (-) 78 (+) 40 (+) 54 (+) 16 (+) 78 (+)</td>
<td>31 (+) 17 (-) 14 (+) 4 (-) 27 (+) 14 (+) 17 (+) 8 (+) 23 (+)</td>
<td>55 (+) 30 (-) 25 (+) 6 (-) 49 (+) 23 (+) 32 (+) 7 (+) 48 (+)</td>
<td>48 (+) 30 (-) 18 (+) 8 (-) 40 (+) 23 (+) 25 (+) 8 (+) 40 (+)</td>
</tr>
<tr>
<td>Mean alcohol intake for drinkers (g/wk)</td>
<td>145.7 177.8 174.0 158.3 161.4 159.8 134.6 165.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No significant associations between risk factors and alcohol consumption. For hypertension $\chi^2=4.2$ (df=4), for diabetes mellitus $\chi^2=1.2$ (df=4), for cigarette smoking $\chi^2=0.5$ (df=4), and for hypercholesterolemia $\chi^2=3.9$ (df=4).
There are biases in our study that may preclude a generalization of our results and require further evaluation in other populations. First, reported intake as the primary measure of alcohol consumption may underestimate heavy drinking; however, in a nonalcoholic population, reported intake may be the most reliable method of assessing alcohol consumption. Second, our study was limited to patients with symptomatic cerebrovascular disease and therefore it may not be a good survey of the role of alcohol consumption in the general population. However, because of referral patterns, we believe that our results are reliable for people >50 years of age who suffer an ischemic stroke; because such patients have several associated risk factors for stroke and atherosclerosis our findings on the effect of alcohol consumption with reference to other risk factors also seem reliable.

The mechanisms by which mild and moderate alcohol consumption affect carotid atherosclerosis cannot be inferred from our data. It has been suggested that the development of atherosclerosis is modified by alterations of the HDL$_2$ and HDL$_3$ subfractions of cholesterol (apolipoprotein components) caused by alcohol itself. We did not find any correlation between carotid atherosclerosis and total cholesterol level, but we did not study the cholesterol subfractions. We found that the presence of some risk factors (hypertension associated with cigarette smoking in men, diabetes associated with cigarette smoking in women) counterbalanced the effect of mild or moderate alcohol consumption. In our patients, drinking did not correlate with cigarette smoking, contrary to that expected in heavier drinkers; such a dissociation has been reported in nonalcoholic patients assessed for coronary heart disease.

Although our data in stroke patients show an association between light-to-moderate alcohol consumption and the absence or low severity of ICA stenosis, our findings cannot be interpreted as showing a "protective" effect of alcohol drinking because we did not perform a follow-up study to assess the evolution of ICA morphology with and without regular alcohol consumption. Potential protection should be studied prospectively with sequential carotid ultrasonography in people with known alcohol intake.

**References**


KEY WORDS • alcohol drinking • carotid artery diseases • stroke registry
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