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). With moderate alcohol consumption (<4 standard drinks/day), the relative risk for coronary heart disease has been estimated to be 0.4-0.7. 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. On the other hand, some authors have suggested that acute alcohol ingestion is a risk factor for ischemic stroke, although it is possible that acute alcohol ingestion does not act independent of other risk factors. 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, 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, hypercholes-
terolemia (fasting level of >6.5 mmol/l), and associ-
ated cardiovascular and other diseases. Cerebral
infarction is diagnosed when CT shows a hypodense
area corresponding to the clinical signs and symp-
toms or when CT excludes a hemorrhage or a non-
vascular lesion.

The 261 patients included in the present study
underwent selective ultrasonography of the carotid
bifurcation using duplex scanning with spectral anal-
ysis of the Doppler signal (Dopscan, Carolina Med-
ical 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 angiog-
raphic 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 investiga-
tor 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 his-
tory, 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
(one glass of wine or one 0.33-l beer or one drink of
hard liquor) to contain 10 g alcohol. One standard
drink per day corresponds to 70 g alcohol/wk or 1 unit
of alcohol. Light drinkers 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 chi² test
and the nonparametric Kruskal-Wallis test. A logistic
regression model was fitted using GLIM software
to predict the presence or absence of stenosis consid-
ering alcohol consumption and the dichotomous vari-
ables age (patients below the median age were con-
sidered to be 60 years old and those above the
median age to be 75 years old), hypertension, diabe-
tes mellitus, cigarette smoking, and hypercholester-
olemia. 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
both 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 terri-
try 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 contralat-
eral 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 consump-
tion 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 (χ²=31.3, df=3, p<0.001; for women χ²=4.6,
df=3, p=0.08; Figure 1 top [bar graph]). When the
carotid score (both ipsilateral and contralateral ICAs)
was considered, this difference was significant for both
men (χ²=31.3, df=3, p<0.001) and women (χ²=6.8,
df=3, p=0.05; Figure 1 bottom [bar graph]). Alcohol
consumption in grams per week decreased while ipsi-
lateral 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
screened according to alcohol consumption in units, this
inverse relation was still observed, for both the ipsilat-
eral (significant for men and women) and the contralat-
eral (sigificant 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 correla-
tion 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 \( \ln(P/Q) = -5.82 + 0.089 \times \text{age} + [(0.87 \times \text{hypertension}) - 0.56] \times \text{units alcohol} \), 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, \( \ln = \text{natural logarithm}, P = \text{probability of ICA lesion of severity classes 2–6}, \) and \( 0 = 1 - P \).

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 with ≥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 \((\leq 4\) 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 stroke\(^7\)–\(^9\) 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>Risk factor</th>
<th>Hypertension</th>
<th>Diabetes mellitus</th>
<th>Cigarette smoking</th>
<th>Hypercholesterolemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>0</td>
<td>94</td>
<td>51</td>
<td>43</td>
<td>16</td>
<td>78</td>
</tr>
<tr>
<td>(&lt; 1)</td>
<td>31</td>
<td>17</td>
<td>14</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>1–2</td>
<td>55</td>
<td>30</td>
<td>25</td>
<td>6</td>
<td>49</td>
</tr>
<tr>
<td>2–3</td>
<td>48</td>
<td>30</td>
<td>18</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>(&gt; 3)</td>
<td>33</td>
<td>13</td>
<td>20</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Mean alcohol intake for drinkers (g/wk)</td>
<td>145.7</td>
<td>177.8</td>
<td>174.0</td>
<td>158.3</td>
<td>161.4</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 HDL₃ and HDL₄ 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


|TABLE 3. Logistic Regression Model for Predicting Carotid Atherosclerosis in Men and Women With and Without Cardiovascular Risk Factors |
|---|---|---|
|Age (yr) | Hypertension interaction† | Alcohol consumption (units)‡ | Predicted (%) | Observed (no.) | Predicted (%) | Observed (no.) |
|60 | No | 0 | 91.01 | 1 | 10 | 39.00 | 1 | 2 |
| | | <1-2 | 69.85 | 4 | 17 | 17.15 | 2 | 0 |
| | | ≥3 | 34.66 | 15 | 7 | 6.28 | 8 | 0 |
|75 | No | 0 | 98.65 | 0 | 7 | 39.00 | 3 | 3 |
| | | <1-2 | 94.37 | 1 | 9 | 53.87 | 2 | 6 |
| | | ≥3 | 79.33 | 2 | 9 | 68.09 | 2 | 1 |
|Total | | | 96.65 | 2 | 19 | 70.99 | 2 | 9 |
| | | | 86.86 | 3 | 23 | 44.20 | 1 | 1 |
| | | | 60.22 | 8 | 13 | 20.41 | 1 | 1 |
| | | | 99.52 | 0 | 5 | 70.99 | 5 | 7 |
| | | | 97.95 | 0 | 6 | 81.72 | 1 | 5 |
| | | | 91.64 | 0 | 8 | 89.09 | 0 | 3 |

*Only women without diabetes or cigarette smoking are considered.
†Interaction with cigarette smoking for men and interaction with alcohol consumption for women.
‡Unit, 70 g/wk (10 g/day).


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