Lifestyle Factors and Risk of Cerebral Infarction

Erik Folmer Ellekjaer, MD; Torgeir Bruun Wyller, MD; Jan Marcus Sverre, MD; and Jostein Holmen, MD

Background and Purpose: We evaluated the impact of lifestyle factors on the risk of ischemic stroke.

Methods: We used a nested case-control design. The cases comprised 163 persons (median age 69 years) admitted to a stroke unit and diagnosed with acute cerebral infarction. All cases had earlier participated in the North Trøndelag Health Survey. The controls comprised 567 participants from the North Trøndelag Health Survey, matched by sex and year of birth.

Results: Raised systolic (p < 0.001) and diastolic (p = 0.02) blood pressure, antihypertensive treatment (p < 0.001), previous myocardial infarction (p < 0.001), prior stroke (p = 0.002), diabetes (p < 0.001), and former daily smoking (p = 0.02) were identified as significant risk factors by univariate conditional logistic regression. No difference in risk was detected at different levels of alcohol consumption, salt intake, physical activity, or body mass index. Current smokers had virtually the same risk as nonsmokers. No association was found between stroke and the number of cigarettes smoked per day or the number of years of smoking. Multivariate conditional logistic regression identified diabetes (p = 0.002), raised systolic blood pressure (p < 0.001), and former daily smoking (p = 0.01) as significant and independent risk factors. Previous myocardial infarction (p = 0.07), previous stroke (p = 0.1), and current daily smoking (p = 0.1) were of marginal significance.

Conclusions: The established medical risk factors for stroke are confirmed. With the possible exception of smoking, we have not identified any lifestyle factor with a significant impact on the risk of ischemic stroke. (Stroke 1992;23:829-834)

Key words: cerebral infarction • cerebrovascular disorders • lifestyle • risk factors

Stroke is an important health problem among the elderly. Efforts to reduce the incidence of stroke are essential for the improvement of public health. Such attempts should be based on knowledge about risk factors that may be influenced, in particular, risk factors related to lifestyle.

Epidemiological research has identified several physical disorders as risk factors for cerebral stroke. High blood pressure is well established as an important risk factor. Many authors have identified diabetes as an independent and significant risk factor for stroke, but in other studies diabetes did not persist as an independent risk factor in multivariate analysis. In a study of the elderly, diabetes was not identified as a risk factor for stroke. Coronary heart disease also seems to be associated with a higher risk of stroke, even if discrepancies are to be found.

The roles of lifestyle factors as risks for stroke are uncertain. Current smoking has been identified as a risk factor in several studies, but not all. Studies have demonstrated that the risk of stroke increases with increasing levels of alcohol consumption, but these results were not confirmed in other studies. The literature regarding the impact of relative weight, physical inactivity, and salt consumption is sparse, and the results are conflicting. The relative importance of different risk factors may vary between countries as well as between ethnic groups. Thus, studies of risk factors should be carried out in different geographic regions, and patients suffering from different types of stroke should be considered separately. Few studies of risk factors for stroke have emerged from Scandinavia. In our nested case-control study we used exposure data from a large health survey, combined with information about later cerebrovascular morbidity. Our main hypothesis is that lifestyle factors influence the risk of cerebral infarction.

Subjects and Methods

North Trøndelag County is situated in the middle part of Norway. Approximately 127,000 of Norway's 4.2 million inhabitants live in this county. Most live in rural areas, and there is little internal migration.

All inhabitants of North Trøndelag County aged 20 years or more (85,100 persons) were invited to participate in the North Trøndelag Health Survey during the period January 1984 to February 1986, and 88.1% attended. Attendance was highest in the group aged 55–64 years (94.3%) and lowest in the group aged 80 years and above (71.6%). At the screening, participants had their blood pressure, height, and weight measured. The participants had filled out a questionnaire before the screening and were asked to return a second questionnaire by mail.

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Innherred Hospital is a district general hospital that serves a defined population corresponding to about two thirds of the inhabitants of North Trøndelag County. Virtually all patients in this population hospitalized on account of stroke are admitted to Innherred Hospital. The exclusion criteria for treatment in the stroke unit of the hospital are subarachnoid hemorrhage, coma at the time of admission, severe dementia diagnosed before the actual stroke, advanced cancer, and terminal failure of respiratory or circulatory function. All acute stroke patients without any exclusion criteria are admitted to the stroke unit provided that a bed is available; otherwise, the patient is admitted to the general medical ward. During the years 1986-1989, 902 patients were admitted to Innherred Hospital due to acute stroke or transient ischemic attack, 225 to the stroke unit and 677 to the general medical ward. Compared with stroke patients treated in the general medical ward, patients treated in the stroke unit were slightly younger (median age 75 and 73 years, respectively). Among the patients in the stroke unit, 185 (82%) were diagnosed with ischemic brain infarction and eight (4%) with nonspecified stroke. In the general medical ward, the corresponding numbers were 233 (34%) and 215 (32%). The rest of the patients had intracerebral hemorrhages, subarachnoid hemorrhages, or transient ischemic attacks.

The cases were 163 patients (95 men and 68 women) treated for acute cerebral infarction in the stroke unit of Innherred Hospital during the years 1986-1989. To improve diagnostic accuracy, we included only patients treated in the stroke unit, all of whom had had a cerebral computed tomogram. We also excluded patients who had not participated in the North Trøndelag Health Survey. The median age was 69 (interquartile range 62-75) years. The cases were identified in the files from the health survey, and the survey data were used to indicate each individual’s exposure to the proposed risk factors. Median interval from the screening until the stroke was 33.4 (interquartile range 22.5-46.4) months. To explore the possible bias introduced by excluding stroke patients treated in the general medical ward, we attempted to investigate the hospital records of the 448 patients with a possible ischemic stroke not treated in the stroke unit (diagnosed with either brain infarction or stroke of unspecified origin); 32 of the records could not be found. Of the 416 records investigated, 35 documented that the patient had suffered from diseases other than stroke, or sequelae of prior strokes, misclassified as acute stroke. Of the remaining 381 patients, the records demonstrated that 53 had been comatose on admission and that five had suffered from terminal cancer, 10 from terminal heart or lung failure, and 20 from severe dementia.

As controls, 652 persons (4:1) were drawn from the health survey summons files, matched by sex and year of birth and living in the same local government areas as the cases. Because the summons files were used for random selection of the controls, 85 of them had not attended the health survey. The analyses were therefore performed using 567 controls.

Data were analyzed according to the methods recommended by Rothman.25 Odds ratios of the exposure variables were calculated using univariate conditional logistic regression, thus taking into account the matching. To identify independent risk factors, the exposure variables with probability values of less than 0.20 were included in a multivariate conditional regression model. The analyses were carried out using the EGRET program.26

Results

Persons with systolic hypertension (above 180 mm Hg) had a tripled risk of ischemic stroke compared with those with a systolic blood pressure of less than 140 mm Hg. The odds ratios increased monotonously in the intermediate groups (Table 1). Persons with a diastolic blood pressure in the upper-normal range (80–95 mm Hg) had a slightly but not significantly increased risk, and persons with diastolic hypertension (above 95 mm Hg) had a nearly doubled risk of cerebral infarction compared with persons with a diastolic blood pressure of less than 80 mm Hg (Table 1). The use of antihypertensive agents was also associated with a higher risk of ischemic stroke (Table 1).

Persons with angina pectoris at the time of the health survey had an approximately 50% higher risk than those without, and persons who had suffered a myocardial infarction had an almost tripled risk compared with people who stated that they had not suffered a myocardial infarction (Table 1). The risk of a new ischemic stroke among those who had had a stroke was increased more than fourfold, and the risk among diabetics was triple that of persons without a history of diabetes (Table 1).

No association was detected between daily smoking at the time of the health survey and later brain infarction (Table 2). However, former daily smokers had a significantly higher risk. No dose–response relation existed between the number of cigarettes smoked per day and the risk of stroke for either former or present smokers. Nor was there any association between the number of years of smoking and the risk of stroke (Table 2).

Participants in the survey were asked how many times they had consumed alcohol-containing beverages during the last 2 weeks and whether they had felt intoxicated at any time during the same period. No association was found between the answers to these questions and the occurrence of later ischemic stroke (Table 2). Regrouping the data on these two variables to study the risk among the respondents with the highest level of alcohol consumption gave the same result (data not shown). Whether the analysis was based on frequency, duration, or intensity of physical activity or on combinations of these factors, no association was detected between physical activity during leisure time and ischemic stroke (Table 2). Adjustment for physical activity during work did not alter this result (data not shown).

The respondents were asked how often they added salt to their dinner portion. The answers to this question showed no relation to later ischemic stroke (Table 2).

Body mass index was calculated, and the participants were divided into quintiles with respect to this variable. Participants in the quintile with the highest body mass index (beyond 29.24 kg/m²) had the highest risk and those in the quintile with the second-lowest body mass index (23.23–25.06 kg/m²) had the lowest risk, but the difference in risk of cerebral infarction between these
TABLE 1. Medical History and Risk of Ischemic Stroke. Results From Univariate Logistic Regression

<table>
<thead>
<tr>
<th>Measurement/question in health survey</th>
<th>Prevalence of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In health survey, %</td>
</tr>
<tr>
<td></td>
<td>(n=74,977)</td>
</tr>
<tr>
<td>Are you taking or have you taken medicines for high blood pressure?</td>
<td>13.0</td>
</tr>
<tr>
<td>Measured systolic blood pressure (reference level &lt;140 mm Hg)</td>
<td>22.7</td>
</tr>
<tr>
<td>140–160 mm Hg</td>
<td>10.1</td>
</tr>
<tr>
<td>&gt;180 mm Hg</td>
<td>6.0</td>
</tr>
<tr>
<td>Measured diastolic blood pressure (reference level &lt;80 mm Hg)</td>
<td>34.4</td>
</tr>
<tr>
<td>90–95 mm Hg</td>
<td>15.4</td>
</tr>
<tr>
<td>&gt;95 mm Hg</td>
<td>16.9</td>
</tr>
<tr>
<td>Do you suffer from or have you ever suffered from diabetes?</td>
<td>2.9</td>
</tr>
<tr>
<td>Do you suffer from or have you ever suffered from myocardial infarction?</td>
<td>2.6</td>
</tr>
<tr>
<td>Do you suffer from or have you ever suffered from angina pectoris?</td>
<td>4.5</td>
</tr>
<tr>
<td>Do you suffer from or have you ever suffered from stroke or cerebral hemorrhage?</td>
<td>1.8</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval for OR.

groups was not significant (odds ratio 1.25, 95% confidence interval 0.72–2.16).

The impact of smoking, alcohol consumption, physical inactivity, body mass index, and salt consumption was reanalyzed using only the younger half of the population (less than 69 years old), but this did not influence the results (data not shown).

The multivariate conditional logistic regression model included 499 persons (107 cases) with complete data for the variables used. Table 3 shows the adjusted odds ratios. Increased systolic blood pressure, diabetes, and previous smoking were identified as independent and significant risk factors for ischemic stroke, while previous stroke, previous myocardial infarction, and current smoking reached the level of only marginal significance. Diastolic blood pressure, angina pectoris, the number of years of smoking, and the use of blood pressure medication did not persist as significant risk factors in the multivariate analysis. Because risk factors for later stroke may differ from those for first stroke, the multivariate analysis was repeated after exclusion of those individuals with a prior stroke. This analysis gave essentially the same results (data not shown).

Discussion

Lifestyle factors seem to play a smaller role as risks for ischemic stroke in our study than has been reported by other groups. The number of responses to some of our questions was low, thus increasing the possibility of type II error, but with the exception of smoking, odds ratios for the lifestyle factors are close to 1.0. High blood pressure, coronary heart disease, diabetes, and prior stroke were identified as significant risk factors for brain infarction in this study. This is in accordance with the results of numerous other groups.

By linking data from a general health survey to the occurrence of later disease, we have avoided recall bias. This can otherwise be a major problem in case-control studies.28 Our control group was population-based, thus avoiding the possible bias connected with the use of hospital controls.27 Due to the high attendance rate, the problem of response bias28 was also minimized. Extensive comparisons have been made between participants and nonparticipants in the North Trøndelag Health Survey.24 District nurses have examined 34.9% of a random sample of nonparticipants, and no significant differences in health habits were found between this sample and the participants. The nonparticipant group as a whole, however, demonstrated increased mortality compared with the participants during the first year after screening. This difference was accounted for by people being severely ill during the survey period and for this reason not participating.24 For some variables there are several persons with missing data due to participants not having answered this particular question. An uneven distribution of health habits between participants answering and not answering the different questions may introduce a bias.

Validity of the diagnosis of cerebral infarction among our cases was probably high because the patients were assessed thoroughly in the stroke unit and all had a computed tomogram of the brain. Some of the controls, however, may have suffered a stroke without being admitted to the hospital. Because Innherred Hospital is the only one serving the population under study, this methodological problem can be regarded as being small. Fifty-three patients were not admitted to the stroke unit because they were comatose when they arrived at the hospital. This means that the proportion of patients with very severe stroke is lower among the cases than among all stroke patients admitted to the hospital. Even though the completeness of data in a retrospective study may be questioned, our review of the records indicated that patients excluded from the stroke unit for reasons
TABLE 2. Lifestyle Factors and Risk of Ischemic Stroke. Results From Univariate Logistic Regression

<table>
<thead>
<tr>
<th>Questions in health survey</th>
<th>Prevalence of exposure</th>
<th>Among cases</th>
<th>Among controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In health survey, % (n=74,977)</td>
<td>No.</td>
<td>n</td>
</tr>
<tr>
<td>Do you smoke daily?</td>
<td></td>
<td>33.2</td>
<td>29</td>
</tr>
<tr>
<td>If you do not smoke cigarettes daily at the moment: Have you ever smoked cigarettes daily?</td>
<td>NA</td>
<td>51</td>
<td>110</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If you smoke cigarettes daily now, or have done so before: How many cigarettes do you smoke or did you smoke per day? (reference level=never smoked)</td>
<td>&lt;20 cigarettes</td>
<td>NA</td>
<td>40</td>
</tr>
<tr>
<td>&gt;20 cigarettes</td>
<td></td>
<td>51</td>
<td>110</td>
</tr>
<tr>
<td>If you smoke cigarettes daily now, or have done so before: For how many years in all have you been smoking daily? (reference level=never smoked)</td>
<td>&lt;10 years</td>
<td>NA</td>
<td>4</td>
</tr>
<tr>
<td>10–30 years</td>
<td></td>
<td>26</td>
<td>112</td>
</tr>
<tr>
<td>&gt;30 years</td>
<td></td>
<td>31</td>
<td>112</td>
</tr>
<tr>
<td>How frequently have you drunk alcohol (beer, wine, or spirits) during the last 14 days? (reference level=teetotaller)</td>
<td>0–10 times</td>
<td>84.7</td>
<td>105</td>
</tr>
<tr>
<td>&gt;10 times</td>
<td></td>
<td>3.1</td>
<td>6</td>
</tr>
<tr>
<td>Exercises (go for walk, skiing, cycling, etc.) on average less than once a week (reference level=once a week or more)</td>
<td>41.1</td>
<td>45</td>
<td>134</td>
</tr>
<tr>
<td>Sprinkles salt on dinner portion always or almost always (reference level=never/rarely/occasionally/frequently)</td>
<td>5.3</td>
<td>3</td>
<td>137</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval for OR. NA, not applicable for variables constructed on basis of >1 question in questionnaire.

TABLE 3. Risk Factors for Ischemic Stroke. Adjusted OR From Multivariate Conditional Logistic Regression Model (n=499)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>p</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>1.384</td>
<td>0.002</td>
<td>3.99</td>
<td>1.66–9.58</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>0.794</td>
<td>0.07</td>
<td>2.21</td>
<td>0.95–5.13</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>1.328</td>
<td>0.10</td>
<td>3.77</td>
<td>0.78–18.37</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140–160 mm Hg</td>
<td>1.277</td>
<td>&lt;0.001</td>
<td>3.59</td>
<td>1.79–7.21</td>
</tr>
<tr>
<td>160–180 mm Hg</td>
<td>1.383</td>
<td>&lt;0.001</td>
<td>3.99</td>
<td>1.83–8.70</td>
</tr>
<tr>
<td>&gt;180 mm Hg</td>
<td>1.460</td>
<td>&lt;0.001</td>
<td>4.31</td>
<td>1.86–9.96</td>
</tr>
<tr>
<td>Prior smoking</td>
<td>0.932</td>
<td>0.01</td>
<td>2.54</td>
<td>1.22–5.29</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.544</td>
<td>0.1</td>
<td>1.72</td>
<td>0.85–3.51</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval for OR.
problem that was not identified through the questionnaire but is associated with a higher risk of ischemic stroke. Other studies have indicated that the risk of stroke decreases gradually after cessation of smoking.11,13

The higher risk of stroke associated with alcohol consumption disclosed in other studies is believed to be related to acute alcohol intoxication23 and seems most clearly associated with heavy drinking.18,33 In the questionnaire used in our study, the highest answer alternative relating to alcohol intake represents a moderate consumption in comparison with other studies, and few persons in our population chose this alternative. Furthermore, alcohol intake seems to be a more important risk factor among younger persons, particularly for brain hemorrhage, even if some authors have also reported an increased risk of brain infarction.17,34 A recent meta-analysis of 62 epidemiological studies indicated that in European populations there is a J-shaped association between alcohol consumption and ischemic stroke.35 It has been argued that the identification of alcohol as a risk factor is due to bias in the selection of control groups in hospital-based studies. Hospital patients without alcohol-related diseases have a lower level of alcohol consumption than the average member of a population and are therefore not representative controls for the evaluation of alcohol effects.28 We used a population-based control group. This can explain the discrepancy between our results and those of other studies regarding the relation between alcohol intake and stroke.

The literature dealing with sedentary lifestyle as a possible risk factor for stroke is very sparse. Our work indicates that this is not an important risk factor.

High salt consumption has been postulated to be an important risk factor for stroke,36 and a decreasing consumption of salt has been suggested to contribute to the decreasing incidence of stroke seen in many European countries as well as in the United States.37,38 Even if uncertainty exists concerning the validity of the question about salt intake in our questionnaire29 and even if the number of respondents with a high level of salt consumption is low, our data weigh against a high salt intake as an important independent risk factor for ischemic stroke.

The data pertaining to body mass index were derived from actual measurements, and we suppose that they have a high validity. Recent research has suggested that abdominal obesity, as part of a metabolic cardiovascular syndrome, is more closely associated with stroke risk than is general obesity.29,40 Unfortunately, this issue cannot be further elucidated from our data.

In conclusion, our study identified hypertension, prior stroke, coronary heart disease, and diabetes as significant risk factors for ischemic stroke, in accordance with the results of others. Among the lifestyle factors, former daily smoking was the only one displaying a statistically significant association with ischemic stroke.

Acknowledgments

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