Relation of Blood Pressure, Serum Lipids, and Smoking to the Risk of Cerebral Stroke
A Longitudinal Study in Eastern Finland

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The impact of blood pressure, serum cholesterol and triglycerides, and smoking on the risk of cerebral infarction and other stroke was studied by a longitudinal design. A random sample of the population aged 35–59 years in two counties of Eastern Finland was examined in 1972, with a participation rate of 92 per cent. In subjects (both sexes) standardized epidemiological measurements on blood pressure, height, weight, and serum lipids were made and questionnaire data were obtained on smoking. The cohort was followed for seven years by means of national hospital discharge and death certificate registers. During the follow-up 77 men and 65 women had a cerebral stroke. Based on multiple logistic risk function analysis, age, smoking, blood pressure, and history of previous stroke and diabetes turned out to be independent predictors of both cerebral infarction and other strokes in men. Diastolic blood pressure of 100 mm Hg or more was associated with a 1.9-fold (90% CI = 1.1–3.6) risk of cerebral infarction in men and 2.5-fold (90% CI = 1.1–5.6) risk in women with no previous stroke. In men 37% (90% CI = 21–53%) of all cerebral strokes were attributable to systolic blood pressure of 150 mm Hg or more and 27% (90% CI = 11–42%) to diastolic blood pressure of 95 mm Hg or more.

CARDIOVASCULAR DISEASES (CVD) are the main cause of death in the developed world. The problem is increased by the frequent permanent disability and loading of health services due to these diseases. In most countries, the most important cardiovascular disease of the middle-aged population is coronary heart disease, and that of the older population is cerebrovascular disease.21,29 In most industrialized countries, cerebrovascular disease is the second most important cause of cardiovascular death.25 In a number of countries, it is the third or fourth most important cause of all deaths in the age-group 45–64.22,28

Since cerebral stroke is often fatal and the impact of treatment on the prognosis is limited, without question the potential to control the disease lies on primary prevention.24,25 This implies reliable information on the factors related to the risk of stroke.

The purpose of this study was to provide information on the relationship of blood pressure, serum cholesterol and triglycerides, and smoking to the risk of cerebral infarction and all strokes in middle-aged men and women in a high-risk area.

Patients and Data Collection

The study was conducted in eastern Finland, a mainly rural area with extremely high mortality rates for cardiovascular diseases.4,13 A random 6.6 per cent sample of the population aged 25–59 of the counties of North Karelia and Kuopio was drawn using the national population register. The subjects received an invitation to a physical examination by mail and a questionnaire to be filled in at home. They were asked to fast for at least four hours before the examination. The participation rate in the field examination was 92 per cent in the age group of 35–59.

Since the occurrence of cerebral stroke is negligible below this average, the 35–59 age group served as the population at risk in the present study. A total of 4,034 men and 4,334 women aged 35–59 participated in the field examination. Blood pressure was recorded of 3,831 men and 4,124 women, and all risk factors analyzed in this paper of 3,750 men and 4,074 women.

The field examination was carried out between February and April of 1972. At the examination, the questionnaire was checked, height, weight, and casual blood pressure were measured in a sitting position using standardized methods, and a venous blood sample was taken. Serum cholesterol and triglycerides were analyzed of the blood samples in a mixed order in the Central Laboratory of the National Pension Institution, which was involved in the international reference system of WHO in Atlanta. All cerebral strokes and transient ischemic attacks (ICD codes 430–437, 8th revision) among the baseline survey participants were noted by means of the national hospital discharge and death certificate data registers of Finland.

This report presents the results based on the follow-up of the cohort up till December 31, 1978. During this approximately seven-year follow-up period, 77 men and 65 women had a stroke or TIA, and of these 34 men and 21 women a cerebral infarction (ICD 433–434).

Statistical Methods

The age-adjusted risk of any cerebral stroke and cerebral infarction was calculated according to the systolic and diastolic blood pressure in the baseline examination, in men and women separately. The direct standardization was used as the method of age-adjustment. Age was broken down in three categories: 35–44, 45–54 and 55–59 years. The age-distribution of the
entire material was used as the reference. The confidence intervals of the risk estimates were based on binomial distribution. Maximum likelihood estimates of relative risks were computed as presented by Miettinen. The confidence intervals of the relative risks were estimated by applying the test-based method of Miettinen and Walker and Duncan.

The joint impact of diastolic blood pressure, serum cholesterol, and smoking on the risk of cerebral stroke and cerebral infarction was studied by calculating the age-specific risks according to the number of elevated values of these factors in the age-groups of 35–49 and 50–59 years for men and women with no previous strokes separately. The cut-off points for the risk factors were: diastolic blood pressure ≥ 100 mm Hg, serum cholesterol ≥ 310 mg/dl, and smoking at least one cigarette a day currently.

The fraction of risk attributable to blood pressure and the three risk factors jointly in the population at risk was calculated as presented by Levin. The variance of the estimate of attributable risk was calculated according to Walter. The independent contributions of diastolic blood pressure, serum cholesterol and triglycerides, and smoking on the risk of stroke were estimated by fitting multiple logistic functions:

\[
\left[1 + \exp \left(- \alpha - \sum \beta_i x_i \right) \right]^{-1},
\]

where \(\alpha\) is the intercept, \(\beta_i\) are the weight coefficients, and \(x_i\) are the independent variables. The iterative procedure of Walker and Duncan was applied. The adjusted relative risks were estimated as antilogarithms of the original coefficients of dichotomous independent variables in the multiple logistic models.

### Results

The age-adjusted risk of any stroke or brain infarction rose steadily with increasing baseline blood pressure. The risk of men with a systolic blood pressure between 150 and 189 mm Hg was 2.1-fold (95% CI = 1.3–3.4) compared with those with a lower pressure (fig. 1). The risk of men having systolic blood pressure at least 190 mm Hg was 4.1-fold (95% CI = 2.2–7.8) compared with the ones whose systolic pressure was below 150 mm Hg. The relative risk associated with a diastolic blood pressure of 95–109 mm Hg in men was 1.5 (95% CI = 0.9–2.4) and that of 110 mm Hg or more was 2.9 (95% CI = 1.7–4.9) (fig. 1). The proportion of all strokes in men attributable to systolic blood pressure of 150 mm Hg or more was 37% (90% CI = 21–53%) and that to diastolic blood pressure of 95 mm Hg or more 27% (90% CI = 11–42%) when analyzed separately.

Women with a systolic blood pressure of 150–189 mm Hg had a 1.1-fold (95% CI = 0.6–1.9) and those with a systolic pressure of at least 190 mm Hg a 2.0-fold (95% CI = 1.0–4.2) age-adjusted risk of stroke compared with the women with a systolic pressure below 150 mm Hg (fig. 2). The relative risk in the diastolic blood pressure level of 95–109 mm Hg was 1.3 (95% CI = 0.8–2.4) and in the level of 110 mm Hg or more 2.3 (95% CI = 1.2–4.2) compared with the diastolic pressure level below 95 mm Hg in women.

The risk of any kind of cerebral stroke or brain infarction rose with increasing number of elevated risk factor values in men with no previous stroke in the preceding 12 months (fig. 3). The age-adjusted risk of any stroke was 15.4-fold (95% CI = 7.1–33.6) among men with a diastolic blood pressure 100 mm Hg or more, a serum cholesterol of 310 mg/dl or more and who were current smokers compared with men who had no risk factor elevations. (Mantel Chi-square = 6.89, one-sided \(p < 0.001\)). This gradient tended to be stronger in men aged below 50 than between 50–59 years (fig. 3).

The age-adjusted risk of any kind of stroke in women with no previous stroke with a high-risk value in any of the three factors was 3.1-fold (95% CI = 1.8–5.3) compared with the women with no risk factor elevations (Mantel Chi-square = 4.22, one-sided \(p < 0.01\)). A more detailed break-down was not possible due to the small number of women with elevations in more than one risk factor.

In a multiple logistic model among all men, age, daily number of cigarettes, diastolic blood pressure, and history of previous stroke were significantly (\(p < 0.05\)) associated with the risk of any kind of stroke and cerebral infarction (table 1). In addition, a history of diabetes was associated with the risk of cerebral infarction in men. In women only age, a history of stroke, and diabetes were significantly related to the risk of cerebral infarction and any kind of stroke (table 1).

In another multiple logistic model in men with no previous stroke in the preceding 12 months diastolic blood pressure of 100 mm Hg or more was associated with a 1.9-fold (95% CI = 1.1–3.6) risk of cerebral infarction and 2.0-fold (95% CI = 1.2–3.4) risk of other strokes consisting mostly of subarachnoidal and cerebral hemorrhages (table 2). Serum triglycerides of 250 mg/dl or more were related to a 2.4-fold (90% CI = 1.2–4.7) risk of brain infarction and 2.3-fold (90% CI = 1.2–4.1) risk of other strokes in men. The men smoking at the time of the survey had a 4.2-fold (90% CI = 2.0–8.9) risk of brain infarction and 2.2-fold (90% CI = 1.3–3.9) risk of other strokes compared with non-smokers (table 2).

Among women only diastolic blood pressure of 100 mm Hg or more was significantly related to an increased risk of brain infarction in the multivariate analysis (table 2). The adjusted relative risk was 2.5 (90% CI = 1.1–5.6).

### Discussion

The design of the present study was a prospective eight-year follow-up of a random sample of a population aged 35–59 from two counties in Eastern Finland, examined in 1972. The stroke events in the cohort were notified by means of the national hospital discharge registers and death certificate data. Since the
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FIGURE 1. Age-adjusted seven-year risk of cerebral stroke and infarctions in men aged 35–59 according to baseline blood pressure. Bars indicate 95% confidence intervals.
FIGURE 2. Age-adjusted seven-year risk of cerebral stroke and infarction in women aged 35–59 according to baseline blood pressure. Bars indicate 95% confidence intervals.
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MOST EPIDEMIOLOGICAL STUDIES HAVE CONFIRMED THAT BLOOD PRESSURE IS AMONG THE MOST IMPORTANT SINGLE RISK FACTORS OF STROKE. 1, 3, 11, 12, 16, 23, 24, 27 THERE IS GOOD EVIDENCE THAT BLOOD PRESSURE CONTRIBUTES TO THE DEVELOPMENT OF ATHEROSCLEROSIS AND ISCHEMIC BRAIN INFARCTION.

FIGURE 3. Seven-year risk of cerebral stroke and infarction in men aged 35-49 and 50-59 according to the number of elevated risk factor values. Elevated values were defined as: diastolic blood pressure \( \geq 100 \text{ mm Hg} \), serum cholesterol \( > 308 \text{ mg/dl} \) and smoking currently at least one cigarette daily. Men with a history of previous stroke in the preceding 12 months are excluded.
In general, 35–75 per cent of the stroke patients, depending on study material and methods, have been found to have elevated blood pressure. The variation can mostly be explained by the different definitions of elevated blood pressure. Hypertension has also been noted to be an important risk-factor for recurrent stroke. Among females, hypertension has not been found to be as strongly associated with the incidence of stroke as among males. In some studies, no association between hypertension and stroke was found, but the material of these studies was only geriatric. 2, 17 Although it has been shown fairly conclusively that serum cholesterol level contributes to the risk of coronary heart disease, the information of the association of blood lipids and stroke is more contradictory. Most studies found no significant relationship between the risk of stroke and the level of serum total cholesterol. 2, 6, 7, 10, 12, 24 In the Framingham study, an increased level of serum cholesterol was not significantly associated with an increased risk of cerebrovascular disease; although such a trend was noticed among people under the age of 50. 10

Elevated serum triglycerides have been found to be associated with an increased risk of stroke. 2, 5, 6, 7 Stroke patients have often shown ECG abnormalities: left ventricular hypertrophy and signs of previous myocardial ischemia. 1, 2, 7, 17 Men with a recurrent stroke commonly have ECG abnormalities. Diabetes associates with an increased risk of stroke. 1, 2, 8, 12, 14 partly because the older age groups with high incidence of stroke rates have also high prevalence rates of diabetes.

Combinations of various risk factors have also been evaluated in some prospective studies. On the basis of the Framingham material, Wolf et al calculated that 10 per cent of the symptom free population that produces half of the subsequent strokes can be identified by combination of five factors: blood pressure, presence of left ventricular hypertrophy in ECG, hypercholesterolaemia, glucose intolerance, and smoking. 30

Because of the enormous human and economic costs of cerebral stroke, preventive measures are of great importance. This implies firm knowledge about the causal factors of stroke. Differences and similarities between populations often help to understand the epidemiology and the role of various risk factors. An interesting question is whether, in the eastern Finnish population with extremely high rate of cardiovascular diseases, the risk factors are the same as elsewhere. In this study the best predictors of stroke were age, blood pressure, a history of diabetes and previous stroke. There was also a positive association between the risk of stroke and smoking as well as serum triglycerides in men but not in women. The lack of any notable association of serum cholesterol and the risk of stroke among the younger people was confirmed in our study, although there was a nonsignificant trend.

Even though several factors contribute to the risk of cerebral stroke, the most important single measure in the prevention of stroke is an effective control of hypertension. On a community level, the effect depends on intervention in groups with relatively low levels of

### TABLE 1  Impact of Multiple Predictors of Cerebral Infarction and Any Stroke in 3,750 Men and 4,074 Women Aged 35–59

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Standardized multiple logistic coefficient*</th>
<th>Cerebral infarction</th>
<th>All cerebral strokes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Age at the baseline</td>
<td></td>
<td>0.87§</td>
<td>0.66†</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td></td>
<td>0.47§</td>
<td>0.15</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td>0.57§</td>
<td>-0.02</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td></td>
<td>0.12</td>
<td>-0.12</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td></td>
<td>0.08</td>
<td>0.12</td>
</tr>
<tr>
<td>Body-mass index</td>
<td></td>
<td>0.08</td>
<td>-0.17</td>
</tr>
<tr>
<td>History of diabetes</td>
<td></td>
<td>0.21‡</td>
<td>0.19†</td>
</tr>
<tr>
<td>History of stroke</td>
<td></td>
<td>0.17‡</td>
<td>0.19§</td>
</tr>
<tr>
<td>Number of events</td>
<td></td>
<td>34</td>
<td>21</td>
</tr>
</tbody>
</table>

*Significance, based on two-sided tests, shown as †p < 0.05, ‡p < 0.01, and §p < 0.001.

### TABLE 2  Adjusted Relative Risk of Cerebral Infarction and Other Strokes Associated With Diastolic Blood Pressures of 100 mm Hg or More, Serum Cholesterol of 300 mg/dl (8 mmol/l) or More, Serum Triglycerides of 250 mg/dl (6.5 mmol/l) or More and Current Smoking in 3,692 Men and 4,023 Women Aged 35–59 With No Previous Stroke in the Preceding 12 Months

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Adjusted relative risk†</th>
<th>90% CI</th>
<th>Adjusted relative risk†</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral infarction*</td>
<td></td>
<td></td>
<td>Other strokes†</td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>1.9§</td>
<td>1.1–3.6</td>
<td>2.0‡</td>
<td>1.2–3.4</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>1.7</td>
<td>0.9–3.3</td>
<td>1.3</td>
<td>0.7–2.3</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>2.4‡</td>
<td>1.2–4.7</td>
<td>2.3‡</td>
<td>1.2–4.1</td>
</tr>
<tr>
<td>Daily no. of cigarettes</td>
<td>4.2‡</td>
<td>2.0–8.9</td>
<td>2.2‡</td>
<td>1.3–3.9</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>2.5§</td>
<td>1.1–5.6</td>
<td>1.6</td>
<td>1.0–2.8</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>0.5</td>
<td>0.2–1.3</td>
<td>1.4</td>
<td>0.8–2.5</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>2.0</td>
<td>0.6–7.3</td>
<td>0.7</td>
<td>0.2–2.5</td>
</tr>
<tr>
<td>Daily no. of cigarettes</td>
<td>1.4</td>
<td>0.4–5.0</td>
<td>0.8</td>
<td>0.3–2.2</td>
</tr>
</tbody>
</table>

*From a multiple logistic model including age in addition and based on 31 events in men and 18 in women.
†Based on 41 events in men and 38 in women.
‡Significance, based on one-sided tests, shown as §p < 0.05, and ‡p < 0.01.
“hypertension,” since only 27 per cent of the cases occurred among men with diastolic blood pressure of 95 mm Hg or more. Since the other harmful consequences of high blood pressure are also well known, a very firm basis exists to establish effective programs to control hypertension in the whole community. Since it would be very beneficial to reach also the relatively large population groups with “border-line” hypertension, health educational measures like general reduction of overweight and salt consumption should be searched for in order to avoid unnecessary wide use of drug intervention among the population.

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