The Impact of History of Hypertension and Type 2 Diabetes at Baseline on the Incidence of Stroke and Stroke Mortality

Gang Hu, PhD; Cinzia Sarti, PhD; Pekka Jousilahti, PhD; Markku Peltonen, PhD; Qing Qiao, PhD; Riitta Antikainen, PhD; Jaakko Tuomilehto, PhD

Background and Purpose—Both hypertension and diabetes are strong predictors of stroke, but very few studies have assessed their joint effect on stroke risk. We evaluated prospectively the joint association of history of hypertension and type 2 diabetes on the incidence of stroke and stroke mortality.

Methods—We prospectively followed 49,582 Finnish subjects aged 25 to 74 years without a history of stroke and coronary heart disease at baseline. Hazards ratios (HRs) for stroke risk were estimated by the hypertension and diabetes status.

Results—During a mean follow-up of 19.1 years, 2978 incident stroke events were recorded, of which 924 were fatal. Age-, sex-, and study year-adjusted HRs of stroke incidence were 1.35 (95% CI, 1.21 to 1.51), 1.98 (95% CI, 1.79 to 2.19), 2.54 (95% CI, 1.61 to 4.01), 3.51 (95% CI, 2.40 to 5.14), and 4.50 (95% CI, 3.60 to 5.61), respectively, among subjects with hypertension I (blood pressure 140 to 159/90 to 94 mm Hg) only, with hypertension II (blood pressure ≥160/95 mm Hg, or using antihypertensive drugs) only, with diabetes only, with both hypertension I and diabetes, and with both hypertension II and diabetes compared with the subjects without either of the diseases. The corresponding HRs of stroke mortality were 1.47, 2.62, 3.06, 5.59, and 9.27, respectively. Additional adjustments for body mass index, cholesterol, education, smoking, alcohol consumption, and physical activity did not appreciably change these risk estimates. Blood pressure affected the risk of stroke similarly in diabetic and nondiabetic subjects.

Conclusions—Hypertension and type 2 diabetes increase stroke risk independently, and their combination increases the risk drastically. A significant proportion of the risk of stroke assumed to be related to hypertension may be attributable to concomitant diabetes. (Stroke. 2005;36:2538-2543.)

Key Words: blood pressure ■ hypertension ■ stroke ■ type 2 diabetes

The epidemiological studies have indicated that hypertension and type 2 diabetes are commonly associated conditions, and their concordance is increased in populations. Hypertension affects up to 40% or more of diabetic patients.1-3 In the general population, high blood pressure is one of the most important risk factors for stroke.2,4-6 However, the independent effect of type 2 diabetes or hyperglycemia on stroke risk has been found inconsistent; some7-14 but not all studies15-17 have identified type 2 diabetes or hyperglycemia as an independent risk factor for stroke. Several studies have demonstrated that high blood pressure is an independent risk factor for stroke in diabetic patients.8,18,19

Although there are few studies12,14 concerning the joint prognostic effect of hypertension and type 2 diabetes on stroke risk in the general population, it is not well known whether the increasing risk of stroke comes from the effect of hypertension or type 2 diabetes alone or from the combined effect of both hypertension and type 2 diabetes. The aim of this study is to evaluate the joint effects of hypertension of different stages and the history of type 2 diabetes on the incidence of stroke and stroke mortality.

Methods

Subjects
Between 1972 and 1997, every 5 years, 6 independent population surveys were carried out in 5 geographic areas of Finland among the population aged 25 to 64 years. The age group of 65 to 74 years was also included in 1997. The sampling methods have been previously described in detail.20 The total sample size of the 6 surveys was 53,166. The participation rate varied by year from 74% to 88%.20 After excluding 2063 subjects with a history of coronary heart disease or stroke at baseline, 105 subjects with type 1 diabetes and 1416 subjects with incomplete data on any required variables, the present analyses are composed of 23,748 men and 25,834 women. The surveys were conducted according to the ethical rules of the National Public Health Institute, and the investigations were carried out in accordance with the Declaration of Helsinki.

Baseline Measurements
A self-administered questionnaire was mailed to the participants in advance. The questionnaire included questions on smoking habits,
alcohol consumption, socioeconomic factors, physical activity, and medical history. Physical activity included occupational, commuting, and leisure-time physical activity and were merged and regrouped into the following 3 categories: low, moderate, and high.21 Measurements of height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), and serum total cholesterol at the baseline examination were carried out using a standardized protocol.20

Assessment of Hypertension and Diabetes at Baseline

The assessment of the diabetes status at baseline was based on self-reporting and on the data from 2 nationwide registers, the National Hospital Discharge Register since 1968 and the National Social Insurance Institution Register since 1964. Antidiabetic drugs prescribed by a physician are free of charge in Finland subject to approval of the case history prepared by the treating physicians. The physician confirms the diagnosis of diabetes applying the World Health Organization criteria.22 All of the patients receiving free-of-charge medication (either oral antidiabetic agents or insulin) are entered into a register maintained by the Social Insurance Institution.

Subjects who reported having diabetes on the questionnaire or had diabetes included among hospital discharge diagnoses or had the approval for free-of-charge medication for diabetes before the baseline survey were classified as having diabetes.

Data on the initiation of antihypertensive drug treatment were also received from the records of the Social Insurance Institution nationwide register on persons entitled to special reimbursement for antihypertensive drugs since 1964. Hypertension stage I was defined as blood pressure 140 to 159 and/or 90 to 94 mm Hg and without any antihypertensive drugs treatment at baseline. Hypertension stage II was defined as blood pressure ≥160/95 mm Hg or use of antihypertensive medicine based on the questionnaire or on the approval of special reimbursement for antihypertensive drugs before the baseline survey. The normotensive reference group was defined as blood pressure <140/90 mm Hg and without any antihypertensive drug treatment at baseline.

Prospective Follow-Up

The study cohorts were followed until the end of 2003 through computerized register linkage by identification numbers. Mortality data were obtained from Statistics Finland, and data on no-fatal events were obtained from the National Hospital Discharge Register. The Eighth, Ninth, and Tenth Revisions of the International Classification of Diseases (ICD) were used to identify subarachnoid (430 to 438 and I63-I66) and intracerebral hemorrhage (431 and I61-I62), intracerebral infarction (432 to 438 and I63-I66), and any stroke (430 to 438 and I60-I66) events. International Classification of Diseases-9 code 432 was classified as an intracerebral hemorrhage. In the data analyses, we combined all of the hemorrhagic strokes, because the number of cases with subarachnoid hemorrhage was small.

The stroke events that occurred before the baseline survey were identified from the Hospital Discharge Register and excluded from the analyses. The validity of the diagnosis of acute stroke in Finland is good for hospital discharge register (agreement in 90% and death register (agreement in 97%).23 End points during follow-up were incident stroke events, defined as either the first nonfatal stroke event or stroke death without a preceding nonfatal event.

Statistical Analyses

Statistical package SPSS for Windows, version 12.0 (SPSS Inc.), was used for statistical analysis. The Cox proportional hazards model was used to estimate the hazard ratios (HRs) of stroke incidence and stroke mortality among participants in 6 groups: subjects with neither hypertension nor type 2 diabetes, with hypertension I only, hypertension II only, type 2 diabetes only, both hypertension I and type 2 diabetes, and subjects with both hypertension II and type 2 diabetes. In addition, the association of blood pressure (as a continuous variable) with the risk of stroke was analyzed stratifying by the diabetes status. Because there was no heterogeneity in the results between sexes, data on men and women were analyzed combined.

The analyses were first carried out adjusting for age, sex, and study year, and additionally for education (tertiles), body mass index (BMI), total cholesterol, smoking (never, past, and current), alcohol consumption (yes/no), and physical activity. A χ² log-likelihood ratio test was carried out to test the significance of the interaction terms of hypertension and diabetes on stroke risk.

Results

General characteristics of the study population at baseline are presented in Table 1. During a mean follow-up of 19.1 years, we identified 2978 cerebrovascular events (618 hemorrhage and 2360 ischemic), of which 924 were fatal.

When blood pressure was used as a continuous variable, age-, sex-, and study year-adjusted HRs for stroke incidence and stroke mortality were 1.13 (95% CI, 1.11 to 1.15) and 1.20 (95% CI, 1.17 to 1.24) for a 10 mm Hg increment in SBP and 1.24 (95% CI, 1.20 to 1.28) and 1.39 (95% CI, 1.32 to 1.46) for a 10 mm Hg increment in DBP, respectively (Table 2). Additional adjustments for BMI, serum total cholesterol, education, smoking, alcohol drinking, and physical activity did not appreciably change the results. The association of blood pressure and the risk of stroke was similar in diabetic and nondiabetic subjects.

Compared with the participants without hypertension or diabetes, the age, sex, and study year adjusted HRs associated with hypertension I only, with hypertension II only, with diabetes only, with both hypertension I and diabetes, and with both hypertension II and diabetes were 1.35 (95% CI, 1.21 to 1.51), 1.98 (95% CI, 1.79 to 2.19), 2.54 (95% CI, 1.61 to 4.01), 3.51 (95% CI, 2.40 to 5.14), and 4.50 (95% CI, 3.60 to 5.61) for stroke incidence, and 1.47 (95% CI, 1.17 to 1.84), 2.62 (95% CI, 2.14 to 3.21), 3.06 (95% CI, 1.25 to 7.49), 5.59 (95% CI, 3.08 to 10.1), and 9.27 (95% CI, 6.58 to 13.1) for stroke mortality, respectively (Table 3). Additional adjustments for other risk factors did not appreciably change these risk estimates. The interaction terms of hypertension and diabetes on both stroke incidence and stroke mortality were not statistically significant, indicating that these 2 factors operated independently for the stroke risk.

Age-, sex-, and study year-adjusted HRs for the incidence of ischemic stroke were 1.13 (95% CI, 1.11 to 1.15) for a 10 mm Hg increment in SBP and 1.22 (95% CI, 1.18 to 1.27) for a 10 mm Hg increment in DBP. The corresponding HRs for the incidence of hemorrhagic stroke were 1.17 (95% CI, 1.12 to 1.21) and 1.31 (95% CI, 1.23 to 1.40), respectively. Diabetic subjects had a 2.8 times higher risk for the incidence of ischemic stroke (95% CI, 2.35 to 3.37), but the increase in the risk of hemorrhagic stroke in diabetic subjects did not differ significantly from that in nondiabetic subjects (HR 1.17; 95% CI, 0.68 to 2.04). Compared with the participants without either hypertension or diabetes, the age-, sex-, and study year-adjusted HRs associated with hypertension I only, with hypertension II only, with diabetes only, with both hypertension I and diabetes, and with both hypertension II and diabetes were 1.29 (95% CI, 1.13 to 1.46), 1.93 (95% CI, 1.73 to 2.17), 2.48 (95% CI, 1.48 to 4.16), 4.26 (95% CI, 2.90 to 6.25), and 4.90 (95% CI, 3.87 to 6.21) for ischemic stroke incidence and 1.62 (95% CI, 1.28 to 2.04), 2.18 (95% CI, 1.75 to 2.71), 2.74 (95% CI, 1.01 to 7.44), 0 (no incident
cases), and 2.47 (95% CI, 1.25 to 4.89) for hemorrhagic stroke incidence, respectively (Table 4).

**Discussion**

This study indicated that both hypertension and type 2 diabetes were independently associated with an increased risk of the incidence of stroke and stroke mortality. Blood pressure was associated with the risk of stroke in a similar fashion both in diabetic and nondiabetic subjects. The highest risk of an incident stroke event and, in particular, of stroke death, was found among subjects who had both hypertension and diabetes.

High blood pressure has been found as the most important determinant of stroke risk in all ethnic groups. The association between blood pressure and stroke mortality is strong and direct, and the absolute risk of stroke mortality associated with high blood pressure increases with age. However, these studies did not stratify for the diabetes status. We found that this direct association between blood pressure and the stroke risk was consistent among both diabetic and nondiabetic subjects. The analyses from another Finnish study and the UK Prospective Diabetes Study have demonstrated that hypertension or an increase in SBP were independently associated with an increased risk of stroke in the diabetic patients. It is also known that hypertension predicts the development of type 2 diabetes. About half of the cases of type 2 diabetes and most of the people with impaired glucose tolerance are unaware of their condition if they not tested for glucose tolerance. Most of the studies that have investigated the relation between hypertension and stroke have not carried out glucose tolerance testing, and the data on the diabetes status has not always been included in the study. Therefore, it is possible that the increased risk of stroke

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Hypertension and No Diabetes (n=21 393)</th>
<th>Hypertension I and No Diabetes (n=12 371)</th>
<th>Hypertension II and No Diabetes (n=14 899)</th>
<th>Diabetes and No Hypertension (n=238)</th>
<th>Both Hypertension I and Diabetes (n=169)</th>
<th>Both Hypertension II and Diabetes (n=512)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>40.0</td>
<td>44.3</td>
<td>49.5</td>
<td>46.8</td>
<td>51.0</td>
<td>55.3</td>
</tr>
<tr>
<td>Male, %</td>
<td>40.0</td>
<td>55.7</td>
<td>52.6</td>
<td>50.8</td>
<td>55.6</td>
<td>48.8</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.6</td>
<td>26.1</td>
<td>28.1</td>
<td>26.1</td>
<td>28.4</td>
<td>30.4</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>124</td>
<td>144</td>
<td>162</td>
<td>126</td>
<td>146</td>
<td>165</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>77</td>
<td>87</td>
<td>98</td>
<td>78</td>
<td>86</td>
<td>95</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>221</td>
<td>242</td>
<td>254</td>
<td>226</td>
<td>241</td>
<td>247</td>
</tr>
<tr>
<td>Education, y</td>
<td>10.6</td>
<td>9.0</td>
<td>8.1</td>
<td>9.7</td>
<td>7.9</td>
<td>7.5</td>
</tr>
<tr>
<td>Low physical activity, %</td>
<td>6.3</td>
<td>7.9</td>
<td>11.7</td>
<td>13.0</td>
<td>19.5</td>
<td>27.3</td>
</tr>
<tr>
<td>Alcohol drinker, %</td>
<td>Male</td>
<td>66.1</td>
<td>65.2</td>
<td>65.1</td>
<td>56.2</td>
<td>57.4</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>43.6</td>
<td>30.0</td>
<td>24.9</td>
<td>36.8</td>
<td>21.3</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>Male</td>
<td>43.8</td>
<td>45.0</td>
<td>40.0</td>
<td>38.8</td>
<td>40.4</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>22.4</td>
<td>14.2</td>
<td>10.4</td>
<td>23.9</td>
<td>16.0</td>
</tr>
</tbody>
</table>

*Characteristics are defined at baseline examination (see Methods).*

**TABLE 2. HRs of Stroke Incidence and Stroke Mortality According to Continuous Blood Pressure Levels or the History of Diabetes at Baseline**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stroke Incidence</th>
<th>Stroke Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age, Sex, and Study Year</td>
<td>Multivariate Adjustment*</td>
</tr>
<tr>
<td>All subjects (n=49 582)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, per 10 mm Hg increment</td>
<td>1.13 (1.11 to 1.15)</td>
<td>1.12 (1.11 to 1.14)</td>
</tr>
<tr>
<td>DBP, per 10 mm Hg increment</td>
<td>1.24 (1.20 to 1.28)</td>
<td>1.22 (1.18 to 1.26)</td>
</tr>
<tr>
<td>Diabetes (yes vs no)</td>
<td>2.50 (2.11 to 2.97)</td>
<td>2.33 (1.96 to 2.77)</td>
</tr>
<tr>
<td>Nondiabetic subjects (n=48 663)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, per 10 mm Hg increment</td>
<td>1.13 (1.11 to 1.15)</td>
<td>1.12 (1.11 to 1.14)</td>
</tr>
<tr>
<td>DBP, per 10 mm Hg increment</td>
<td>1.24 (1.20 to 1.28)</td>
<td>1.22 (1.18 to 1.26)</td>
</tr>
<tr>
<td>Diabetic subjects (n=919)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, per 10 mm Hg increment</td>
<td>1.13 (1.05 to 1.21)</td>
<td>1.12 (1.04 to 1.21)</td>
</tr>
<tr>
<td>DBP, per 10 mm Hg increment</td>
<td>1.20 (1.05 to 1.37)</td>
<td>1.16 (1.01 to 1.34)</td>
</tr>
</tbody>
</table>

*Multivariate models included age, sex, study year, BMI, serum cholesterol, education, smoking, alcohol drinking, and physical activity.*
usually seen in hypertensive subjects may sometimes be
related not only to the hypertension itself but also to undiag-
nosed diabetes or glucose intolerance.

Most of the previous studies have focused on ischemic
stroke alone,10–12,14,16,17 because type 2 diabetes is not a
prominent risk factor for hemorrhagic stroke.18 The recent
joint report from the Honolulu Heart Program and the
Framingham Stroke Study, however, suggested that type 2
diabetes promoted hemorrhagic stroke.26 Another study from
Lausanne Stroke Registry indicated that diabetic patients had
a lower prevalence of intracerebral hemorrhage compared
with nondiabetic subjects.27 In the present study, we found
that type 2 diabetes was associated with an increased risk for
ischemic stroke, but, overall, the 17% increment of the risk
of hemorrhagic stroke in diabetic subjects was not statisti-
cally significant. When we stratified the analysis by both the
hypertension and diabetes status, the subjects with diabetes
only and the subjects with both hypertension II and diabetes
showed a significantly increased risk of hemorrhagic stroke
compared with those without either hypertension or diabetes.
Thus, diabetes seems to be a risk factor for hemorrhagic
stroke, too.

Although subjects with hypertension are more likely to
develop type 2 diabetes,24 and hypertension is very common
in patients with type 2 diabetes,1 only 2 studies12,14 assessed
the joint effect of hypertension and type 2 diabetes on the
stroke risk in the general population. A Japanese study
analyzed the relation between diabetes and the risk of

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Hypertension and No Diabetes</th>
<th>Hypertension I and No Diabetes</th>
<th>Hypertension II and No Diabetes</th>
<th>Diabetes and No Hypertension</th>
<th>Both Hypertension I and Diabetes</th>
<th>Both Hypertension II and Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke incidence</td>
<td>569</td>
<td>730</td>
<td>1538</td>
<td>19</td>
<td>28</td>
<td>94</td>
</tr>
<tr>
<td>Person-years</td>
<td>391 630</td>
<td>249 939</td>
<td>276 208</td>
<td>3456</td>
<td>2651</td>
<td>6520</td>
</tr>
<tr>
<td>Age, sex, and study year adjustment</td>
<td>1.00</td>
<td>1.35</td>
<td>1.79</td>
<td>2.19</td>
<td>2.54</td>
<td>4.01</td>
</tr>
<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>1.33</td>
<td>1.71</td>
<td>2.11</td>
<td>2.50</td>
<td>4.84</td>
</tr>
</tbody>
</table>

| Stroke mortality | 121 | 199 | 540 | 5 | 12 | 47 |
| Person-years | 394 995 | 254 155 | 284 346 | 3551 | 2766 | 6818 |
| Age, sex, and study year adjustment | 1.00 | 1.47 | 1.74 | 2.11 | 2.50 | 4.16 |
| Multivariate adjustment* | 1.00 | 1.47 | 1.74 | 2.11 | 2.50 | 4.16 |

*Multivariate models included age, sex, study year, BMI, cholesterol, education, smoking, alcohol drinking, and physical activity.

TABLE 4. HRs for Different Types of Stroke Incidence According to the History of Hypertension and Diabetes at Baseline*

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Hypertension and No Diabetes</th>
<th>Hypertension I and No Diabetes</th>
<th>Hypertension II and No Diabetes</th>
<th>Diabetes and No Hypertension</th>
<th>Both Hypertension I and Diabetes</th>
<th>Both Hypertension II and Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke</td>
<td>439</td>
<td>557</td>
<td>1236</td>
<td>15</td>
<td>28</td>
<td>85</td>
</tr>
<tr>
<td>Cases, n</td>
<td>392 043</td>
<td>250 548</td>
<td>277 140</td>
<td>3486</td>
<td>2651</td>
<td>6528</td>
</tr>
<tr>
<td>Person-years</td>
<td>1.00</td>
<td>1.29</td>
<td>1.73</td>
<td>2.17</td>
<td>2.48</td>
<td>4.16</td>
</tr>
<tr>
<td>Age, sex, and study year adjustment</td>
<td>1.00</td>
<td>1.25</td>
<td>1.59</td>
<td>2.02</td>
<td>2.41</td>
<td>4.04</td>
</tr>
<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>1.25</td>
<td>1.59</td>
<td>2.02</td>
<td>2.41</td>
<td>4.04</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>130</td>
<td>173</td>
<td>302</td>
<td>4</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Cases, n</td>
<td>394 247</td>
<td>253 430</td>
<td>283 266</td>
<td>3516</td>
<td>2766</td>
<td>6801</td>
</tr>
<tr>
<td>Person-years</td>
<td>1.00</td>
<td>1.62</td>
<td>1.75</td>
<td>2.71</td>
<td>2.74</td>
<td>7.44</td>
</tr>
<tr>
<td>Age, sex, and study year adjustment</td>
<td>1.00</td>
<td>1.70</td>
<td>1.88</td>
<td>2.97</td>
<td>2.75</td>
<td>7.45</td>
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<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>1.70</td>
<td>1.88</td>
<td>2.97</td>
<td>2.75</td>
<td>7.45</td>
</tr>
</tbody>
</table>

*Multivariate models included age, sex, study year, BMI, cholesterol, education, smoking, alcohol drinking, and physical activity.
ischemic stroke stratifying for the hypertension status and BMI and found that the excess risk of ischemic stroke associated with diabetes was primarily observed in nonhypertensive subjects or those with high BMI but not in hypertensive subjects or subjects with low BMI. The Greater Cincinnati/Northern Kentucky Stroke Study determined the relative risk of ischemic stroke attributable to diabetes, hypertension, or both. It indicated that the risk of stroke attributable to a history of both diabetes and hypertension was substantially greater than for either condition alone, and diabetes alone had a higher relative risk of stroke than hypertension alone, in keeping with our results.

Recently, clinical trials have shown that pharmacological treatments of hypertension are efficient ways to prevent stroke in hypertensive patients. A meta-analysis based on 18 randomized trials found that both β-blocker therapy and diuretic-based therapy were effective in preventing stroke. For diabetic patients, blood pressure-lowering therapy seems to offer a greater reduction in the risk of macrovascular disease than do interventions for blood glucose control. This is probably in part because of the fact that currently we have more efficient tools to lower blood pressure than to control hyperglycemia. Several clinical trials have demonstrated that adequate control of hypertension attenuates the risk of stroke in hypertensive diabetic patients.

There are several strengths and limitations in our study. The number of participants was large and from a homogeneous population. The mean follow-up, 19.1 years, was long and resulted in the largest number of stroke events reported in any prospective study thus far. Baseline data also included a large number of variables related to hypertension, type 2 diabetes, and the stroke risk, which were included in the multifactorial analyses in order to overcome bias and confounding effects. A limitation of our study was that we did not carry out a glucose tolerance test at the baseline. Therefore, we have missed cases of asymptomatic diabetes, although the clinical diagnosis of diabetes in the hospital discharge register has included some of the patients not using drugs, thus reducing this potential underdiagnosis. We did not have data on individual drugs used for the treatments of hypertension and diabetes, but with such a long duration of the observational study it would be almost impossible to reveal effects attributable to specific pharmacological agents, because their use has varied drastically over time in most if not all of the hypertensive and diabetic patients.

In conclusion, our study confirmed that hypertension and type 2 diabetes increased the risk of stroke independently, and, having both together, the risk increased dramatically. Because hypertension and type 2 diabetes often occur concomitantly, it is possible that part of the risk of stroke assumed to be related to high blood pressure may primarily be because of undiagnosed disorders in glucose metabolism. This has to be assessed in studies where data on glucose tolerance have been collected. Although we confirmed that type 2 diabetes is an independent risk factor for ischemic stroke, we revealed evidence that type 2 diabetes is also associated with the risk of hemorrhagic stroke.

Acknowledgments

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