Subtype Hypertension and Risk of Stroke in Middle-Aged and Older Chinese
A 10-Year Follow-Up Study

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Background and Purpose—Hypertension is the most important indicator of stroke. We aim to compare the long-term effects of the subtypes of hypertension on the risk of stroke in a Chinese cohort.

Methods—A total of 26 587 subjects ≥35 years of age and free of stroke were recruited in 5 cities in 1987. The subtypes of hypertension were defined as isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH), systolic and diastolic hypertension (SDH), as well as managed hypertension (MHT), according to the criteria of systolic blood pressure ≥140 or diastolic blood pressure >90 mm Hg or under antihypertensive treatment. The relative risks of stroke with the subtypes of hypertension, compared with normotensives, were estimated using the Cox model after adjustments for age, sex, and other confounders.

Results—The prevalence of hypertension was: ISH 7.1%, SDH 18.4%, IDH 6.7%, and MHT 3.9%. During a total of 233 437 person years of follow-up, 1107 subjects developed stroke (614 ischemic and 451 hemorrhagic events and 42 unclassified). SDH patients were at the highest risk of stroke among all the hypertensives. The hazard ratio and 95% CI was 2.96 (2.49 to 3.52) for all stroke, 4.05 (3.10 to 5.30) for hemorrhagic, and 2.33 (1.84 to 2.95) for ischemic stroke. Although the incidence of stroke was higher in the older population, the effect of hypertension, especially SDH, on hemorrhagic stroke is stronger in the middle-aged population.

Conclusion—ISH and IDH are similarly prevalent in the population; both are independent predictors of stroke. Patients with SDH are at the highest risk of stroke and should be treated more aggressively. (Stroke. 2006;37:38-43.)

Key Words: cohort studies hypertension incidence stroke

The incidence and mortality of stroke in China are at high levels.¹ A 16-year surveillance study showed that the stroke attack rates were continuously increasing annually: by 4.5% in men and 4.2% in women from 1984 to 1999.² A substantial number of epidemiological studies in China have demonstrated that stroke is associated with hypertension³⁻⁵ and that the prevalence of hypertension has been increasing rapidly in China.⁶ Stroke is a strongly age-dependent disease, and the incidence of stroke among people >60 years of age was 2 to 3 times higher than those <60 years of age in the Chinese population.⁷ As the aging of the Chinese population continues, the distribution of hypertension subtypes is likely to change; for instance, the proportion of isolated systolic hypertension (ISH) will increase. However, the impact of the subtypes of hypertension, especially of isolated diastolic hypertension (IDH), on the risk of total, hemorrhagic, and ischemic stroke, has not been assessed in the Chinese population because of the lack of enough event numbers in each subtype of hypertension group in most studies. The stroke prevention project in China was a community-based program for primary prevention of stroke, implemented in 7 major cities in 1987,⁴,⁸,⁹ The analysis here intended to explore the association of subtypes of hypertension (ie, ISH, IDH, combined systolic and diastolic hypertension [SDH], and managed hypertension [MHT]), with the risk of stroke incidence in total and in different age groups.

Subjects and Methods

Study Summary
The design, recruitment experience, and intervention results of the project have been described in detail previously.⁴,⁸,⁹ Briefly, 7 urban

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clinical medical centers located in Beijing, Shanghai, Changsha, Harbin, Yinchuan, Changchun, and Zhengzhou participated in the study. In each city, 2 geographically separated communities with approximate registered populations of 10,000 each were chosen as study communities. One of the 2 communities was randomly assigned as intervention community with intensive health education and promotion of healthy lifestyle, including consultation on dietary intake, quitting smoking, doing more exercises, and encouraging hypertensives to maintain the treatment, etc, whereas the other community was assigned as control with common practice. In each of the communities, ~2700 subjects ≥35 years of age and free of stroke were recruited. There were ~5400 subjects in each city and altogether 37,622 subjects in the cohort. The baseline survey was conducted from May to July 1987. Demographic information and the medical history and drinking and smoking habits were collected with a standardized questionnaire administered by the interviewers. An extensive physical and neurological examination was performed in the study clinics. Seated blood pressure was measured twice in the right arm with standard sphygmomanometer by clinic personnel who had been trained to assess it in a routine fashion. The subjects were required to rest ≥5 minutes, avoiding eating, smoking, and strenuous activity during the previous 30 minutes. The average of the 2 measurements was used to calculate systolic blood pressure (SBP) and diastolic blood pressure (DBP). An intensive surveillance system for identifying and ascertaining new stroke cases was established. The project was organized and cooperated between neurological institutes in the 7 cities.

Data from cohorts in Shanghai and Changchun were excluded from the analysis because the end point information was not available because of the reconstruction of the areas and the residences moved out.

Definition of Hypertension Subtypes
Subtypes of hypertension were defined according to the baseline SBP, DBP, and the antihypertensive treatment: ISH (SBP ≥140 mm Hg and DBP <90 mm Hg); SDH (SBP ≥140 mm Hg and DBP ≥90 mm Hg); IDH (SBP <140 mm Hg and DBP ≥90 mm Hg) for the participants with or without antihypertensive treatment; MHT was defined as blood pressure under control by antihypertensive treatment (SBP <140 mm Hg and DBP <90 mm Hg); and normotensives including those without a history of hypertension and SBP <140 mm Hg and DBP <90 mm Hg at the baseline survey.

Statistical Methods
Baseline characteristics of the different groups were compared using χ² or Mann–Whitney tests for categorical variables and 2-sample t tests or ANOVA for continuous variables. The Kaplan–Meier method was used to estimate the cumulative incidence to assess the prospective association of hypertension subtypes and the development of stroke. Relative risk (hazard ratio) and the corresponding 95% CIs were derived from Cox proportional hazards regression models for different hypertension subtypes compared with the normotensive group. Covariance in the model include age, body mass index (BMI), smoking (never versus ever), and alcohol drinking (never versus ever regular drinking habits), and history of heart disease (coronary heart disease, pulmonary heart disease, rheumatic heart disease, any kind of heart failure, etc; yes versus no).

There was no detailed information collected in the baseline survey to clarify the types of heart disease and diabetes (yes versus no), treatment status (regularly or irregularly took antihypertensive medication during the last year; yes versus no); subtypes of hypertension as explanatory variables (each subtype of hypertension group contrast to normotension group), and stratified by sex at the none sex-specific analysis. The age specific estimation was performed in the middle-aged (35 to 59 years of age) and older population (≥60 years of age), with the same adjustment for confounders as the analysis with all subjects. SAS system for Windows version 8.02 (SAS Institute Inc.) was used for the statistical analysis.

Results
A total of 26,587 subjects with adequate data at baseline survey and outcomes recorded during the follow-up were included in the analysis. Subjects who died during the follow-up or were lost to follow-up were verified by the surveillance teams. The date of death or the date of last known as alive were treated as censored date and included in the analysis. During 233,437 person years of follow-up (mean duration of follow-up 9.5 years; median 11.6 years), 1107 participants developed stroke, and the proportion of ischemic, hemorrhagic, and unclassified stroke was 55.5% (614 of 1107), 40.7% (451 of 1107), and 3.8% (42 of 1107), respectively. The stroke cases were diagnosed by the neurologists in each study center following the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (WHO-MONICA) criteria, and 68.4% (757 of 1107) of them had computed tomography (CT) or MRI evidences.

Characteristics at Baseline
Baseline characteristics by hypertension subtypes are listed in Table 1. The prevalence of hypertension at baseline was ∼37.1% in this cohort; the most common type of hypertension was SDH (18%); ISH and IDH were similar at ∼7%. Among 3698 hypertensives, 28% of them were under control.

Compared with the normotensive group, the hypertensive groups were older and heavier, with a higher prevalence of comorbidity of heart disease or diabetes, especially in the MHT group (25.0% had heart disease and 2.9% had diabetes). The differences were statistically significant. But the differences between hypertensive and normotensive on drinking and smoking habits were not consistent in men: the MHT group, which were known hypertensives and under effective control, had significantly lower smoking and drinking rates in men than other groups. In women, the prevalence of smoking and alcohol drinking were very low compared with men but significantly higher in the hypertensive than in the normotensive group.

Among the subtypes of hypertensive groups, the ISH group was ∼11.7 years older (61.9 versus 50.2) and had 17.7% fewer male participants (40.6% versus 58.3%) than the IDH group.

Subtypes of Hypertension and the Risk of Stroke
The crude incidence rate of total stroke was 4.7 per 1000 person years in the cohort, with the lowest in the normotensive group (1.9) and the highest in the SDH group (12.6), followed by the ISH group (11.2), MHT group (6.7), and IDH group (5.4) (Table 2).

After adjusting for the confounders mentioned above, the patients with SDH had 3 times the risk of developing any kind of stroke (hazard ratio, 2.96; 95% CI, 2.49 to 3.52), 4 times risk of developing hemorrhagic stroke (4.05; 3.10 to 5.30), and twice the risk of ischemic stroke (2.33; 1.76 to 3.07) compared with the normotensive group. The association of SDH with the risk of all stroke or hemorrhagic stroke was statistically and significantly greater than the association between other subtypes of hypertension and stroke (P<0.05). The ISH group had a slightly higher relative risk than the IDH group for all kinds of stroke (2.35; 1.91 to 2.90 versus 2.16;
1.69 to 2.76), hemorrhagic stroke (2.58; 1.86 to 3.59 versus 1.99; 1.29 to 3.07), and ischemic stroke (2.33; 1.76 to 3.07 versus 2.24; 1.65 to 3.03), but the differences were not statistically significant (P > 0.05). The MHT group had a higher risk of stroke than the normotensive group, but the differences were not statistically significant for the analysis with all subjects. The gender-specific association between the subtypes of hypertension and stroke was similar to the

TABLE 1. Baseline Characteristics of the Participants According to Blood Pressure Status

<table>
<thead>
<tr>
<th></th>
<th>Normotension</th>
<th>ISH</th>
<th>SDH</th>
<th>IDH</th>
<th>MHT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>16 984 (63.9)</td>
<td>1885 (7.1)</td>
<td>4883 (18.4)</td>
<td>1803 (6.7)</td>
<td>1032 (3.9)</td>
<td>26 587 (100.0)</td>
</tr>
<tr>
<td>Antihypertensive treatment (%)</td>
<td>0 (0)</td>
<td>370 (19.6)</td>
<td>2017 (41.3)</td>
<td>274 (15.1)</td>
<td>1032 (14.0)</td>
<td>3698 (100.0)</td>
</tr>
<tr>
<td>Age, y</td>
<td>49.0±10.2</td>
<td>61.9±11.1*</td>
<td>56.4±10.3*</td>
<td>50.2±9.4*</td>
<td>53.6±10.7*</td>
<td>51.5±11.0</td>
</tr>
<tr>
<td>Male (%)</td>
<td>8116 (47.8)</td>
<td>766 (40.6)*</td>
<td>2197 (45.0)*</td>
<td>1051 (58.3)*</td>
<td>430 (41.7)*</td>
<td>12 560 (47.2)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>114.3±11.5</td>
<td>150.4±13.1*</td>
<td>160.8±18.6*</td>
<td>127.9±7.0*</td>
<td>122.2±9.8*</td>
<td>126.6±22.8</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>74.1±7.6</td>
<td>79.5±6.0*</td>
<td>98.6±8.3*</td>
<td>92.1±3.8*</td>
<td>77.8±6.6*</td>
<td>80.3±12.3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.3±3.1</td>
<td>22.7±3.7*</td>
<td>24.1±3.6*</td>
<td>23.7±3.2*</td>
<td>23.6±3.5*</td>
<td>22.8±3.4</td>
</tr>
<tr>
<td>No. and prevalence (%) of Heart diseases</td>
<td>920 (5.4)</td>
<td>247 (13.1)*</td>
<td>845 (17.3)*</td>
<td>185 (10.3)*</td>
<td>258 (25.0)*</td>
<td>2455 (9.2)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>108 (0.6)</td>
<td>40 (2.1)*</td>
<td>73 (1.5)*</td>
<td>21 (1.2)*</td>
<td>30 (2.9)*</td>
<td>272 (1.0)</td>
</tr>
<tr>
<td>Smoking</td>
<td>Male 5798 (71.4)</td>
<td>598 (78.1)</td>
<td>1593 (72.5)</td>
<td>682 (64.9)</td>
<td>286 (66.5)</td>
<td>8957 (71.3)</td>
</tr>
<tr>
<td></td>
<td>Female 559 (6.3)</td>
<td>101 (9.0)</td>
<td>251 (9.3)</td>
<td>76 (10.1)</td>
<td>61 (10.1)</td>
<td>1048 (7.5)</td>
</tr>
<tr>
<td>Drinking</td>
<td>Male 3743 (46.1)</td>
<td>343 (44.8)</td>
<td>1114 (50.7)</td>
<td>519 (49.4)</td>
<td>197 (45.8)</td>
<td>5916 (47.1)</td>
</tr>
<tr>
<td></td>
<td>Female 209 (2.4)</td>
<td>42 (3.8)</td>
<td>85 (3.2)</td>
<td>23 (3.1)</td>
<td>20 (3.3)</td>
<td>379 (2.7)</td>
</tr>
<tr>
<td>At intervention group</td>
<td>8574 (50.5)</td>
<td>884 (46.9)*</td>
<td>2483 (50.8)</td>
<td>762 (42.3)*</td>
<td>509 (49.3)</td>
<td>13 212 (49.7)</td>
</tr>
</tbody>
</table>

*P < 0.05, for t-test or χ² test, compared with normotensive group.

TABLE 2. Cumulative Incidence (per 1000 person-years during follow-up) and the Relative Risk of Stroke by Subtypes of Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Normotension</th>
<th>ISH</th>
<th>SDH</th>
<th>IDH</th>
<th>MHT</th>
<th>All Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years of follow-up</td>
<td>154 417</td>
<td>14 322</td>
<td>40 056</td>
<td>16 244</td>
<td>8398</td>
<td>23 437</td>
</tr>
</tbody>
</table>

All stroke

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>Incidences</th>
<th>Relative risk of all stroke: hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men Reference</td>
<td>296</td>
<td>1.9</td>
<td>2.47 (1.85–3.28)</td>
</tr>
<tr>
<td>Women Reference</td>
<td>161</td>
<td>11.2</td>
<td>2.20 (1.62–2.99)</td>
</tr>
<tr>
<td>Total Reference</td>
<td>457</td>
<td>12.6</td>
<td>2.35 (1.91–2.90)</td>
</tr>
</tbody>
</table>

Hemorrhagic stroke

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>Incidences</th>
<th>Relative risk of hemorrhagic stroke: hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men Reference</td>
<td>109</td>
<td>0.7</td>
<td>2.25 (1.42–3.57)</td>
</tr>
<tr>
<td>Women Reference</td>
<td>66</td>
<td>4.6</td>
<td>2.98 (1.85–4.81)</td>
</tr>
<tr>
<td>Total Reference</td>
<td>175</td>
<td>5.8</td>
<td>2.58 (1.86–3.59)</td>
</tr>
</tbody>
</table>

Ischemic stroke

<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>Incidences</th>
<th>Relative risk of ischemic stroke: hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men Reference</td>
<td>174</td>
<td>1.1</td>
<td>2.69 (1.86–3.88)</td>
</tr>
<tr>
<td>Women Reference</td>
<td>91</td>
<td>6.4</td>
<td>1.92 (1.25–2.94)</td>
</tr>
<tr>
<td>Total Reference</td>
<td>265</td>
<td>6.3</td>
<td>2.33 (1.76–3.07)</td>
</tr>
</tbody>
</table>

The relative risk (hazard ratio) of stroke, for subtypes of hypertensives or total hypertensive (#) compared with normotensives, was estimated using the Cox model, adjusting for age, body mass index, smoking (ever vs never), alcohol drinking (ever regularly drinking vs not), existing any kind of heart disease and diabetes (yes vs no), community lived (control vs intervention community), and antihypertensive treatment (yes vs no).
in the elderly population.10–13 But few studies have focused on the effect of isolated DBP on the risk of stroke. We found that SBP and DBP were strong predictors of stroke, but SBP was more important than DBP.4 However, we cannot reach any conclusions about the association of hypertension subtypes and development of stroke in the long-term follow-up study from this population. In this article, we examined the associations between 4 types of hypertension and the incidence of stroke in the cohort consisting of participants from 5 large cities in China with 233,437 person years of follow-up. Mounting evidence from prospective epidemiological studies indicates that SBP is an important risk factor, whereas ISH is the single greatest risk factor, other than age, for the development of cardiovascular diseases in the elderly population.10–13 But few studies focused on the effect of isolated DBP on the risk of stroke. Our findings demonstrate that SDH was the most common type of hypertension and the greatest predictor for stroke of any type. The association of SDH with ischemic and all stroke were significantly stronger than that of other subtypes of hypertension in this Chinese urban cohort.

The prevalence of IDH and ISH were similar in general but differed by age groups; IDH in the 35- to 59-year age group was 8% and in the older group was 4%, whereas for ISH, it was 4% and 18%, respectively, in the current study, which is similar to a nationwide survey in China in 2001.14 The similar strength of the association of stroke with IDH and ISH in the studied population suggested that IDH should be at least as important as ISH in predicting stroke. It has significant public health consequences as the proportion of the middle-aged population is greater than that of the older population, and hypertension of any type had a higher impact on the risk of stroke in the middle-aged than in the older population, although the older population had a higher prevalence of ISH and a higher incidence of stroke.

### Discussion

This is the first study to evaluate the long-term association of subtypes of hypertension with the risk of stroke incidence from a large prospective cohort study in the Chinese population. The results revealed that: (1) IDH was as common as ISH in the Chinese population; (2) the highest relative risk of stroke was among the patients with elevated SBP and DBP; (3) the IDH and ISH had similar predictive values for stroke incidence; (4) middle-aged hypertensives tended to have a higher relative risk of stroke than older patients; and (5) the higher risk of stroke in the MHT group may attribute to the higher prevalence of heart disease and other factors, as well as the possible longer duration of elevated blood pressure. In the previous short-term follow-up (3.5 years of follow-up) of this study, the association between risk of stroke and blood pressure was evaluated. We found that SBP and DBP were strong predictors of stroke, but SBP was more important than DBP.4 However, we cannot reach any conclusions about the association of hypertension subtypes and development of stroke in the long-term follow-up study from this population. In this article, we examined the associations between 4 types of hypertension and the incidence of stroke in the cohort consisting of participants from 5 large cities in China with 233,437 person years of follow-up. Mounting evidence from prospective epidemiological studies indicates that SBP is an important risk factor, whereas ISH is the single greatest risk factor, other than age, for the development of cardiovascular diseases in the elderly population.10–13 But few studies focused on the effect of isolated DBP on the risk of stroke. Our findings demonstrate that SDH was the most common type of hypertension and the greatest predictor for stroke of any type. The association of SDH with ischemic and all stroke were significantly stronger than that of other subtypes of hypertension in this Chinese urban cohort.

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Another finding from the present study is that the MHT group (SBP and DBP were <140 and 90 mm Hg, respectively) still had higher risk of stroke compared with normotensives. After further adjustments for the SBP and DBP, the relative risk was only reduced moderately. This suggested that either the level of SBP or DBP should be controlled more tightly, or risk factors other than blood pressure should be accounted for the increased risk. The remarkably high prevalence of heart disease (25%; any type; most of them could be attributable to rheumatic heart disease and pulmonary heart diseases, which are not strongly associated with hypertension) in this group, and the possible longer duration (nonmeasurable) of hypertension of the patients may partly explain the high risk of stroke.

The strength of the study is that the cohort is large, with 233,437 person years of follow-up and 1,107 stroke events to allow us to do this analysis by subtypes of hypertension and subtypes of stroke. Because the study was conducted in the major cities and led by neurological institutes in China, all stroke events were ascertained by specialists and with relatively higher CT scan and MRI exams compared with the studies conducted in rural or remote areas during the same time period.
The weakness is that a great proportion of participants were lost during follow-up because of migration, which might reduce the study power. The ignorable differences of age (0.4 years), 0.85 mm Hg DBP, and 0.22 U of body mass index between the participants remained in the cohort, and those lost to follow-up would not affect the estimates of the association of the risk of stroke and the subtypes of hypertension (Table 4).

In summary, to explore the association of stroke incidence with 4 subtypes of hypertension, we estimated the relative risk of stroke in 4 subtypes of hypertension groups using the data from a cohort initiated for a community-based intervention program to prevent stroke in 5 major Chinese cities. The results indicated that: all types of hypertension had a substantially increased risk of stroke compared with the normotension group; SDH subjects were at the highest risk of stroke among all types of hypertension, in middle-aged and older populations; and ISH and IDH had similar predictive values for stroke of any type after the adjustment for other confounders. MHT was still in the high risk of stroke; this could be attributable to the high comorbidity of heart diseases in the group.

**Acknowledgments**

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