Prevalence and Magnitude of Classical Risk Factors for Stroke in a Cohort of 5092 Chinese Steelworkers Over 13.5 Years of Follow-up

Xiao-Fei Zhang, MD, MS; John Attia, MD, PhD; Catherine D’Este, PhD; Xue-Hai Yu, MD

Background and Purpose—Stroke is the most common manifestation of cardiovascular disease (CVD) among Chinese men. This study addresses the prevalence and magnitude of classic CVD risk factors associated with total, ischemic, and hemorrhagic stroke in a Chinese cohort of at-risk men, compared with white populations. We also address which blood pressure index: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and pulse pressure (PP) is the best predictor of stroke.

Methods—A cohort of 5092 male steelworkers (aged 18 to 74 years) recruited between 1974 to 1980 was followed up for an average of 13.5 years. The results showed that the risk ratios (RRs) of stroke associated with classic risk factors in this Asian population were not different than in whites, except for blood pressure. The RRs of total stroke for each 10mm Hg rise in SBP and DBP in this Asian group (1.4 and 1.8, respectively) were higher than in whites (1.2 to 1.3 and 1.2 to 1.5, respectively). The population attributable risk (PAR) for hypertension (160/95 mm Hg cutoff) to stroke was higher in Asians (ie, 31% for ischemic and 42% for hemorrhagic stroke) than in whites (25% and 34%, respectively).

Conclusion—Our results indicate that hypertension is a greater risk factor for stroke in Asians than whites, especial for hemorrhagic stroke. The most predictive blood pressure (BP) index for stroke is MAP. However, the prevalence or magnitude of these traditional risk factors appears unlikely to explain the differing spectrum of CVD among Asians.

Key Words: blood pressure • body mass index • cardiovascular diseases • cholesterol • cigarette smoking • cohort studies • race, Asiatic • stroke

Stroke is the second and third leading cause of death in urban and rural China, respectively.1 The profile of cardiovascular disease (CVD) among Asians is very different than among whites. Cerebrovascular disease predominates in Asians; the number who die from stroke is more than 3 times that for coronary heart disease.1–3 The age-standardized, gender-specific stroke mortality rate is 44 to 102.6/100 000

Methods—Our results indicate that hypertension is a greater risk factor for stroke in Asians than whites, especial for hemorrhagic stroke. The most predictive blood pressure (BP) index for stroke is MAP. However, the prevalence or magnitude of these traditional risk factors appears unlikely to explain the differing spectrum of CVD among Asians.

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Methods

Population
Subjects were selected from among the workforce of the Beijing Iron and Steel Complex. The total number of male workers in a representative sample of 7 of these factories was 7933, of which up to 70% were men aged 35 years or more. In 3 separate waves of recruitment (1974, 1979, and 1980), 5298 male workers attended a health check, of which 5092 were free of vascular disease, as judged by history and clinical examination.

The project health practitioners conducted follow-up until 1993, by way of face-to-face, relative or telephone interviews, and checking hospital records. Loss to follow-up was only 144 subjects (2.9%).

Measurements
At baseline examination, blood pressure, total serum cholesterol (TC), height, and weight were measured. Smoking status was assessed using a questionnaire. Blood pressure was measured in the right arm using a standard mercury sphygmomanometer on a single occasion after participants had been seated at least 5 minutes. PP was calculated as SBP–DBP and MAP as 1/3(SBP) + 2/3(DBP). TC was also determined on the same single occasion from a fasting venous blood sample, using the enzyme reagent method. Height and weight were measured with subjects in light underclothes and bare feet using a stadiometer and scale. Body mass index (BMI) was calculated as weight (kg)/height (m)^2. Smoking status was self-reported and defined as nonsmoker, light (<10 cigarettes per day), medium (11 to 19 per day), and heavy (>20 per day).

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From the Centre for Clinical Epidemiology and Biostatistics (X.-F.Z, J.A., C.D.), School of Medical Practice and Population Health, The University of Newcastle, Australia; Department of Epidemiology (X.-F.Z.), Cardiovascular Institute and Fu Wai Hospital, Peking Union Medical College, China; Hospital of the Capital Iron and Steel Complex (X.-H.Y.), Beijing, China.
Correspondence to Xiao-Fei Zhang, Centre for Clinical Epidemiology and Biostatistics, The University of Newcastle, Newcastle, NSW 2300, Australia.
Email xiaofei.zhang@studentmail.newcastle.edu.au
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Outcomes
Self-reported outcomes were confirmed by reviewing hospital records, and adjudicated by a panel of several experienced clinicians. Incidence of fatal and nonfatal stroke included hemorrhagic and ischemic stroke (ICD-9 Codes: 430 to 438). The definition of stroke was confirmed by review of the hospital record according to WHO criteria, namely, rapidly developing clinical symptoms and/or signs of focal, global, and at times, loss of cerebral functions with symptoms lasting more than 24 hours or with death, with no apparent cause other than of vascular origin. A fatal stroke was defined as one from which the patient died within 28 days from the onset of symptoms. Death certificates were also obtained for all fatalities to confirm cause of death.

Statistical Analyses
TC and BMI were categorized into 5 groups as follows: TC (mmol/L) with ranges <4.5, 4.5 to 4.9, 5.0 to 5.4, 5.5 to 5.9, >6.0 and BMI with ranges <20, 20 to 22.4, 22.5 to 24.9, 25 to 29.9, >30. Smoking status was defined as smokers and nonsmokers. Diabetes was not included because only 6 workers had diabetes at baseline. Multivariate Cox models were undertaken with stroke incidence as the outcome variable, with age, TC, BMI, and smoking as the independent variables. For the various BP indices, three different analysis strategies were used, all of which were adjusted for age (in years), BMI (kg/m^2), TC (mg/dL), and smoking history (yes or no): (1) a Cox model using each BP index as a continuous variable for a 10 mm Hg increase separately. No more than two of the indices could be included in any one model because of problems of multicollinearity; (2) a Cox model using each BP index as a categorical variable (4 levels). The cutoffs for PP and MAP were chosen according to quartile levels; (3) a Cox model using clinical definitions of hypertension as follows: normotension (SBP <140 and DBP <90), isolated systolic hypertension (ISH) (SBP >140 mm Hg and DBP <90), isolated diastolic hypertension (IDH) (SBP <140 and DBP >90 mm Hg), and combined hypertension (SDH) (SBP >140 mm Hg and DBP >90 mm Hg).

The Akaike Information Criteria (AIC) and standardized coefficients were calculated in order to compare different (non-nested) models and to determine which BP measure was the best predictor for stroke. A lower AIC and higher standardized coefficient indicate a better model. Data were censored at the last point of follow-up (ie,
1993). This analysis was performed with the 4400 individuals that had serum cholesterol measurements available, and was repeated excluding the 388 participants under 35 years of age (with no significant change). Population attributable risk (PAR) was calculated as \[ \frac{f(RR-1)}{1+f(RR-1)} \], where \( f \) is the frequency of the risk factor in the population at baseline. Stata 7.0 (Stata Corp) was used for all analyses.

### Results

#### Baseline Characteristics of the Study Population

The characteristics of the 4400 individuals in the study were representative of the original cohort (Table I, available online at http://stroke.ahajournals.org). The characteristics of the 144 males lost to follow-up were also similar except for age; those lost to follow-up were on average 4 years younger than the remaining of cohorts. The average age of the study population was aged 45 years (aged 18 to 74 years), with an average blood pressure of 123/81; 31% of the cohort was hypertensive (cutoff ≥140/90 mm Hg). Average TC was 186 mg/dL (4.8 mmol/L), with only 6.3% having a reading over 250 mg/dL (6.5 mmol/L). Average BMI was 23, with only 1.3% being frankly obese (BMI >30). There was a high proportion of smokers (74%), with most being medium users. At the conclusion of the study in 1993, representing a mean follow-up time of 13.5 years, there was a total of 152 strokes, including 55 fatal cases. Among these total events, 87 were ischemic strokes, 58 were hemorrhagic, and 7 were unclassified.

### Multivariate Analysis of Classical Risk Factors

#### Total Cholesterol

There appeared to be no relationship between TC and total stroke (Table 1). However, conducting a stratified analysis by stroke subtype seemed to indicate an increased risk of TC on ischemic stroke, and a deceased risk for hemorrhagic stroke, regardless of whether TC was treated as a continuous (Table 2) or categorical variable (Table 1). The PAR% for hypercholesterolemia (cutoff 4.5 mmol/L) was 25.6 for ischemic stroke.

#### Body Mass Index (BMI)

BMI was a consistent risk factor for ischemic stroke but not hemorrhagic stroke, whether as a categorical (Table 1) or continuous (Table 2) measure. Using a cutoff of 25, the PAR% for overweight was 16.9 for ischemic stroke.

#### Smoking

Smoking was a risk factor for ischemic stroke but not hemorrhagic stroke, whether analyzed categorically (Table 1) or continuously (Table 2). Taken as a continuous measure, this translates into a RR of ischemic stroke of ≈3 for every

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**TABLE 2.** Age-Adjusted and Risk-Factor–Adjusted Relative Risk of Ischemic and Hemorrhagic Stroke for the Given Change in the Variables, from Selected Studies for Men

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age-adjusted</th>
<th>Risk Factor-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TC</td>
<td>BMI</td>
</tr>
<tr>
<td></td>
<td>Δ=1</td>
<td>Δ=3</td>
</tr>
<tr>
<td>Ischemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honolulu</td>
<td>2.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Framingham</td>
<td>2.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Beijing</td>
<td>4.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honolulu</td>
<td>3.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Framingham</td>
<td>3.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Beijing</td>
<td>5.6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

*Hypertension: 160/95 mm Hg.

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**TABLE 3.** Hazard Ratios and 95% Confidence Intervals per 10 mm Hg Increase in BP Indices, and Akaike Information Criterion (AIC) From Cox Proportional Hazard Models for Stroke

<table>
<thead>
<tr>
<th>Variable</th>
<th>M 1</th>
<th>M 2</th>
<th>M 3</th>
<th>M 4</th>
<th>M 5</th>
<th>M 6</th>
<th>M 7</th>
<th>M 8</th>
<th>M 9</th>
<th>M 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>1.38</td>
<td>1.17</td>
<td>1.71</td>
<td>0.97</td>
<td>1.29–1.49</td>
<td>1.03–1.33</td>
<td>1.50–1.95</td>
<td>0.78–1.20</td>
<td>1.58–2.03</td>
<td>1.19–1.80</td>
</tr>
</tbody>
</table>
increase of 1 pack year, compared with nonsmokers (Table 2). The PAR% for smoking was 44.9 for ischemic stroke.

**Blood Pressure**

There was a continuous, graded increase in risk for total stroke, ischemic stroke and hemorrhagic stroke (Table 1) for each of the 4 blood pressure indices. Using a cutoff of 140/90 mm Hg, the PAR% for hypertension was 56% for total stroke; 46%, ischemic stroke; and 67%, hemorrhagic stroke: with a cutoff of 160/95 mm Hg, PAR% was 35%, 31%, and 42%, respectively. According to the standardized coefficients and Akaike Information Criterion (AIC) (Table 3), MAP was the single best predictor for stroke, followed closely by the combination of SBP and DBP. Based on the AIC, none of the models with two BP indices were better than the best individual model (Table 3).

Although the greatest risk is for combined hypertension (140/90 mm Hg) with a RR of 5.47 (95% CI 3.55 to 8.43), isolated systolic and diastolic hypertension are also risk factors, with RRs of 2.43 (95% CI 1.01 to 5.84) and 3.2 (95% CI 1.8 to 5.6), respectively (Table 4).

**Discussion**

It has been well established that the incidence of stroke in Asians is substantially higher than in whites.1-3 The rates of stroke we noted in our cohort are roughly consistent with those in Sino-MONICA.4 Our specific focus in this study was to contrast the stroke incidence rates in our Asian cohort to known white rates and to compare the prevalence and magnitude of risk factors.

**Prevalence of Risk Factors**

The prevalence of most risk factors was lower in our Asian cohort compared with a white cohort, the MONICA cohort in Augsburg, except that smoking was much more prevalent in our cohort (Table II, available online at http://stroke.ahajournals.org).

**Magnitude of Risk Factors**

**Total Cholesterol**

The magnitude of the risk for all ischemic and hemorrhagic stroke events associated with a 1 mmol/L rise in TC in our cohort was similar to that found in a number of other studies.5-9

**Body Mass Index**

Our results are consistent with another large Chinese cohort10 and other white cohorts (Table 5).

**Smoking**

The age-adjusted magnitude of the RR for ischemic stroke events for smokers was 2.4 per pack of cigarettes per day, slightly higher than the Framingham study, but similar to other white cohorts11-12 and other Asian cohorts.13

**Blood Pressure**

We compared the results of our study with similar studies conducted in white populations,14-16 and with other regression coefficients across a number of studies (listed in Tables 2 and 5). On average the RR of stroke events of ≈1.7 associated with a 15 mm Hg rise in our cohort is somewhat higher than the average RR of ≈1.4 seen in other white studies,5-8 and consistent with a previous meta-analysis.17

Compared with the results of the Framingham study,18 RRs were ≈5 to 8 for whites in the >160 to 180 mm Hg and >180 mm Hg groups (compared with <120 mm Hg) versus 6.6≈15 in our Asian cohort. The PAR% for hypertension was higher in our cohort than in whites.19-20 Furthermore, in the PROGRESS trial, a drop in 9/4 mm Hg reduced the risk of stroke by 28% in whites versus 36% in Chinese.21-22 These data consistently point to the fact that BP is a greater risk factor for stroke in Asians than in whites. In addition, isolated systolic and isolated diastolic hypertension also carry a similarly increased risk of stroke, consistent with a previous Chinese meta-analysis.23

**Best Blood Pressure Predictor of Stroke Risk**

Our results indicate that MAP was the most powerful predictor of stroke; this makes sense physiologically in that the MAP is the perfusion pressure of the cerebral circulation.24 These results are consistent with a French study24 and the MRC Mild Hypertension Trial.25 Other studies, however, (eg, Copenhagen City Heart Study26 and the Cardiovascular Health Study27) found that SBP was a better predictor of stroke than DBP. It is difficult to find any clear explanation for these differences, although differences between models are very small.

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**Table 4.** Hazard Ratios and 95% Confidence Intervals for Hypertension Categories (140/90 mm Hg) and Stroke

<table>
<thead>
<tr>
<th>Blood Pressure Category</th>
<th>N of Events</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension (n=3035)</td>
<td>38</td>
<td>1.00</td>
</tr>
<tr>
<td>ISH (150)</td>
<td>6</td>
<td>2.43</td>
</tr>
<tr>
<td>IDH (452)</td>
<td>19</td>
<td>3.22</td>
</tr>
<tr>
<td>SDH (763)</td>
<td>61</td>
<td>5.47</td>
</tr>
</tbody>
</table>

*Adjusted for age, total cholesterol, BMI, and smoking.

**Table 5.** Age-Adjusted and Risk-Factor-Adjusted Relative Risk of Total Stroke for the Given Change in the Variables, From Selected Studies for Men (Cox Model)

<table>
<thead>
<tr>
<th>Age-adjusted</th>
<th>Risk factor-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SBP</strong></td>
<td><strong>DBP</strong></td>
</tr>
<tr>
<td>Δ=15 mm Hg</td>
<td>Δ=7.5 mm Hg</td>
</tr>
<tr>
<td>Firingmark</td>
<td>1.5 (1.3–1.7)</td>
</tr>
<tr>
<td>Lithuanian</td>
<td>1.4 (1.2–1.8)</td>
</tr>
<tr>
<td>Oslo</td>
<td>1.4 (1.3–1.5)</td>
</tr>
<tr>
<td>Scotland</td>
<td>1.4 (1.2–1.5)</td>
</tr>
</tbody>
</table>

*Associated with >20 cigarettes/day. †Not age-adjusted.
Caveats

Our study has a number of limitations: baseline blood pressure was based on a single measurement; smoking was self-reported, and dose was ascertained only at baseline; and events were self-reported. An additional consideration is that CT was not widely used in China during the period of the study, and most stroke diagnoses and classifications were based on clinical information alone. This would be likely to cause nondifferential misclassification and, if anything, would minimize the magnitude of the effects. It is further reassuring that CT data were available for the Sino-MONICA study,\(^{24}\) and comparison of the stroke rates and mortality was similar in both studies. Strengths of the study are the relatively large size of the cohort, the length of follow-up, the small loss during that time, and the documentation of events using hospital records and death certificates.

Conclusions

Prevalence of classical risk factors is generally lower among Asian men than white men, except for smoking. Our major findings are that (1) hypertension is a greater risk factor for stroke in Asians than in whites, with diastolic blood pressure being particularly implicated; (2) TC, BMI, and smoking carry the same risk in Asians as in whites; (3) the PAR% indicates that \(\approx 50\%\) of more of all strokes in Asians could be avoided if hypertension were controlled (ie, \(<140/90\) mm Hg); and (4) it appears unlikely that the prevalence or magnitude of classical risk factors can fully account for the differing spectrum of CVD among Asians. Such ethnic comparisons may help dissect genetic and environmental effects in CVD.

References

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