Proportion of Different Subtypes of Stroke in China

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Background and Purpose—The goal of this article is to clarify the proportion of stroke subtypes in China, where stroke is the most common cause of death.

Methods—A total of 16,031 first-ever strokes in subjects ≥25 years of age were identified in 1991 to 2000 from 17 Chinese populations through a community-based cardiovascular disease surveillance program in the China Multicenter Collaborative Study of Cardiovascular Epidemiology. World Health Organization diagnosis criteria were used for classification of stroke subtypes.

Results—CT scan rate of stroke cases reached a satisfactorily high level only after 1996 in the study populations. In 8,268 first-ever stroke events from 10 populations with CT scan rate >75% in 1996 to 2000, 1.8% were subarachnoid hemorrhage, 27.5% were intracerebral hemorrhage, 62.4% were cerebral infarction, and 8.3% were undetermined stroke. The proportion of intracerebral hemorrhage varied from 17.1% to 39.4% and that for cerebral infarction varied from 45.5% to 75.9% from population to population. The ratio of ischemic to hemorrhagic stroke ranged from 1.1 to 3.9 and averaged 2.0. The 28-day fatality rate was 33.3% for subarachnoid hemorrhage, 49.4% for intracerebral hemorrhage, 16.9% for cerebral infarction, and 64.6% for undetermined stroke.

Conclusions—In our study, ischemic stroke was more frequent and its proportion was higher than hemorrhagic stroke in Chinese populations. Although hemorrhagic stroke was more frequent in Chinese than in Western populations, the variation of the proportion of stroke subtypes among Chinese populations could be as large as or larger than that between Chinese and Western populations.

Key Words: China ■ epidemiology ■ stroke

Stroke is the most common cause of death in China. The risk factor profiles and prevention strategies are different for ischemic and hemorrhagic stroke, so it is important to clarify the proportion of stroke subtypes. Most previous studies suggested that at least 30% of strokes in China were hemorrhagic strokes; some studies even reported that >50% of strokes were hemorrhagic, which was significantly different from the findings in whites. However, most of these previous studies either limited the study population to a confined area or based the diagnosis criteria mainly on clinical presentations. In recent years, CT scan rate of stroke patients has increased rapidly, which makes it possible to examine the stroke subtypes more accurately in Chinese populations. In this article, we use data from the China Multicenter Collaborative Study of Cardiovascular Epidemiology, a long-term, ongoing, large-scale project supported by the Chinese central government, to clarify the relative proportions of stroke subtypes in Chinese populations and stroke fatality by different subtypes to provide a scientific base for making an appropriate stroke prevention strategy in the most populous country in the world.

Subjects and Methods

China Multicenter Collaborative Study of Cardiovascular Epidemiology

The China Multicenter Collaborative Study of Cardiovascular Epidemiology was initiated in 1982 by the Department of Epidemiology, Cardiovascular Institute and Fu Wai Hospital, Chinese Academy of Medical Sciences, supported by the China Ministry of Science and Technology through a series of national 5-year plans. It was originally designed as a cross-sectional multicenter comparison of cardiovascular diseases risk factors and was later developed into a comprehensive epidemiological study that included 3 major components: population disease surveillance of cardiovascular disease morbidity and mortality, population sampling surveys of cardiovascular disease risk factors, and cohort follow-up of cardiovascular outcomes to monitor the trends of cardiovascular disease and risk factors and to pinpoint the major determinants of cardiovascular disease.
Study Populations

As part of the China Multicenter Collaborative Study of Cardiovascular Epidemiology, the population disease surveillance program (of cardiovascular disease morbidity and mortality) from 1991 to 2000 used the World Health Organization Monitoring of Trends and Determinants in Cardiovascular Disease (WHO MONICA) diagnosis criteria\(^{18,19}\) for cardiovascular disease events. It began with 14 populations in 1991, and 2 of them stopped in 1995. However, the study expanded to 15 populations in 1996 by adding 3 new populations in 1991, and 2 of them stopped in 1995. Thus, we have data for analysis of 14 populations from 1991 to 1995, of 15 populations from 1996 to 2000, and of 12 populations from 1991 to 2000. These populations were not selected randomly from the whole nation but were selected on the basis of the main characteristics of the population in terms of socioeconomic status, geographical locations, and dietary patterns. The geographical locations of these populations are shown in the Figure. The study duration and population characteristics are listed in Table 1. Of the 17 populations overall, 9 were from rural residential areas and 8 were from urban residential areas. Among the rural populations, 2 were from islets at the east coast of China, 1 in the north part and 1 in the south part. Among the urban populations, 3 were from living areas mainly for families of workers in the large industrial manufacturers, the Capital Iron-Steel Complex (CISC) in Beijing, the Guangzhou Shipyard in Guangzhou, and the CISC mine in Qian’an. In each population, we chose a geographically and administratively well-defined community with \(\approx 100,000\) residents in all ages as the study population, except for Changdao, according to its representativeness of the local population in terms of economy development, standard of living, education level, and occupation. All populations were covered by the governmental household register system, which documented the entering of the subjects as newborns or by moving into the area and the leaving of the subjects when they moved from the area or died. Thus, information on the exact size, age, and sex structure of the study populations was obtained annually from the local administration offices. The population size in mid-2000 was given by the study populations in Table 1.

### Definition of Stroke and Classification of Stroke Subtypes

Stroke was defined according to the WHO MONICA criteria\(^{18}\): a sudden onset of focal (or global) disturbance of cerebral function lasting \(\geq 24\) hours (unless interrupted by surgery or death) with no apparent nonvascular cause. The definition included patients presenting with clinical signs and symptoms suggestive of complete stroke, including cerebral infarction (CI), intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH). Transient ischemic attacks and silent brain infarctions (cases without clinical symptoms or signs) were not included; neither were events associated with trauma, blood disease, or malignancy. All suspected stroke events were first classified into “definite stroke,” “definite stroke associated with definite myocardial infarction,” “not stroke,” or “insufficient event documentation.”

### Table 1. Characteristics of First-Ever Stroke Events in Subjects ≥25 Years of Age

<table>
<thead>
<tr>
<th>Population</th>
<th>Study Duration</th>
<th>Socioeconomic Status</th>
<th>Population in 2000, n</th>
<th>First-Ever Stroke Events, n</th>
<th>Cases by Age, %</th>
<th>Male Cases, %</th>
<th>Cases Hospitalized, %</th>
<th>28-Day Case Fatality Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xicheng, Beijing</td>
<td>1991-2000</td>
<td>Developed urban</td>
<td>154,805</td>
<td>2984</td>
<td>3.5</td>
<td>51.5</td>
<td>45.0</td>
<td>56.4</td>
</tr>
<tr>
<td>Shanghai</td>
<td>1991-2000</td>
<td>Developed urban</td>
<td>93,350</td>
<td>1043</td>
<td>1.2</td>
<td>22.0</td>
<td>76.8</td>
<td>53.0</td>
</tr>
<tr>
<td>Shijingshan, Beijing</td>
<td>1991-2000</td>
<td>Developed rural</td>
<td>117,300</td>
<td>1129</td>
<td>4.0</td>
<td>53.0</td>
<td>43.0</td>
<td>68.7</td>
</tr>
<tr>
<td>CISC, Beijing</td>
<td>1991-2000</td>
<td>Developed urban</td>
<td>127,452</td>
<td>2338</td>
<td>4.0</td>
<td>38.7</td>
<td>57.3</td>
<td>63.8</td>
</tr>
<tr>
<td>Yuxian</td>
<td>1991-2000</td>
<td>Rural</td>
<td>116,343</td>
<td>2170</td>
<td>4.1</td>
<td>37.6</td>
<td>58.3</td>
<td>52.8</td>
</tr>
<tr>
<td>Deyang</td>
<td>1991-2000</td>
<td>Urban</td>
<td>108,398</td>
<td>650</td>
<td>3.8</td>
<td>49.7</td>
<td>46.5</td>
<td>61.1</td>
</tr>
<tr>
<td>Shipyard, Guangzhou</td>
<td>1991-2000</td>
<td>Developed urban</td>
<td>93,295</td>
<td>1201</td>
<td>1.8</td>
<td>24.4</td>
<td>73.8</td>
<td>52.1</td>
</tr>
<tr>
<td>Panyu, Guangzhou</td>
<td>1991-2000</td>
<td>Developed rural</td>
<td>97,525</td>
<td>353</td>
<td>4.5</td>
<td>36.3</td>
<td>59.2</td>
<td>60.6</td>
</tr>
<tr>
<td>Jintan</td>
<td>1991-2000</td>
<td>Rural</td>
<td>107,239</td>
<td>848</td>
<td>3.3</td>
<td>31.8</td>
<td>64.9</td>
<td>59.7</td>
</tr>
<tr>
<td>Zhoushan</td>
<td>1991-2000</td>
<td>Coastal islets</td>
<td>106,427</td>
<td>176</td>
<td>2.3</td>
<td>40.9</td>
<td>56.8</td>
<td>70.5</td>
</tr>
<tr>
<td>Hanzhong</td>
<td>1991-2000</td>
<td>Rural</td>
<td>101,587</td>
<td>322</td>
<td>5.0</td>
<td>32.3</td>
<td>62.7</td>
<td>58.4</td>
</tr>
<tr>
<td>Wuming</td>
<td>1991-2000</td>
<td>Rural</td>
<td>119,429</td>
<td>524</td>
<td>3.6</td>
<td>37.8</td>
<td>58.6</td>
<td>65.6</td>
</tr>
<tr>
<td>Qian-an</td>
<td>1991-1995</td>
<td>Large industry residential area</td>
<td>39,698*</td>
<td>186</td>
<td>16.1</td>
<td>76.3</td>
<td>7.6</td>
<td>85.5</td>
</tr>
<tr>
<td>Harbin</td>
<td>1991-1995</td>
<td>Urban</td>
<td>107,254*</td>
<td>454</td>
<td>6.2</td>
<td>59.0</td>
<td>34.8</td>
<td>63.0</td>
</tr>
<tr>
<td>Mudanjiang</td>
<td>1996-2000</td>
<td>Urban</td>
<td>105,169</td>
<td>727</td>
<td>9.2</td>
<td>51.9</td>
<td>38.9</td>
<td>62.2</td>
</tr>
<tr>
<td>Zhengding</td>
<td>1996-2000</td>
<td>Rural</td>
<td>117,882</td>
<td>689</td>
<td>4.4</td>
<td>37.7</td>
<td>57.9</td>
<td>53.3</td>
</tr>
<tr>
<td>Changdao</td>
<td>1996-2000</td>
<td>Coastal islets</td>
<td>44,524</td>
<td>239</td>
<td>4.2</td>
<td>38.1</td>
<td>57.7</td>
<td>58.6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>1641,844</td>
<td>16,031</td>
<td>4.0</td>
<td>41.2</td>
<td>54.8</td>
<td>59.0</td>
</tr>
</tbody>
</table>

by the centrally trained local physician responsible for event diagnosis on the basis of all available information, as done in the MONICA project. Classification was done entirely on clinical presentations. A stroke episode that occurred >28 days after the previous one was considered a recurrent stroke. Then, all cases identified as definite stroke and definite stroke associated with definite myocardial infarction were further classified into SAH, ICH, CI, and undetermined stroke (UND) and coded with the ninth revision of the International Classification of Diseases (ICD-9). The classification of SAH, ICH, and CI was done on the basis of clinical presentation, and confirmation by CT was required, with reference to the MONICA criteria. UND included all cases that either had not had CT scan or could not be classified by CT scan findings. Although the stroke events included first-ever and recurrent stroke, only first-ever strokes were used for analysis.

Case Ascertainment
A 3-level case reporting and ascertainment system was established to function in the disease surveillance program in the China Multicenter Collaborative Study of Cardiovascular Epidemiology. All suspected cases were first reported to the local centers by the primary healthcare workers in rural populations, household administrative workers, and doctors in primary hospitals or health stations in urban populations. The local center would send a trained staff member to the location of the suspected patient, after receiving information from the first-level monitors, to collect all information related to the diagnosis of stroke to complete the registration. If a patient was hospitalized, discharge information was obtained. If a patient died, information on the death certificate was required. If a patient was not admitted to the hospital, disease information was collected from either the relatives (fatal) or the patient (nonfatal). The registration form was then brought back to the diagnosis committee, which was composed of 2 or 3 qualified physicians at the local center. The local diagnosis committee then made a preliminary diagnosis on the basis of all available information and coded each event according to ICD-9. Then, all registration forms were sent to the coordinating center, where all the information was rechecked and the final diagnosis was given by the central diagnosis committee, which consisted of neurologists, cardiologists, and epidemiologists.

Data Quality and Statistical Analysis
The registration form was centrally designed with reference to that used in the MONICA project and distributed to all local centers. The responsible physicians at the local centers were trained and certified centrally by the Coordinating Center, and were responsible for training of the first-level monitors under the local center according to a uniform protocol. The event-missing rate was estimated annually by local centers using data obtained from a door-to-door survey in a random sample of 5% to 10% of the study populations. The characteristics of the cases are 25 years of age were identified among all study populations. Of these, 59.0% were men, 4.0% were <44 years of age, 41.2% were 45 to 64 years of age, and 54.8% were ≥65 years of age. The mean age was 64.9 years for men and 66.6 years for women. The number of cases hospitalized was generally high, ≈83.3% on average (higher for developed urban populations and lower for rural populations). The 28-day case fatality was generally lower in developed urban populations and higher in rural populations and was 35% on average. The characteristics of the cases are shown in detail in Table 1.

Results

Characteristics of First-Ever Stroke Cases
During 1991 through 2000, a total of 16,031 first-ever stroke events in persons ≥25 years of age were identified among all study populations. Of these, 59.0% were men, 4.0% were <44 years of age, 41.2% were 45 to 64 years of age, and 54.8% were ≥65 years of age. The mean age was 64.9 years for men and 66.6 years for women. The number of cases hospitalized was generally high, ≈83.3% on average (higher for developed urban populations and lower for rural populations). The 28-day case fatality was generally lower in urban populations and higher in rural populations and was 35% on average. The characteristics of the cases are shown in detail in Table 1.

Changes in Proportion of Stroke Subtypes and CT Scan Rate in China From 1991 to 2000
Table 2 shows the changes in frequency and proportion of stroke subtypes, as well as the CT scan rate over 10 years (from 1991 to 2000), among 12 populations that had complete data during the period. Data clearly showed that the CT scan rate in China increased markedly during the 10 years, from <50% to >90%. As a result, the proportion of UND decreased remarkably from >50% to <10%; at the same time, the proportions of both hemorrhagic stroke and ischemic stroke increased significantly. In 2000, SAH, ICH, CI, and UND accounted for 1.1%, 28.5%, 61.9%, and 8.6%, respectively, of the overall population.

Proportion of Stroke Subtypes in Different Populations in China
To minimize the influence of CT scan rate on study results, Table 3 limited the analysis to data from 1996 and 2000 and to the populations with the CT scan rate >75% to analyze the proportion of different stroke subtypes. As a result, on average, 1.8% were SAH, 27.5% were ICH, 62.4% were CI, and 8.3% were UND. The proportions of ICH and CI varied from population to population, but SAH did not vary much. IS/HS ranged from 1.1 to 3.9 and averaged 2.0. Although the variations in the proportions could not be explained fully by
the variance in CT scan rate, ischemic stroke was demonstrated to be the dominant subtype.

Proportion of Stroke Subtypes in Relation to Age and Sex
To further understand the factors besides CT scan rate that may affect the proportions of stroke subtypes, the proportion of stroke subtypes by age and sex in the 10 populations with CT scan rate >75% during the period of 1996 through 2000 is shown in Table 4. The proportion of stroke subtypes was similar in men and women, but there were more hemorrhagic strokes in the younger group than in the older group in both sexes.

Case Fatality Within 28 Days in Relation to Stroke Subtypes, Age, and Sex
Table 5 gives the number and rate of death at 28 days for first-ever stroke cases by subtype of stroke, age of onset, and sex. On average, 33.3% of the first-ever SAH stroke cases died within 28 days, 49.4% of ICH cases, 16.9% of CI cases, and 64.6% of UND cases. The 28-day fatality rate increased significantly with age for both CI and ICH in both sexes, increased significantly for SAH in women, but did not vary much with age for UND.

Discussion
Generalizability of Our Findings
Population-based epidemiological studies on stroke are scarce in China; multicenter studies are even fewer. In fact, there were only 2 population-based multicenter studies of stroke that used WHO MONICA diagnosis criteria. Because CT scan became popular only very recently (as shown by our data), it made our study unique, with accurate data from multiple populations to clarify the proportion of stroke subtypes in Chinese populations. Furthermore, a uniform protocol and registration form and central training were used in all study populations from start to end, which allowed the comparability in different populations in the present study.

Although the study populations were not randomly selected from the whole nation, they were selected after careful consideration of main residential districts, major strata of socioeconomic development, and dietary lifestyles. Some industrial residential areas were selected to take advantage of their administration systems to increase the feasibility of conducting the study, but the whole population was put into the case registration system of the study. Thus, findings from our study should well reflect the current actual pictures in China with different populations at different stages of social development.

What is the Dominant Subtype of Stroke in China?
Our data from 1996 to 2000 in populations with CT scan rate >75% demonstrated that the proportions of CI ranged from 49.3% to 75.9%, and IS/HS ratios were all >1. On average, one third were hemorrhagic and two thirds were ischemic. Thus, we concluded that ischemic stroke was the dominant subtype in terms of quantity of incident cases in Chinese populations, as long as high-quality data were available. This finding was similar to those reported elsewhere in the world7–16 but contradicted findings from some studies in Chinese populations6 in which hemorrhagic stroke was reported to account for as much as 52.2%. The reasons for the difference between our study and the previous studies include differences in methodology, CT scan rate, age limitations of study population, etc.

On the other hand, our data indicated that the 28-day fatality was <20% for ischemic stroke but as high as 60% for hemorrhagic (ICH and SAH) stroke. Thus, in terms of risk of mortality (by multiplying proportion of stroke subtype with the 28-day fatality), the 2 types of stroke were almost identical in Chinese populations. This implies that the prevention and treatment of hemorrhagic stroke are as important as that of ischemic stroke from the public health point of view.

Stroke Subtypes in Chinese Populations Compared With Western Populations
Racial-ethnic differences in the subtypes of stroke have previously been reported between Asians21–25 and whites7–16.
Factors Associated With the Variance of Subtypes of Stroke

Our study is the first in the world to find a great variance in the proportion of stroke subtypes among different populations with the same ethnic background and within the same country. Thus, the difference induced by genetic diversity, if it exists, may not play a major role in the large variance between Chinese and Western populations. Further analysis showed that the proportion of hemorrhagic stroke among all strokes varied from 19.4% to 42.2% in the 10 populations, although all the study populations came from the same race, Han people. In comparison, a population-based study in Australia found that 18.8% were hemorrhagic stroke. This suggested that racial-ethnic differences in stroke subtypes identified previously may actually underline differences in lifestyles, diet, and other environmental factors rather than genetics.

TABLE 5. The 28-Day Case Fatality Rates of Different Stroke Subtypes by Age and Sex

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>SAH</th>
<th>ICH</th>
<th>CI</th>
<th>UND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–44</td>
<td>6</td>
<td>35.3</td>
<td>32</td>
<td>46.4</td>
</tr>
<tr>
<td>45–64</td>
<td>5</td>
<td>18.5</td>
<td>220</td>
<td>41.2</td>
</tr>
<tr>
<td>≥65</td>
<td>11</td>
<td>57.9</td>
<td>392</td>
<td>53.8</td>
</tr>
<tr>
<td>P for trend</td>
<td>&gt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–44</td>
<td>1</td>
<td>12.5</td>
<td>12</td>
<td>30.8</td>
</tr>
<tr>
<td>45–64</td>
<td>7</td>
<td>17.1</td>
<td>156</td>
<td>42.2</td>
</tr>
<tr>
<td>≥65</td>
<td>19</td>
<td>54.3</td>
<td>311</td>
<td>58.2</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>All men</td>
<td>22</td>
<td>34.9</td>
<td>644</td>
<td>48.3</td>
</tr>
<tr>
<td>All women</td>
<td>27</td>
<td>32.1</td>
<td>479</td>
<td>50.8</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>33.3</td>
<td>1123</td>
<td>49.4</td>
</tr>
</tbody>
</table>

Previous studies in China, Hong Kong, Taiwan, and Japan generally found that 23% to 52.2% of strokes were hemorrhagic, in contrast to only 9% to 18% in whites. In the present study, 29.6% of stroke cases overall in 2000 were hemorrhagic in Chinese populations, which supported the above idea that an ethnic difference existed between Eastern and Western populations. Further analysis showed that racial-ethnic differences in stroke subtypes identified previously may actually underline differences in lifestyles, diet, and other environmental factors rather than genetics. erably lower (as shown by our data), so less severe or silent cases presenting minimum symptoms or signs or cases who died before being admitted to a hospital and without autopsy might be missed; this might lead to a higher proportion of hemorrhagic stroke in rural populations. However, this could not be the main reason because, in our study, a population-based case-reporting system instead of a hospital-based registration was used, and the event-missing rates were mostly <5%, within an acceptable limit. We compared the hospitalized cases and unhospitalized cases in terms of age and sex distribution and found no differences. In addition, there was still significant variation just in the developed urban populations. Further analysis indicated that there were more hemorrhagic strokes in the younger group than in the older group. The age-standardized proportions of stroke subtypes, however, still varied to about the same extent as the unstandardized proportions. Thus, the age difference among these populations cannot be the main reason for such a variation.

The most probable reasons were the differences in stroke risk factor profiles between the populations studied. Our previous study indicated that high serum cholesterol and body mass index would increase the risk of ischemic stroke but not hemorrhagic stroke, which was in accordance with findings from other studies. Studies in China also showed that serum cholesterol was higher in urban than in rural populations and higher in northern than in southern populations. The present study also showed a higher proportion of ischemic stroke and a lower proportion of hemorrhagic stroke in urban and northern populations in China. Compared with Western populations, Eastern populations like Chinese and Japanese have a lower level of serum cholesterol and body mass index, mostly because of their very different lifestyle and dietary patterns, and have relatively more hemorrhagic strokes. This hypothesis can explain not only the variance among Chinese populations but also the difference between Chinese and Western populations.
In summary, our study found that ischemic stroke was more frequent and the proportion was higher than hemorrhagic stroke in Chinese populations. Although hemorrhagic stroke was not the predominant subtype of stroke in Chinese, it was more frequent in Chinese than in Western populations. The difference in stroke subtypes between Chinese and Western population and between Chinese populations may be due mainly to different cardiovascular risk factor profiles induced by lifestyles, dietary patterns, and other environmental factors.

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References
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