



Sex Differences in Trends of Incidence and Mortality of First-Ever Stroke in Rural Tianjin, China, From 1992 to 2012

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and 40% in women for residents aged 35 to 74 years in 1991.¹¹ Few residents were covered by national medical insurance before 2008.¹² The residents used to live in the same village for generations based on the household registration system and traditional habit, except married daughters or those going to the universities. Ten percent of men aged 35 to 64 years usually go to cities for seasonal work and go back home for harvests and festivity at least four times a year.

The events and death because of stroke have been monitored in this population since 1985. In this study, we analyzed the events and death because of first-ever stroke from 1992, because there was no imaged diagnosis technique before 1992 in this area.

The population size by 5-year age strata for men and women was obtained from the local Permanent Resident Registry. The population was adjusted by adding births and migrants as well as deducting deaths and emigrants from January 1 through December 31 of each year.

The ethics committee of Tianjin Medical University General Hospital approved the study, and informed consent for each resident was obtained during recruitment.

Definition and Registration of Stroke

A first-ever stroke event was defined as the first occurrence of rapidly developing signs of focal neurological disturbance with a presumed vascular cause lasting >24 hours.¹³ Transient ischemic attacks and silent strokes (diagnosed by imaging without clinical symptoms and signs) were excluded. During the early phase of this study (1992–1998), the diagnosis of stroke events among patients with no imag-

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| | 1992 1998 | | 1999 2005 | | 2006 2012 | |
|----------------------------|-----------|----------|-----------|----------|-----------|----------|
| | Men | W men | Men | W men | Men | W men |
| Case number | 3644 | 30162 | 2073 | 48224 | 2344 | 47813 |
| Case rate, n (%) | 113 (63) | 63 (37) | 137 (61) | 102 (39) | 272 (38) | 199 (42) |
| HS | 17 (13) | 9 (14) | 30 (19) | 23 (23) | 61 (23) | 43 (23) |
| IS | 34 (30) | 21 (32) | 84 (34) | 34 (33) | 172 (63) | 120 (60) |
| UND | 62 (33) | 33 (34) | 43 (27) | 23 (24) | 39 (14) | 34 (17) |
| Age group, n (%) | | | | | | |
| <45 | 4 (4) | 4 (6) | 6 (4) | 7 (7) | 14 (3) | 11 (6) |
| 45-64 | 33 (29) | 30 (46)* | 37 (36) | 33 (32) | 131 (48) | 88 (44) |
| ≥65 | 76 (67) | 31 (48)* | 94 (60) | 62 (61) | 127 (47) | 100 (30) |
| Age range, mean (SD) | 68 (11) | 64 (12) | 66 (12) | 63 (13) | 63 (12) | 66 (13) |
| Diagnosis by CT/MRI, n (%) | | | | | | |
| <45 | 3 (7) | 4 (100) | 3 (83) | 7 (100) | 14 (100) | 11 (100) |
| 45-64 | 23 (70) | 21 (70) | 48 (84) | 31 (94) | 123 (93) | 83 (94) |
| ≥65 | 23 (33) | 3 (16) | 61 (63) | 39 (63) | 94 (74) | 71 (71) |

CT indicates computed tomography; HS, hemorrhagic stroke; IS, ischemic stroke; and UND, undetermined (nonimaged) stroke.
 * $P < 0.01$; $P < 0.05$ by χ^2 test between men and women during the study period.

(Table 2): 1.9 (1.4–2.8; $P < 0.001$) in 1992 to 1998, 1.5 (1.1–2.0; $P = 0.005$) in 1999 to 2005, and 1.4 (1.1–1.8; $P = 0.002$) in 2006 to 2012; particularly in individuals ≥ 65 years of age, the corresponding rate ratio was 2.6 (1.7–3.9; $P < 0.001$), 1.6 (1.2–2.2; $P = 0.004$), and 1.3 (1.0–1.7; $P = 0.055$). The sex differences of incidence of first-ever stroke diminished over time in ≥ 65 years of age (Figure).

Annual Proportion of Change in Incidence in First-Ever Stroke by Age

Between 1992 and 2012, the incidence of first-ever stroke increased by 5.8% in men and 8.0% in women annually and by 6.4% in women and 2.7% in men aged ≥ 65 years.

Secular Trend in Mortality <30 Days of First-Ever Stroke by Age and Period

There were no significant sex differences in trends of stroke mortality by age throughout the entire study period (Table 3).

Trends in Cardiovascular Risk Factors in the Study Population From 1991 to 2011

The prevalence of hypertension, diabetes mellitus, obesity, and alcohol consumption was significantly higher in 2011 than in 1991, both in men and in women; the prevalence of smoking, in contrast, decreased in men. The prevalence of obesity appeared significantly higher in women than in men in

| Age Group | 1992 1998 | | | 1999 2005 | | | 2006 2012 | | |
|-----------|-----------|-------|-----------------|-----------|-------|-----------------|-----------|-------|-----------------|
| | Men | W men | RR (95% CI) | Men | W men | RR (95% CI) | Men | W men | RR (95% CI) |
| <35 | 0 | 0 | | 8 | 16 | 0.3 (0.1, 3.1) | 8 | 3 | 1.3 (0.1, 16.8) |
| 35-44 | 36 | 33 | 1.0 (0.3, 4.1) | 60 | 36 | 1.1 (0.3, 4.3) | 180 | 143 | 1.2 (0.3, 2.9) |
| 45-64 | 108 | 102 | 1.1 (0.4, 2.7) | 280 | 206 | 1.4 (0.7, 2.3) | 306 | 313 | 1.6 (1.0, 2.6) |
| 35-64 | 303 | 246 | 1.2 (0.7, 2.2) | 479 | 207* | 2.3 (1.3, 4.2)* | 1180 | 733* | 1.6 (1.1, 2.2)* |
| 65-74 | 1300 | 332* | 2.4 (1.4, 4.2)* | 1631 | 1311 | 1.3 (0.8, 1.9) | 1767 | 1428 | 1.2 (0.8, 1.8) |
| ≥75 | 1733 | 619* | 2.8 (1.3, 3.3)* | 1831 | 760* | 2.4 (1.4, 4.3)* | 3232 | 2238 | 1.4 (1.0, 2.0) |
| Overall | 166 | 86 | 1.9 (1.3, 2.8) | 227 | 148 | 1.3 (1.1, 2.0) | 376 | 264 | 1.4 (1.1, 1.8) |
| <65 | 49 | 43 | 1.2 (0.6, 2.1) | 92 | 62 | 1.4 (0.9, 2.3) | 201 | 132 | 1.3 (1.1, 2.1) |
| ≥65 | 1448 | 363 | 2.6 (1.7, 3.9) | 1723 | 1083 | 1.6 (1.2, 2.2) | 2306 | 1790 | 1.3 (1.0, 1.7) |

CI indicates confidence interval; and RR, relative risk.
 * $P < 0.01$ by χ^2 test between men and women during the study period.
 $P < 0.05$ by χ^2 test between men and women during the study period.
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 $P < 0.001$ by χ^2 test between men and women during the study period.

4. S... A S...
1991 2011

| Risk Factor | 1991 | | 2011 | |
|-------------------------|-------------------|--------------|-------------------|---------------|
| | Men | Women | Men | Women |
| n (%) | 1032 (47) | 1164 (53) | 865 (45) | 1074 (52) |
| Illiteracy, n (%) | 312 (30) | 470 (40) | 56 (6) | 217 (20) |
| Hypertension, % | 39 (37, 41) | 41 (38, 44) | 50 (47, 54) | 54 (51, 57) |
| <45 | 24 (19,28) | 24 (20,27) | 31 (25,37) | 40 (32,48) |
| 45-64 | 42 (38,47) | 45 (41,50) | 59 (54,63) | 58 (54,61) |
| ≥65 | 66 (58,74) | 71 (64,79) | 68 (62,75) | 74 (68, 80) |
| Obesity, % | 3 (0, 9) | 8 (3, 14) | 18 (15, 20) | 21 (16, 26) |
| <45 | 2 (1, 3) | 7 (5, 9) | 17 (12, 22) | 19 (12, 24) |
| 45-64 | 3 (2, 9) | 10 (7,12) | 18 (15,22) | 22 (19,25) |
| ≥65 | 4 (1, 6) | 7 (3, 11) | 18 (13, 24) | 21 (16, 27) |
| Diabetes mellitus, % | 1 (0, 8) | 3 (0, 9) | 4 (0,10) | 6 (0, 9) |
| <45 | 1 (0, 2) | 3 (1, 4) | 1 (0, 2) | 1 (0, 2) |
| 45-64 | 2 (1, 3) | 5 (3, 7) | 5 (3, 7) | 6 (4, 8) |
| ≥65 | 1 (0, 2) | 1 (0, 2) | 4 (2, 7) | 8 (4,12) |
| Smoking, % | 46.0 (41.6, 50.5) | 3.7 (0, 9.3) | 36.8 (31.5, 42.2) | 4.8 (0, 10.6) |
| Alcohol consumption, % | 18.9 (13.4, 24.4) | 0.3 (0, 6.0) | 31.6 (26.1, 31.6) | 4.5 (0, 10.3) |
| Fasting glucose, mmol/L | 4.8 (1.5) | 4.6 (0.9) | 5.2 (1.7) | 5.3 (1.8) |
| Cholesterol, mmol/L | 4.3 (0.9) | 4.3 (1.0) | 4.6 (1.1) | 4.8 (1.2) |
| Triglyceride, mmol/L | 1.3 (0.3) | 1.3 (0.3) | 1.5 (1.1) | 1.6 (1.0) |
| Age at menarche, | | 16.3 (1.8) | | 16.3 (2.0) |
| Age at menopause, | | 48.6 (3.6) | | 49.8 (3.0) |
| Reproductive years, | | 32.3 (4.2) | | 33.2 (3.4) |

*Prevalence of hypertension, diabetes mellitus, obesity, smoking, drinking alcohol, illiteracy (95% confidence interval), and age at menarche, age at menopause, and reproductive years are the mean (SD).
P<0.001; P<0.01; P<0.05 on a χ^2 test between men and women during the study period.

This is not in accordance with the findings of most previous studies that women tend to develop first-ever stroke at an older age compared with men.^{15,22,26-28} The younger age of stroke among women in the early period of this study could not be explained with the present population-based studies or associated with protective sex hormones.²⁹⁻³¹ Previous research has found that women were protected from stroke relative to men up until menopause.³¹ Unsurprisingly, we observed a younger age of menopause and short reproductive years in 1991 compared with 2011, which resulted in the earlier disappearance of protective sex hormones. In our study, we observed a higher prevalence of obesity and diabetes mellitus in women than in men among those aged 45 to 64 years in 1992 to 1998.

Lower education level is also associated with increased stroke risk in middle-aged women; it is partially mediated by known risk factors, particularly lifestyle and biological factors.³² Diabetes mellitus and obesity are clearly important risk factors for stroke.³³⁻³⁵ A higher proportion of illiteracy and a higher prevalence of diabetes mellitus and obesity in women than in men may partially explain the sex differences in stroke incidence during the early period. The link between education and stroke is a novel finding in this population, because no previous studies have reported it in China.

Our study was restricted to a county sample in northern China, which limits the generalization of our results.

Cardiovascular risk factors were only monitored twice during the study. The low percentage of imaging by brain computed tomographic scan during the early period of 1992 to 1998 may lead to over- or underestimation of the incidence of stroke and limits further analysis for stroke subtypes. However, the present study also has numerous strengths: first is the availability of >21 years of prospective follow-up data from the large population-based longitudinal study design; second is the high efficiency of follow-up by village doctors, and the restricted living area of every participant provided thorough follow-up registration of stroke events and mortality during the past 21 years; third is ≥100 000 person-years of observations were recorded in all 3 study periods, fulfilling the criteria for population studies of stroke incidence.³⁶

Our study provides the first longitudinal data on sex differences in stroke incidence during a 21-year period in a low-income rural area in China. There has recently been a remarkable increase in the incidence of stroke in women compared with men. Sex disparities in stroke incidence indicate that more attention should be given to cardiovascular health prevention in women in China, such as the Go for Red campaign initiated by the American Heart Association. We also found a concurrent increase in the levels of stroke-related risk factors. Our data suggest that stroke will eventually become the major disease with the highest impact on women; the incidence of stroke in China may continue to increase

in future decades, without immediate implementation of an effi-