Effect of Measurement on Sex Difference in Stroke Mortality

Kazim Sheikh, MD; Claudia M. Bullock, BS

Abstract—The 1994 to 1997 administrative data on 40,450 elderly Medicare beneficiaries and general population of 2 states were used to measure “case mortality” (deaths attributable to any cause among cases of acute stroke), “case fatality” (deaths caused by cerebrovascular diseases among cases of acute stroke), and “population mortality” (deaths caused by stroke in the elderly general population). Mortality was higher in men than in women according to all measures except population mortality caused by subarachnoid hemorrhage. There was no sex difference in 1-year case fatality. One-year all-cause mortality among cases of nonhemorrhagic stroke or all types of stroke was higher in men than in women. Similar sex differences were found in 4-year population mortality caused by nonhemorrhagic stroke or all types of stroke combined. The 3 measures differed with respect to sex difference in stroke mortality. How stroke is defined and how mortality is measured does affect sex difference. (Stroke. 2007;38:1085-1087.)

Key Words: measurement ■ sex difference ■ stroke mortality

Disparity in the outcome of chronic diseases may be a useful indicator of an opportunity for improving preventive or therapeutic care. The natural history of stroke has been studied by many researchers who have found age, sex, and race differences in mortality.

Some studies of stroke mortality did not find a significant sex difference; others found a relatively higher risk among men or among women. Some of these investigations studied mortality associated with only 1 type of stroke. Many investigations studied mortality from all types of stroke combined. Two of the 3 studies of sex difference in mortality caused by nonhemorrhagic stroke in the general population found increased risk among women whereas 2 of the 3 corresponding studies that measured case fatality rates among patients with acute stroke found increased risk among men.

There are many reasons for discrepancy between these studies with respect to the magnitude and the direction of sex difference in stroke mortality. This study addressed 2 factors—how stroke was defined and how mortality was measured—by estimating 3 different measures of sex-specific stroke mortality in the same geographically defined population during the same time period. The objective was to determine the effect of using different measures on sex difference in stroke mortality.

Materials and Methods

The measures of stroke mortality used in this study were (a) 1-year case mortality defined as deaths attributable to any cause among cases of acute stroke, (b) 1-year case fatality defined as deaths caused by cerebrovascular diseases among cases of acute stroke, and (c) 4-year population mortality defined as deaths caused by stroke in the general population in a 4-year period. The study cohort was 40,450 fee-for-service Medicare beneficiaries aged 65 to 99 years who were hospitalized in Indiana and Kentucky for acute stroke from January 1, 1994 to December 31, 1996. Medicare administrative data were used to identify the demographics and hospitalizations with primary discharge diagnosis of acute stroke. The International Classification of Diseases, 9th Revision, Clinical Modification codes were used to define the types of stroke: subarachnoid hemorrhage (code 430), intracerebral hemorrhage (431), ischemic stroke (433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, and 434.91), and unspecified type or non-specific stroke (436, 438, 997.02). Codes 430 to 438 were used to define cerebrovascular diseases. Mortality ascertainment period was 1 year from hospital admission for acute stroke. Death certificate data for 1994 to 1997 from the state vital statistics agencies were used to determine the date and the immediate cause of death. Social security numbers were used to match study subjects with death certificates. Sex-specific, age-adjusted case mortality and fatality rates were estimated.

The death certificate data for 1994 to 1997 and the 1995 census data on 65 years old or older general population of the same 2 states were used to estimate sex-specific, age-adjusted, 4-year cumulative stroke mortality rates for the general population. Stroke deaths in the general population were also stratified into 4 categories: subarachnoid hemorrhage (codes 430), intracerebral hemorrhage (431), ischemic stroke (434.0, 434.1, 434.9), and non-specific stroke (436, 438). The direct standardization method was used to adjust all fatality and mortality rates for age, both sexes together being the standard. These rates were not adjusted for the prevalence of coexistent or incidental conditions.

Results

Descriptive statistics for the study cohort are provided in Table 1 according to sex and the type of stroke. The type of 33.2% of all strokes was not specified in the Medicare claims data. The proportion of male cases with their stroke coded as ischemic stroke (434.0, 434.1, and 434.9) was 55.6% compared with 51.8% of females. This study used the International Classification of Diseases, 9th Revision, Clinical Modification codes to define the types of stroke: subarachnoid hemorrhage (code 430), intracerebral hemorrhage (431), ischemic stroke (433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, and 434.91), and unspecified type or non-specific stroke (436, 438, 997.02). Codes 430 to 438 were used to define cerebrovascular diseases.
ischemic was a little higher than that of female cases ($P=0.03$), and subarachnoid hemorrhage was more frequent in women ($P=0.000$). During the 1-year follow-up period, 12,898 (31.9%) cases died. Twenty-two percent of all deaths occurred within the first 5 days. Forty-five percent and 51% of deaths among male and female cases respectively were caused by cerebrovascular diseases. In 1995, the general population of Indiana and Kentucky aged 65 years and older comprised of 488,006 men and 731,660 women. Women were older than men. In 1994 to 1997, there were 276,678 deaths in this general population, the immediate cause of 7.5% of these deaths was stroke. The type of 78% of fatal strokes could not be established because of the death certification and coding practices.

The 3 sets of measures of sex-specific stroke mortality and sex difference are given in Table 2. There was no sex difference in case fatality and there were small sex differences in the other 2 measures. The age-adjusted all-cause mortality among cases of all types of stroke was 16% higher in men than in women. Similarly, the age-adjusted, 4-year mortality in the general population caused by all types of stroke was 10% greater among men. Table 3a shows the age-adjusted all-cause case mortality rates and sex differences stratified by the type of stroke. There was no significant sex difference in mortality among cases of hemorrhagic stroke, but the relative risk was higher among male cases of ischemic and nonspecific stroke. There were significant sex differences in the age-adjusted stroke mortality in the general population regardless of the type of stroke causing death (Table 3b). The relative risk was lower among men for mortality caused by subarachnoid hemorrhage and higher for mortality caused by intracerebral hemorrhage, ischemic stroke and stroke of unspecified type.

### TABLE 1. Descriptive Statistics for Stroke Cases

<table>
<thead>
<tr>
<th>Type of Stroke</th>
<th>Male Cases</th>
<th>Female Cases</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>Mean Age (years)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>212 (1.29)*</td>
<td>73.7</td>
<td>502 (2.09)*</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>1501 (9.16)</td>
<td>76.2</td>
<td>2194 (9.12)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>9364 (57.1)*</td>
<td>76.2</td>
<td>13 251 (55.1)*</td>
</tr>
<tr>
<td>Other (nonspecific)</td>
<td>5314 (32.4)</td>
<td>77.6</td>
<td>8112 (33.7)</td>
</tr>
<tr>
<td>All types</td>
<td>16 391 (100)</td>
<td>76.6</td>
<td>24 059 (100)</td>
</tr>
</tbody>
</table>

*Sex difference, $P<0.05$.

### TABLE 2. Sex-Specific Age-Adjusted Case Fatality or Mortality and Sex Differences Among Cases of All Types of Stroke and the Elderly General Population

<table>
<thead>
<tr>
<th>Measure of Mortality</th>
<th>Men</th>
<th>Women</th>
<th>Male/Female Rate Ratio (95% CIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause 1-year case mortality</td>
<td>5385 34.9</td>
<td>7 513 30.1</td>
<td>1.16 (1.13–1.20)</td>
</tr>
<tr>
<td>One-year case fatality (caused by cerebrovascular diseases)</td>
<td>2432 15.8</td>
<td>3 844 15.3</td>
<td>1.03 (0.99–1.08)</td>
</tr>
<tr>
<td>General population 4-year stroke mortality</td>
<td>7684 1.85</td>
<td>13 623 1.68</td>
<td>1.10 (1.07–1.13)</td>
</tr>
</tbody>
</table>

### Discussion

In this study, 49% of deaths among cases of all types of stroke were attributable to cerebrovascular diseases. Although there was no sex difference in case fatality, all-cause mortality was higher in men. This disagreement between the 2 case rates was expected because the latter measure included deaths caused by conditions other than cerebrovascular diseases, and the age-adjusted risk of death attributable to cancer, cardiovascular and respiratory diseases was 38% higher in male stroke cases than in female cases. Previous stroke mortality studies of the general population included deaths attributable to cerebrovascular diseases other than subarachnoid and intracerebral hemorrhage and ischemic stroke. Mortality in our study’s general population was restricted to deaths caused by stroke, and there was agreement on sex difference (higher risk in men) between this measure and all-cause mortality among cases of nonhemorrhagic stroke, not with case fatality.

Despite the basic differences between case fatality and population mortality rates, sex difference (increased risk in men) in most of the measures in our study was $<27\%$ and in the same direction. The only exception was the higher risk of mortality caused by subarachnoid hemorrhage among women in the general population, which was consistent with the findings of previous studies of subarachnoid hemorrhage mortality based on the national death certificate data for all ages. This finding is significant because the lower age-limit of our study population was 65 years. In 1994, the median age at death attributable to subarachnoid hemorrhage was reported to be 60 years. If some subarachnoid hemorrhage cases in Indiana and Kentucky died at younger age, an unknown number of deaths may have been excluded from our study. However, there is no evidence to suggest that there is a difference between cases of subarachnoid hemorrhage older than 64 years and those younger than 65 years with respect to the magnitude or the direction of sex difference in mortality.
In conclusion, how stroke is defined and how mortality is measured does affect sex difference. Studies using different definitions of stroke or different measures of mortality are not comparable. No one measure of stroke mortality is right or wrong. Each measure has specific use and application. Case fatality rate is usually used to track the natural history of stroke and to determine the outcome of medical care and the risk factors for fatality. Case mortality, also used in clinical studies such as the outcome of carotid endarterectomy, includes deaths caused by conditions other than cerebrovascular diseases, mostly the complications of stroke and comorbid conditions. The general population mortality rate is based on cross-sectional, often death certificates, data and it includes deaths caused by acute stroke (incident stroke) as well as old (prevalent or “chronic”) stroke. This public health measure is useful for surveillance and estimation of the disease burden. Spatial and temporal trends and patterns are examined.

Disclosures
None.

References

TABLE 3. Sex-Specific Age-Adjusted Mortality Rates and Sex Difference in Mortality

<table>
<thead>
<tr>
<th>Type of Acute/Fatal Stroke</th>
<th>Men</th>
<th>Women</th>
<th>Male/Female Rate Ratio (95% CIs)</th>
<th>No. Rate/1000</th>
<th>Women Rate/1000</th>
<th>Male/Female Rate Ratio (95% CIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>119 59.1</td>
<td>266 52.0</td>
<td>1.13 (0.99–1.30)</td>
<td>144 0.31</td>
<td>306 0.41</td>
<td>0.74 (0.61–0.91)</td>
</tr>
<tr>
<td>Intracerebral Hemorrhage</td>
<td>771 53.2</td>
<td>1174 52.6</td>
<td>1.01 (0.95–1.08)</td>
<td>917 2.03</td>
<td>1 396 1.80</td>
<td>1.13 (1.04–1.22)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>2730 31.3</td>
<td>3697 26.7</td>
<td>1.17 (1.13–1.22)</td>
<td>715 1.73</td>
<td>1 196 1.46</td>
<td>1.19 (1.08–1.30)</td>
</tr>
<tr>
<td>Other (nonspecific)</td>
<td>1765 35.4</td>
<td>2376 28.1</td>
<td>1.26 (1.20–1.33)</td>
<td>5908 14.4</td>
<td>10 725 13.1</td>
<td>1.10 (1.07–1.13)</td>
</tr>
</tbody>
</table>
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