Elderly Women Have Lower Rates of Stroke, Cardiovascular Events, and Mortality After Hospitalization for Transient Ischemic Attack

Judith H. Lichtman, PhD; Sara B. Jones, MPH; Emi Watanabe, MPH; Norrina B. Allen, MPH; Yun Wang, PhD; Virginia J. Howard, PhD; Larry B. Goldstein, MD

Background and Purpose—Patients with transient ischemic attack (TIA) are at increased risk for stroke, cardiovascular events, and death, yet little is known about whether these risks differ for men and women. We determined whether there are sex-based differences in these outcomes 30 days and 1 year after TIA using a national sample of elderly patients.

Methods—Rates of 30-day and 1-year hospitalization for TIA (International Classification of Diseases, 9th Revision Code 435), stroke (International Classification of Diseases, 9th Revision Codes 433, 434, and 436), coronary artery disease (International Classification of Diseases, 9th Revision Codes 410 to 414), all-cause readmission, and mortality were determined for fee-for-service Medicare patients 65 years of age discharged with a TIA in 2002. Cox proportional hazards models and random-effects logistic models compared outcomes with risk adjustment for demographics, medical history, comorbidities, and prior hospitalizations.

Results—The study included 122,063 TIA hospitalizations (mean age, 79.0±7.6 years; 62% women; 86% white). Men were younger but had higher rates of cardiac comorbidities than women. Women had lower unadjusted rates of stroke, coronary artery disease, and mortality at 30 days and 1 year after TIA admission. These relationships persisted in risk-adjusted analyses at 30 days for stroke (hazard ratio, 0.70; 95% CI, 0.64 to 0.77), coronary artery disease (hazard ratio, 0.86; 0.74 to 1.00), and mortality (odds ratio, 0.74; 0.68 to 0.82) as well as at 1 year for stroke (hazard ratio, 0.85; 0.81 to 0.89), coronary artery disease (hazard ratio, 0.81; 0.77 to 0.86), and mortality (odds ratio, 0.78; 0.75 to 0.81).

Conclusion—These data suggest that women have a better prognosis than men within the first year after hospital discharge for a TIA. Additional research is needed to identify factors that may explain these sex-related differences in outcomes. (Stroke. 2009;40:2116-2122.)

Key Words: sex ▪ transient ischemic attack (TIA) outcome

Stroke is the third leading cause of death in the United States and a leading cause of disability. Because of their longer lifespan, women have a higher stroke burden than men, accounting for 61% of all stroke deaths in 2004.1 Transient ischemic attack (TIA) precedes approximately 15% to 23% of strokes2,3 and carries a 90-day stroke risk of 9% to 17%.2 In addition to stroke, patients with TIA are also at increased risk for recurrent TIA, coronary artery disease, and death.3,7 With an estimated 240,000 TIs diagnosed annually in the United States, TIA represents an important target for secondary stroke prevention and is an indicator of a patient’s risk for myocardial infarction and vascular death.9–13 Rapid evaluation and treatment of patients with TIA can reduce subsequent morbidity.5,14

Relatively little is known about whether elderly women and men have comparable risks for recurrent events and mortality within the first year after TIA. Findings from studies that examined potential sex-related differences in outcomes after TIA are inconsistent.4,6–8,15–21 Some report a lower unadjusted 7-day stroke risk for women as well as reduced risk-adjusted long-term rates of stroke, death, and the composite outcome of stroke, myocardial infarction, or death.7,15,20 Others report no sex-related differences in unadjusted4,17–19,21 or risk-adjusted8,16 analyses of stroke and cardiac risk. Many of these studies combined TIA and stroke in the index cohort and in the assessment of outcomes,7,15,16 were conducted in European populations,7,15,17,19–21 used clinical trial cohorts,7,15 or were restricted to specific US geographic areas.4,8,16,18 Thus, only limited information is available reflecting both early and long-term prognosis after TIA in a US national cohort of elderly patients. In the present study, we compared 30-day and 1-year outcomes for elderly...
women and men after hospital discharge for TIA in a US national cohort. Outcomes included hospitalization for recurrent TIA, stroke, cardiovascular events, all-cause rehospitalization, and mortality.

Methods

Study Population

The study population included all fee-for-service Medicare beneficiaries ≥65 years hospitalized with a primary discharge diagnosis of TIA from January 1, 2002, through December 31, 2002, who were identified based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM 435.x). Data were obtained from the Medicare Provider Analysis and Review files that included demographic information, primary and secondary discharge diagnosis codes, and procedure codes for each hospitalization. We excluded patients who were <65 years of age, discharged from nonacute care facilities, or transferred from another facility. We further limited the cohort to patients with at least 12 months of continuous fee-for-service status before the index TIA hospitalization to allow assessment of comorbid conditions.

Outcomes

Rehospitalization rates at 30 days and 1 year after the index TIA hospital discharge were determined for recurrent TIA (ICD-9 435), ischemic stroke (ICD-9 433, 434, 436), coronary artery disease (CAD; ICD-9 410 to 414), and all-cause readmission. Mortality at 30 days and 1 year was obtained from the Medicare Enrollment Database. The accuracy of ascertainment of vital status using these data resources is high for this age group.22 Length of stay was determined for each index hospitalization and discharge disposition was categorized as home, skilled nursing facility, or other location.

Table 1. Characteristics of Medicare Beneficiaries Hospitalized for TIA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N=122,063), %</th>
<th>Women (N=76,108), %</th>
<th>Men (N=45,955), %</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean±SD</td>
<td>79.0±7.6</td>
<td>79.7±7.7</td>
<td>77.8±7.3</td>
<td>&lt;0.0001</td>
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<tr>
<td>65–74</td>
<td>30.2</td>
<td>27.1</td>
<td>35.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>75–84</td>
<td>44.8</td>
<td>44.3</td>
<td>45.6</td>
<td></td>
</tr>
<tr>
<td>85+</td>
<td>25.0</td>
<td>28.6</td>
<td>19.0</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>White</td>
<td>85.7</td>
<td>85.0</td>
<td>86.9</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>9.8</td>
<td>10.6</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2.4</td>
<td>2.3</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.2</td>
<td>2.1</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Source of admission</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Emergency department</td>
<td>78.6</td>
<td>78.3</td>
<td>79.1</td>
<td></td>
</tr>
<tr>
<td>Skilled nursing facility</td>
<td>0.7</td>
<td>0.8</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>20.7</td>
<td>20.9</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>Hospitalizations in past year ≥2</td>
<td>15.6</td>
<td>16.0</td>
<td>14.8</td>
<td>&lt;0.0001</td>
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<td>Deyo score ≥3</td>
<td>16.4</td>
<td>15.1</td>
<td>18.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medical history and comorbidity</td>
<td></td>
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<td></td>
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<tr>
<td>Cancer</td>
<td>2.5</td>
<td>1.8</td>
<td>3.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dementia</td>
<td>9.9</td>
<td>10.6</td>
<td>8.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>18.4</td>
<td>16.9</td>
<td>20.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>11.4</td>
<td>11.6</td>
<td>11.2</td>
<td>0.0697</td>
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<tr>
<td>Diabetes</td>
<td>26.5</td>
<td>25.6</td>
<td>27.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>6.2</td>
<td>4.8</td>
<td>8.6</td>
<td>&lt;0.0001</td>
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<td>Hypertension</td>
<td>65.4</td>
<td>68.6</td>
<td>60.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>9.2</td>
<td>7.5</td>
<td>12.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10.3</td>
<td>10.6</td>
<td>9.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>15.8</td>
<td>15.2</td>
<td>16.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior coronary artery bypass graft</td>
<td>7.3</td>
<td>4.3</td>
<td>12.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior percutaneous transluminal coronary angioplasty</td>
<td>2.7</td>
<td>2.1</td>
<td>3.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Discharge disposition</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Home</td>
<td>70.6</td>
<td>68.0</td>
<td>74.9</td>
<td></td>
</tr>
<tr>
<td>Skilled nursing facility</td>
<td>13.5</td>
<td>15.3</td>
<td>10.6</td>
<td></td>
</tr>
<tr>
<td>In-hospital death</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>15.6</td>
<td>16.5</td>
<td>14.3</td>
<td></td>
</tr>
<tr>
<td>Length of stay, days, mean±SD</td>
<td>3.4±2.6</td>
<td>3.5±2.6</td>
<td>3.3±2.6</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*P value is for difference between men and women using t-tests for continuous variables and χ² statistics for categorical variables.
†Excludes 2174 patients due to in-hospital death, transfer to another acute care facility, and length of stay ≥61 days.
Covariates
Comorbidities were identified from Medicare Provider Analysis and Review files in the year before the index hospitalization to avoid misclassifying pre-existing conditions as complications. Demographic characteristics included age, sex, and race. Medical history included previous diagnosis of cancer, dementia, chronic obstructive pulmonary disease, ischemic stroke, diabetes, smoking status, hypertension, acute myocardial infarction, congestive heart failure, atrial fibrillation, prior receipt of coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty, Deyo score for comorbidities (3),23 and number of hospitalizations in the year before the index TIA (dichotomized as <2 or ≥2).

Statistical Analysis
Bivariate analyses were conducted to compare patient characteristics by sex using t tests for continuous variables and $\chi^2$ statistics for categorical variables. Readmission rates were compared using Cox proportional hazards models with censoring for deaths. Random-effects logistic models were used to compare 30-day and 1-year mortality from admission by sex taking into account the correlation among patients treated at the same hospital. Models were adjusted for demographics, medical history, comorbidities, and prior hospital events. Risk-adjusted survival curves were used to illustrate the timing of follow-up events by sex. All analyses were conducted using SAS Version 9.1.3 (SAS Institute Inc, Cary, NC).

Results
The final study cohort included 122,063 patients (mean age, 79.0±7.6 years; 86% white) with a discharge code of TIA in 2002 (Table 1). Women represented 62% of TIA cases and were more likely to be older (mean age, 79.7±7.7 versus 77.8±7.3) and of black race ($P<0.0001$ for each). Women were more likely to have been hospitalized 2 or more times in the prior year but less likely to have 3 or more comorbidities using the Deyo score. They had lower rates of cancer, chronic obstructive pulmonary disease, and diabetes, but higher rates of hypertension and congestive heart failure ($P<0.0001$ for each). Men had a higher prevalence of cardiovascular risk factors, including diabetes and smoking history as well as prior acute myocardial infarction and cardiovascular procedures, than women. Discharge disposition varied by sex with a higher percentage of women discharged to skilled nursing facilities or other location and a greater percentage of men discharged home ($P<0.0001$).

Unadjusted 30-day readmission rates were similar for women and men for all-cause readmission (10.6% versus 10.6%) and recurrent TIA (1.1% versus 1.1%), but women...
had lower rates of stroke (1.3% versus 1.8%; \(P < 0.0001\)) and CAD hospitalizations (0.5% versus 0.7%; \(P < 0.0001\); Table 2). At 1 year, women had higher rates of all-cause readmission (48.8% versus 47.6%; \(P = 0.0002\)) and TIA (5.3% versus 4.9%; \(P < 0.0001\)) but lower readmission rates for stroke (5.9% versus 6.9%; \(P < 0.0001\)) and CAD (4.5% versus 5.8%; \(P < 0.0001\)). Mortality rates were lower for women at 30 days (1.4% versus 1.8%; \(P < 0.0001\)) and 1 year (12.9% versus 14.7%; \(P < 0.0001\)) as compared with men.

In risk-adjusted analyses, there were no sex-related differences in all-cause readmission (hazards ratio [HR], 1.00; 95% CI, 0.97 to 1.04) or hospitalizations for TIA (HR, 1.01; CI, 0.90 to 1.13), but women had a lower risk of stroke (HR, 0.70; CI, 0.64 to 0.77), CAD events (HR, 0.86; CI, 0.74 to 1.00), and death (OR, 0.74 to 1.00) at 30 days (Figure 1). At 1 year, women had a slightly higher risk of recurrent TIA relative to men (HR, 1.06; CI, 1.00 to 1.11; \(P < 0.05\)) but lower risk of stroke (HR, 0.85; CI, 0.81 to 0.89), CAD events (HR, 0.81; CI, 0.77 to 0.86), and death (OR, 0.78; CI, 0.75 to 0.81). The risk of adverse events, including hospitalization for TIA, stroke, cardiovascular events, all-cause readmission, and mortality, in the first year after TIA in women and men are shown in Figures 2 and 3. Men had a higher risk of hospital admission for stroke, CAD, and death compared with women throughout the 365-day period with increasing differences over time.

## Discussion

Among elderly fee-for-service Medicare beneficiaries who were hospitalized for a TIA, women had a lower risk of subsequent hospitalization for major vascular events and death within the first year as compared with men. Women were 30% less likely to have a stroke, 14% less likely to have a cardiac event, and 26% less likely to die within the first 30 days even after adjustment for comorbid conditions, including pre-existing coronary heart disease. Within 1 year, women were 15% less likely to have a stroke, 19% less likely to have a cardiac event, and 22% less likely to die. Women had a marginally higher risk of recurrent TIA (6%) within 1 year, which was not evident within the first month.

Our findings are consistent with 2 European studies from the Dutch TIA Trial, which included 3127 patients with TIA or minor ischemic stroke.\(^{7,15}\) The first study reported an increased combined risk of vascular death, stroke, or myocardial infarction for men (HR, 1.6; 95% CI, 1.3 to 2.0) and a marginally higher risk of fatal or nonfatal stroke (HR, 1.3; 1.0 to 1.8) over an average 2.6-year follow-up.\(^{15}\) The second, more recent study reported a higher 10-year risk of vascular death, stroke, or myocardial infarction (HR, 1.38; 1.22 to 1.56) as well as fatal or nonfatal stroke (HR, 1.31; 1.07 to 1.59) for men.\(^{7}\) Our findings extend these results by providing data on outcomes after TIA for recurrent TIA, stroke, and other cardiovascular events as well as mortality using a more contemporary, national population of elderly patients with TIA in the United States.

Several studies reported no sex-related differences in outcomes after TIA.\(^{4,8,16–19,21}\) Many of these were based on international populations,\(^{17,19,21}\) had relatively small samples,\(^{8,17–19,21}\) were not representative of the national elderly population,\(^{4,8,16,18}\) combined TIA and mild stroke events,\(^{16}\) included patients <65 years,\(^{4,8,17–19,21}\) and provided only unadjusted rates by sex.\(^{4,17–19,21}\) Moreover, studies have generally focused on stroke risk\(^{4,17–19,21}\) with few analyzing cardiac risk\(^{16}\) or mortality\(^{8}\) after TIA. A study of Michigan Medicare beneficiaries discharged with TIA or stroke found a nonsignificant lower stroke risk (inclusive of TIA) for women in adjusted analysis (HR, 0.83; 0.64 to 1.07).\(^{16}\) We found an opposite risk profile for men and women; women had a lower...
stroke risk but a slightly higher risk of recurrent TIA than men. Some prior studies may have masked these sex effects by combining TIA and stroke outcomes.

There are a number of plausible explanations for the observed sex-based differences in outcomes after TIA. First, they may be due to etiologic differences in TIA. Men may have a higher proportion of TIAs caused by large artery atherosclerosis, which is associated with greater stroke risk. Lower event rates among women could also be attributable to differences in care-seeking behaviors, initial diagnostic evaluation, or in the receipt of and/or compliance with secondary prevention measures. Studies of patients with TIA, however, found no sex-related differences in recognition of TIA nor were there differences in care-seeking behavior. It is unlikely that women receive more aggressive diagnostic evaluations. In fact, women receive comparable care or may be less likely to receive acute therapies and discharge medications than men. Finally, women may be hospitalized more often for conditions such as migraine that could potentially be misclassified as a TIA. A study that validated an ICD-9 TIA diagnosis with review by a neurologist, however, found that fewer than 6% were attributable to these other causes, although this was not analyzed by sex. Use of ICD-9 codes for diagnosis of TIA is reasonably valid with positive predictive values between 70% and 90%, but data are not available to compare the validity of these codes by sex. Two European studies evaluated the validity of international administrative data for diagnosis of ischemic stroke and did not find a sex-based difference.

In our sample, the overall 30-day stroke risk of 1.5% is lower than cited in other studies, whereas our estimate of 30-day mortality is more consistent with previous work. There are no data directly comparable with our study because we used national Medicare administrative data. The relatively lower stroke rate could be due to demographic differences of our cohort; Medicare patients are on average older and consist of a higher percentage of women, who we found to have lower short-term stroke risk after TIA. This may also be due to our use of administrative discharge codes for case selection and outcome ascertainment. The majority of other studies used neurologist review to verify TIA cases, identified events through patient follow-up interviews, and/or included nonadmitted patients. For these reasons, findings from our national study likely underestimate the true risk in the community but accurately reflect the use of hospital resources after hospital admission for TIA among fee-for-service Medicare beneficiaries in the United States.

We found that the risk of recurrent stroke is almost 3 times higher than the risk of cardiovascular events within the first 30 days after TIA, but the rates became roughly equivalent by 1 year. Similarly, Brown et al reported that an ischemic stroke after a stroke or TIA is more common as the first recurrent

Figure 3. Risk-adjusted 365-day survival curves for TIA, stroke, and coronary artery disease readmission, and mortality.
event than an ischemic cardiac event.16 Other studies have also found that cardiovascular events tend to rival stroke events over longer periods of follow-up.3,7,40

The present study has a number of limitations. First, assessment of comorbid conditions is dependent on the accuracy of recorded secondary administrative codes, but we would not expect sex-based differences in data coding. There are additional unmeasured factors such as clinical data on neurological symptoms, symptom duration, or etiology and test results that are not part of the administrative record. Medicare data does not contain information on medication use; therefore, we are unable to address potential differences in secondary stroke care by sex, although current research indicates that women are not likely to receive more aggressive care than men.26–29 The index TIA cases and vascular outcomes were ascertained using ICD-9 codes and were restricted to hospitalized events. Two population-based studies reported that 82% to 86% of TIA cases presented at the emergency department,8,18 with 79% of these patients admitted to the hospital.8,18 Positive predictive values for the selected codes for TIA, ischemic stroke, and CAD are relatively high,41,42 and evidence suggests these do not vary by sex.33,34

Patients hospitalized with TIA represent a high-risk population for stroke, cardiovascular events, and all-cause readmission. Almost one in 10 patients will be rehospitalized within the first month, and half are rehospitalized within the first year. Furthermore, women have better outcomes after hospitalization for TIA than men, even after adjusting for demographic and clinical factors. These short-term sex-based differences persist for the first year after TIA. Our analysis has the advantage of providing information about prognosis after TIA based on a 100% national fee-for-service Medicare population with a broad range of vascular outcomes. Further investigation of the underlying causes for these sex-based differences may help improve care and outcomes for both men and women after TIA and will be critical in planning for the future healthcare needs of these patients.

Acknowledgments

The Centers for Medicare & Medicaid Services reviewed and approved the use of its data for this work, and approved submission of the manuscript; this approval is based on data use only, and does not represent a Centers for Medicare & Medicaid Services endorsement of or comment on the manuscript content.

Source of Funding

The project described was supported by Grant R01NS043322 from the National Institute of Neurological Disorders and Stroke. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Neurological Disorders and Stroke or the National Institutes of Health.

Disclosures

None.

References


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Stroke. 2009;40:2116-2122; originally published online February 19, 2009;
doi: 10.1161/STROKEAHA.108.543009

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