Sex-Related Differences of Acute Stroke Unit Care
Results From the Austrian Stroke Unit Registry

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Background and Purpose—Sex-related differences in quality of acute stroke care are an important concern with limited data available, specifically regarding stroke unit (SU) setting. We used the prospective nationwide Austrian SU registry to address this issue.

Methods—Our analysis covered an 8-year time period (January 2005 to December 2012) during which all patients with transient ischemic attack or ischemic stroke admitted to 1 of 35 Austrian SU had been captured in the registry. These data were analyzed for age-adjusted preclinical and clinical characteristics and quality of acute stroke care in men and women.

Results—A total of 47,209 individuals (47% women) had received SU care. Women were significantly older (median age: 77.9 versus 70.3 years), had higher pre-existing disability and more severe strokes. Correcting for age, no significant sex-related differences in quality of care were identified with comparable onset-to-door times, times to and rates of neuroimaging, as well as door-to-needle times and rates of intravenous thrombolysis (14.5% for both sexes). Despite equal acute stroke care and a comparable rate of neurorehabilitation, women had a worse functional outcome at 3-month follow-up (modified Rankin scale 3–5: odds ratio, 1.26; 95% confidence interval [1.17–1.36]), but a lower mortality (odds ratio, 0.70; 95% confidence interval [0.78–0.88]) after correcting for confounders.

Conclusions—We identified no disproportions in quality of care in the acute SU setting between men and women, but the outcome was significantly different. Further studies on the poststroke period including socioeconomic aspects are needed to clarify this finding. (Stroke. 2014;45:00-00.)

Key Words: ischemic attack, transient ischemic stroke, sex

In recent years, a considerable number of studies have addressed sex-specific aspects of stroke. Whether there are differences in stroke symptom presentation, pathogenesis, risk factors, and outcome between men and women has been widely studied. Most studies focused on differences in outcome after cerebrovascular events and showed almost consistently higher rates of dependency in women.4,5 Because women are ≈4 to 5 years older than men at their first stroke,5,6 age certainly represents an important confounder. Both sex- and age-related disparities potentially influence preclinical management, the access to and timing of acute stroke diagnostics, and treatment strategies. It is therefore unfortunate that differences in quality of care between men and women have been infrequently studied. Specifically, incomplete knowledge is available concerning this aspect in the stroke unit setting, although organized stroke unit care is one of the mainstays of acute stroke management with proven efficacy.7 In Austria, acute stroke care is provided by a network of stroke units, which are accessible within 45 to 60 minutes for the majority of the population. These stroke units are requested to collect data on a variety of patient and management-related variables to allow quality control by individual benchmarking. At the same time, these data provide an excellent means to explore possible sex-related differences in quality of care and their relation to outcome parameters.

Methods

Since 2003, a network of stroke units has been collecting data on characteristics and acute management of all patients with transient ischemic attack and stroke admitted to these units in Austria. Data collection and clinical ratings are performed by experienced stroke neurologists using standardized definitions of variables and scores. To ensure high quality of data, immediate data entry is obligatory. The Web-based database includes online plausibility checks and help. In biannual meetings of stroke neurologists, details about scoring...
procedures and variable assessment are thoroughly discussed. The registry is a part of a governmental quality assessment program for stroke care in Austria financed by the Federal Ministry of Health. Anonymized data are centrally administrated by the Gesundheit Österreich GmbH, and scientific analyses are approved and supervised by an academic review board. Formal approval for each data analysis by a local ethics committee is therefore not needed. The registry contains epidemiological, clinical, diagnostic, and therapeutic data, as well as clinical scores (National Institutes of Health Stroke Scale score, modified Rankin Scale [mRS] score, and Barthel Index). The initial stroke syndrome is categorized according to the Oxfordshire Community Stroke Project, and stroke pathogenesis is defined by using the Trial of Org 10172 in Acute Stroke Treatment criteria. The mRS score 3 months after the index event served for rating of the outcome. Details on this registry and the definition of variables and ratings have been described previously. The tight network of stroke units in Austria allows to care for about two thirds of all acute strokes admitted to a hospital with their data therefore entered into the present registry.

Our analysis was based on all patients (>18 years) with ischemic stroke or clinically defined transient ischemic attack who were admitted to 35 of 36 Austrian stroke units and registered from January 1, 2005, and December 31, 2012. It was presupposed to adjust baseline characteristics and quality of care parameters for age in case of significant disproportions between sexes. Follow-up information, including data on subsequent neurorehabilitation after stroke unit care, mortality, and functional outcome (according to the mRS), was assessed at 3 months after the cerebrovascular index event and was analyzed in a multivariate model, correcting for demographic and clinical confounders (age, pre-existing disability [mRS], stroke severity [National Institutes of Health Stroke Scale score], vascular risk factors [hypertension, diabetes mellitus, hypercholesterolemia], atrial fibrillation [AF], thrombolytic therapy, and stroke pathogenesis). These covariates were shown to influence the target variables significantly (P≤0.01). Neurologists obtained follow-up data by personal or phone contact.

Statistics

All data were processed using the statistical environment R, version 2.15.2. Numeric variables regarding differences between men and women were tested using the Kruskal–Wallis rank-sum test for equality of the location parameters. Categorical variables were tested with the χ² test for independence. Age-adjusted tests were performed by fitting a multiple linear regression model in case of numeric variables and a multiple logistic regression model in case of categorical variables. The target variables were transformed as appropriate (log-transformation for onset-to-door time, time to first neuroimaging and door-to-needle time, square root for severity measured by the National Institutes of Health Stroke Scale score). Age as explanatory variable was included as third-order polynomial. The P value was obtained by testing the coefficient for sex-related differences with the t test, respectively, the Wald test in case of logistic regression. Based on the large number of study data and an associated high statistical power, the level of significance was set at a P value of ≤0.01 for all analyses. Odds ratios and respective P values are given in the Tables 1–3 and in the Table in the online-only Data Supplement.

Results

During the 8-year study period, a total number of 47209 patients were identified. Of these, 22329 (47.3%) stroke unit patients were women. A total of 5198 (23.3%) women and 5673 (22.8%) men had a transient ischemic attack. Demographics and clinical characteristics dichotomized for sex are summarized in Table 1. Women were significantly older (median age: 77.9 versus 70.3 years). Therefore, all statistical analyses were performed with and without age adjustment.

After accounting for age, the following clinical differences remained: women had more severe pre-existing disability and more severe strokes at admission (according to National Institutes of Health Stroke Scale scores), and they more often had a total anterior circulation stroke syndrome and had a higher rate of AF. Posterior circulation stroke syndromes, cardiovascular risk factors, such as diabetes mellitus, hypercholesterolemia, smoking as well as previous stroke and myocardial infarction, peripheral artery disease, and regular alcohol consumption were more prevalent in men with stroke. Hypertension was almost equally distributed after adjusting for age. Among identified stroke pathogeneses, cardiac embolism predominated in women, whereas macroangiopathy, as the presumed cause of stroke, was more frequent in men (Table 1).

In Table 2, preclinical and clinical quality of care parameters are summarized. In univariate analyses, a higher proportion of transfer via ambulance (with or without accompanying emergency physician) was noted in women, whereas private transportation to the hospital and secondary transports (transport via another hospital to a stroke unit) were more frequent in men. Symptom onset was more often unknown in women. Time from stroke symptom onset to hospital admission (onset-to-door time) was higher in men in univariate analyses. Regarding in-hospital stroke care, median time to neuroimaging was 30 minutes and comparable between both sexes. Overall, men were more likely to receive MRI as the first brain imaging study after the index event. Although there was no imbalance in neurosonographic examinations, women were less likely to receive extracranial magnetic resonance angiography (women 11.3% versus men 14.2%; P=0.001). There were no differences in door-to-needle times (women 49 minutes versus men 48 minutes; P=0.989) and rates of intravenous thrombolysis (14.5% for women and men). The median stay at the stroke unit was 3 days for both sexes. After age adjustment, the trend continued to show a higher proportion of private transportation to the hospital in men and a more often unknown onset of stroke symptoms in women. There were no sex differences in onset-to-door times, and times to first neuroimaging and the more frequent allocation of men to cerebral MRI, as the first brain imaging method, also disappeared after correcting for age. Door-to-needle times and thrombolysis rates remained comparable in age-adjusted analyses.

Ninety days follow-up data were available in 38.4% women and in 39.5% men (P=0.825). The Table in the online-only Data Supplement lists demographics and clinical characteristics of patients with follow-up data compared with those without. There were minor statistically significant differences regarding age, risk factors, and pre-existing disability (ie, patients with available follow-up data were 1 year older, slightly more disabled, and had slightly more often hypertension and previous stroke), but a similar distribution regarding sex. Three months after the cerebrovascular index event, women had a higher mortality, a worse functional outcome defined as an mRS score of 3 to 5, a higher proportion of dependence on nursing care, and a lower rate of poststroke neurorehabilitation in univariate analyses. The proportion of receiving nursing care allowance (ie, nursing care for disabled people living at home that is covered by the Austrian
healthcare system) was 2× higher for women, who also were less likely to live at home. Despite a considerably higher frequency of AF in women (32.3% versus 22.7% in men), there was no difference in the use of oral anticoagulants (Table 3).

Statin therapy was more often noted in men. After performing multivariate analyses accounting for age, pre-existing disability, stroke severity, administration of intravenous thrombolysis, stroke pathogenesis, and vascular risk factors, the rate of neurorehabilitation was comparable, women still had a higher grade of disability (mRS 3–5: odds ratio, 1.26; 95% confidence interval [1.17–1.36]), but now showed a lower mortality rate (odds ratio, 0.70; 95% confidence interval [0.78–0.88]). Moreover, the chance of receiving antiplatelets (odds ratio, 1.11; 95% confidence interval [1.04–1.19]) turned higher in women, whereas all other parameters did not significantly change.

Discussion

This analysis of data from the nationwide Austrian Stroke Unit Registry shows no significant differences in quality of acute stroke care between men and women admitted to a specialized stroke unit when correcting for age, based on available variables. Multivariate analyses also demonstrated a comparable rate of neurorehabilitation therapy in the postacute period after ischemic cerebrovascular events. This indicates that once admitted to an Austrian stroke unit, women seem to receive equal care and neurorehabilitation after having a transient ischemic attack or an ischemic stroke. Regarding

Table 1. Demographics and Clinical Characteristics of Women Compared With Those of Men (n=47 209) With Ischemic Cerebrovascular Events (Stroke and TIA) at the Stroke Unit

| Variables                                      | Women n=22 329 (47.3%) | Men n=24 880 (52.7%) | OR (95% CI) | PValue   | OR (95% CI)     | PValue
|-----------------------------------------------|-------------------------|----------------------|-------------|-----------|----------------|-------
| Age, y, median (Q1, Q3)                      | 77.9 (67.9, 84.3)       | 70.3 (60.8, 78.5)    | ...         | <0.001*   | ...            | ...   
| Previous functional status, n (%)            |                         |                      |             |           |                |       
| mRS 0                                         | 13 835 (62.2)           | 18 361 (74)          | 0.56 (0.56–0.60) | <0.001†   | 0.86 (0.83–0.90) | <0.001‡   
| mRS 1–2                                       | 4550 (20.4)             | 4178 (16.8)          | 1.27 (1.21–1.33) | <0.001†   | 0.97 (0.93–1.02) | 0.29‡    
| mRS 3–5                                       | 3876 (17.4)             | 2289 (9.2)           | 2.08 (1.96–2.19) | <0.001†   | 1.37 (1.29–1.45) | <0.001‡   
| NIHSS at admission, Median (Q1, Q3)           | 4 (2, 11)               | 3 (1, 7)             | ...         | <0.001*   | ...            | <0.001§  
| Stroke syndrome, n (%)                        |                         |                      |             |           |                |       
| Lacunar                                       | 6353 (28.5)             | 7541 (30.3)          | 0.91 (0.88–0.95) | <0.001†   | 0.97 (0.94–1.02) | 0.225‡    
| Total anterior circulation                    | 3186 (14.3)             | 2318 (9.3)           | 1.62 (1.53–1.71) | <0.001†   | 1.37 (1.29–1.45) | <0.001‡   
| Partial anterior circulation                  | 8818 (39.5)             | 9367 (37.7)          | 1.08 (1.04–1.12) | <0.001†   | 1.02 (0.98–1.06) | 0.341‡    
| Posterior circulation                         | 3268 (14.6)             | 4738 (19)            | 0.73 (0.69–0.77) | <0.001†   | 0.82 (0.78–0.86) | <0.001‡   
| Other                                         | 704 (3.2)               | 915 (3.7)            | 0.85 (0.77–0.94) | 0.002†    | 0.92 (0.83–1.03) | 0.138‡    
| Risk factors, n (%)                           |                         |                      |             |           |                |       
| Hypertension                                  | 17 994 (80.8)           | 19 623 (79.1)        | 1.11 (1.06–1.16) | <0.001†   | 0.96 (0.91–1.01) | 0.121‡    
| Diabetes mellitus                             | 5451 (24.5)             | 6568 (26.5)          | 0.9 (0.86–0.94) | <0.001†   | 0.9 (0.86–0.94) | <0.001‡    
| Hypercholesterolemia                          | 11 441 (51.3)           | 14 245 (57.4)        | 0.78 (0.76–0.81) | <0.001†   | 0.9 (0.87–0.94) | <0.001‡    
| Atrial fibrillation                           | 7190 (32.3)             | 5623 (22.7)          | 1.63 (1.56–1.69) | <0.001†   | 1.14 (1.09–1.12) | <0.001‡    
| Smoking                                       | 2440 (11.1)             | 5977 (24.1)          | 0.39 (0.37–0.41) | <0.001†   | 0.55 (0.52–0.58) | <0.001‡    
| Previous stroke                               | 5203 (23.3)             | 6066 (24.4)          | 0.94 (0.9–0.98) | 0.006†    | 0.82 (0.78–0.86) | <0.001‡    
| Myocardial infarction                         | 1654 (7.4)              | 2832 (11.4)          | 0.62 (0.58–0.66) | <0.001†   | 0.54 (0.51–0.58) | <0.001‡    
| Peripheral artery disease                     | 1258 (5.6)              | 2181 (8.8)           | 0.62 (0.58–0.67) | <0.001†   | 0.57 (0.53–0.61) | <0.001‡    
| Regular alcohol consumption                   | 570 (2.6)               | 3150 (12.7)          | 0.18 (0.16–0.2) | <0.001†   | 0.23 (0.21–0.26) | <0.001‡    
| TIA, n (%)                                    | 5198 (23.3)             | 5673 (22.8)          | 1.03 (0.98–1.07) | 0.218†    | 1.09 (1.04–1.14) | <0.001‡    
| Final stroke pathogenesis                     |                         |                      |             |           |                |       
| Cardiac embolism                              | 6531 (29.2)             | 5710 (23)            | 1.39 (1.33–1.45) | <0.001†   | 1.1 (1.05–1.15) | <0.001‡    
| Macroangiopathy                               | 2321 (10.4)             | 3862 (15.5)          | 0.63 (0.6–0.67) | <0.001†   | 0.67 (0.63–0.71) | <0.001‡    
| Microangiopathy                               | 5823 (26.1)             | 6620 (26.8)          | 0.97 (0.93–1.01) | 0.192‡    | 1.01 (0.97–1.06) | 0.596§    
| Unknown/Indefinite                            | 7155 (32)               | 8053 (32.4)          | 0.99 (0.95–1.02) | 0.452‡    | 1.12 (1.08–1.17) | <0.001‡    

CI indicates confidence interval; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; Q1, lower quartile; Q3, upper quartile; and TIA, transient ischemic attack.

*Kruskal–Wallis rank-sum test for equality of the location parameters.

†χ² test for independence.

‡Wald test for logistic regression parameters.

§t test for regression parameters.
outcome 3 months after the acute cerebral ischemic event, however, women were more often disabled but had a lower mortality when correcting for confounding demographic and clinical variables.

There are a considerable number of studies that have explored sex differences in cerebrovascular and cardiovascular events. However, work that has investigated putative sex-related disproportions in acute stroke care is limited, and, to date, no study has been performed that has explicitly focused on the stroke unit setting, although stroke unit treatment is one of the most effective and evidence-based strategies to improve outcome in ischemic stroke.7

A previous large-scale study by Reeves et al14 has analyzed >380000 patients with acute ischemic stroke within the Get With the Guidelines Stroke program, who were treated in 1139 hospitals between the years 2003 and 2008 in the United States, and found a lower quality of in-hospital care, regarding 7 predefined performance measures for women including a lower use of intravenous thrombolysis. The lower use of intravenous thrombolysis in women is supported by a meta-analysis of 18 studies that showed a 30% lower odds for women to receive intravenous recombinant tissue-type plasminogen activator than men.15 Although women were >7 years older and stroke symptom onset was more often unknown in women, our study depicted no sex differences in the use of intravenous recombinant tissue-type plasminogen activator with a thrombolysis rate of 14.5% for men and women. This is in accordance with a recent analysis by the Promoting Acute Thrombolysis for Ischaemic Stroke (PRACTISE) study investigators16 and might be explained by a nowadays generally more wider application of intravenous thrombolysis beyond the previous classical contraindications such as especially higher age.17 Regarding the use of thrombolysis, it is also crucial to highlight that in our specialized stroke unit care setting, no clinically significant sex-related differences in onset-to-door time, door to neuroimaging time, and door-to-needle time were identified. The acquisition of such performance measures (ie, time to critical in-hospital events) is a prerequisite for analyzing potential group differences in time-dependent acute stroke treatment strategies and has been a limitation in former studies.14

Table 2. Quality of Care Parameters at the Stroke Unit for Women and Men

<table>
<thead>
<tr>
<th>Variables</th>
<th>Women n=22329 (47.3%)</th>
<th>Men n=24880 (52.7%)</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>OR Age Adjusted (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Way of admission, n (%)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Private transport</td>
<td>2954 (13.2)</td>
<td>4296 (17.2)</td>
<td>0.71 (0.68–0.75)</td>
<td>&lt;0.001†</td>
<td>0.94 (0.89–0.99)</td>
<td>0.021†</td>
</tr>
<tr>
<td>Ambulance with physician</td>
<td>4840 (21.7)</td>
<td>5002 (20.1)</td>
<td>1.08 (1.03–1.13)</td>
<td>&lt;0.001†</td>
<td>1 (0.96–1.05)</td>
<td>0.963†</td>
</tr>
<tr>
<td>Ambulance without physician</td>
<td>10919 (48.9)</td>
<td>11157 (44.8)</td>
<td>1.17 (1.12–1.21)</td>
<td>&lt;0.001†</td>
<td>1.05 (1.01–1.09)</td>
<td>0.052†</td>
</tr>
<tr>
<td>Helicopter transport</td>
<td>579 (2.6)</td>
<td>687 (2.8)</td>
<td>0.92 (0.82–1.03)</td>
<td>0.271*</td>
<td>0.96 (0.85–1.07)</td>
<td>0.447†</td>
</tr>
<tr>
<td>Secondary transport</td>
<td>2631 (12.7)</td>
<td>3483 (14)</td>
<td>0.89 (0.85–0.94)</td>
<td>&lt;0.001†</td>
<td>1.01 (0.95–1.06)</td>
<td>0.818†</td>
</tr>
<tr>
<td>Onset of stroke symptoms, n (%)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Known</td>
<td>15409 (69)</td>
<td>18142 (72.9)</td>
<td>0.83 (0.79–0.86)</td>
<td>&lt;0.001†</td>
<td>0.89 (0.86–0.93)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Unknown</td>
<td>3822 (17.1)</td>
<td>2963 (11.9)</td>
<td>1.53 (1.45–1.61)</td>
<td>&lt;0.001†</td>
<td>1.35 (1.28–1.42)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Wakeup stroke</td>
<td>3098 (13.9)</td>
<td>3775 (15.2)</td>
<td>0.9 (0.86–0.95)</td>
<td>&lt;0.001†</td>
<td>0.9 (0.86–0.95)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Onset-to-door time</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median, min (Q1, Q3)</td>
<td>115 (64, 224)</td>
<td>120 (63, 243)</td>
<td>...</td>
<td>&lt;0.002‡</td>
<td>...</td>
<td>0.966§</td>
</tr>
<tr>
<td>Time to first neuroimaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median, min (Q1, Q3)</td>
<td>30 (19, 60)</td>
<td>30 (19, 60)</td>
<td>...</td>
<td>0.005‡</td>
<td>...</td>
<td>0.941§</td>
</tr>
<tr>
<td>Acute neuroimaging, n (%)</td>
<td></td>
<td></td>
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<tr>
<td>Computed tomography</td>
<td>20089 (90.5)</td>
<td>21830 (88.2)</td>
<td>1.27 (1.2–1.35)</td>
<td>&lt;0.001*</td>
<td>1.04 (0.98–1.11)</td>
<td>0.203†</td>
</tr>
<tr>
<td>MRI</td>
<td>3694 (16.6)</td>
<td>5087 (20.6)</td>
<td>0.77 (0.74–0.81)</td>
<td>&lt;0.001*</td>
<td>0.95 (0.91–1)</td>
<td>0.066†</td>
</tr>
<tr>
<td>Extracranial vessel studies, n (%)</td>
<td></td>
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<tr>
<td>Neurosonography</td>
<td>17026 (76.7)</td>
<td>19166 (77.5)</td>
<td>0.96 (0.92–1)</td>
<td>0.058*</td>
<td>0.96 (0.92–1)</td>
<td>0.081†</td>
</tr>
<tr>
<td>Magnetic resonance angiography</td>
<td>2513 (11.3)</td>
<td>3507 (14.2)</td>
<td>0.77 (0.73–0.82)</td>
<td>&lt;0.001*</td>
<td>0.92 (0.87–0.98)</td>
<td>0.005†</td>
</tr>
<tr>
<td>Thrombolysis (IV), n (%)</td>
<td>3217 (14.5)</td>
<td>3592 (14.5)</td>
<td>1 (0.95–1.05)</td>
<td>0.954*</td>
<td>1 (0.95–1.06)</td>
<td>0.990†</td>
</tr>
<tr>
<td>Door-to-needle time</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Median, min (Q1, Q3)</td>
<td>49 (34, 70)</td>
<td>48 (35, 68)</td>
<td>...</td>
<td>0.989‡</td>
<td>...</td>
<td>0.968§</td>
</tr>
<tr>
<td>Stay at stroke unit</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Median, d (Q1, Q3)</td>
<td>3 (2, 5)</td>
<td>3 (2, 5)</td>
<td>...</td>
<td>0.809‡</td>
<td>...</td>
<td>0.441‡</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; IV, intravenous; OR, odds ratio; Q1, lower quartile; and Q3, upper quartile.
*χ² test for independence.
†Wald test for logistic regression parameters.
‡Kruskal–Wallis rank-sum test for equality of the location parameters.
§t test for regression parameters.
Another specific scope of the present work was to assess the use of acute brain and vessel imaging strategies related to sex. In previous analyses, it has been suggested that there might be a sex gap in stroke diagnostics with a disadvantage for women.1,18 Overall and in accordance with other studies,19,20 we could not confirm this assumption. Although men had a higher proportion of brain MRI in univariate analysis, this difference disappeared after correcting for age. This finding might be explained by the well-known phenomenon that younger women present themselves more often with atypical, nontraditional, and more diffuse stroke symptoms, which more often might prompt clinicians to perform a brain MRI.21,22

Although our study was unable to detect sex differences in the use of neurosonographic examinations of the extracranial vasculature, men more often received an acute magnetic resonance angiography of brain supplying vessels. This could be explained by the higher prevalence of atherosclerotic risk factors and macroangiopathic strokes, that is, carotid artery disease in men (Table 1).

Irrespective of an equal quality of acute stroke unit care and a comparable allocation to poststroke neurorehabilitation, we found that women had a worse functional outcome with higher rates of disability, dependency, and the need of permanent nursing 3 months after the ischemic cerebrovascular index event when correcting for important epidemiological and clinical confounders. Regarding mortality, the rate was higher for women in the unadjusted analysis, but this difference reversed after multivariate modeling with a higher probability of being alive for women at 3-month follow-up. Although this will remain a controversial issue, such a scenario has also been described by other authors4,23 and stresses the importance to consider also demographic and clinical aspects besides sex when analyzing stroke mortality rates. Such investigations should also encompass the more complex construct of gender-related diversity.

A higher dependency after stroke in women has been consistently reported1,3,4,24–26 and is confirmed by our results. Intriguingly, we did not identify any difference in management or treatment strategies in the acute phase between men and women that could serve to explain this fact. It has been suggested that worse functional outcome in women might be related to their weaker social situation with more often being widowed, less caring relatives, and a minor socioeconomic background or more accompanying diseases like depression and other (nonvascular) comorbidities (eg, dementia, malignancies) that are not covered in our database and in previous stroke databases.6,27 In line with our results, data from the Swedish National Quality Register for Stroke Care also demonstrated that women are more frequently institutionalized after stroke, which could be explained by sociodemographic factors in that women were more often living alone before stroke and women’s spouses tended to be generally older.1,6 The higher proportion of unknown stroke symptom onset in women and the predominant private transportation of men to hospital, which were observed in our analysis, can probably also be attributed to these factors.

Our follow-up data identified 2 sex-specific differences regarding long-term medication. Although women had a higher proportion of AF and cardioembolic strokes, the rate of oral anticoagulation was similar between sexes. This implies undertreatment and is especially worrisome because sex (ie, female sex), increases the risk for cardioembolism.

### Table 3. Sex-Specific Poststroke Follow-Up Data at 3 Months After the Index Event

<table>
<thead>
<tr>
<th>Variables</th>
<th>Women</th>
<th>Men</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>OR Adjusted* (95% CI)</th>
<th>P Value Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (% follow-up rate)</td>
<td>8567 (38.4)</td>
<td>9822 (39.5)</td>
<td>...</td>
<td>0.825†</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Outcome, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS 0–2</td>
<td>4515 (53.4)</td>
<td>6570 (68.8)</td>
<td>0.52 (0.49–0.55)</td>
<td>&lt;0.001†</td>
<td>0.84 (0.77–0.91)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>mRS 3–5</td>
<td>2756 (32.7)</td>
<td>2156 (22.6)</td>
<td>1.66 (1.55–1.77)</td>
<td>&lt;0.001†</td>
<td>1.26 (1.17–1.36)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>mRS 6 (mortality)</td>
<td>1178 (13.9)</td>
<td>827 (8.6)</td>
<td>1.71 (1.56–1.88)</td>
<td>&lt;0.001†</td>
<td>0.70 (0.78–0.88)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Barthel Index, median (Q1, Q3)</td>
<td>80 (35, 100)</td>
<td>95 (60, 100)</td>
<td>...</td>
<td>&lt;0.001†</td>
<td>...</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing home, n (%)</td>
<td>1143 (15.6)</td>
<td>555 (6.3)</td>
<td>2.75 (2.47–3.05)</td>
<td>&lt;0.001†</td>
<td>1.60 (1.42–1.81)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Neurorehabilitation, n (%)</td>
<td>2715 (37.1)</td>
<td>3592 (40.9)</td>
<td>0.85 (0.80–0.91)</td>
<td>&lt;0.001†</td>
<td>0.94 (0.87–1.01)</td>
<td>0.072†</td>
</tr>
<tr>
<td>Permanent nursing, n (%)</td>
<td>1199 (16.4)</td>
<td>742 (8.4)</td>
<td>2.12 (1.93–2.34)</td>
<td>&lt;0.001†</td>
<td>1.53 (1.38–1.70)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Nursing allowance, n (%)</td>
<td>1973 (26.9)</td>
<td>1203 (13.7)</td>
<td>2.33 (2.15–2.52)</td>
<td>&lt;0.001†</td>
<td>1.55 (1.41–1.69)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Secondary stroke prevention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>3604 (51.2)</td>
<td>4407 (51.7)</td>
<td>0.98 (0.92–1.04)</td>
<td>0.527‡</td>
<td>1.11 (1.04–1.19)</td>
<td>0.003‡</td>
</tr>
<tr>
<td>Oral anticoagulants</td>
<td>1540 (21.1)</td>
<td>1841 (21)</td>
<td>1.01 (0.93–1.09)</td>
<td>0.858‡</td>
<td>0.92 (0.84–1.00)</td>
<td>0.063‡</td>
</tr>
<tr>
<td>Statins</td>
<td>4024 (55.2)</td>
<td>5630 (64.2)</td>
<td>0.69 (0.64–0.73)</td>
<td>&lt;0.001†</td>
<td>0.85 (0.79–0.92)</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>5348 (73.4)</td>
<td>6474 (73.9)</td>
<td>0.97 (0.91–1.04)</td>
<td>0.458‡</td>
<td>0.97 (0.91–1.04)</td>
<td>0.665‡</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; mRS, modified Rankin scale; OR, odds ratio; Q1, lower quartile; and Q3, upper quartile.

*Adjusted for age, pre-existing disability, initial stroke severity, thrombolytic therapy, stroke pathogenesis, diabetes mellitus, hypercholesterolemia, atrial fibrillation because these variables showed a significant effect in univariate analyses.

†P<test for independence.

‡Wald test for logistic regression parameters.
from AF, as also reflected in the CHA$_2$DS$_2$-VASc score.$^{28}$ Furthermore, females seem to have a higher net clinical benefit of oral anticoagulation therapy especially at higher age as recently shown in an elderly (>80 years) population of patients with AF.$^{29}$ Thus, many reasons should actually favor a proactive attitude toward oral anticoagulation of women with stroke with AF but this is obviously not the case and may indicate insufficient information of prescribing doctors. Other potential explanations for the undertreatment of women with stroke with oral anticoagulants could again be a lower social support as well as other concomitant diseases like cognitive disorders, a higher burden of vascular brain disease and epilepsy, or an increased risk of falls. Unfortunately, these suggestions have to remain speculative because respective data are not captured in our registry. Second, women had a distinctly lower prescription rate of statins, even after correcting for stroke pathogenesis and vascular risk factors including hypercholesterolemia. This potential disadvantage for women has also been noticed in previous studies$^6$ and might be associated with a lower general burden of vascular disease and athero-sclerosis or history of cardiovascular events in women.

A main concern with our study and the finding of equal quality of acute stroke care between sexes has to be the fact that our cohort of patients admitted to a stroke unit is not representative for all patients with ischemic cerebrovascular events in Austria. Thus, the likelihood of women to be admitted to a stroke unit could be a priori lower. Although we cannot fully exclude this possibility, the higher median age and grade of pre-existing disability in women admitted to the stroke unit strongly argue against such an assumption. Another major limitation is that follow-up data were available in only 40% of patients. The large proportion of patients for whom no follow-up information was available therefore prohibits a solid statement on 3 months outcome. However, it is reassuring to note that patients with and without follow-up data were comparable in relation to sex and stroke severity at admission, and that there were only slight differences regarding age, pre-existing disability, and risk factors. Furthermore, our analysis shows that more detailed and prospective information on social aspects, postacute stroke care, and comorbidities will be needed to clarify obvious differences in sex-specific functional outcomes after 3 months, which cannot be explained by the acute treatment setting.

Conclusions

In conclusion, our work identifies several demographic and clinical sex-related differences in patients with acute stroke admitted to the stroke unit; however, it does not show significant disadvantages in quality of care for women. Three months after stroke, women had a worse functional outcome, but a lower mortality. Women had a higher rate of AF. There were no sex differences in the prescription of oral anticoagulants, and women were less likely to be treated with statins. Additional prospective studies are needed to explore the background of sex-specific differences in outcome and the lower rate of women in receiving certain medications for secondary stroke prevention. These studies would need to include comprehensive information on socioeconomic aspects and nonvascular comorbidities.

Disclosures

None.

References


Sex-Related Differences of Acute Stroke Unit Care: Results From the Austrian Stroke Unit Registry
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