Gender Differences in Acute Stroke Treatment
The University of California San Diego Experience
Gilda M. Tafreshi, MD; Rema Raman, PhD; Karin Ernstrom, MS; Brett C. Meyer, MD; Thomas M. Hemmen, MD, PhD

Background and Purpose—To assess the gender differences in patients with acute ischemic stroke treated with and without tissue plasminogen activator. The primary purpose is to evaluate for differences in baseline risk factors, treatment times, and 90-day outcomes. Data regarding gender differences in acute stroke treatment shows a delayed treatment and evaluation in women with stroke, associated with poorer outcome.

Methods—Review of the University of California San Diego Specialized Program for Translational Research in Acute Stroke (SPOTRIAS) database from 2001 to 2009. All “code stroke” patients with the admitting diagnosis of acute ischemic stroke were classified based on gender and tissue plasminogen activator treatment (group 1 with tissue plasminogen activator, group 2 without).

Results—A total of 848 patients were included, group 1: 294 patients, baseline median NIHSS and mean age in men was 10 and 67.6±16.5 years, in women 13 and 72.4±16.5 years. group 2: 554 patients, baseline median NIHSS and mean age in men was 4 and 68.4±14.0 years, in women 5 and 72.2±14.0 years. Women and men had a similar tissue plasminogen activator treatment rate (women = 38%, men = 32%). Men were more likely to use tobacco and have a history of coronary artery disease and less likely to take a history of atrial fibrillation. In both groups, men had higher rates of a 90-day modified Rankin scale score of 0 to 1 compared to women (group 1 35.5% vs 22.6%; group 2 57.3% vs 47.3%). Multivariable analysis adjusting for observed confounders, namely admission NIHSS, coronary artery disease/myocardial infarction, and atrial fibrillation, indicate that this difference was not statistically significant. We found no significant difference between genders when assessing for treatment times in either group.

Conclusions—Treatment times and patient outcomes after treatment for acute ischemic stroke were similar between genders. Previously identified gender differences in stroke treatment times and outcome were not found in our sample. (Stroke. 2010;41:1755-1757.)

Key Words: gender ▪ stroke treatment ▪ tissue plasminogen activator ▪ women

Intravenous tissue plasminogen activator (t-PA) is currently the only approved therapy for acute ischemic stroke. Only 2% to 3% of acute stroke patients receive this treatment.1,2 The primary reason for this low rate is delayed presentation to an emergency department.3 Because women have a longer life expectancy than men, and because age is associated with a higher incidence of stroke, more women than men die of stroke.4 Women with acute myocardial infarction receive less medical therapy, experience longer treatment delays, undergo fewer invasive procedures, and have a higher risk of adverse outcome than men.5,6 Data suggest that women with ischemic stroke experience similar delays in treatment and lower frequency of thrombolysis.7 Women present later to the emergency department8 and are less likely to receive brain imaging within 1 hour of emergency department arrival.8 There is limited data regarding the differences between gender regarding stroke risk factors, treatment times, and outcome after acute ischemic stroke. Previous studies have shown that women are older and more often have a history of atrial fibrillation and are less likely to be smokers or have a history of coronary artery disease than men.8,10–11 Data also show that women tend to have more severe strokes and are more likely to have a poorer modified Rankin scale score (mRS) at discharge.12 Delays in arrival to the emergency department may explain why women have a reported lower rate of t-PA treatment.8,11–13 This could be critical in targeting women for improving stroke symptom awareness and urgency of rapid emergency department assessment.

Women have worse functional outcome even 5 years after their first stroke as compared to men.14 A pooled analysis of gender-based differences in response to t-PA treatment demonstrated that women with acute ischemic stroke appeared to have significantly more benefit at 90 days from t-PA than men.9 We evaluated the University of California San Diego Stroke Center experience regarding gender differences in acute stroke diagnosis and treatment.

Materials and Methods
We reviewed all “code stroke” calls from January 2001 to April 2009 for subjects who were entered into the University of California San Diego Stroke Center database. Data were analyzed by gender for baseline characteristics and outcomes.

Received March 10, 2010; accepted April 1, 2010.
From the University of California San Diego, San Diego, Calif.
Correspondence to Gilda M. Tafreshi, MD, 200 W. Arbor Drive #8466, San Diego, CA 92103-8466. E-mail gtafreshi@ucsd.edu
© 2010 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.110.584136
Results

In the time period undergoing study, 2027 code stroke alerts were registered. A total of 848 patients had an emergency department admitting diagnosis of acute ischemic stroke with a decision regarding t-PA and were included in our study. Baseline characteristics are summarized by group in Table 1. There were 294 patients (148 women and 146 men) who were treated with t-PA (group 1) and 554 patients (242 women and 312 men) without t-PA (group 2). Women and men had a similar t-PA treatment rate (women, 38%; men, 32%). Women in both groups were older than men (group 1, 72.4 ± 16.5 vs 67.6 ± 16.5; P = 0.008; group 2, 72.2 ± 14.0 vs 68.4 ± 14.0; P = 0.001). In both groups, men had a significantly higher rate of coronary artery disease (group 1, 30.1% vs 14.9%; P = 0.02; group 2, 26.3% vs 17.8%; P = 0.02) and a higher rate of tobacco use (group 1, 33.6% vs 16.2%; P = 0.001; group 2, 29.8% vs 16.5%; P < 0.001). In group 1, men more often had a history of myocardial infarction (21.2% vs 8.1%; P = 0.002) and were less likely to have atrial fibrillation (18.5% vs 34.5%; P = 0.002). In group 2, men were significantly more likely to have a history of peripheral arterial disease when compared to women (5.5% vs 0.8%; P = 0.04). There were no significant differences between gender in either group when comparing history of diabetes, hypertension, or hyperlipidemia. The median NIHSS on admission was higher for women in both groups (group 1, 13 vs 10; P = 0.10; group 2, 5 vs 4; P = 0.06). In group 2, more women than men had a pre-stroke mRS >1 (28.9% vs 19.5%; P = 0.01). There were no differences in pre-stroke mRS between gender in group 1 (mRS, 2–6; 18.9% vs 16.6%; P = 0.65). There were no significant differences in discharge destination between gender in group 1 (P = 0.17). In group 2, however, there was an overall difference in discharge destination (P = 0.02). Men were more likely to be discharged home or to acute rehabilitation facilities than to any other discharge destination compared to women (73% vs 62%). Out of the 294 patients included in group 1, 209 had 90-day outcome data (102 women and 107 men; Table 3). In group 1, 35.5% of the men and 22.6% of the women had a good clinical outcome (90-day mRS, 0–1). When controlling for observed confounders, namely admission NIHSS, history of coronary artery disease/myocardial infarction, and history of atrial fibrillation, the rates of good clinical outcome were not statistically significant (odds ratio, 0.58; 95% confidence interval, 0.28–1.18; P = 0.13). Out of 554 patients included in group 2, 194 had 90-day outcome data (91 women and 103 men). In this group, 57.3% of the men and 47% of the women had a good clinical outcome (90-day mRS, 0–1). However, when controlling for observed confounding variables, namely admission NIHSS and history of coronary artery disease/myocardial infarction, the comparison was not statistically significant (odds ratio, 0.83; 95% confidence interval, 0.43–1.58; P = 0.56; Table 2). We found no significant difference between genders when assessing for treatment times in either group (Table 3).

Discussion

We examined a prospectively collected case series of “code stroke” patients from 6 hospitals regarding gender differences in acute stroke treatment. In our analysis, men with acute stroke were younger, had lower admission NIHSS, and were more likely to have a positive smoking history, coronary artery disease, and myocardial infarction; they were less likely to have
The limitations of our study are that not all code stroke patients received a 90-day evaluation and therefore bias may have been introduced into our outcome analysis. We do, however, show close to 100% follow-up on hospital discharge.

The conclusions we make may not be applied to other acute stroke populations. Using a dedicated stroke team and stroke treatment algorithms, no gender differences in treatment times and t-PA utilization were found.

Sources of Funding
This work was supported by the National Institute of Neurological Disorders and Stroke (NINDS) 2P50NS044148.

Disclosures
None.

References
13. Tafreshi et al. Gender Differences in Acute Stroke Treated in Community Hospitals.

Table 2. Dichotomized Day 90 Modified Rankin Score

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>N=102</td>
<td>N=107</td>
</tr>
<tr>
<td>0–1</td>
<td>23 (22.6%)</td>
<td>38 (35.5%)</td>
</tr>
<tr>
<td>2–6</td>
<td>79 (77.5%)</td>
<td>69 (64.5%)</td>
</tr>
<tr>
<td>Group 2</td>
<td>N=91</td>
<td>N=103</td>
</tr>
<tr>
<td>0–1</td>
<td>43 (47.3%)</td>
<td>59 (57.3%)</td>
</tr>
<tr>
<td>2–6</td>
<td>48 (52.8%)</td>
<td>44 (42.7%)</td>
</tr>
</tbody>
</table>

When controlling for observed confounding variables, the comparison between genders was not found to be statistically significant.

Table 3. Treatment Times

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset to arrival, min</td>
<td>78±38</td>
<td>64±38</td>
<td>0.951</td>
</tr>
<tr>
<td>Onset to decision</td>
<td>137±41</td>
<td>119±41</td>
<td>0.286</td>
</tr>
<tr>
<td>Onset to bolus</td>
<td>157±51</td>
<td>139±51</td>
<td>0.259</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset to arrival</td>
<td>348±609</td>
<td>372±609</td>
<td>0.379</td>
</tr>
<tr>
<td>Onset to decision</td>
<td>415±609</td>
<td>440±609</td>
<td>0.539</td>
</tr>
</tbody>
</table>
Gender Differences in Acute Stroke Treatment: The University of California San Diego Experience
Gilda M. Tafreshi, Rema Raman, Karin Ernstrom, Brett C. Meyer and Thomas M. Hemmen

Stroke. 2010;41:1755-1757; originally published online June 10, 2010;
doi: 10.1161/STROKEAHA.110.584136

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/41/8/1755

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/