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Background and Purpose**—**Prior studies have suggested worse poststroke outcomes in women. We sought to examine sex differences in quality of care (QOC) in the Get With The Guidelines-Stroke (GWTG-Stroke) program.

Methods**—**We analyzed the relationships between sex and QOC as well as outcomes (in-hospital mortality and discharge home) using multivariable logistic regression models in 383 318 acute ischemic stroke admissions from 1139 hospitals that participated in the GWTG-Stroke program between 2003 to 2008. QOC was measured using 7 predefined performance measures and a defect-free care summary measure (defined as the proportion of patients who received all eligible interventions).

Results**—**Compared to men, women were older and more likely to present by ambulance. They were also more likely to have a past medical history of atrial fibrillation or hypertension, and less likely to have a history of heart disease, dyslipidemia, or smoking. Although sex differences in individual performance measures were relatively modest they consistently identified women as being less likely to receive care compared to men. Overall, women received less defect-free care than men (66.3% versus 71.1%, adjusted odds ratio [aOR]=0.86; 95% confidence interval [CI] 0.85 to 0.87) and were less likely to be discharged home (41.0% versus 49.5%, aOR=0.84, 95% CI 0.83 to 0.85). Although crude mortality was higher in women (6.0% versus 5.2%), this difference was eliminated after risk adjustment (aOR=1.03, 95% CI 0.99 to 1.06).

Conclusions**—**Quality of care for women with ischemic stroke was lower than that for men, and women were less likely to be discharged home. Further study is warranted to identify the causes and consequences of these sex-based differences in care. **(*Stroke*. 2009;40:00-00.)**

Key Words: acute stroke ■ quality of health care ■ sex differences ■ women

Stroke in women is increasingly recognized as an important clinical and public health problem.[1] Because women have a longer life expectancy and have higher stroke mortality in the oldest age groups, more stroke events occur in women than in men.[2] Moreover, this sex difference in the number of stroke events is expected to increase dramatically over the next few decades.[1] Women have worse functional outcomes after a stroke than men, and these differences continue despite adjustment for baseline differences in age, stroke risk factors, and other comorbidities.[3–8] At the time of their stroke event women are about 4 to 5 years older on average than men, and this difference could impact the appropriateness or timeliness of acute stroke care.[3,8–10] Lower quality of acute stroke care in women could contribute to poorer poststroke outcomes in women. Our objective was to examine sex differences in the quality of care in the Get With The Guidelines-Stroke (GWTG-Stroke) population.

Methods

The GWTG-Stroke program has been in development since 2000. Details of the design and conduct of the GWTG-Stroke program have been previously described.[11–13] After an initial pilot phase conducted in 8 states,[11] the program was made available in April 2003 to any hospital in the United States. Data from hospitals that joined the program anytime between April 2003 and June 2008 were included in this analysis. Each participating hospital received either human research approval to enroll cases without individual patient consent under the common rule, or a waiver of authorization and exemption from subsequent review by their Institutional Review Board. Outcome Sciences Inc serves as the data collection and coordination center for GWTG. The Duke Clinical Research Institute serves as the data analysis center and has an agreement to analyze the aggregate deidentified data for research purposes.

Case Identification and Data Abstraction

Trained hospital personnel were instructed to ascertain consecutive acute stroke admissions by either prospective clinical identification, retrospective identification using International Classification of Dis-

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eases (ICD)-9 discharge codes, or a combination. Methods used for prospective identification varied, but included regular surveillance of emergency department records (ie, presenting symptoms and chief complaints), ward census logs, or neurological consultations.[14] The eligibility of each acute stroke admission was confirmed at chart review before abstraction.

Patient data were abstracted by trained hospital personnel using an Internet-based Patient Management Tool (PMT) (Outcome Sciences). These included demographics, medical history, initial head computerized tomography findings, in-hospital treatment and events, discharge treatment and counseling, mortality, and discharge destination. All patient data were deidentified before submission. Data on hospital-level characteristics (ie, bed size, academic or nonacademic status, annual volume of stroke discharges, and geographical region) were obtained from the American Hospital Association.[15]

Patient Population

Among all ischemic stroke admissions from hospitals that participated in the program between April 2003 and June 2008, we excluded 7562 (2.0%) cases from 17 hospitals that provided incomplete medical history data, and 365 (0.01%) cases were excluded because of missing information on sex or age. The final analysis sample consisted of 383 318 ischemic stroke admissions from 1139 hospitals.

Quality of Care Definitions

The following 7 predefined performance measures, selected by the GWTG-Stroke program as primary targets for stroke quality improvement efforts,[16] were used to compare the quality of care (QOC) in male and female ischemic stroke admissions:

Acute Performance Measures

- IV tPA in patients who arrive <2 hours after symptom onset (IV tPA <2 hours)
- Antithrombotic medication within 48 hours of admission (early antithrombotics)
- DVT prophylaxis within 48 hours of admission (DVT prophylaxis)

Discharge Performance Measures

- Antithrombotic medication (antithrombotics)
- Anticoagulation for atrial fibrillation (anticoagulation for AF)
- Cholesterol treatment if LDL >100 mg/dL or LDL not documented (LDL 100 or ND)
- Counseling or medication for smoking cessation (smoking cessation)

We used two different measures to summarize the overall QOC in male and female patients.[13,17] We calculated the binary defect-free measure of care,[17] which is defined as the proportion of patients who received all of the interventions that they were eligible for. A composite measure of care,[13,17] defined as the total number of interventions performed among eligible patients divided by the total number of possible interventions among eligible patients, was also calculated. The composite score is a summary of performance on all 7 individual performance measures and represent the proportion of care opportunities that were fulfilled by the hospitals.

Statistical Analysis

Contingency tables were generated to explore the relationship between sex and other demographic and clinical variables, and hospital-level characteristics. Similarly, contingency tables were generated to explore the relationship between sex and compliance with the individual and summary QOC measures. Pearson Chi-square test for nominal data and Wilcoxon rank sum tests for ordinal and continuous data were used as tests for statistical associations. Because of the large size of the data set statistical significance was defined as $P \leq 0.01$.

The relationship between sex (female versus male) and compliance with individual QOC measures was further examined using multivariable logistic regression models. To account for within-hospital clustering, generalized estimating equations (GEE) were used to generate both unadjusted and adjusted models.[18] Given the large data set, traditional model building approaches that identify independent predictors based on statistical significance were not used. Instead, the final models were adjusted for the following prespecified potential confounders: age, race, past medical history and risk factors (including atrial fibrillation, previous stroke/TIA, coronary heart disease or prior myocardial infarction [CAD/prior MI], carotid stenosis, diabetes, peripheral vascular disease, hypertension, dyslipidemia, and current smoking), and hospital size and type. An identical modeling approach was used to explore the relationship between sex and 3 binary outcome measures ie, in-hospital mortality, discharged status (home versus other), and length of stay (LOS; >4 days versus <=4 days; this cut point represented the median LOS).

We examined the relationship between sex and the two summary measures of care using separate multivariable logistic regression models adjusted for the same prespecified set of potential confounders. Because the composite measure was highly skewed and not normally distributed we used a previously developed modeling approach,[13] where each care opportunity for which a patient was eligible for contributed an observation to the logistic regression model (value=1 if measure was met; 0 if not). GEE based models were again was used to account for within-hospital clustering.[18]

Finally, we also explored interaction effects between sex and age for the defect-free care and mortality models, with interactions deemed statistically significant at $P \leq 0.001$ level. All statistical analyses were performed using SAS Version 9.1 software (SAS Institute).

Results

Of 383 318 ischemic stroke admissions, just over half (52.6%) were women. Table 1 compares the demographic and clinical characteristics of female and male patients. Women were older (mean 73.3 versus 68.5) with many more in the >80 year category (40% versus 25%). Women were also more likely to present by ambulance (60.1% versus 56.8%), to have a past medical history of atrial fibrillation (20.4% versus 15.6%) and hypertension (76.5% versus 71.9%), but were less likely to have a history of CAD/prior MI (24.0% versus 32.0%), dyslipidemia (34.2 versus 38.1%), or current smoking (15.2% versus 23.7%; Table 1).

Performance on all individual QOC measures was lower in female patients compared to males, although most of these differences were small, despite being statistically significant (Table 2). The largest differences were seen in the proportion of women arriving within 2 hours treated with IV tPA (ie, 55.8% versus 59.4%), and in the appropriate treatment of lipid disorders (69.3% versus 76.1%). However, the 2 summary measures demonstrated that women received defect-free care (66.3% versus 71.1%) or composite care (86.3% versus 88.5%) less often than men (Table 2).

We observed important sex differences in unadjusted stroke-related outcomes at discharge (Table 3). Women had a higher in-hospital case fatality rate (6.0% versus 5.2%), were less likely to be discharged home (41.0% versus 49.5%), and were more likely to be discharged to a skilled nursing facility (24.0% versus 16.3%) or hospice (4.2% versus 2.3%) compared to men. Length of stay was similar in men and women.

After multivariable adjustment, the modest sex differences in the compliance with individual performance measures remained. Compared to men, the adjusted ORs for receiving any of the 7 individual measures were all <1.0 for women—

Table 1. Association Between Demographics, Clinical Characteristics and Hospital Characteristics, and Sex Among Ischemic Stroke Admissions

		Total		Male		Female		
Variable	Level	n	(%)	n	(%)	n	(%)	*P* Value+
Total		383 318	100	181 612	47.4	201 706	52.6	
Demographics								
Age, y	Median	73.0		70.0		77.0		<0.0001
	Mean	71.0		68.5		73.3		
Age, y	≥80	128 537	33.5	45 173	24.9	83 364	41.3	<0.0001
	70 and <80	96 798	25.3	46 799	25.8	49 999	24.8	
	60 and <70	71 866	18.8	40 741	22.4	31 125	15.4	
	50 and <60	52 075	13.6	30 814	17.0	21 261	10.5	
	<50	34 042	8.9	18 085	10.0	15 957	7.9	
Race*	White	282 430	73.7	133 820	73.7	148 610	73.7	<0.0001
	Black	56 554	14.8	25 442	14.0	31 112	15.4	
	Hispanic	17 076	4.5	8891	4.9	8185	4.0	
	Other	27 258	7.1	13 459	7.4	13 799	6.8	
Arrival mode								
Arrival mode	Ambulance	224 386	58.5	103 108	56.8	121 278	60.1	<0.0001
	Other	124 297	32.4	61 869	34.0	62 428	31.0	
	Not documented	34 635	9.0	16 635	9.2	18 000	8.9	
Medical history								
Atrial fibrillation*		68 974	18.1	28 167	15.6	40 807	20.4	<0.0001
Previous stroke/TIA*		115 923	30.4	53 368	29.6	62 555	31.2	<0.0001
CAD/prior MI*		105 931	27.8	57 791	32.0	48 140	24.0	<0.0001
Carotid stenosis*		17 179	4.5	9183	5.1	7996	4.0	<0.0001
Diabetes mellitus*		114 609	30.1	56 176	31.1	58 433	29.1	<0.0001
PVD*		19 558	5.1	10 337	5.7	9221	4.6	<0.0001
Hypertension*		283 188	74.3	129 810	71.9	153 378	76.5	<0.0001
Dyslipidemia*		137 407	36.1	68 830	38.1	68 577	34.2	<0.0001
Current smoker*		73 303	19.2	42 815	23.7	30 488	15.2	<0.0001
Hospital characteristics								
No. of beds	Median	379 229	380.0	179 718	382.0	199 511	375.0	<0.0001
	Mean		448.0		453.5		443.0	
Hospital type*	Academic	235 696	61.5	113 110	62.3	122 586	60.8	<0.0001
	Nonacademic	142 946	37.3	66 313	36.5	76 633	38.0	
No. of stroke discharges	0 to 100	30 918	8.1	14 125	7.8	16 793	8.3	<0.0001
	101 to 300	142 988	37.3	67 519	37.2	75 469	37.4	
	301+	151 383	39.5	72 389	39.9	78 994	39.2	
	Missing	58 029	15.1	27 579	15.2	30 450	15.1	

+*P* values are based on Pearson chi-square tests for categorical row variables, or chi-square rank based group means score statistics for continuous/ordinal variables. *Missing observations were <2% of the total.

CAD/PriorMI indicates coronary heart disease or myocardial infarction; PVD, peripheral vascular disease.

varying from 0.95 (DVT prophylaxis and smoking cessation) to 0.82 (lipid therapy; Table 4). The adjusted OR for the defect-free measure of care was 0.86, indicating that the odds of receiving defect-free care was 14% lower in women. Similar results were found for the composite measure of care (Table 4).

Adjustment for potential confounding variables had a larger impact when stroke-related outcomes were analyzed. The OR for the sex difference in discharge home changed from 0.71 (unadjusted) to 0.84 in the final multivariable model. (Table 4). The unadjusted OR for in-hospital mortality was 1.18, but after adjustment the risk of mortality was no longer significantly elevated in women (OR=1.03, 95% CI 0.99 to 1.06). After adjustment the OR for women being hospitalized longer than 4 days was modestly elevated (OR=1.09, 95% CI 1.07 to 1.10).

There was a strong interaction between sex and age in the defect-free care model ($P<0.001$). Comparison of the pro-

Table 2. Association Between Performance Measures and Summary Measures of Care and Sex Among Ischemic Stroke Admissions

	Total		Male		Female		
Variable	n	(%)	n	(%)	n	%	*P* Value+
Total	383 318	100.0	181 612	47.4	201 706	52.6	
Performance measures							
IV tPA<2 hour[1]	14 460	57.6	7424	59.4	7036	55.8	<0.0001
Early antithrombotics[2]	245 500	94.2	113 843	94.7	131 657	93.6	<0.0001
DVT prophylaxis[3]	212 436	88.6	96 022	89.4	116 414	87.9	<0.0001
Antithrombotics[4]	308 163	94.7	148 672	95.2	159 491	94.3	<0.0001
Anticoagulation for AF[5]	39 086	88.7	17 159	89.7	21 927	88.0	<0.0001
LDL 100 or ND [6]	182 267	72.6	91 789	76.1	90 478	69.3	<0.0001
Smoking cessation[7]	52 787	86.0	30 927	86.4	21 860	85.5	0.0021
Defect-free measure[8]	255 260	68.6	125 656	71.1	129 604	66.3	<0.0001
Composite measure[9]	255 260	87.3	125 656	88.5	129 604	86.3	<0.0001

+*P* values are based on Pearson chi-square tests for categorical row variables, or chi-square rank based group means score statistics for continuous/ordinal variables. *Missing observations were <2% of the total. D/C indicates discharge.

[1]Patients presenting within 2 hours of symptom onset who receive IV tPA within 3 hours of symptom onset.

[2]Antithrombotic therapy prescribed within 48 hours of hospitalization, includes antiplatelet or anticoagulant therapy.

[3]Patients who are at risk of DVT (nonambulatory) who receive DVT prophylaxis within 48 hours of hospitalization, includes warfarin, heparin, other anticoagulants, or pneumatic pressure devices.

[4]Antithrombotic therapy prescribed at discharge.

[5]Anticoagulation therapy prescribed at discharge for patients with AF documented during hospitalization, including therapeutic doses of warfarin, heparin, or other anticoagulants.

[6]Lipid lowering agent prescribed at discharge in eligible patients. Eligible patients were defined as: (1) if LDL>100, (2) if patient on lipid lowering agent at admission, or (3) if LDL was not measured.

[7]Smoking cessation intervention (medication or counseling) provided at discharge.

[8]Defect-free care represents the proportion of subjects who received all of the measures that they were eligible for.

[9]Composite care represents the proportion of all eligible care opportunities that were completed.

portions of male and female patients who received defect-free care by age showed a consistent sex disparity (Figure). After including a sex*age interaction term in the multivariable model, the ORs for defect-free care in females decreased in a linear fashion as age increased. For example, OR=0.90 (at age 50), OR=0.88 (at age 60), OR=0.86 (at age 70), OR=0.84 (at age 80), and OR=0.82 (at age 90). All of these estimates were statistically significant at $P<0.001$. This

Table 3. Association Between Stroke-Related Outcomes at Discharge and Sex Among Ischemic Stroke Admissions

		Total		Male		Female		
Variable	Level	n	(%)	n	(%)	n	(%)	*P* Value+
Total		383 318	100	181 612	47.4	201 706	52.6	
Discharge status								
Died		21 426	5.6	9360	5.2	12 066	6.0	<0.0001
Discharge destination (if alive)	Home	172 607	45.0	89 959	49.5	82 648	41.0	<0.0001
	Skilled nursing facility	77 970	20.3	29 590	16.3	48 380	24.0	
	Rehabilitation	80 167	20.9	38 780	21.4	41 387	20.5	
	Hospice	12 679	3.3	4224	2.3	8455	4.2	
	Transfer to acute care facility	11 081	2.9	5871	3.2	5210	2.6	
	Other	7388	1.9	3828	2.1	3560	1.8	
Ambulatory status	Independent	165 038	43.1	87 177	48.0	77 861	38.6	<0.0001
	With assistance	107 863	28.1	47 804	26.3	60 059	29.8	
	Unable	73 596	19.2	29 267	16.1	44 329	22.0	
	Not documented	36 821	9.6	17 364	9.6	19 457	9.7	
Length of stay, days*	Median	4.0		4.0		4.0		
	Mean	5.8		5.8		5.8		

*Excludes subjects who were transferred to another facility or did not have a valid admission or discharge date (final n=329 747).

Table 4. Unadjusted and Adjusted Odds Ratios (OR) With 95% Confidence Intervals (CI) for Sex Differences (Female vs Male) in Performance Measures and Outcome Measures

		Unadjusted			Adjusted+		
Outcome	Total n*	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Performance measures							
IV tPA 2 hour	24 445	0.88	0.84, 0.92	<0.001	0.91	0.86, 0.95	<0.001
Early antithrombotics	255 172	0.84	0.81, 0.86	<0.001	0.87	0.85, 0.90	<0.001
DVT prophylaxis	234 477	0.91	0.89, 0.92	<0.001	0.95	0.92, 0.97	<0.001
Antithrombotics	319 277	0.86	0.83, 0.88	<0.001	0.91	0.88, 0.94	<0.001
Anticoagulation for AF	43 108	0.86	0.81, 0.90	<0.001	0.93	0.88, 0.98	0.008
LDL 100 or ND	246 217	0.74	0.73, 0.76	<0.001	0.82	0.80, 0.84	<0.001
Smoking cessation	60 455	0.94	0.90, 0.98	0.007	0.95	0.91, 0.99	0.031
Defect-free measure	363 868	0.82	0.81, 0.84	<0.001	0.86	0.85, 0.87	<0.001
Composite measure	363 868	0.86	0.85, 0.87	<0.001	0.90	0.89, 0.91	<0.001
Outcomes							
Length of stay (> 4 days)	322 346	1.13	1.11, 1.15	<0.001	1.09	1.07, 1.10	<0.001
Discharge home	349 705	0.71	0.70, 0.72	<0.001	0.84	0.83, 0.85	<0.001
Mortality (all patients)	370 745	1.18	1.15, 1.22	<0.001	1.03	0.99, 1.06	0.088

+Variables included in multivariable models were age, race, prior medical history of Arial fibrillation, stroke/TIA, coronary heart disease or myocardial infarction, carotid stenosis, diabetes, peripheral vascular disease, hypertension, dyslipidemia, smoking, hospital size, and hospital type.

*No. of observations used in the unadjusted and adjusted analyses.

See Table 2 footnotes for variable definitions.

interaction demonstrates that the sex disparity in QOC was present in all age groups, and that the disparity was greater in older age groups.

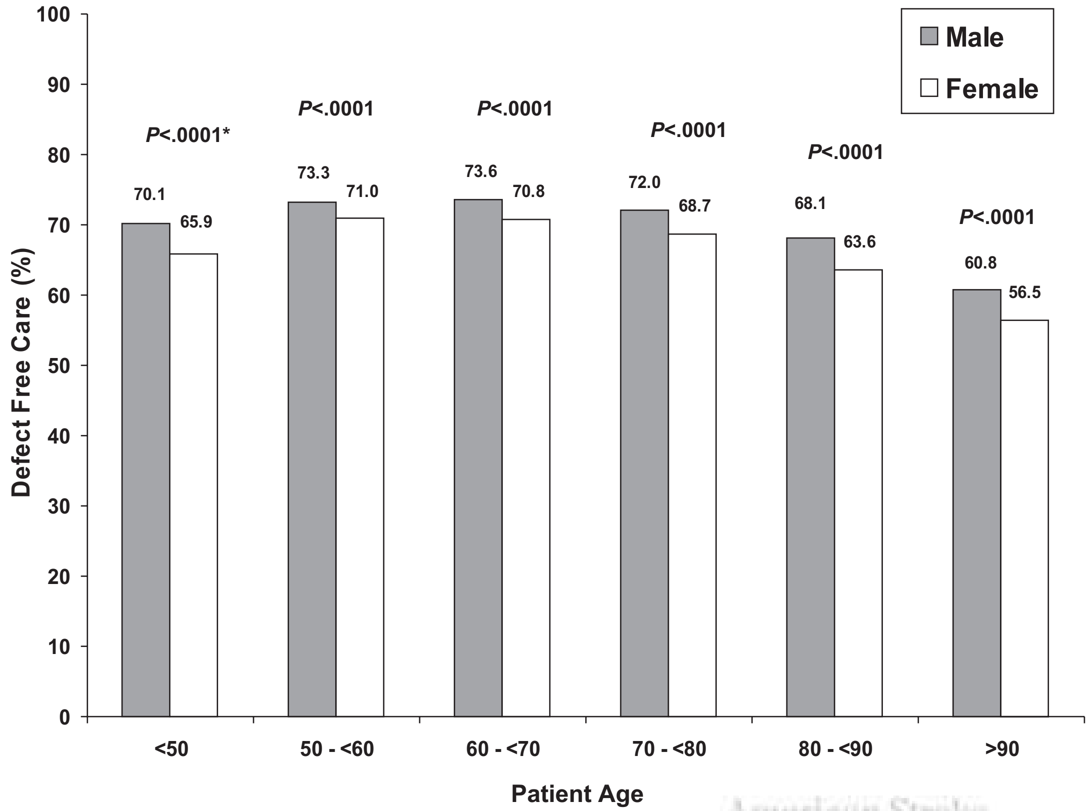
Discussion

In this analysis of over 380 000 acute ischemic stroke admissions, women received poorer quality of care than men. Although the absolute differences in individual performance measures were small, taken together they amounted to a modest disparity in the proportion of women and men who received defect free care (66.3% of women versus 71.1% of men). Baseline differences in age, risk factors, and comorbidities are often used to explain sex-based differences in stroke care and outcomes.[19,20] However, in this large study of hospital-based stroke care, adjustment for these baseline differences had little impact on the sex disparities in individual or summary quality of care measures. Adjustment did have an impact on reducing the magnitude of the sex difference in some stroke-related outcomes—particularly in-hospital mortality, which became nonsignificant after risk adjustment.

The number of studies that have examined sex differences in the care of acute stroke patients has been relatively small. Although some of these studies have found differences in the use of specific diagnostic and treatment procedures,[3,10,21,22] overall the number and magnitude of these findings have been relatively small, suggesting that there are not major sex differences in the quality of in-hospital care.[1] Among the studies that have identified sex differences in hospital-based stroke care, a European study found that after adjusting for age, women received less brain imaging, carotid ultrasound, and echocardiograms than men.[3] In the United States, a study in Corpus Christi, Texas found that after adjusting for confounders including age, women with stroke were less likely to receive echocardiography (OR=0.64) or carotid imaging (OR=0.57).[10] More recently, two registry-based studies from Canada and Michigan examined a large number of treatments and procedures and found few sex differences after accounting for age and other baseline differences.[8,9] The two most consistent findings in the literature are that women are less likely to have lipids investigated and treated while hospitalized,[8,9] and are less likely to receive IV tPA treatment.[23] Both of these findings were confirmed in our data. Several studies in the United States, Canada, and Germany have reported on sex differences in intravenous (IV) tPA use.[8,24–27] The findings from this current study confirm the presence of a modest sex difference in IV tPA use (adjusted OR=0.91), although it should be noted that the measure used in our study is different from most previously reported studies which report tPA treatment rates among all ischemic stroke admissions or those arriving within 3 hours of onset.

Our study found evidence of modest sex differences in the use of stroke-related medications at discharge—namely, antiplatelet, anticoagulation, and cholesterol treatments. Use of aspirin and warfarin at discharge was lower in women in the Swedish Riks-Stroke hospital-based registry,[7] whereas use of antiplatelet medications was lower only among older women (>85 years of age) in a study of administrative data from Ontario.[28] A Michigan registry study found no sex difference in the use of statin drugs at discharge, despite the lower use of lipid testing in women hospitalized with acute stroke.[9] Finally, a study of Medicare patients in Michigan found no sex differences in the use of antithrombotic medications at discharge among stroke patients.[29]

Consistent with prior reports, women in our study had a higher in-hospital case fatality than men (6.0% versus 5.2%),



* P-values represent unadjusted comparisons.

Figure. Percent of patient receiving defect-free care by age and sex in the GWTG-Stroke Program.

but this difference was greatly reduced after risk adjustment for age and other baseline differences. Reports assessing sex differences in stroke case fatality are quite variable with many providing little evidence of a substantial difference,[7,8,28,30,31] although some studies have shown that baseline differences in age, stroke characteristics, and cardiovascular risk factors account for much of the observed sex difference.[5]

The reasons why sex disparities in the quality of care remain after adjustment for baseline differences needs further study.[1,20] One possible explanation is that these differences are attributable to residual confounding by other unmeasured factors. For example, given the substantially higher proportion of women stroke admissions that are in the oldest age group (ie, >80 years), decisions regarding the extent and intensity of medical care may be heavily influenced by the presence of previously expressed limitations of care delivery, ie, comfort measures only (CMO) or do not resuscitate (DNR) orders. In the GWTG-Stroke database, patients who are identified as having CMO orders are excluded from the denominator of the performance measures, thus this factor should not explain the observed sex disparities. It should be noted that in this database, DNR orders were not explicitly collected as a reason for nontreatment. For patients who arrived to the hospital within 2 hours of symptom onset but do not receive IV tPA treatment, more detailed data are collected on the presence of severe comorbid illness, poor patient prognosis (ie, life expectancy <1 year), or patient refusal (eg, CMO orders). The proportion of subjects who had one or more of these listed was very low and similar between men and women (1.0% versus 1.5%, respectively), and so this also does not appear to be an explanation for the observed treatment discrepancy for IV tPA. Of course, less frequent use of evidence-based care may be the choice of the patient or family, or may be a reflection of physician-related factors including discrimination. Only limited information on these factors is obtained in the GWTG-Stroke program, so additional studies are needed to address these important questions.

This study has several limitations. First, the GWTG program is voluntary and the hospitals that participate are more likely to be larger teaching hospitals with a strong interest in stroke and QI. However, the population in GWTG-Stroke is similar in racial makeup when compared to the global U.S. population, and has a similar proportion of female patients and stroke risk factors compared with other large stroke registries.[14] Second, it was not possible to account for stroke severity in this analysis because the NIHSS is inconsistently documented in the database, and so it's inclusion in the multivariable models would have introduced significant selection bias. The absence of information in the GWTG-Stroke database relevant to understanding the details of other patient or physician decisions with respect to medical care has already been noted. Third, hospitals are instructed to include all consecutive admissions or to take a systematic sample after selecting a random starting point. However, because these processes are not audited the potential exists for selection bias.[11] Only in-hospital QOC and mortality were assessed, so sex differences in postdischarge care and outcomes could not be determined. Discharge home was included as a stroke-related outcome in this study, but it should be noted that many factors beyond those directly related to the stroke event and its treatment influence whether a given patient is discharged home—for example the availability of caregivers. Finally, we defined quality of care using only 7 predefined performance measures that address acute and discharge care. While we did not find large clinically important differences in these individual measures, sex differences in other interventions and treatments, such as the time to critical in-hospital events (eg, door-to-doctor and door-to-image times)[32] or surgical interventions such as endarterectomy[3,21,33] could exist and should be studied further.

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Disclosures

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References

1. Reeves MJ, Bushnell CD, Howard G, Gargano JW, Duncan PW, Lynch G, Khatiwoda A, Lisabeth L. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. *Lancet Neurol*. 2008; 7:915–926.
2. American Heart Association. *Heart Disease and Stroke Statistics - 2007 Update.* Dallas, Tex; 2007.
3. Di Carlo A, Lamassa M, Baldereschi M, Pracucci G, Basile AM, Wolfe CD, Giroud M, Rudd A, Ghetti A, Inzitari D. Sex differences in the clinical presentation, resource use, and 3-month outcome of acute stroke in Europe: data from a multicenter multinational hospital-based registry. *Stroke*. 2003;34:1114–1119.
4. Gargano JW, Reeves MJ. Sex differences in stroke recovery and stroke-specific quality of life - Results from a statewide stroke registry. *Stroke*. 2007;38:2541–2548.
5. Niewada M, Kobayashi A, Sandercock PA, Kaminski B, Czlonkowska A. Influence of gender on baseline features and clinical outcomes among 17,370 patients with confirmed ischaemic stroke in the international stroke trial. *Neuroepidemiology*. 2005;24:123–128.
6. Lai SM, Duncan PW, Dew P, Keighley J. Sex differences in stroke recovery. *Prev Chronic Dis*. 2005;2:A13.
7. Glader EL, Stegmayr B, Norrving B, Terent A, Hulter-Asberg K, Wester PO, Asplund K. Sex differences in management and outcome after stroke: a Swedish national perspective. *Stroke*. 2003;34:1970–1975.
8. Kapral MK, Fang J, Hill MD, Silver F, Richards J, Jaigobin C, Cheung AM. Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network. *Stroke*. 2005;36:809–814.
9. Gargano JW, Wehner S, Reeves M. Sex differences in acute stroke care in a statewide stroke registry. *Stroke*. 2008;39:24–29.
10. Smith MA, Lisabeth LD, Brown DL, Morgenstern LB. Gender comparisons of diagnostic evaluation for ischemic stroke patients. *Neurology*. 2005;65:855–858.
11. LaBresh KA, Reeves MJ, Frankel MR, Albright D, Schwamm LH. Hospital treatment of patients with ischemic stroke or transient ischemic attack using the "Get With The Guidelines" program. *Arch Intern Med*. 2008;168:411–417.
12. Reeves MJ, Smith E, Fonarow G, Hernandez A, Pan W, Schwamm LH. Off-hour admission and in-hospital stroke case fatality in the Get With The Guidelines-Stroke Program. *Stroke.* In press.
13. Schwamm LH, Fonarow GC, Reeves MJ, Pan W, Frankel MR, Smith EE, Ellrodt G, Cannon CP, Liang L, Peterson E, LaBresh KA. Get With the Guidelines-Stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or TIA. *Circulation.* 2009;119: 107–115.
14. Reeves MJ, Arora S, Broderick JP, Frankel M, Heinrich JP, Hickenbottom S, Karp H, LaBresh KA, Malarcher A, Mensah G, Moomaw CJ, Schwamm L, Weiss P. Acute stroke care in the US: results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry (vol 36, pg 1232, 2005). *Stroke*. 2005;36:1820–1820.
15. Association. AH. *American Hospital Association Hospital Statistics 2007.* Chicago, Ill: American Hospital Association; 2007.
16. Get with the Guidelines-Stroke. Accessed November 12th, 2008. http://www.strokeassociation.org/presenter.jhtml?identifier=3002728.
17. Nolan T, Berwick DM. All-or-none measurement raises the bar on performance. *JAMA*. 2006;295:1168–1170.
18. Kleinbaum D, Klein M *Logistic Regression- A Self Learning Text, II Edition.* New York; 2002.
19. Kelly-Hayes M, Beiser A, Kase CS, Scaramucci A, D'Agostino RB, Wolf PA. The influence of gender and age on disability following ischemic stroke: the Framingham study. *J Stroke Cerebrovasc Dis*. 2003;12: 119–126.
20. Mitka M. Studies explore stroke's gender gap. *JAMA*. 2006;295: 1755–1756.
21. Patrick SJ, Concato J, Viscoli C, Chyatte D, Brass LM. Sex differences in the management of patients hospitalized with ischemic cerebrovascular disease. *Stroke*. 1995;26:577–580.
22. Ramani S, Byrne-Logan S, Freund KM, Ash A, Yu W, Moskowitz MA. Gender differences in the treatment of cerebrovascular disease. *J Am Geriatr Soc*. 2000;48:741–745.
23. Lisabeth LD, Brown DL, Morgenstern LB. Barriers to intravenous tissue plasminogen activator for acute stroke therapy in women. *Gend Med*. 2006;3:270–278.
24. Brown DL, Lisabeth LD, Garcia NM, Smith MA, Morgenstern LB. Emergency department evaluation of ischemic stroke and TIA - The BASIC Project. *Neurology*. 2004;63:2250–2254.
25. Reed SD, Cramer SC, Blough DK, Meyer K, Jarvik JG. Treatment with tissue plasminogen activator and inpatient mortality rates for patients with ischemic stroke treated in community hospitals. *Stroke*. 2001;32: 1832–1839.
26. Foerch C, Misselwitz B, Humpich M, Steinmetz H, Neumann-Haefelin T, Sitzer M. Sex disparity in the access of elderly patients to acute stroke care. *Stroke*. 2007;38:2123–2126.
27. Deng YZ, Reeves MJ, Jacobs BS, Birbeck GL, Kothari RU, Hickenbottom SL, Mullard AJ, Wehner S, Maddox K, Majid A. IV tissue plasminogen activator use in acute stroke - Experience from a statewide registry. *Neurology*. 2006;66:306–312.
28. Holroyd-Leduc JM, Kapral MK, Austin PC, Tu JV. Sex differences and similarities in the management and outcome of stroke patients. *Stroke*. 2000;31:1833–1837.
29. Lisabeth LD, Roychoudhury C, Brown DL, Levine SR. Do gender and race impact the use of antithrombotic therapy in patients with stroke/TIA? *Neurology*. 2004;62:2313–2315.
30. Rothwell PM, Coull AJ, Silver LE, Fairhead JF, Giles MF, Lovelock CE, Redgrave JNE, Bull LM, Welch SJV, Cuthbertson FC, Binney LE, Gutnikov SA, Anslow P, Banning AP, Mant D, Mehta Z. Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study). *Lancet*. 2005;366:1773–1783.
31. Roquer J, Campello AR, Gomis M. Sex differences in first-ever acute stroke. *Stroke*. 2003;34:1581–1585.
32. Menon SC, Pandey DK, Morgenstern LB. Critical factors determining access to acute stroke care. *Neurology*. 1998;51:427–432.
33. Kapral MK, Redelmeier DA. Carotid endarterectomy for women and men. *J Womens Health Gend Based Med*. 2000;9:987–994.