Sex Disparities in Ischemic Stroke Care

FL-PR CReSD Study (Florida–Puerto Rico Collaboration to Reduce Stroke Disparities)

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Background and Purpose—Sex-specific disparities in stroke care including thrombolytic therapy and early hospital admission are reported. In a large registry of Florida and Puerto Rico hospitals participating in the Get With The Guidelines—Stroke program, we sought to determine sex-specific differences in ischemic stroke performance metrics and overall thrombolytic treatment.

Methods—Around 51 317 (49% women) patients were included from 73 sites from 2010 to 2014. Multivariable logistic regression with generalized estimating equations evaluated sex-specific differences in the prespecified Get With The Guidelines—Stroke metrics for defect-free care in ischemic stroke, adjusting for age, race-ethnicity, insurance status, hospital characteristics, individual risk factors, and the presenting stroke severity.

Results—As compared with men, women were older (73±15 versus 69±14 years; $P<0.0001$), more hypertensive (67% versus 63%, $P<0.0001$), and had more atrial fibrillation (19% versus 16%; $P<0.0001$). Defect-free care was slightly lower in women than in men (odds ratio, 0.96; 95% confidence interval, 0.93–1.00). Temporal trends in defect-free care improved substantially and similarly for men and women, with a 29% absolute improvement in women ($P<0.0001$) and 28% in men ($P<0.0001$), with P value of 0.13 for time-by-sex interaction. Women were less likely to receive thrombolysis (odds ratio, 0.92; 95% confidence interval, 0.86–0.99; P=0.02) and less likely to have a door-to-needle time <1 hour (odds ratio, 0.83; 95% confidence interval, 0.71–0.97; P=0.02) as compared with men.

Conclusions—Women received comparable stroke care to men in this registry as measured by prespecified Get With The Guidelines metrics. However, women less likely received thrombolysis and had door-to-needle time <1 hour, an observation that calls for the implementation of interventions to reduce sex disparity in these measures. **(*Stroke*. 2016;47:2618-2626. DOI: 10.1161/STROKEAHA.116.013059.)**

Key Words: Get With The Guidelines ■ National Institute of Neurological Disorders and Stroke ■ sex characteristics ■ stroke

Stroke affects a greater number of women than men; partly related to women's increased longevity, higher incidence of stroke with aging, and unique vascular risk factors.[1] Sex differences in access to stroke care therapeutic management and the quality of care (QOC) exist and may contribute to the poorer stroke-related outcomes in women.[2,3] Many stroke routine investigations are performed less frequently in women.[4,5] Among patients with acute ischemic stroke, women are less likely to receive acute revascularization therapies.[6,7] Other potential reasons for poor stroke-related outcomes in women include differences in stroke severity, risk factor profile, stroke subtype profiles, premorbid disability, marital status, atypical stroke symptoms, and differential response to therapies.[8–10]

Participation in stroke registries such as Get With The Guidelines—Stroke (GWTG-S) has been shown to improve the overall delivery of acute stroke care and stroke outcomes.[11] The Florida–Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) study, a National Institute of

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Neurological Disorders–funded multicenter initiative, was developed to create high-impact, culturally tailored interventions aimed at identifying race-ethnic, sex, and regional disparities in stroke care among a diverse population with significant Hispanic representation. Thus, the FL-PR Stroke Registry was created, making it the first comprehensive look into race-ethnic, sex and geographic stroke disparities in Florida and Puerto Rico. Our goal was to design and evaluate the interventions to reduce identified stroke disparities in this region. It is expected that such data analysis, together with specific feedback to hospitals comparing their performance by race/ethnicity/sex and educational programs created to implement specific culturally tailored interventions to address disparities in stroke care, will have a direct impact on the QOC at all participating institutions. Hispanics comprise 22% of Florida's and the vast majority of Puerto Rico's population, compared with 17% nationally (United States Census, update 2013), and includes more Latin and Caribbean Hispanic population than other regions of the country. In this study, we sought to investigate the sex-specific differences in risk factor profile, presentation, thrombolysis rates, and performance on the GWTG quality of stroke care measures within this registry.

Methods

Case Identification and Data Abstraction

The current study represents data collected in the FL-PR Stroke Registry from January 2010 to September 2014, across 73 hospitals in Florida (64) and Puerto Rico (9), and includes patients with the primary diagnosis of ischemic stroke, transient ischemic attack, subarachnoid hemorrhage, intracerebral hemorrhage, and stroke not otherwise specified. Data were collected according to the American Heart Association GWTG program as previously described.[12] The FL-PR Stroke registry contacted all GWTG-S–participating hospitals in Florida (n=132) and Puerto Rico (n=10) about amending their contract to include their data within the registry and ≈50% of hospitals agreed to participate. Each participating center received institutional ethics approval to enroll cases in the FL-PR Stroke Registry without requiring individual patient consent under the common rule or a waiver of authorization and exemption from subsequent review by their institutional review board.

Trained personnel at hospitals used GWTG-S data-collection tools to collect information on patients presenting to the hospital with stroke symptoms. Data were collected using an interactive internet-based Patient Management Tool. Information collected for each hospitalization included patient demographics, race/ethnicity (non-Hispanic white, non-Hispanic black, or Hispanic), medical history, stroke onset time (time last known well), mode of hospital arrival (via emergency medical services [EMS] from home/scene, private transport, transfer from other hospital, or unknown), the onset-to-door time (time from stroke onset to the arrival time of arrival to the emergency department), time from arrival to the initial head computed tomography (door-to-CT [DTC]), time from hospital arrival to the initiation of intravenous tissue-type plasminogen activator (door-to-needle [DTN] time), in-hospital treatment and events, discharge medications, in-hospital mortality, and discharge disposition. Stroke severity at presentation was measured by the National Institutes of Health Stroke Scale (NIHSS).[13] Case ascertainment for the diagnosis of ischemic stroke was performed by prospective clinical identification and retrospective chart review using *International Classification of Diseases*, Ninth revision, and discharge codes followed by chart review to confirm the final diagnosis.

Data on hospital-level characteristics (ie, number of beds, academic or nonacademic status, annual stroke volume, and number of years in GWTG) were obtained from the American Hospital Association database in addition to a self-reported hospital characteristics survey distributed to all hospitals participating in the FL-PR Stroke Registry.

Study Population

A total of 78466 patients were enrolled, and 51317 were included in this study with a final diagnosis of ischemic stroke. Patients with intracerebral hemorrhage (10.9%), subarachnoid hemorrhage (4.5%), transient ischemic attack (14.1%), stroke not otherwise specified (0.5%), no stroke-related diagnosis (1.6%), and admission for elective carotid intervention only (2.6%) were excluded.

QOC Measures

Seven stroke performance measures were used to compare the QOC between men and women as previously described[2] (1) intravenous tissue-type plasminogen activator administered to patients who arrived at the hospital within 2 hours and received treatment within 3 hours of symptom onset; (2) antithrombotic therapy by the end of hospital day 2 (3) deep venous thrombosis prophylaxis by the end of hospital day 2 for nonambulatory patients; (4) discharged on antithrombotic therapy; (5) anticoagulation therapy at discharge for atrial fibrillation (AF)/flutter; (6) discharged on statin medication for patients with low-density lipoprotein >100 or on lipid-lowering agents before admission or with unmeasured low-density lipoprotein in the previous 30 days; and (7) counseling or medication for smoking cessation). The composite variable of defect-free care (DFC) was used to identify the proportion of patients who received all applicable stroke measures that they were eligible to receive. In addition, sex disparities in thrombolytic utilization, DTC, DTN were studied in all eligible patients.

Statistical Analysis

For patient characteristics, continuous variables were summarized as means with SD and categorical variables were presented as frequencies with percentages. For continuous variables, sex differences were assessed using the Student t test, or Wilcoxon–Mann–Whitney test if data were not normally distributed. For categorical variables, the Pearson χ^2 test was used to compare the distributions between men and women. Multivariable logistic regression analyses were performed to examine the sex differences in the thrombolysis outcomes, DTN, and for each of stroke care performance measures, with generalized estimating equations to account for within-hospital clustering. To account for the contribution of the patient-level and hospital characteristics in explaining the sex differences in the performance measures, 3 sequential models were constructed to include patient-level and hospital-level covariates. Model 1 was age-adjusted, model 2 was adjusted for individual characteristics (age, race/ethnicity, health insurance status, and mode of arrival) and hospital level characteristics (number of beds, years in GWTG, and academic versus not), and model 3 included Model 2 with additional adjustment for the NIHSS score and differences in the vascular risk factors (current smoking, medical history of hypertension, AF, coronary artery disease/prior myocardial infarction). For the thrombolysis subgroup, results were adjusted for differences in the baseline characteristics (age, smoking, coronary artery disease/prior myocardial infarction, AF, academic hospital status, and stroke severity by NIHSS). In addition, standardized differences for each performance measure were calculated and considered as clinically significant for differences greater than 10. Most variables had missing values in fewer than 5% of cases, except for health insurance status (16.6% missing), NIHSS (37.7% missing), and mode of arrival (7.2% missing). The missing indicator approach was used to include the full sample for variables with a large proportion of missingness as previously described.[14] Given the high missing rate of NIHSS, sensitivity analyses were also performed by excluding those without missing NIHSS. All patient-level and hospital factors were selected in the regression models if there was a sex difference in the distribution of the factor. All statistical

Table 1. Patient and Hospital-Level Characteristics of Ischemic Stroke Patients in the Florida–Peurto Rico Stroke Registry Stratified by Sex

Clinical Characteristics	All (n=51 317)	Men (n=25 936)	Women (n=25 381)	*P* Value
Age, y; mean±SD; range (min–max)	70.8±14.3 (18–112)	68.8±13.5 (18–103)	73±14.7 (18–112)	<0.0001
Vascular risk factor, %				
Current smoker	16.6	20.2	13.0	<0.0001
Hypertension	64.8	63.1	66.6	<0.0001
Diabetes mellitus	28.1	28.3	27.9	0.3515
Dyslipidemia	36.7	36.9	36.6	0.4405
Medical history, %				
AF	17.1	15.7	18.6	<0.0001
CAD/prior MI	22.6	25.6	19.5	<0.0001
Previous stroke/TIA	25.3	24.5	26.1	<0.0001
Ethnicity, %				0.008
NH-white	63.7	63.9	63.4	
NH-black	17.5	17.0	18.0	
Hispanic	18.9	19.2	18.6	
Medical insurance, %				<0.0001
Private*	37.6	39.0	36.2	
Medicare	33.9	30.7	37.2	
Medicaid†	11.9	13.1	10.6	
Unknown	16.6	17.2	16.0	
NIHSS, %				<0.0001
≤5	33.9	35.6	32.2	
6–15	17.6	17.4	17.9	
≥16	10.8	9.2	12.4	
Missing	37.7	37.8	37.6	
Mode of arrival EMS, %				<0.0001
Yes	48.7	46.6	50.9	
No	44.1	45.7	42.5	
Missing	7.2	7.7	6.6	
State, %				0.94
Florida	94.8	94.7	94.8	
Puerto Rico	5.3	5.3	5.2	
Hospital characteristics				
Hospital size, % (n=No. of beds)				0.1478
Small (<250)	15.0	14.7	15.3	
Mid (250–450)	31.4	31.4	31.4	
Large (>450)	53.6	53.9	53.3	
Academic hospital, %	30.8	31.6	30.0	<0.0001
Years in GWTG-S, mean±SD	7.9±2.3	7.9±2.3	7.9±2.3	0.4258

AF indicates atrial fibrillation; CAD, coronary artery disease; EMS, emergency medical services; GWTG-S, Get With The Guidelines—Stroke; MI, myocardial infarction; NH-white, non-Hispanic white; NH-black, non-Hispanic black; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; and VA, Veterans Affairs.

*Includes private insurance, VA, and other.

†Includes Medicaid, self-pay, and no insurance.

analyses were performed using SAS version 9.3 software (SAS Institute).

Results

A total of 51 317 cases (49% women) with a primary diagnosis of acute ischemic stroke were studied (Table 1). As compared with men, women were older (73±15 versus 69±14years), more likely to be non-Hispanic-black (18% versus 17%), had higher prevalence of hypertension (66.6% versus 63.1%), AF (18.6% versus 15.7%), and were more likely to have previous history of stroke/transient ischemic attack (26.1% versus 24.5%), but were less likely to have a history of coronary artery disease/prior myocardial infarction (19.5% versus 25.6%) or current smoking (13.0% versus 20.2%).

GWTG QOC Measures and DFC

Table 2 compares the performance of the individual QOC measures and DFC between men and women. A total of 77.8% of women received DFC in the registry compared with 78.5% of men (adjusted odds ratio (OR), 0.96; 95% confidence interval (CI), 0.93–1.00; P=0.04). Overall, women consistently received a lower QOC in all of the predefined measures compared with men (Table 2). Accounting for confounders in all 3 models, the difference remained statistically significant for discharge antithrombotic therapy, anticoagulation for AF, and statin therapy (Table 2).

However, these statistically significant differences in performance measures and DFC did not reach the prespecified threshold for a clinically significant difference as measured by standardized differences (Table I in the online-only Data Supplement). Women were less likely treated at an academic institution, but adjusting for this confounder did not alter the results (Table II in the online-only Data Supplement). Similarly, sensitivity analyses showed similar results when those with a missing NIHSS were excluded (Table III in the online-only Data Supplement). The overall percentage of patients receiving DFC improved substantially and similarly for men and women over time, with a 29% absolute improvement in the percentage of eligible patients receiving DFC in women from 2010 to 2014 (P for trend <0.0001) and a 28% absolute improvement in men from 2010 to 2014 (P for trend <0.0001; Figure 1; P value for time-by-sex interaction=0.13).

We also tested for potential modification effect by race/ethnicity or by region (Florida/Puerto Rico). We did not find significant sex-by-race interaction for any performance metrics and DFC.

However, sex-by-region interaction analysis showed a greater sex disparity in deep venous thrombosis prophylaxis performance measure (odds ratio of 0.90 in Puerto Rico versus odds ratio of 0.99 in Florida; P value for interaction=0.04) and DFC (odds ratio of 0.85 in Puerto Rico versus odds ratio of 0.96 in Florida, P value for interaction=0.002). No other significant sex-by-region interactions were found.

Hospital Arrival and Time From Symptom Onset to Presentation

Among 51 317 patients, 31% (30.6% women; 31.4% men) arrived in ≤6 hours of stroke onset (19.3% presented ≤2hours [19.1% women; 19.6% men], 5.8% presented at 2–3.5 hours [5.8% women; 5.8% men], and 5.9% at 3.5-6hours [5.7% women; 6.0% men]) and 27.2% (26.9% women; 27.4% men) presented within the thrombolytic (<4.5 hours) time window. A total of 64.9% of patients presented within 6 hours of symptom onset and arrived to the hospital via EMS. Women were more

Table 2. Distribution of the Get With The Guidelines—Stroke Measures and Defect-Free Care Based on Sex

Outcome	Total No. of Eligible Patients	Men	Women	Unadjusted			Model 1*			Model 2†			Model 3‡		
		% Treated	% Treated	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Intravenous tPA 2 h§	3878	88.1	87.8	0.98	0.88–1.09	0.78	0.96	0.86–1.08	0.50	0.98	0.88–1.08	0.64	0.96	0.83–1.11	0.57
Early antithrombotic	39869	96.2	95.6	0.86	0.79–0.94	<0.001	0.87	0.80–0.95	0.002	0.88	0.81–0.97	0.006	0.90	0.80–1.01	0.08
DVT prophylaxis	46652	84.7	84.5	0.98	0.95–1.02	0.46	0.98	0.94–1.02	0.33	0.99	0.96–1.03	0.59	1.00	0.96–1.03	0.87
Antithrombotic at discharge	41059	97.4	97.0	0.86	0.78–0.93	<0.001	0.86	0.79–0.94	0.001	0.87	0.80–0.94	0.0004	0.87	0.76–0.99	0.03
Anticoagulation at discharge	6434	95.9	94.9	0.81	0.70–0.94	0.005	0.81	0.70–0.95	0.008	0.84	0.73–0.97	0.02	0.82	0.70–0.96	0.01
Statins at discharge for low-density lipoprotein >100 or ND	31906	92.7	91.3	0.83	0.76–0.89	<0.0001	0.84	0.77–0.91	<0.0001	0.84	0.78–0.91	<0.001	0.86	0.79–0.94	0.007
Smoking cessation	7295	96.8	96.3	0.85	0.69–1.03	0.11	0.87	0.72–1.05	0.16	0.85	0.69–1.03	0.10	0.86	0.69–1.06	0.16
Defect-free care	47520	78.5	77.8	0.95	0.92–0.98	0.009	0.95	0.92–0.98	0.003	0.96	0.93–0.99	0.02	0.96	0.93–1.00	0.04

All measures reflect the proportion of eligible patients (those without documented reasons for nontreatment) who received the intervention described. CI indicates confidence interval; DVT, deep venous thrombosis; ND, not determined; OR, odds ratio; and tPA, tissue-type plasminogen activator.

*Model 1: age adjusted.

†Model 2: adjusting for age, race-ethnicity, hospital level factors (academic vs not), health insurance status, and mode of arrival.

‡Model 3: Model 2 with additional adjustment for the NIHSS and vascular risk factors.

§Intravenous tPA 2 h: the group of eligible patients who arrived by 2 h and treated by 3 h.

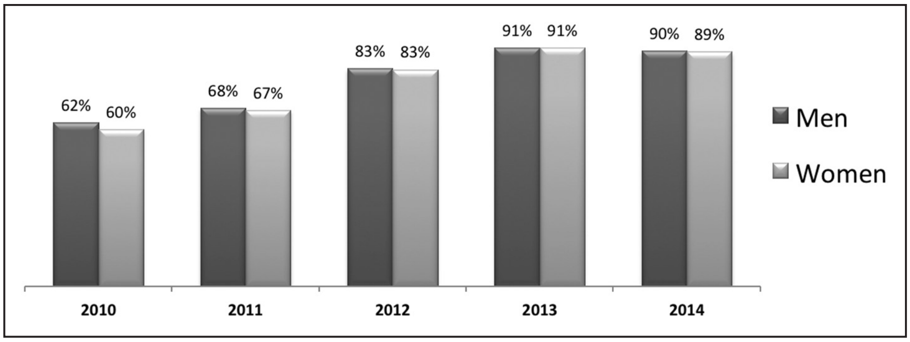

Figure 1. The distribution of defect-free care from 2010 to 2014 stratified by sex.

likely to arrive by EMS relative to men: 73.3% versus 69.7% within 2 hours (*P*=0.002), 61.6% versus 55.2% at 2 to 3.5 hours (*P*=0.009), and 51.5% versus 47.7% at 3.5 to 6 hours (*P*=0.27).

The median DTC time for patients with onset-to-door time ≤6 hours was 25min (Q1=15 min; Q3=45 min). Women were less likely to have a DTC ≤25min as compared with men (50% versus 52%; adjusted odds ratio, 0.86; 95% confidence interval, 0.82–0.92; *P*<0.0001)

Thrombolytic Therapy

In total, 10% (n=5003) of patients received intravenous tissue-type plasminogen activator at a registry participating hospital. Table 3 shows the clinical and hospital characteristics of thrombolyzed patients based on sex. Rapid improvement and mild stroke symptoms were the main reasons tissue-type plasminogen activator exclusion within the first 4.5 hours in both sexes. However, as compared to men, women were more likely to refuse thrombolysis and to be excluded because of advanced age (Figure 2).

Adjusting for all significant differences described in Table 3, women were significantly less likely to receive thrombolysis (9.6%; n=2397) compared with men (10.2%; n=2606; *P*=0.02); adjusted odds ratio of 0.92 (95% confidence interval, 0.86–0.99; *P*=0.02). Thrombolyzed women were older than thrombolyzed men (73.0±14.4 versus 68.4±13.8 years) and had a similar risk factor profile to the overall women participants of the registry (Tables 1 and 3). Over the study period, the annual rate of thrombolysis increased over time (8.0% in 2010 to 12.1% in 2014), with no significant difference in thrombolytic rates between men and women in 2010 (8% versus 8%; *P*=0.96) and in 2014 (12.7% versus 11.5%; *P*=0.11). Stroke severity was greater in thrombolyzed women relative to men (median NIHSS, 12 [interquartile range=11] versus median NIHSS, 10 [interquartile range=10]; *P*<0.0001).

Women had a longer median DTN time (73 minutes; interquartile range=55–97) relative to men (69 minutes; interquartile range=52–91; *P*=0.005) and were less likely to have a DTN ≤60 min (29.2% versus 32.7% men, unadjusted *P*=0.02 adjusted for significant difference in Table 3 (odds ratio, 0.83; 95% confidence interval, 0.71–0.97; *P*=0.02). However, when treatment was stratified by onset to time of arrival (arrived by 2 hours and treated by 3 hours, arrived by 3.5 hours and treated by 4.5 hours, and arrived after 3.5 hours and treated after 4.5 hours), there was no significant difference in percentage of thrombolyzed men and women (94.9% versus 94.1%, *P*=0.29; 99% versus 99.3%, *P*=0.24; and 70.9% versus 67.3%, *P*=0.68; respectively).

Discussion

In this study of over 51 000 patients with ischemic stroke, women and men received comparable overall stroke care as measured by DFC, one of the main GWTG-S QOC measures. However, women were less likely to receive thrombolysis and had a longer assessment time in the emergency room before thrombolysis initiation (a DTN time less than an hour) relative to men. Sex-based stroke treatment disparity was noted among Puerto Rican Hispanics where it was not present in patients from other race/ethnic origin in Florida. Our results are consistent with that of the national GWTG publication on sex disparity that was collected from 2003 to 2008.[2] Compared with that study, our registry represents a younger cohort with a greater representation of Hispanics (by >10%) and blacks. Almost a decade later, the current study shows an overall higher compliance with all stroke QOC measures across both sexes and a significant improvement in the percentage of patients receiving a DFC (78% in this study) relative to the previous publication (68.6%).[2] We also show a much smaller gap in performance measures between men and women. Our findings emphasize that adherence with a stroke performance program not only improves care but also resolves disparity.

In our population, women were older than men, more likely to have suffered a prior stroke, had a higher prevalence of AF, and had a higher presenting stroke severity. Some of these characteristics have been linked to a worse premorbid functional status in the secondary prevention of small subcortical strokes[15] and higher stroke severity in the Framingham study.[16] Premorbid disability and high stroke severity are in turn associated with poor stroke-related functional outcomes.[17] Moreover, certain risk factors such as diabetes mellitus[9] and hypertension[18] carry a higher risk for development of stroke in women relative to men. It is therefore conceivable that the sex differences noted in the quality of stroke care may be related to advanced age, higher stroke severity, and differential effects of vascular risk factors. Accounting for major possible confounding factors in 3 different statistical models, we found only a small gap in sex-related stroke care, without a clinically meaningful difference in the quality of stroke care between men and women.

Many of the factors that could cause worse stroke-related outcomes in women result from delays in hospital presentation or acute treatment after stroke.[19] Inability to identify the common stroke symptoms,[20] living alone,[21] and use of transportation modes other than the EMS[19] have also been linked to delayed hospital presentation among women. In our study,

Table 3. Clinical and Hospital Characteristics of Patients With Acute Ischemic Stroke Who Received Intravenous Thrombolysis Based on Sex

	All (n=5003)	Men (n=2606)	Women (n=2397)	*P* Value
Clinical characteristics of patients who received tPA				
Age, y, mean±SD	70.6±14.3	68.4±13.8	73.0±14.4	<0.0001
Vascular risk factor, %				
Current smoker	16.2	19.2	13.0	<0.0001
Hypertension	63.9	62.2	65.7	0.0092
Diabetes mellitus	22.8	23.1	22.4	0.5123
Dyslipidemia	34.7	34.7	34.7	0.9896
Medical history, %				
AF	21.7	18.7	25.0	<0.0001
CAD/prior MI	22.8	26.3	19.0	<0.0001
Previous stroke/TIA	80.4	81.2	79.4	0.1009
Ethnicity, %				0.9569
NH-white	64.8	65.3	64.3	
NH-black	13.6	13.2	14.1	
Hispanic	21.6	21.6	21.5	
Mode of arrival EMS, %				0.1939
Yes	72.8	71.9	73.8	
No	24.7	25.3	24.0	
Missing	2.5	2.8	2.2	
NIHSS, %				<0.0001
≤5	19.8	21.7	17.8	
6–15	40.4	42.6	38.1	
≥16	28.9	25.3	32.7	
Missing	10.9	10.4	11.5	
Door to CT time, %				0.08
≤25 min	63.2	64.2	62.2	
>25 min	28.0	26.6	29.4	
Missing	8.8	9.2	8.4	
Door to needle time, %				0.02
≤60 min	31.0	32.7	29.2	
>60 min	58.2	56.5	60.1	
Missing	10.8	10.9	10.7	
Hospital characteristics				
Hospital size, % (n=No. of beds)				0.5414
Small (n<250)	14.8	14.4	15.3	
Mid (n≤450)	29.0	29.5	28.4	
Large (n>450)	56.2	56.1	56.4	
Academic hospital, %	37.9	39.5	36.1	0.0133
Years in GWTG, mean±SD	7.7±2.1	7.7±2.1	7.7±2.1	0.5800

AF indicates atrial fibrillation; CAD, coronary artery disease; CT, computed tomography; EMS, emergency medical services; GWTG, Get With The Guidelines; MI, myocardial infarction; NIHSS, National Institutes of Health Stroke Scale; NH-white, non-Hispanic white; NH-black, non-Hispanic black; TIA, transient ischemic attack; and tPA, tissue-type plasminogen activator.

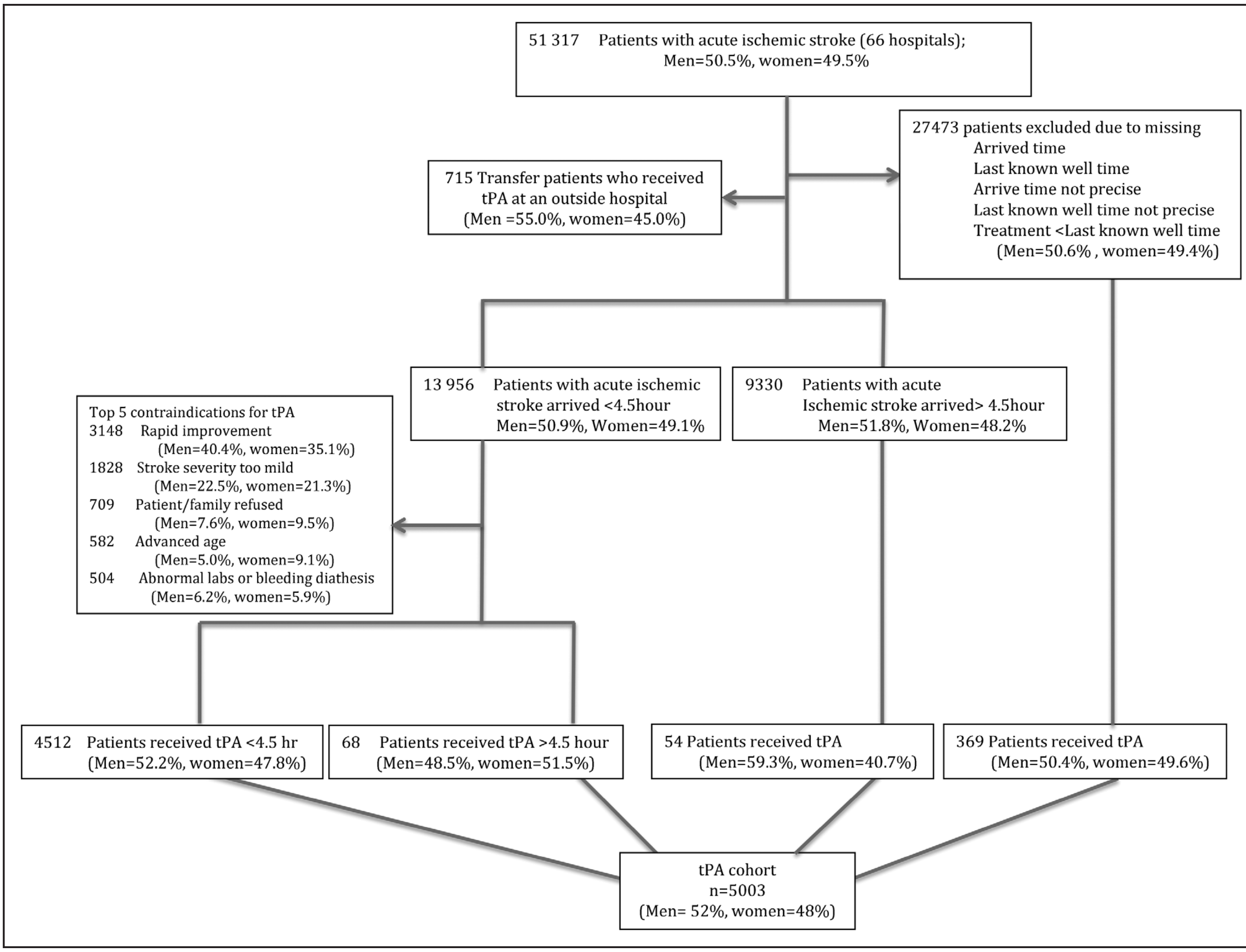

Figure 2. Outline of patients who received thrombolysis. tPA indicates tissue-type plasminogen activator.

men and women had similar representations in the acute period, and women were even more likely to arrive to the hospital via EMS. However, they were less likely to be treated in academic hospitals, a factor associated with overall higher thrombolysis utilization and shorter DTN time.[22] Adjusting for these confounders, women had longer assessment time in the ER as measured by DTC, lower thrombolysis utilization, and longer DTN times relative to men. These findings can have major implications on stroke outcomes.[2,6,23,24] Fonarow et al[25] demonstrated that a 10-minute reduction in the median DTC over their study period was the major factor behind significant reductions in stroke mortality and symptomatic intracranial hemorrhage post thrombolysis. The same study showed that improved DTN resulted in increased likelihood of being discharged home as compared with other dispositions such as admission to nursing home and long-term care facilities. In our study, the absolute difference in the median DTN time between men and women alone was 4 minutes. Assuming that the same relationship exists between the prolonged DTN and poorer thrombolysis outcomes, the financial implication of this DTN difference even without accounting for other forms of sex disparity is enormous. Between 2012 and 2030, the total direct medical stroke-related costs are projected to triple, from $71.55 billion to $184.13 billion in the United States.[26] The rise in the nursing home admission requirements and long-term care is the major driver of this increased cost in the US aging population, which has >60% representation of women. Therefore, although the absolute difference in treatment rates and DTN times between men and women is small, this disparity is relevant and has an implication on outcomes and burden of stroke.

The drivers for these in-hospital delays are not clear; it is hypothesized that greater deliberations over the risks and benefits of thrombolysis in elderly women with greater stroke severity can lead to treatment delays.[27] Others have suggested atypical stroke symptoms[28] and higher concerns regarding thrombolytic risks[29] as factors prolonging the timelines to obtain imaging and initiating treatment. In fact, in our study, more women (or their families) refused thrombolysis as compared with men.

Our study has several limitations. The FL-PR Stroke Registry is a voluntary program including only hospitals that are members of the GWTG-S program. It is more likely that our registry includes larger teaching hospitals with stronger interest in quality improvement of stroke compared with nonparticipating hospitals. Our study population has a higher representation of Hispanics (19%) and non-Hispanic-blacks (17.5%), as compared with the general US population

(17.1% and 13.2%, respectively [updated US Census, 2013]). As such, sex disparity is possibly greater in our population with higher representation of minorities. However, given the projected rise in the US Hispanic population, our study provides important data to address this fastest growing subgroup. The NIHSS as a stroke severity variable was inconsistently recorded in our database with the highest rate of missing values for both sexes, which could have affected our findings. Finally, we did not collect information regarding the use of different diagnostic modalities and carotid intervention therapies that had been suggested as a source of sex disparity in ischemic stroke care in multiple reports[4,5] and is an area that merits further research. Despite these limitations, our study is the largest cohort of ethnically diverse ischemic stroke patients to look at sex disparity in both GWTG-S QOC and acute stroke measures.

In summary, we found that women had a similar overall quality of stroke care in the FL-PR Stroke Registry as compared with their men counterparts. Participation in GWTG-S resulted in temporal reductions in overall sex disparities. However, women less likely received thrombolysis and DTN <1 hour. The reasons for sex disparities are multifactorial and require further refinement in stroke quality improvement programs and the implementation of interventions to reduce sex-specific disparities in stroke care that will improve care for all.

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Disclosures

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Sex Disparities in Ischemic Stroke Care: FL-PR CReSD Study (Florida–Puerto Rico Collaboration to Reduce Stroke Disparities)

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SUPPLEMENTAL MATERIAL

Outcome		Men	Women	Unadjusted
	Total number of eligible patients	**% Treated**	**% Treated**	**Standardized Difference, %**
IV tPA 2 hour[£]	3878	88.1	87.8	0.9
Early antithrombotic	39869	96.2	95.6	3
DVT prophylaxis	46652	84.7	84.5	5.5
Antithrombotic at Discharge	41059	97.4	97	2.4
Anticoagulation at Discharge	6434	95.9	94.9	4.7
Statins at discharge for LDL> 100 or ND	31906	92.7	91.3	5.1
Smoking cessation	7295	96.8	96.3	2.7
Defect-free care	47520	78.5	77.8	1.6

Supplemental Table I: Distribution of the Get With the Guidelines-Stroke measures and defect-free care, showing standardized difference for each measure based on sex. All measures reflect the proportion of eligible patients (those without documented reasons for non-treatment) who received the intervention described.

Outcome		Men	Women	Adjusting for Academic Hospital Admission			Adjusting for Age and Academic Hospital Admission		
	Total number of eligible patients	% treated	% treated	OR	95% CI	P Value	OR	95% CI	P Value
IV tPA 2 hour[£]	3878	88.1	87.8	0.98	0.89-1.08	0.76	0.96	0.86-1.06	0.48
Early antithrombotic	39869	96.2	95.6	0.86	0.79-0.93	0.0005	0.87	0.80-0.95	0.003
DVT prophylaxis	46652	84.7	84.5	0.98	0.95-1.02	0.46	0.98	0.95-1.02	0.43
Antithrombotic at Discharge	41059	97.4	97	0.85	0.78-0.93	0.0007	0.86	0.79-0.93	0.0003
Anticoagulation at Discharge	6434	95.9	94.9	0.81	0.70-0.94	0.005	0.83	0.73-0.96	0.01
Statins at discharge for LDL> 100 or ND	31906	92.7	91.3	0.82	0.76-0.89	<0.0001	0.84	0.77-0.91	<0.0001
Smoking cessation	7295	96.8	96.3	0.84	0.70-1.02	0.09	0.85	0.70-1.03	0.11
Defect-free care	47520	78.5	77.8	0.95	0.92-0.98	0.009	0.95	0.92-0.98	0.006

Supplemental Table II: The Distribution of the Get With the Guidelines Stroke Measures and Defect Free Care based on Sex, adjusting for Academic Hospital Admission and Age. All measures reflect the proportion of eligible patients (those without documented reasons for non-treatment) who received the intervention described.

		Men	Women	Sensitivity analysis		
Outcome	**Total # of eligible patients**	**% treated**	**% treated**	**OR**	**95% CI**	**P Value**
IV tPA 2 hour[£]	3489	91.2	91.6	1.00	0.80-1.25	0.97
Early antithrombotic	24647	98.1	97.6	0.85	0.65-1.10	0.21
DVT prophylaxis	30419	86.0	86.1	1.01	0.96-1.06	0.77
Antithrombotic at Discharge	26412	98.8	98.6	0.84	0.70-1.02	0.07
Anticoagulation at Discharge	4518	96.9	96.2	0.88	0.69-1.12	0.31
Statins at discharge for LDL> 100 or ND	20308	95.1	93.6	0.80	0.70-0.91	0.0007
Smoking cessation	4781	97.7	97.6	0.93	0.69-1.27	0.66
Defect-free care	30955	80.9	80.2	0.95	0.91-1.00	0.04
* Model 3 among those without NIHSS missing data.						

Supplemental Table III: sensitivity analyses among those without NIHSS missing data. Model was adjusted for age, race-ethnicity, hospital level factors (academic vs not), health insurance status, mode of arrival and NIHSS.