Original Contribution

Predictors of Thrombolysis Administration in Mild Stroke

Florida-Puerto Rico Collaboration to Reduce Stroke Disparities

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Background and Purpose—Mild stroke is the most common cause for thrombolysis exclusion in patients acutely presenting to the hospital. Thrombolysis administration in this subgroup is highly variable among different clinicians and institutions. We aim to study the predictors of thrombolysis in patients with mild ischemic stroke in the FL-PR CReSD registry (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities).

Methods—Among 73 712 prospectively enrolled patients with a final diagnosis of ischemic stroke or TIA from January 2010 to April 2015, we identified 7746 cases with persistent neurological symptoms and National Institutes of Health Stroke Scale ≤5 who arrived within 4 hours of symptom onset. Multilevel logistic regression analysis with generalized estimating equations was used to identify independent predictors of thrombolytic administration in the subgroup of patients without contraindications to thrombolysis.

Results—We included 6826 cases (final diagnosis mild stroke, 74.6% and TIA, 25.4%). Median age was 72 (interquartile range, 21); 52.7% men, 70.3% white, 12.9% black, 16.8% Hispanic; and median National Institutes of Health Stroke Scale, 2 (interquartile range, 3). Patients who received thrombolysis (n=1281, 18.7%) were younger (68 versus 72 years), had less vascular risk factors (hypertension, diabetes mellitus, and dyslipidemia), had lower risk of prior vascular disease (myocardial infarction, peripheral vascular disease, and previous stroke), and had a higher presenting median National Institutes of Health Stroke Scale (4 versus 2). In the multilevel multivariable model, early hospital arrival (arrive by 0–2 hours versus ≥3.5 hours; odds ratio [OR], 8.16; 95% confidence interval [CI], 4.76–13.98), higher National Institutes of Health Stroke Scale (OR, 1.87; 95% CI, 1.77–1.98), aphasia at presentation (OR, 1.35; 95% CI, 1.12–1.62), faster door-to-computed tomography time (OR, 1.81; 95% CI, 1.53–2.15), and presenting to an academic hospital (OR, 2.02; 95% CI, 1.39–2.95) were independent predictors of thrombolysis administration.

Conclusions—Mild acutely presenting stroke patients are more likely to receive thrombolysis if they are young, white, or Hispanic and arrive early to the hospital with more severe neurological presentation. Identification of predictors of thrombolysis is important in design of future studies to assess the use of thrombolysis for mild stroke. **(*Stroke*. 2018;49:00-00. DOI: 10.1161/STROKEAHA.117.019341.)**

Key Words: Florida ■ Puerto Rico ■ risk factors ■ stroke ■ therapy

The majority of patients with ischemic stroke have either mild or transient neurological symptoms on the initial presentation.[1] Despite a seemingly benign presentation, close to one third of these patients are dead or disabled at 3 months of follow-up.[2–5] The role of thrombolysis in this subgroup of patients with ischemic stroke is not well understood, and the current practice is widely variable. Patients with rapidly improving or mild neurological symptoms, including isolated sensory deficit, ataxia, dysarthria, and facial palsy, were excluded from randomization in the NINDS trial (National Institute of Neurological Disorders and Stroke).[6] However, these features are not individually considered as a contraindication for thrombolysis, whereas mild and rapidly improving stroke is listed as a relative thrombolytic contraindication in the current guidelines.[7,8] Furthermore, mild stroke is no longer mentioned as a contraindication for ischemic stroke treatment in the updated package insert of Alteplase by Genetech.[9–11]

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To date, no large-scale study has evaluated the clinical practice and predictors of thrombolysis administration in patients with mild ischemic stroke who do not have contradictions to thrombolytic treatment. In a large FL-PR CReSD study (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities), we aimed to study the clinical and hospital characteristics that are associated with the thrombolytic use in ischemic patients with mild stroke who otherwise do not have contraindications to thrombolysis.

Methods

Case Identification and Data Abstraction

The FL-PR Stroke registry consists of hospitalized patient data collected from participating hospitals in Florida and Puerto Rico and includes patients with the primary diagnosis of ischemic stroke, transient ischemic attack (TIA), subarachnoid hemorrhage, intracerebral hemorrhage, and stroke not otherwise specified. Briefly, FL-PR Stroke registry is a NINDS-funded multicenter initiative, as part of the Get With The Guidelines-Stroke program,[12] to create high-impact, culturally tailored interventions to identify disparities in delivery of stroke care among a diverse population of patients with significant Hispanic representation.

Information collected included patient demographics (age, sex, race/ethnicity [non-Hispanic white, non-Hispanic black, Hispanic in Florida, and Hispanic in Puerto Rico]), clinical characteristics (vascular risk factors and relevant medical history), arrival characteristics (mode of hospital arrival [via emergency medical services from home/scene, private transport, transfer from other hospital, or unknown], presenting National Institutes of Health Stroke Scale [NIHSS], presenting neurological symptoms [to identify disability-producing symptoms not captured by the NIHSS], the onset-to-door time [time from the stroke onset to arrival to the time of emergency department]), assessment characteristics (time from arrival to the initial head computed tomography [CT; door to CT (DTC)]), time from hospital arrival to initiation of intravenous thrombolysis (door-to-needle [DTN] time), and hospital-level characteristics (number of beds, academic status, annual stroke volume, and number of years in Get With The Guidelines-Stroke). Stroke severity at presentation was measured by the NIHSS. 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.

Study Population

From the total of 88 978 patients in the registry from January 2010 through April 2015 from 66 hospitals in Florida and 9 in Puerto Rico, 27 178 patients with ischemic stroke and TIA with documented NIHSS ≤5 at presentation were included in the current study. We further excluded those who arrived after 4 hours of symptom onset (n=19 432) and those with other known contraindications to thrombolysis (n=920; Figure 1). Thrombolysis was defined as any patient who has received intravenous recombinant tPA (tissue-type plasminogen activator) alteplase.

Statistical Analysis

The level of statistical significance was set at $P<0.05$. The data that support the findings of this study are available from the corresponding author on reasonable request.

We selected 3 categories of variables based on our understanding of the disease processes and factors influencing the clinician's decision to thrombolyze patients with mild stroke and thus affecting the therapeutic conduct of the clinicians. These factors included patient's clinical characteristics (demographics, vascular risk factors, time and mode of arrival, and stroke severity), hospital-based characteristics (size, experience, and academic status of the hospital), and geographic characteristics (4 regions in Florida and Puerto Rico). For patient characteristics, continuous variables were summarized as median with interquartile range (IQR), and categorical variables were presented as frequencies with percentages. For continuous variables, differences were assessed using the Student *t* test (mean comparison) if normally distributed or Wilcoxon–Mann–Whitney *U* test (median comparison). For categorical variables, the Pearson χ^2 test was used to compare the distributions between groups. Univariate analysis was performed to identify the specific characteristics of patients with mild stroke who received thrombolysis. To reduce multicollinearity among the correlated factors, we first conducted stepwise logistic regression to select the independent factors. We then conducted multivariable analysis with generalized estimating equations to account for clustering effect within each hospital and evaluated the associations between factors and thrombolysis administration. Potential interactions between hospital characteristics and race–ethnicity, region, and arrive time were also examined by including their interaction terms in the regression model. The goodness of fit of the regression was assessed by the quasi-likelihood information criterion—a modification of Akaike information criterion to apply to models fit by the generalized estimating equations approach. The final model (parsimonious model, quasi-likelihood information criterion, 5041) was close to the full model (quasi-likelihood information criterion, 5033) in goodness of fit.

Most variables had missing values in <5% of cases, except for the mode of arrival and insurance variables (18.9%, 7.2% missing, respectively). The complete case approach and the missing indicator approach were used to include the full sample for variables with a large proportion of missingness as described previously.[13] All statistical analyses were performed using SAS, version 9.3, software (SAS Institute).

Results

We included 6826 cases with acute mild ischemic stroke (documented NIHSS, ≤5) within 4 hours of symptom onset and no contraindications to thrombolysis (Figure 1). Median age was 72 (IQR, 21), 52.7% were men, 70.3% white, 12.9% black, 16.8% Hispanic, and the median presenting NIHSS was 2 (IQR, 3). A total of 1281 (18.7%) patients received thrombolysis.

Baseline characteristics of patients based on thrombolysis treatment are summarized in the Table. Patients who were thrombolyzed were younger, more likely to be men, and less likely to have preexisting vascular risk factors, including hypertension, diabetes mellitus, and dyslipidemia as compared with those who did not receive thrombolysis. Similarly, they were less likely to have had a history of stroke/TIA or coronary artery disease/myocardial infarction.

As described in the Table, thrombolyzed patients had a higher NIHSS (4 versus 2) and were more likely to have weakness (57.6% versus 48.4%) and aphasia (41.6% versus 31.0%) compared with those who did not receive thrombolysis. Presenting with altered level of consciousness (5.2% versus 7.7%) or other neurological symptoms (14.7% versus 16.8%) was inversely related to thrombolysis utilization.

Thrombolyzed patients were more likely to arrive early to the hospital after symptom onset than nonthrombolyzed patients (63 versus 81 minutes) and were more likely to have arrived via emergency medical services (64.1% versus 52.8%). The rate of thrombolysis administration decreased from 22% for those presenting between 0 and 2 hours from symptom onset to 4% in those presenting between 3.5 and 4 hours. The median DTC time was shorter in patients who received thrombolysis relative to those who did not (20 versus 30 minutes). Compared with nonthrombolyzed patients with mild stroke, thrombolyzed patients were more likely assessed

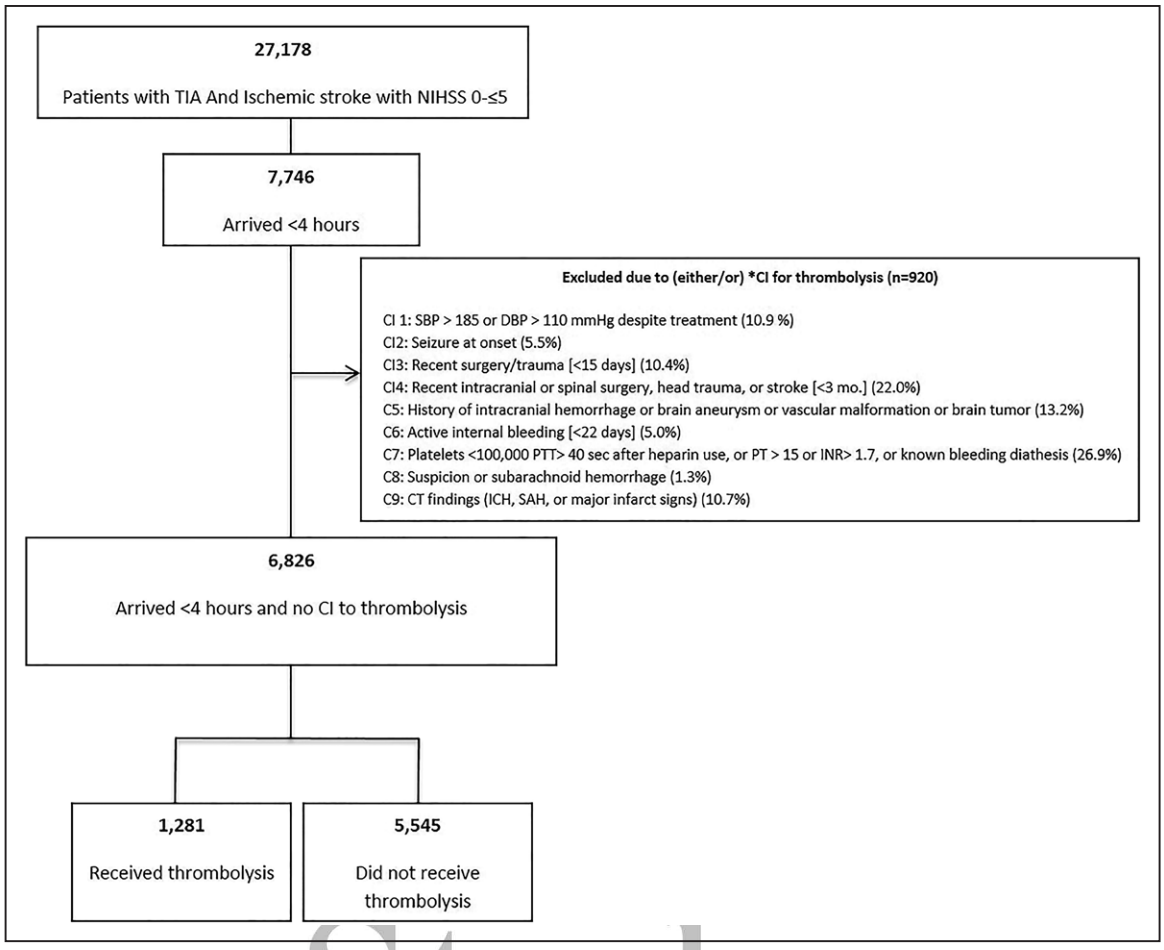

Figure 1. Flowchart of patients included in the study. CI indicates contraindication; CT, computed tomography; DBP, diastolic blood pressure; ICH, intracerebral hemorrhage; INR, international normalized ratio; NIHSS, National Institutes of Health Stroke Scale; PT, prothrombin time; PTT, partial thromboplastin time; SAH, subarachnoid hemorrhage; SBP, systolic blood pressure; and TIA, transient ischemic attack. *Contraindication.

in an academic hospital (31.1% versus 14.6%), hospitals with greater annual thrombolysis volumes (≥100; 60.7% versus 49.7%) and comprehensive stroke centers versus primary stroke centers (58.5% versus 51.6%), and were less likely treated at smaller hospitals (<250 beds; 15.7% versus 20.8%). Regional analysis of thrombolysis utilization showed a disproportionately higher rate of thrombolysis use in South Florida relative to all other regions in Florida.

After stepwise logistic regression, age, race, medical history of stroke/TIA, medical history of hypertension, medical history of peripheral vascular disease, final diagnosis stroke type, onset-to-arrival time, arrival time of day, NIHSS, aphasia language disturbance, DTC time, academic status, and region were retained for inclusion in multivariable analysis (Table I in the online-only Data Supplement). In the final multilevel multivariable model, early hospital arrival (arrive by 0–2 hours versus ≥3.5 hours; odds ratio [OR], 8.16; 95% confidence interval [CI], 4.76–13.98), higher NIHSS (OR, 1.87; 95% CI, 1.77–1.98), aphasia at presentation (OR, 1.35; 95% CI, 1.12–1.62), faster DTC time (OR, 1.81; 95% CI, 1.53–2.15), and presenting to an academic hospital (OR, 2.02; 95% CI, 1.39–2.95) were independent predictors of thrombolysis administration. In contrast, the odds of thrombolysis administration were lower in older patients (OR, 0.98; CI, 0.97–0.98), non-Hispanic blacks versus non-Hispanic whites (OR, 0.80; 95% CI, 0.69–0.93), those with a history of stroke/TIA (OR, 0.61; 95% CI, 0.52–0.72), history of hypertension (OR, 0.74; 95% CI, 0.64–0.87), history of peripheral vascular disease (OR, 0.67; CI, 0.46–0.97), arriving during off hours versus on hours (OR, 0.87; CI, 0.77–0.99), and hospitals in west central versus south (OR, 0.38; CI, 0.24–0.61). No significant interactions between hospital characteristics and race–ethnicity, region, and arrive time were found.

The overall rate of thrombolysis in patients with mild stroke presenting within the thrombolytic window increased over time from 15% in 2010 (10%) to 25% in 2015 (*P* value for trend, <0.0001; Figure 2).

In patients who received thrombolysis, the rate of symptomatic intracerebral hemorrhage within 36 hours of treatment was 2.5% and that of life-threatening, serious systemic hemorrhage was 0.3%.

Predictors of Fast Thrombolysis (DTN ≤60 Minutes) in Patients With Mild Ischemic Stroke

The median DTN time was 71 minutes (IQR, 43). Over time, DTN decreased from median 89 minutes (IQR, 44) in 2010 to 62 minutes (IQR, 46) in 2015 (P<0.0001). A

Table. Patient- and Hospital-Level Characteristics of Patients With Mild Ischemic Stroke (NIHSS≤5) in the FL-PR Stroke Registry Stratified by Thrombolysis Treatment

	All (n=6826)	Thrombolysis (n=1281)	No Thrombolysis (n=5545)	*P* Value
Clinical Characteristics				
Age, y; median (IQR)	72 (21)	68 (20)	72 (21)	<0.0001
Sex (men), %	3598 (52.7)	718 (56.1)	2880 (51.9)	<0.0001
Vascular risk factor, %				
Current smoker	1048 (15.4)	248 (19.4)	800 (14.4)	<0.0001
Hypertension	4713 (69.0)	745 (58.2)	3968 (71.6)	<0.0001
Diabetes mellitus	1839 (26.9)	304 (23.7)	1535 (27.7)	0.004
Dyslipidemia	2990 (43.8)	428 (33.4)	2562 (46.2)	<0.0001
Medical history, %				
AF	1067 (15.6)	187 (14.6)	880 (15.9)	0.26
CAD/prior MI	1733 (25.4)	260 (20.3)	1473 (26.6)	<0.0001
Previous stroke/TIA	1911 (28.0)	233 (18.2)	1678 (30.3)	<0.0001
Ethnicity, %				<0.0001
NH-white	4798 (70.3)	855 (66.7)	3943 (71.1)	
NH-black	881 (12.9)	174 (13.6)	707 (12.8)	
FL-Hispanic	889 (13.0)	173 (13.5)	716 (12.9)	
PR-Hispanic	258 (3.8)	79 (6.2)	179 (3.2)	
Medical insurance, %				<0.0001
Private*	2777 (40.7)	498 (38.9)	2279 (41.1)	
Medicare	2112 (30.9)	311 (24.3)	1801 (32.5)	
Medicaid/no insurance†	645 (9.5)	147 (11.5)	498 (9.0)	
Unknown	1292 (18.9)	325 (25.4)	967 (17.4)	
Arrival time, %				0.20
On hours	3241 (47.5)	629 (49.1)	2612 (47.1)	
Off hours	3585 (52.5)	652 (50.9)	2933 (52.9)	
Arrival time from onset, min (median, IQR)	76 (85)	63 (64)	81 (92)	0.001
Arrival time from onset, h				<0.0001
0–2	4861 (71.2)	1061 (82.8)	3800 (68.5)	
2–3.5	1600 (23.4)	206 (16.1)	1394 (25.1)	
≥3.5	365 (5.4)	14 (1.1)	351 (6.3)	
Final diagnosis TIA	1735 (25.4)	32 (2.5)	1703 (30.7)	<0.0001
NIHSS (median), IQR	2 (3)	4 (2)	2 (2)	<0.0001
Clinical signs/symptoms, %				
Weakness	3420 (50.1)	738 (57.6)	2682 (48.4)	<0.0001
Aphasia	2253 (33.0)	533 (41.6)	1720 (31.0)	<0.0001
Altered level of consciousness	494 (7.2)	67 (5.2)	427 (7.7)	0.002
Other neurological signs/symptoms	1120 (16.4)	188 (14.7)	932 (16.8)	0.06
No neurological signs/symptoms	57 (0.8)	2 (0.2)	55 (1.0)	0.003
Mode of arrival EMS				<0.0001
Yes	3748 (54.9)	821 (64.1)	2927 (52.8)	
No	2585 (37.9)	346 (27.0)	2239 (40.4)	

(*Continued*)

Table. Continued

	All (n=6826)	Thrombolysis (n=1281)	No Thrombolysis (n=5545)	*P* Value
Missing	493 (7.2)	114 (8.9)	379 (6.8)	
DTC time, min (median, IQR)	27(35)	20 (20)	30 (40)	<0.0001
DTC time (<25 min), %	3029 (46.7)	792 (65.0)	2237 (42.5)	<0.0001
Hospital characteristics				
Hospital size				<0.0001
Median bed (IQR)	468 (387)	466 (462)	468 (396)	
Small (<250 beds)	1355 (19.8)	201 (15.7)	1154 (20.8)	
Mid (250–450 beds)	1658 (24.3)	367 (28.7)	1291 (23.3)	
Large (>450 beds)	3813 (55.9)	713 (55.7)	3100 (55.9)	
Academic hospital, %				<0.0001
Yes	1207 (17.7)	398 (31.1)	809 (14.6)	
No	5619 (82.3)	883 (68.9)	4736 (85.4)	
GWTG, y; median (IQR)	8 (2)	7 (3)	8 (2)	<0.0001
No. of tPA-treated patients per y				<0.0001
Low volume (<100)	3291 (48.2)	503 (39.3)	2788 (50.3)	
High volume (≥100)	3535 (51.8)	778 (60.7)	2757 (49.7)	
State				
FL	6568 (96.2)	1202 (93.8)	5366 (96.8)	<0.0001
PR	258 (3.8)	79 (6.2)	179 (3.2)	
Stroke center type				
Primary	3054 (44.7)	477 (37.2)	2577 (46.5)	<0.0001
Comprehensive	3611 (52.9)	749 (58.5)	2862 (51.6)	
Not primary/comprehensive	161 (2.4)	55 (4.3)	106 (1.9)	
Region in FL				
South	2402 (36.6)	517 (43.0)	1885 (35.1)	<0.0001
East Central	918 (14.0)	205 (17.1)	713 (13.3)	
West Central	2286 (34.8)	232 (19.3)	2054 (38.3)	
North and Panhandle	962 (14.7)	248 (20.6)	714 (13.3)	

AF indicates atrial fibrillation; CAD, coronary artery disease; CT, computed tomography; DTC, door to computed tomography; EMS, emergency medical services; FL, Florida; GWTG, Get With The Guidelines; IQR, interquartile range; MI, myocardial infarction; NH, Non-Hispanic; NIHSS, National Institutes of Health Stroke Scale; PR, Puerto Rico; TIA, transient ischemic attack; and tPA, tissue-type plasminogen activator.

*Includes private insurance, Veterans Affairs, and other.

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

total of 461 (39%) patients had fast thrombolysis, defined as a DTN of ≤60 minutes. The characteristics of thrombolyzed patients based on fast versus slow DTN time are shown in Table II in the online-only Data Supplement. Accounting for all significant variables, presenting with aphasia (OR, 1.36; 95% CI, 1.01–1.84; *P*=0.04) and arrival via emergency medical services (OR, 1.89; 95% CI, 1.41–2.54; *P*<0.0001) to an academic institution (OR, 1.93; 95% CI, 1.28–2.91; *P*=0.0016) were independently associated with an increased chance of receiving fast thrombolysis. In contrast, a history of ischemic stroke was associated with reduced odds of fast thrombolysis treatment (OR, 0.64; 95% CI, 0.47–0.88; *P*=0.0067).

Similarly, onset-to-door time was inversely associated with faster DTN time, which decreased from a median of 72 minutes (IQR, 45) in those presenting within 0 to 2 hours of symptoms to the hospital to 36 minutes (IQR, 12) in those presenting between 3.5 and 4 hours from symptom onset. The median symptom onset-to-arrival time was longer in patients with fast DTN (67 minutes; IQR, 68) relative to those with delayed DTN (60 minutes; IQR, 53). In multivariable analysis, delay in hospital presentation was associated with higher odds of receiving fast thrombolysis (OR, 1.08 per every 10-minute delay; 95% CI, 1.05–1.11; *P*<0.001). Patients with fast DTN times had also rapid DTC times relative to those with delayed DTNs (15 versus 23 minutes).

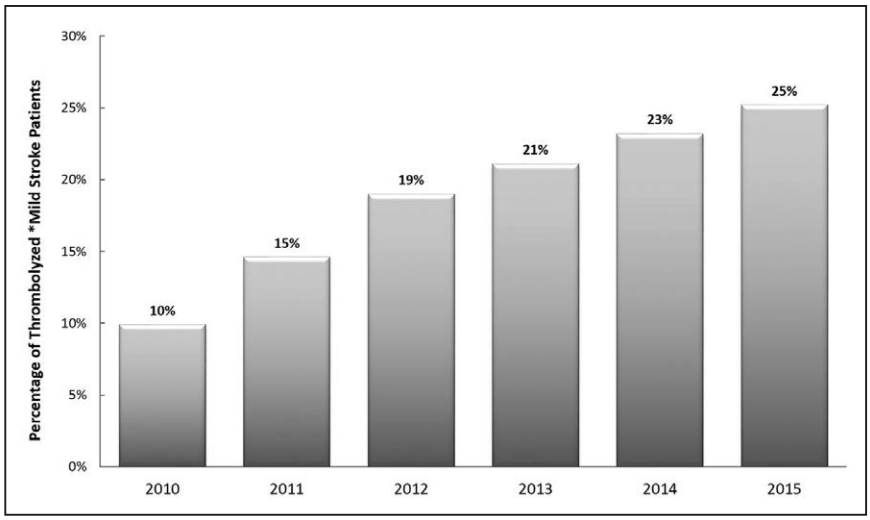

Figure 2. Trends of thrombolysis administration in patients with mild ischemic stroke by year (2010–2015). *Among patients with mild stroke who presented within 4 hours of symptom onset and did not otherwise have contraindications to thrombolysis.

Discussion

In this large cohort of patients with acute mild ischemic stroke without contraindications to thrombolysis, we identified multiple demographic, clinical, and hospital characteristics associated with administration of thrombolytic therapy. Treatment patterns in mild stroke differ by age, race, and neurological symptoms. Patients were more likely to receive thrombolysis if they arrived early, via emergency medical services, to a large academic hospital with more thrombolysis experience.

In clinical practice, the majority of patients with low NIHSS do not receive thrombolysis therapy, and physicians are inclined to withhold therapy because symptoms are perceived as nondisabling.[2] However, a low score on the NIHSS can still be associated with disabling symptomatology.[14] A subanalysis of the patients with baseline NIHSS ≤6 in the Trial of ORG 10172 in Acute Stroke showed neither the individual NIHSS items nor the type of neurological syndrome to be independent predictors of disability and long-term outcome.[15] More recent studies suggest that the majority of persistent neurological deficits, however mild, do affect functional outcomes and are, therefore, disability producing.[14] Indeed, recent scientific statements have emphasized that mild but disabling symptoms should be treated with thrombolytic therapy.[16] Despite this, our results show that >80% of patients with mild stroke do not receive thrombolysis, even if they present within the time window and have no other contraindications for treatment. Uncontrolled hypertension and a history of stroke in combination with diabetes mellitus are considered as relative thrombolysis contraindications in certain patients with all severity strokes.[8] In our study, the lower rates of thrombolysis in those with a history of stroke and hypertension may represent the clinician's uncertainty on thrombolysis utilization in patients with mild stroke with concurrent other relative thrombolysis contraindications. Our results suggest that many factors beyond the clinical characteristics play a role in the clinician's decision to use thrombolysis therapy in a mild stroke patient, including time of presentations, mode of hospital arrival, and the type and the size of the hospital.

In recent years, an increase in the proportion of patients with mild stroke treated with thrombolysis has been reported.[17–19] Our study supports these trends, with the frequency of thrombolysis more than doubling in our study population during a span of 5 years. This further emphasizes the importance of completing studies to look at the safety and efficacy of thrombolysis in mild stroke. Two randomized controlled trials have aimed to answer these questions, although the eligibility criteria differ between the studies,[10,11] and one recently stopped enrollment because of slow recruitment.[10]

The efficacy of thrombolytic therapy in ischemic stroke is highly time dependent, and guidelines recommend a DTN time of ≤60 minutes.[20] Early treatment is associated with reduced mortality and lower complication rates.[21,22] In prior studies, greater stroke severity, arrival by ambulance, and arrival during regular hours have been shown to be factors most strongly associated with fast DTN times.[21] In our study, the overall rate of thrombolytic administration for patients with mild stroke significantly dropped with later presentation to the hospital. Patients arriving at the emergency department within the first 2 hours of symptoms had a 5.5-fold higher rate of IV thrombolytic therapy than did patients arriving between 3.5 and 4.5 hours. Of concern, DTN was significantly slower in those arriving earlier. The absolute DTN time was 2-fold faster in patients arriving between 3.5 and 4.5 hours compared with those arriving within the first 2 hours. Other groups have reported a similar inverse relationship between onset-to-door and DTN in patients with all severity strokes.[23,24] One possible explanation is selection bias, where the majority of cases in whom treatment could take too long to be initiated within the determined timelines were excluded from receiving the therapy. Alternatively, the shorter treatment times could also reflect a more rapid response time on the part of emergency and stroke teams to implement a therapy when the available time is limited. The fact that DTN times were shorter in comprehensive stroke centers is a testament to the latter, where systems of care have been modified to improve the delivery of care in a more expedited manner.

There is a natural tendency on the part of the patients with mild symptoms to wait and watch rather than to immediately present to the emergency department. Similarly, physicians are inclined to obtain additional information and advanced neuroimaging to improve their diagnostic certainty. The perception that these patients have good outcomes and the fear of

intracranial hemorrhage among other side effects of treatment may all play a role in withholding or delaying thrombolysis. In this study, we identified a 2.5% symptomatic intracranial hemorrhage rate, which compares favorably with the 4.7% reported for all thrombolyzed patients within Get With The Guidelines-Stroke.[25] Efficacy of thrombolysis in this population is difficult to ascertain from retrospective data given the many confounders and bias by indication. One ongoing prospective study of patients with mild and rapidly improving stroke[26] and randomized clinical trials[10,11] will shed light on the impact of thrombolysis in mild stroke.

Our study has several limitations. The FL-PR Stroke registry is a voluntary program, including only Get-With-The-Guidelines participating hospitals, which are generally larger teaching hospitals with higher than average thrombolytic volumes as compared with nonparticipating hospitals. It is, therefore, likely that our data overrepresent the percentage of patients with mild stroke treated with thrombolysis. Furthermore, mild stroke was defined using NIHSS and not level of disability, and we excluded those with missing NIHSS value at presentation. It is plausible that patients with mild deficits are more likely to have missing NIHSS values, as compared with those with more severe symptoms, which may decrease the estimated rate of thrombolysis in this population. Brain imaging information was inconsistently documented in our registry and not analyzed as part of this report. Advanced imaging findings predict outcomes in TIA and minor stroke[27,28] and, therefore, can affect the decision to administer thrombolysis treatment. Finally, we do not report on the outcomes of mild stroke with thrombolysis because this article focuses on identifying characteristics that are associated with thrombolysis utilization, not thrombolysis outcome. Despite these limitations, our study is the largest cohort to report the current practice pertaining to acute thrombolytic treatment of patients with mild stroke.

Although randomized controlled trials are needed to provide robust clinical evidence for use of thrombolysis in mild stroke, data from large multicenter registries, such as ours, offer an insight to the practice patterns in the real world and can guide design and implement successful educational interventions and future studies to improve the care of those with mild strokes.

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Disclosures

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Predictors of Thrombolysis Administration in Mild Stroke: Florida-Puerto Rico Collaboration to Reduce Stroke Disparities

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SUPPLEMENTAL MATERIAL

Predictors of Thrombolysis Administration in Mild Stroke: Florida Puerto Rico Collaboration to Reduce Stroke Disparities

Supplemental Table I: Stepwise logistic regression to determine the effect of each factor included in the final model of multivariate analysis among mild stroke patients with thrombolysis treatment as outcome.

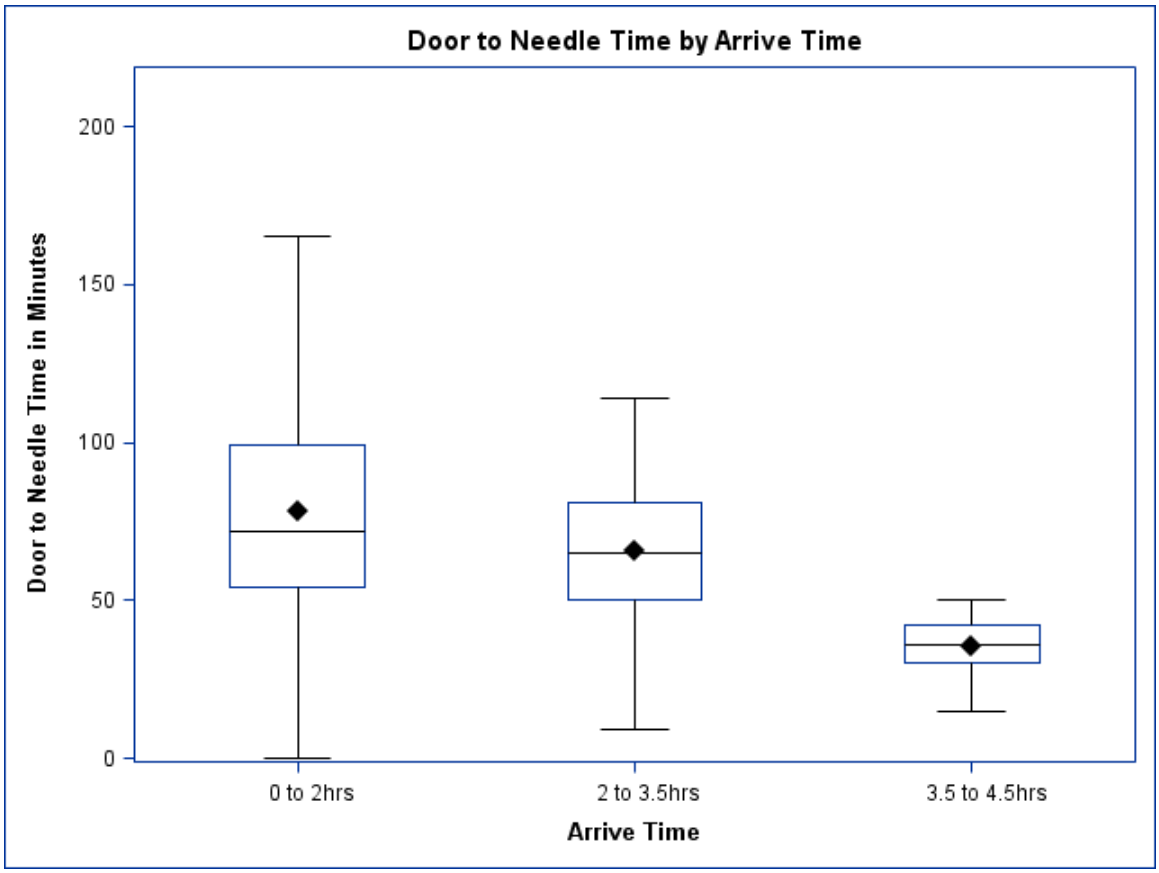
Demographics	**Univariate analysis**	**OR (CI)**	**P Value**
Age	Increase by 1 year	0.98 (0.97,0.98)	<.0001
Race	NH-Black vs NH-White	0.80 (0.69,0.93)	0.00
Race	FL-Hispanic vs NH-White	0.95 (0.75,1.19)	0.63
Race	PR-Hispanic vs NH-White	0.90 (0.53,1.53)	0.71
Medical history Stroke/TIA	Yes vs No	0.61 (0.52,0.72)	<.0001
Medical history Hypertension	Yes vs No	0.74 (0.64,0.87)	0.00
Peripheral Vascular Disease	Yes vs No	0.67 (0.46,0.97)	0.04
Onset to arrival	0 to 2 hrs vs 3.5 hrs and above	8.16 (4.76,13.98)	<.0001
Onset to arrival	2 to 3.5 hrs vs 3.5 hrs and above	3.83 (2.29,6.39)	<.0001
Arrive time of day	Off hours vs On hours	0.87 (0.77,0.99)	0.04
NIHSS	Increase by 1	1.87 (1.77,1.98)	<.0001
Aphasia	Yes vs No	1.35 (1.12,1.62)	0.00
Door to CT within 25 mins	Missing vs No	1.03 (0.65,1.63)	0.92
Door to CT within 25 mins	Yes vs No	1.81 (1.53,2.15)	<.0001
Teaching hospital	Yes vs No	2.02 (1.39,2.95)	0.00
Region	East Central vs South	1.02 (0.62,1.67)	0.94
Region	North and Panhandle vs South	1.24 (0.68,2.28)	0.49
Region	West Central vs South	0.38 (0.24,0.61)	<.0001

Supplemental Table II: Clinical and hospital characteristics of thrombolyzed mild ischemic stroke patients by arrival to treatment time

Clinical Characteristics	All thrombolyzed (n=1,190)	Door to Needle ≤ 60 min (n=461)	Door to needle > 60 min (n=729)	p value
Age (yrs), median (IQR)	68 (20)	68 (21)	69 (19)	0.34
Sex (male), %	669 (56.2)	266 (57.7)	403 (55.28)	0.41
Vascular Risk Factor, %				
Current smoker	221 (18.6)	88(19.1)	133 (18.2)	0.71
Hypertension	698 (58.7)	252 (54.7)	446 (61.2)	0.02
Diabetes mellitus	277 (23.3)	96 (20.8)	181 (24.8)	0.11
Dyslipidemia	405 (34.0)	134 (29.1)	271 (37.2)	0.004
Medical History, %				
AF	182 (15.3)	64 (13.8)	118 (16.2)	0.28
CAD/prior MI	246 (20.7)	88 (19.1)	158 (21.7)	0.28
Previous stroke/TIA	212 (17.8)	58 (12.6)	154 (21.1)	<.0001
Ethnicity, %				<.0001
NH- white	789 (66.3)	281 (61.0)	508 (69.7)	
NH- black	165 (13.9)	61 (13.2)	104 (14.3)	
FL-Hispanic	164 (13.8)	87 (18.9)	77 (10.6)	
PR-Hispanic	72 (6.1)	32 (6.9)	40 (5.5)	
Medical Insurance, %				<.0001
Private*	448 (37.7)	144 (31.2)	304 (41.7)	
Medicare	287 (24.1)	99 (21.5)	188 (25.8)	
Medicaid/no insurance**	137 (11.5)	55 (11.9)	82 (11.3)	
Unknown	318 (26.7)	163 (35.4)	155 (21.3)	
Arrival Time from Onset (min), median (IQR)	61 (58)	67 (68)	60 (53)	<.0001
Arrival Time (%)				0.01
On –hours	48.5	52.9	45.7	
Off- hours	51.5	47.1	54.3	
Arrival time				

0-2 hours 2-3.5 hours 3.5-4.5 hours	1015 (85.3) 166 (14.0) 9 (0.8)	376 (81.6) 76 (16.5) 9 (2.0)	639 (87.7) 90 (12.4) 0 (0.0)	<.0001
NIHSS , median (IQR)	4(2)	4 (2)	4(3)	0.04
Clinical Signs/symptoms, %				
Weakness	672 (56.4)	243 (52.7)	429 (58.9)	0.03
Aphasia	491 (41.3)	183 (39.7)	308 (42.3)	0.38
Altered level of Consciousness	56 (4.7)	26 (5.6)	30 (4.1)	0.22
Other Neurological Signs/symptoms	177 (14.9)	60 (13.0)	117 (16.1)	0.15
No Neurological Signs/symptoms	2 (0.2)	0 (0.0)	2 (0.3)	0.26
Mode of Arrival EMS Yes No Missing	 788 (66.2) 290 (24.4) 112 (9.4)	 339 (73.5) 79 (17.1) 43 (9.3)	 449 (61.6) 211 (28.9) 69 (9.5)	<.0001
Door to CT time (% <25 min)	755 (66.1)	363 (83.6)	392 (55.4)	<.0001
Hospital Characteristics				
Hospital Size Small (<250beds) Mid (250-450 beds) Large (>450)	 189 (15.9) 357 (30.0) 644 (54.1)	 75 (16.3) 144 (31.2) 242 (52.5)	 114 (15.6) 213 (29.2) 402 (55.1)	0.66
Academic hospital, %	348 (29.2)	156 (33.8)	192 (26.3)	0.006
Years in GWTG, median (IQR)	7 (3)	7 (3)	8 (3)	0.06
State FL PR	 1118 (94.0) 72 (6.1)	 429 (93.1) 32 (6.9)	 689 (94.5) 40 (5.5)	0.31

AF=atrial fibrillation, CAD= Coronary Artery Disease, MI=Myocardial Infarction. NH-White= Non-Hispanic White, NH-black= Non-Hispanic black. EMS= Emergency Medical Services. *Includes Private insurance, VA and other.** Includes Medicaid, self-pay and No insurance.



Supplemental Figure I: The distribution of Door to Needle time (DTN) based on symptoms onset to hospital arrival time.