

# Characteristics, Hospital Factors, and Temporal Trends in Door-to- Needle Times within 60 Minutes for Acute Ischemic Stroke

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# Disclosures

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## Author Disclosure Information:

Dr. Fonarow receives research support from the NIH (significant), served as a consultant to Pfizer, Merck, Schering Plough, Bristol Myers Squibb, and Sanofi-Aventis (all modest); received honoraria from Pfizer, Merck, Schering Plough, Bristol Myers Squibb, and Sanofi-Aventis (all significant); and is an employee of the UCLA, which holds a patent on retriever devices for stroke (significant). Dr. Smith receives research support from the NIH (NINDS R01 NS062028), the Canadian Stroke Network, the Canadian Institutes of Health Research, and the Heart and Stroke Foundation of Canada, and has served on an advisory board for Genentech. Dr. Saver is a scientific consultant regarding trial design and conduct to CoAxia, Concentric Medical, Talacris, Ferrer, Photothera, Brainsgate, Sygnis, and Ev3; received lecture honoraria from Ferrer; and is an employee of UCLA, which holds a patent on retriever devices for stroke. Dr. Reeves receives salary support from the Michigan Stroke Registry. Dr. Bhatt receives research support (significant) from Astra Zeneca, Bristol-Myers Squibb, Eisai, Sanofi Aventis, and The Medicines Company. Dr. Grau-Sepulveda is a member of the Duke Clinical Research Institute. Dr. Olson is a member of the Duke Clinical Research Institute. Dr. Hernandez is a member of the Duke Clinical Research Institute. Dr Hernandez is a recipient of an AHA Pharmaceutical Roundtable grant (0675060N) and has received a research grant from Johnson & Johnson; has received honoraria from AstraZeneca and Amgen. Dr. Peterson has received research grants from Lilly, Johnson & Johnson, and Bristol-Myers Squibb, Sanofi-Aventis, and Merck-Schering Plough partnership. Dr. Schwamm serves as a consultant to the Research Triangle Institute and to the Massachusetts Department of Public Health and serves on the Steering Committee for Lundbeck's DIAS4 clinical trial.

# Background

- Tissue plasminogen activator (tPA) is a proven intervention for acute ischemic stroke and the benefits of tPA are strongly time dependent.
- Because of the importance of rapid treatment, national guidelines recommend an arrival to treatment initiation (door-to-needle [DTN]) time of 60 minutes or less.
- However, patient characteristics and hospital factors associated with DTN times  $\leq$  60 minutes have not been well studied.

# Objectives

- The objectives of this study were to evaluate the presenting characteristics of acute ischemic stroke patients treated with intravenous tPA in whom a DTN time  $\leq 60$  minutes was achieved, patient and hospital characteristics associated with DTN times  $\leq 60$  minutes, hospital level variation in DTN, and temporal trends in timely thrombolytic care.

# Methods

- GWTG Stroke is an ongoing, voluntary, observational registry and a continuous performance improvement program for patients hospitalized with stroke or TIA.
- A web-based Patient Management Tool provides decision support at the point-of-care, on-demand reporting and patient education features (Outcome, Cambridge, MA).
- Patient data were abstracted by trained hospital personnel. These included demographics, medical history, initial CT findings, in-hospital treatment and events, discharge treatments, treatment contraindications, counseling, in-hospital mortality, and discharge destination.
- The eligibility of all acute stroke admissions was confirmed prior to chart abstraction.

# Methods: Study Population

- Between April 1, 2003 and September 30, 2009, 595,172 acute ischemic stroke admissions were submitted by 1259 participating hospitals.
- We excluded 465,269 patients who did not present within 3 hours symptom onset. There were 2823 patients arriving to the hospital within 3 hours of symptom onset, but treated with tPA beyond 3 hours after symptom onset, who were excluded.
- There were 472 patients treated with experimental thrombolytic therapy who were also excluded.
- Of the 129,431 ischemic stroke cases presenting during the study period and time eligible, 25,504 (19.7%) were treated with intravenous tPA within 3 hours of symptom onset in 1082 hospitals.

# Statistical Methods

- Patient demographic and clinical variables and hospital-level characteristics were compared between patients with and without DTN time  $\leq 60$  minutes.
- Pearson Chi-square test and Wilcoxon rank-sum tests were used to compare the categorical and continuous variables.
- The relationships between patient and hospital characteristics associated with DTN times  $\leq 60$  minutes were 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.
- Temporal trends in DTN times  $\leq 60$  minutes by both calendar time and program time participating in GWTG-Stroke were evaluated.

# Results

- During the 6.5 year study time period, 25,504 acute ischemic stroke patients were treated with tPA within 3 hours of symptom onset at 1082 hospital sites.
- Among patients arriving within 3 hours of onset and receiving intravenous tPA within 3 hours of last known well time, the mean DTN time for tPA administration was  $79.3 \pm 28.1$  minutes and the median 78 minutes (25<sup>th</sup>-75<sup>th</sup> 60-98 minutes).
- There were 6790 (26.6%) patients with DTN times  $\leq 60$  minutes and 18,714 (73.4%) with DTN times  $>60$  minutes.

# Patient Characteristics

	DTN Times ≤60 Minutes N=6790	DTN Times >60 Minutes N=18,714	P value
Age, Years, Mean, (SD)	68.9 (14.5)	70.1 (14.8)	<0.0001
Sex, Female	46.0%	50.3%	<0.0001
Race-Ethnicity			
White, Non-Hispanic	77.0%	75.7%	0.0115
Black	10.9%	12.7%	
Asian	2.0%	2.1%	
Hispanic	5.4%	5.3%	
Arrival by EMS (vs. Private Transport)	85.9%	84.2%	<0.0001
Arrival On Hours (vs. Off Hours)	50.7%	45.5%	<0.0001
Time from Symptom Onset to Arrival, Minutes, Median, (25 <sup>th</sup> -75 <sup>th</sup> )	60 (40-95)	49 (34-65)	<0.0001
NIHSS*, Median, (25 <sup>th</sup> 75 <sup>th</sup> )	12 (8-18)	12 (7-18)	0.1113
0-9	29.8%	30.9%	0.1111
10-14	20.2%	18.8%	
15-20	21.8%	19.2%	
21-42	13.0%	13.8%	
Not documented	15.2%	17.3%	

# Patient Characteristics

	DTN Times ≤60 Minutes N=6790	DTN Times >60 Minutes N=18,714	P value
<i>Past Medical History</i>			
Atrial Fibrillation/Flutter	22.1%	25.0%	<0.0001
Prior Stroke/Transient Ischemic Attack	20.7%	25.1%	<0.0001
Coronary Artery Disease/Prior MI	27.7%	29.5%	0.0099
Carotid Stenosis	3.2%	3.3%	0.7782
Peripheral Vascular Disease	3.2%	3.8%	0.0367
Prosthetic Heart Valve	1.1%	1.4%	0.0588
Diabetes Mellitus	23.5%	24.5%	0.1032
Hypertension	75.0%	76.5%	0.0168
Smoker	22.8%	20.1%	<0.0001
Dyslipidemia	38.0%	39.0%	0.1444

# Patient Characteristics

	DTN Times ≤60 Minutes N=6790	DTN Times >60 Minutes N=18,714	P value
<i>Hospital Diagnostics and Treatment Intervals</i>			
Time from Arrival to CT Scan, Minutes, Median, (25 <sup>th</sup> -75 <sup>th</sup> )	18 (11-26)	24 (15-36)	<0.0001
Door to CT Scan ≤ 25 Minutes	68.5%	53.0%	<0.0001
Time from Symptom Onset to tPA Treatment, Minutes, Median, (25 <sup>th</sup> -75 <sup>th</sup> )	110 (88-144)	145 (124-165)	<0.0001
DTN Time, Minutes, Mean (SD) Median (25 <sup>th</sup> -75 <sup>th</sup> )	46.0 (12.2) 49 (40-55)	91.4 (21.7) 88 (74-105)	<0.0001

# Hospital Characteristics

	DTN Time ≤60 Minutes	DTN Time >60 Minutes	P value
Annual Volume of Ischemic Stroke Admissions			
301+	15.6%	14.7%	0.0003
101-300	64.5%	63.2%	
0-100	19.8%	22.1%	
Annual Volume of tPA Administration			
20+	23.5%	15.4%	<0.0001
11-20	34.8%	32.3%	
0-10	41.7%	52.4%	
Hospital Size, Beds, Median, (25 <sup>th</sup> -75 <sup>th</sup> )	400 (270-588)	380 (267-558)	0.0002
Hospital Type			
Non-Academic	33.5%	36.0%	0.0005
Academic	62.9%	60.9%	
TJC Primary Stroke Center	68.5%	65.9%	<0.0001
Hospital Region			
West	21.8%	21.0%	<0.0001
South	30.9%	33.0%	
Midwest	17.0%	18.3%	
Northeast	30.4%	27.7%	

## Patient and Hospital Characteristics Associated with DTN ≤60 Minutes

Variables	Adjusted Odds Ratio	Lower 95% CI	Upper 95% CI	P-Value
<b>Demographics</b>				
Age, Per 10 Year Increase	0.92	0.90	0.95	<.0001
Sex, Female	0.87	0.81	0.93	0.0001
Race/Ethnicity (reference Non-Hispanic Whites)				
Black	0.80	0.71	0.89	0.0001
Hispanic	0.96	0.82	1.13	0.6598
Other	0.98	0.83	1.15	0.7916
<b>Admission Characteristics</b>				
Arrival Mode Emergency Medical Services	1.10	0.97	1.23	0.1275
Arrival Time On Hours	1.27	1.18	1.37	<.0001
Symptom Onset to Arrival Times, Per 10 Minutes Increase	1.23	1.22	1.25	<.0001
NIHSS (Reference: 0-9)				
10-14	1.37	1.25	1.51	<.0001
15-20	1.58	1.44	1.73	<.0001
21-42	1.37	1.23	1.54	<.0001

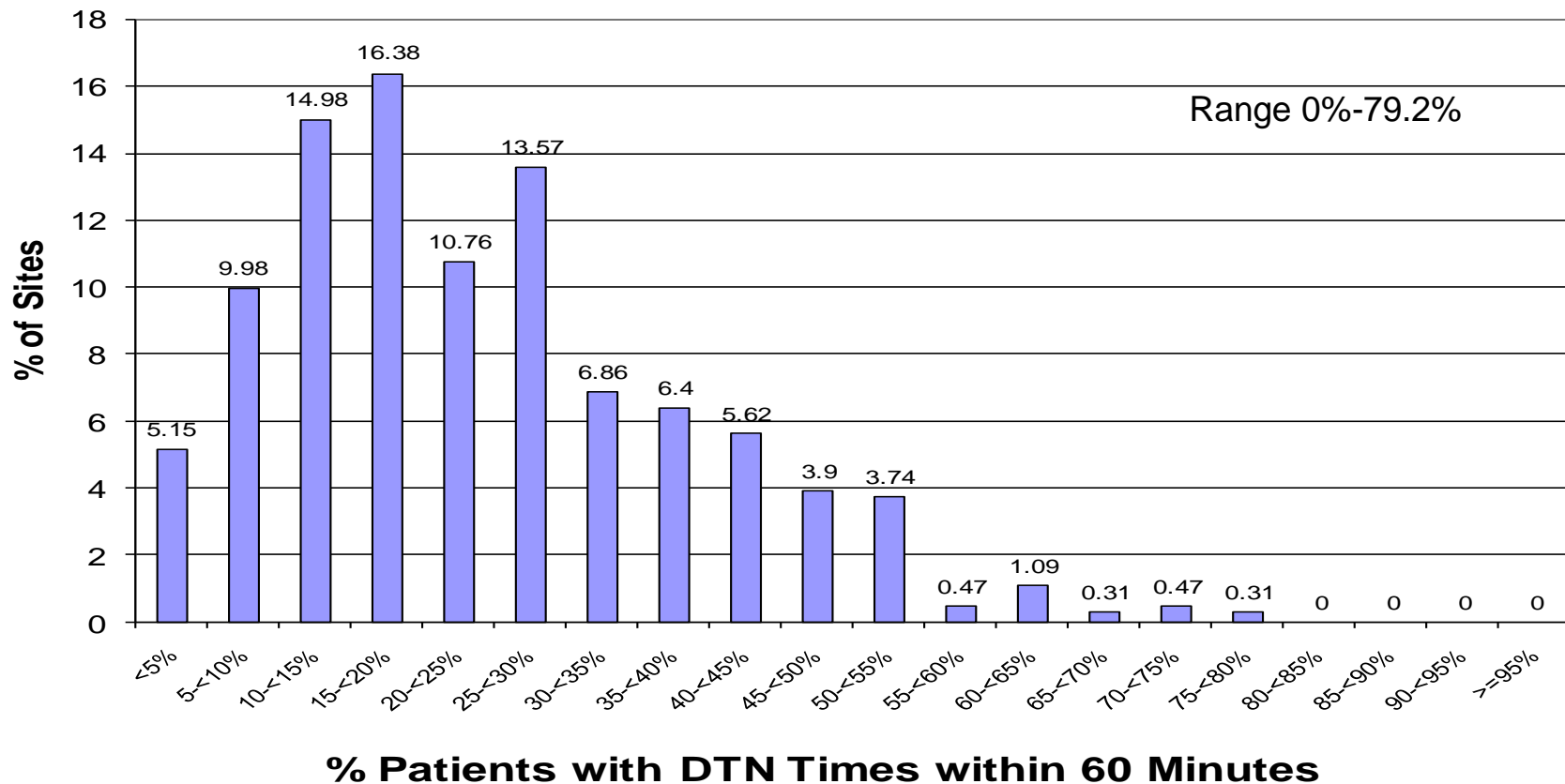
## Patient and Hospital Characteristics Associated with DTN ≤60 Minutes

Variables	Adjusted Odds Ratio	Lower 95% CI	Upper 95% CI	P-Value
<b>Medical History</b>				
Atrial Fibrillation	0.89	0.81	0.97	0.0077
Prosthetic Heart Valve	0.75	0.55	1.00	0.0539
Coronary Artery Disease/Prior Myocardial Infarction	0.95	0.86	1.04	0.2313
Carotid Stenosis	1.01	0.84	1.22	0.9225
Diabetes Mellitus	0.89	0.83	0.97	0.0051
Peripheral Vascular Disease	0.89	0.73	1.08	0.2444
Hypertension	1.01	0.94	1.08	0.8625
Smoker	1.00	0.92	1.10	0.9637
Dyslipidemia	1.01	0.94	1.09	0.7223
Stroke/Transient Ischemic Attack	0.81	0.74	0.88	<.0001

## Patient and Hospital Characteristics Associated with DTN ≤60 Minutes

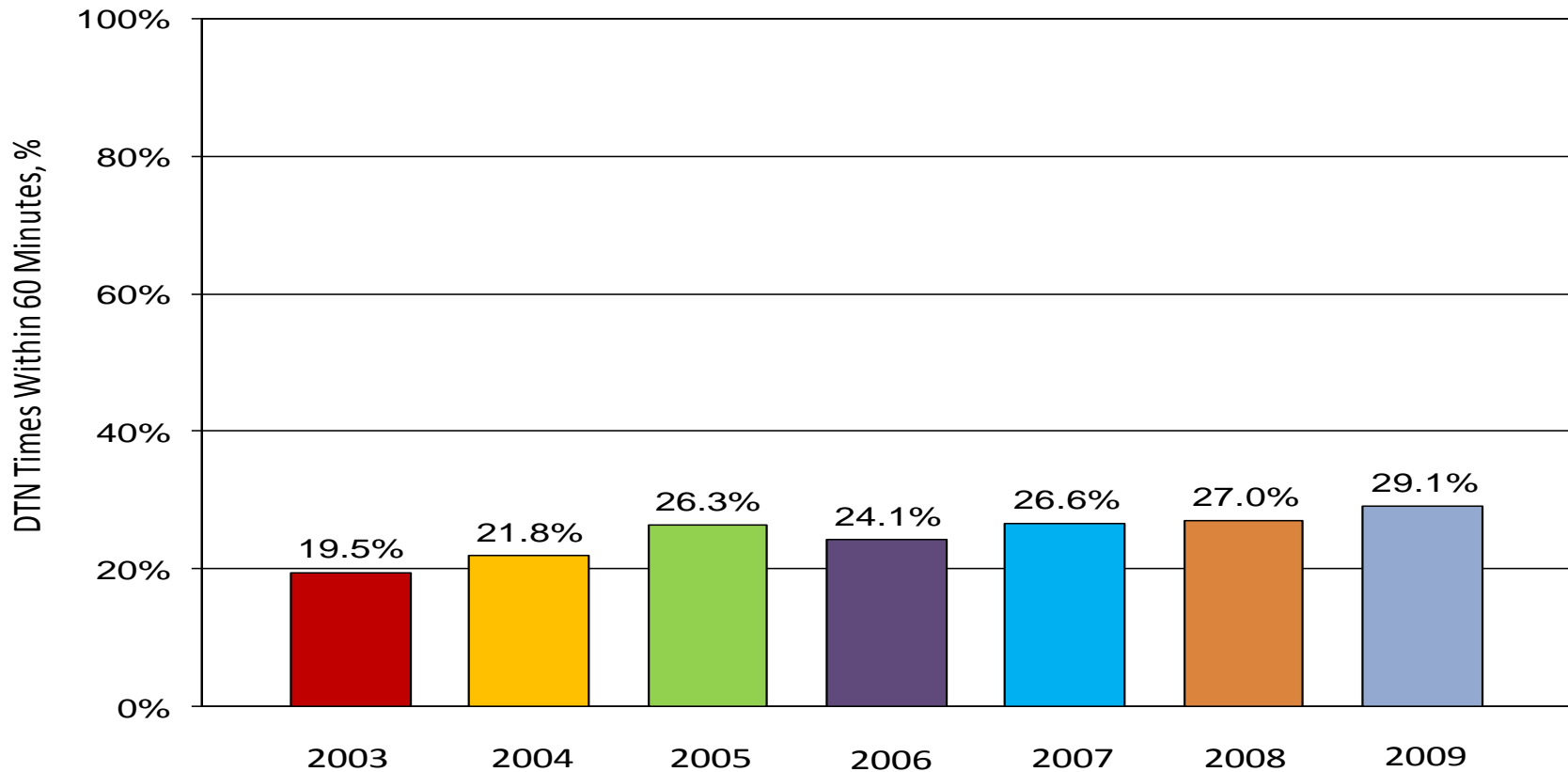
Variables	Adjusted Odds Ratio	Lower 95% CI	Upper 95% CI	P-Value
<b>Hospital Characteristics</b>				
The Joint Commission Primary Stroke Center	1.02	0.88	1.17	0.7903
Number of Hospital Beds, Per 200 Beds Increase	0.96	0.91	1.01	0.1260
Academic hospital	1.01	0.89	1.15	0.8233
Hospital Region (Reference Northeast)				
Midwest	1.05	0.88	1.25	0.5826
South	0.97	0.83	1.14	0.7273
West	0.89	0.74	1.07	0.2237
Ischemic Stroke Admits/Year (Reference ≤100)				
>100-300	0.86	0.74	1.00	0.0467
>300	0.53	0.38	0.75	0.0003
Intravenous tPA Patients/Year (Reference ≤10)				
>10-20	1.38	1.18	1.61	<.0001
>20	2.03	1.51	2.74	<.0001

# Hospital Variation in the Proportion of Ischemic Stroke Patients with DTN Times ≤60 Minutes



Among hospitals with at least 10 tPA patients (N=641)

## Temporal Trends in the Proportion of Patients with DTN Times $\leq 60$ Minutes 2003-2009



# Limitations

- Data were collected by medical chart review and are dependent upon the accuracy of documentation and abstraction.
- A number of additional factors that may be important in timely reperfusion were not captured in GWTG-Stroke and could not be analyzed.
- Residual measured and unmeasured confounding variables may have influenced the findings.
- Hospitals participating in GWTG-Stroke are self-selected and tend to be larger, teaching institutions, and have an interest in stroke quality improvement.
- These findings may not apply to hospitals that differ in patient characteristics or care patterns from GWTG-Stroke Hospitals.

# Conclusions

- Less than one-third of patients treated with intravenous tPA had DTN times  $\leq 60$  minutes.
- Patient factors most strongly associated with DTN times  $\leq 60$  minutes included younger age, male, white race, no prior stroke, arrival during regular hours, arrival times closer to 3 hours, and greater stroke severity. Hospital factors included greater annual volumes of tPA treated stroke patients, but not primary stroke center or teaching hospital status.
- There is wide variation among hospitals in the proportion of patients treated within 60 minutes of arrival.
- There has been only modest improvement in the proportion of patients with DTN times  $\leq 60$  minutes over the past 6.5 years.

# Clinical Implications

- These findings support the need for a targeted initiative to improve the timeliness of intravenous tPA in acute ischemic stroke to maximize the clinical benefit.
- The ASA has recently launched the Target: Stroke initiative to increase the portion of patients with DTN times  $\leq 60$  minutes.

These results have been published online in the journal *Circulation*