

Timeliness of Tissue-Type Plasminogen Activator Therapy in Acute Ischemic Stroke: Patient Characteristics, Hospital Factors, and Outcomes Associated With Door-to-Needle Times Within 60 Minutes

Real-world retrospective, multi-center analysis

Objective

- To determine the presenting characteristics of acute ischemic stroke patients treated with tPA within 3 hours of symptom onset who had door-to-needle times of ≤ 60 minutes, patient and hospital characteristics associated with ≤ 60 -minute door-to-needle treatment time, in-hospital clinical outcomes of tPA treatment within ≤ 60 minutes, and temporal trends in timely thrombolytic care

This retrospective, multi-center study analyzed data from the Get With the Guidelines-Stroke (CWTG-Stroke) national registry of acute ischemic stroke patients who were treated with intravenous tissue-type plasminogen activator (tPA) within 3 hours of symptom onset from April 1, 2003 to September 30, 2009. National guidelines recommend that hospitals complete the clinical and imaging evaluation of acute ischemic stroke patients and initiate intravenous tPA therapy within 60 minutes of patient arrival. This study aimed to determine the presenting characteristics of acute ischemic stroke patients treated with tPA who had door-to-needle times of ≤ 60 minutes, patient and hospital characteristics associated with door-to-needle treatment times of ≤ 60 minutes, in-hospital clinical outcomes of tPA treatment in ≤ 60 minutes, and temporal trends in timely thrombolytic care.

The GWTG-Stroke database included 595,172 acute ischemic stroke admissions submitted by 1,259 hospitals between April 1, 2003 and September 30, 2009. This study used only patients who were treated with intravenous tPA within 3 hours of symptom onset, resulting in 25,504 (19.7%) patients from 1,082 hospitals. Patient data included demographics, medical history, onset time of stroke symptoms, arrival time, in-hospital diagnostic studies, treatments and procedures, discharge treatments and counseling, tPA treatment initiation time, tPA complications, in-hospital mortality, discharge destination, and stroke severity.

The analysis compared patient demographic and clinical variables, hospital level characteristics, and clinical outcomes between patients with and without door-to-needle time of ≤ 60 minutes. These relationships were further examined with multivariable logistic regression models. The study used generalized estimation equations (GEEs) to generate unadjusted and adjusted models and to determine significant confounders, including but not limited to age, race, sex, stroke severity, onset-to-arrival time, and average number of patients treated with tPA annually at each hospital. Additionally, the study used GEE models to analyze the relationship between door-to-needle time and tPA complications and the long-term temporal trends in door-to-needle time of ≤ 60 minutes.

Among the 25,504 ischemic stroke patients treated with tPA, door-to-needle time was ≤ 60 minutes in only 6,790 (26.6%) patients. The mean door-to-needle time for intravenous tPA administration was 79.3 ± 28.1 minutes. Patient factors most strongly associated with door-to-needle time of ≤ 60 minutes were younger age, male gender, white race, no prior stroke, greater time since symptom onset, and arrival during on-hours (Monday through Friday, 7 AM to 5 PM) and by emergency medical service transport. Hospital characteristics associated with ≤ 60 -minute door-to-needle time included greater number of patients treated with intravenous tPA annually and lower annual number of stroke admissions. The proportion of patients with door-to-needle times of ≤ 60 minutes varied widely by hospital (0% to 79.2%) and increased by approximately 1.6% per year from 19.5% in 2003 to 29.1% in 2009 ($P < 0.0001$). Despite similar stroke severity, in-hospital mortality was lower and symptomatic intracranial hemorrhage was less frequent for patients with door-to-needle times of ≤ 60 minutes compared with patients with door-to-needle times of > 60 minutes.

The authors acknowledged some limitations of this analysis. Lower mortality had not previously been reported with timelier tPA therapy, so the authors urged replication of their analysis. The hospitals in this study were self-selected, so it is likely that other U.S. hospitals would have a smaller portion of patients with door-to-needle time of ≤ 60 minutes than those in this study. Some additional factors that may be important for timely treatment with tPA were not captured or analyzed in this study, including prehospital notification by emergency medical service, existence of a regional stroke system of care with routing of stroke patients directly to designated stroke centers, and availability of stroke neurologists. Finally, no information was collected on post-discharge stroke-related outcomes in the GWTG-Stroke Program. Therefore, whether door-to-needle times of within 60 minutes have longer term impacts on functional outcomes was not able to be ascertained.

The study concluded that older patients, non-white patients, women, and those with less severe strokes or arriving during off-hours were less likely to receive timely treatment. Additionally, hospitals with less experience in providing tPA to ischemic stroke patients were less likely to provide thrombolytic therapy within 60 minutes. The authors argued that their findings support the need for a targeted initiative to improve the timeliness of reperfusion in acute ischemic stroke. They suggested that aspects of the GWTG-Stroke toolkit, intervention strategies, and recognition system be updated to highlight the importance of the ≤ 60 -minute door-to-needle target.

Table 3 from the paper summarizes how patient and hospital characteristics were associated with door-to-needle time of ≤ 60 minutes.

Conclusions

The authors concluded that:

- Patient factors most strongly associated with door-to-needle time of ≤ 60 minutes were younger age, male gender, white race, no prior stroke, greater time since symptom onset, and arrival during on-hours, and by emergency medical service transport
- Hospital factors associated with ≤ 60 -minute door-to-needle time included greater number of patients treated with intravenous tPA annually and lower annual number of stroke admissions
- These findings support the need for a targeted initiative to improve the timeliness of reperfusion in acute ischemic stroke

Tables recreated from original article

Table 3. Patient- and Hospital-Level Characteristics Associated With Door-to-Needle Time ≤ 60 Minutes

VARIABLES	ADJUSTED OR	LOWER 95% CI	UPPER 95% CI	P
Demographics				
Age, per 10-y increase	0.92	0.90	0.95	<0.0001
Sex, female	0.87	0.81	0.93	0.0001
Race/ethnicity (reference non-Hispanic white)				
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
Admission characteristics				
Arrival mode, emergency medical services	1.10	0.97	1.23	0.1275
Arrival time, on-hours	1.27	1.18	1.37	<0.0001
Symptom-onset-to-arrival times, per 10-min increase	1.23	1.22	1.25	<0.0001
NIHSS (reference: 0–9)				
10–14	1.37	1.25	1.51	<0.0001
15–20	1.58	1.44	1.73	<0.0001
21–42	1.37	1.23	1.54	<0.0001
Medical history				
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/TIA	0.81	0.74	0.88	<0.0001
Hospital characteristics				
The Joint Commission primary stroke center	1.02	0.88	1.17	0.7903
No. of hospital beds, per 200-bed 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 admissions per 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 per year (reference: ≤ 10)				
>10–20	1.38	1.18	1.61	<0.0001
>20	2.03	1.51	2.74	<0.0001

The table reflects multivariable modeling performed with 20,358 patients with full data available, including NIHSS. No major differences (apart from NIHSS) were observed when the model was constructed using the more complete cohort of patients (n=24,385) without recorded NIHSS. The findings were also similar when hospital characteristics of annual ischemic stroke admissions and annual tPA patients treated were analyzed as continuous variables and interaction terms were included in the model.

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