Emergency Medical Service Hospital Prenotification Is Associated With Improved Evaluation and Treatment of Acute Ischemic Stroke

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Background—The benefits of intravenous tissue-plasminogen activator (tPA) in acute ischemic stroke are time-dependent. Emergency medical services (EMS) hospital prenotification of an incoming patient with potential stroke may provide a means of reducing evaluation and treatment times and improving treatment rates; yet, available data are limited.

Methods and Results—We examined 371,988 patients with acute ischemic stroke transported by EMS and enrolled in Get With The Guidelines–Stroke from April 1, 2003, to March 31, 2011. Prenotification occurred in 249,197 (67.0%) of EMS-transported patients. Among eligible patients arriving by 2 hours, patients with EMS prenotification were more likely to be treated with tPA within 3 hours (82.8% versus 79.2%, absolute difference +3.5%, \( P<0.0001 \), the National Institutes of Health Stroke Scale-documented cohort; 73.0% versus 64.0%, absolute difference +9.0%, \( P<0.0001 \), overall cohort). Patients with EMS prenotification had shorter door-to–imaging times (26 minutes versus 31 minutes, \( P<0.0001 \)), shorter door-to–needle times (78 minutes versus 80 minutes, \( P<0.0001 \)), and shorter symptom onset-to–needle times (141 minutes versus 145 minutes, \( P<0.0001 \)). In multivariable and modified Poisson regression analyses accounting for the clustering of patients within hospitals, use of EMS prenotification was independently associated with greater likelihood of door-to–imaging times ≤ 25 minutes, door-to–needle times for tPA ≤ 60 minutes, onset-to–needle times ≤ 120 minutes, and tPA use within 3 hours.

Conclusions—EMS hospital prenotification is associated with improved evaluation, timelier stroke treatment, and more eligible patients treated with tPA. These results support the need for initiatives targeted at increasing EMS prenotification rates as a mechanism from improving quality of care and outcomes in stroke. (Circ Cardiovasc Qual Outcomes. 2012;5:00-00.)

Key Words: stroke • emergency medicine services • thrombolytics • hospitals • registry

Despite advances in the field, stroke remains the fourth leading cause of death in the United States and one of the leading causes for adult disability.1 Treatment with intravenous tissue plasminogen activator (tPA) has been shown to significantly improve stroke outcomes; yet, the benefits of tPA are strongly time-dependent.2,3 The American Heart Association (AHA)/American Stroke Association (ASA) have set guidelines for a 3- to 4.5-hour window from symptom onset to thrombolytic therapy and recommend rapid evaluation and treatment, with a targeted time of patient arrival to the hospital facility to intravenous tPA administration (door-to–needle time) of ≤ 60 minutes.2 Achieving timely evaluation and treatment of stroke is a challenge, and currently less than one third of patients with acute ischemic stroke treated with tPA receive treatment within 60 minutes of hospital arrival.4

The use of emergency medical services (EMS) is a potentially important means of improving medical response and treatment for acute ischemic stroke. Prenotifying hospitals that a patient with potential stroke is being transported could facilitate earlier activation of the stroke evaluation team and play an important role in increasing the number of eligible patients receiving timely tPA therapy. National recommendations from the AHA/ASA and the National Association of...
Emergency Medical Services Physicians endorse EMS stroke prenotification.6,7 Prior smaller studies and those performed outside of the United States have suggested an association between EMS stroke prenotification and more rapid assessment, faster access to imaging, and shorter door-to-needle times.5,12; however, there is little contemporary data that establishes the association of EMS prenotification with improved timeliness of evaluation and treatment of stroke in a broad cohort of patients with stroke from throughout the United States.

Using data from the AHA/ASA’s Get With The Guidelines-Stroke and GWTG-Stroke registry, our study goals were to evaluate the association of EMS prenotification with acute ischemic stroke evaluation and treatment, including door-to-imaging times, door-to-needle times, onset-to-door times, and rates of tPA treatment in eligible patients.

WHAT IS KNOWN
- Treatment with intravenous tissue plasminogen activator has been shown to significantly improve outcomes in acute ischemic stroke; yet, the benefits are highly time-dependent.
- Emergency Medical Service hospital prenotification of an incoming patient with potential stroke may provide a means of reducing evaluation and treatment times and improving treatment rates; however, available data are limited.

WHAT THE STUDY ADDS
- Drawing from data collected from all regions of the country, Emergency Medical Service hospital prenotification was demonstrated to be associated with significantly more eligible patients with acute ischemic stroke being treated with tissue plasminogen activator therapy.
- Emergency Medical Service prenotification was also associated with shorter door-to-imaging times, shorter door-to-needle times, and shorter symptom onset-to-needle times in patients with acute ischemic stroke.
- These results support the need for initiatives targeted at increasing Emergency Medical Service prenotification rates as a mechanism from improving quality of care and outcomes in stroke.

Methods
Data collected from hospitals participating in AHA/ASA’s GWTG-Stroke were used for this study. GWTG–Stroke is an initiative undertaken by the AHA/ASA to improve the quality of care delivered to patients with stroke and transient ischemic attacks through changes implemented at the hospital level. Details of the design and conduct of the GWTG–Stroke program have previously been described.5,13 GWTG uses a Web-based patient management tool (Outcome Sciences, Inc) to collect clinical data on consecutively admitted patients, provide decision support, and enable real-time online reporting features. After a yearlong pilot phase, the GWTG–Stroke program was made available to all hospitals across the United States in April 2003.5,13 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, de-identified data for research purposes.

Hospital site personnel were trained to collect data on consecutive patients admitted with the principal clinical diagnosis of acute stroke or transient ischemic attack (TIA) by prospective clinical identification, retrospective identification through the use of discharge codes, or a combination. Methods used for the prospective clinical identification of cases involved regular review of a combination of data sources, including emergency department admission logs, ward census logs, intensive care unit logs, and neurology service consultations. Methods used for the retrospective clinical identification of cases included regular surveillance of discharge codes, specifically International Classification of Disease, Ninth Revision, codes 433.xx, 434.xx, and 436 for ischemic stroke. The eligibility of all acute stroke admissions was confirmed before chart abstraction.5,13

Patient data (such as demographics, medical history, onset time of stroke symptoms [defined as last known well time], mode of arrival, arrival time, in-hospital diagnostic studies, treatments and procedures, time of initial imaging study, tPA treatment initiation time, tPA complications, in-hospital mortality, and discharge treatments, counseling and destination) were abstracted by trained hospital personnel. The National Institutes of Health Stroke Scale (NIHSS) was used to index stroke severity, when documented. Data collectors at hospital facilities indicated mode of patient arrival as EMS from home/scene, hospital transferred/transport, private transport/walk in, or not documented. If applicable, they further recorded if there was EMS prenotification to hospital for the patient in question, based on explicit documentation anywhere in the records that advanced notification by EMS had occurred and that this notification included that the patient had a suspected stroke, through the use of the word stroke or any documentation of signs and symptoms consistent with stroke. All patient data were de-identified before submission. Data on hospital-level characteristics (eg, bed size, geographical region, teaching status) was accessed from the American Hospital Association.

There were 936,702 patients with acute ischemic stroke from 1635 hospitals enrolled between April 1, 2003, and April 2, 2011 (Figure). Patients who had in-hospital strokes (n=159,985) and those transferred in from other acute care facilities (n=94,061) were excluded for the purpose of this study. Of the remaining patients, 404,031 did not arrive by EMS from home/scene. Another 50,637 (12.0%) patients who were transported by EMS had missing or nonapplicable prenotification data and were therefore excluded, leaving 371,988 EMS-transported patients that constituted the study population.

Statistical Analysis
Sociodemographic factors, clinical variables, hospital characteristics, and quality of care measures were compared between patients transported by EMS with prenotification versus those without. Categorical and continuous variables were reported in percentages and median (25th and 75th percentiles) as appropriate. The acute ischemic stroke process of care, including door-to-imaging time ≤25 minutes (overall and confined to patients presenting within 3 hours of symptom onset), door-to-needle time for intravenous tPA ≤60 minutes, and onset-to-door time for intravenous tPA ≤120 minutes, use of intravenous tPA in eligible patients without documented contraindications arriving within 2 hours and treated within 3 hours, and door-to-imaging, door-to-needle, and onset-to-needle times as continuous variables were compared between patients transported by EMS with prenotification versus those without. The Pearson Chi2 and Wilcoxon rank-sum test were used to compare the binary process of care measures and continuous time measures, respectively. The time intervals and proportion of eligible patients evaluated or treated within recommended time windows were also estimated, using modified Poisson regression with the generalized estimating equations (GEE) approach to account for clustering of patients within hospitals. For the time variables, log transformation
was performed first, and then regression analysis was conducted for the log-transformed time variable, with the geometric mean report-
ed. The analyses were also examined with multivariable modified
Poisson regression models and adjusted for the potential confounder
variables that may have impacted the association of EMS prenoti-
fication with stroke evaluation and treatment, including age, sex,
race/ethnicity (white, black, Hispanic, Asian, and other), medical
history (including atrial fibrillation/flutter, coronary artery disease/
prior myocardial infarction, cardiac stenosis, diabetes mellitus,
hyperlipidemia, heart failure, hypertension, smoking status, prior
stroke/TIA, peripheral vascular disease, and prosthetic heart valve),
insurance status (Medicare, Medicaid, no insurance, or other, in-
cluding health maintenance organization/Veterans Affairs/private),
arrival during regular working hours (defined as Monday to Friday
between 7AM and 6PM), hospital bed size, geographic region
(Midwest, Northeast, West, South), teaching status, average num-
ber of ischemic stroke/TIA patients annually, and average number
of patients treated with tPA annually. These relationships were also
examined with multivariable logistic regression models using the
GEE approach to adjust for within-hospital clustering. Because the
degree of stroke severity is a potential factor impacting both EMS
prenotification and stroke care but was not available in all patients,
sensitivity analyses were performed on the subset of patients with
complete NIHSS data available (N=199154), including NIHSS as
an additional covariate in the multivariable modified Poisson regres-
sion models using GEE.

Similar analyses were conducted to investigate the relationship
between EMS prenotification and complications of intravenous tPA
therapy (symptomatic intracranial hemorrhage within 36 hours and
major bleeding). GEE was similarly employed in these models to ac-
count for within-hospital clustering, and the same set of previously
mentioned potential confounders were used for risk adjustment.
All tests were 2-tailed, with \( P<0.05 \) considered as the level of statistical
significance. All statistical analyses were performed using SAS ver-
sion 9.2 software (SAS Institute). The authors had full access to the
data and take responsibility for its integrity. All authors have read and
agree to the manuscript as written.

Results

This study analyzed 371988 patients with acute ischemic
stroke from 1585 participating sites arriving by EMS
transport from 2003 to 2011. Of patients transported by
EMS during the 8-year study period, EMS hospital preno-
tification occurred in 249197 (67.0%). When the analysis
is confined to patients arriving by EMS within 4.5 hours
from symptom onset, EMS prenotification occurred in
97511 of 135308 patients (72.1%). Among patients arriv-
ing with symptom duration ≤2 hours, the rate of prenotifi-
cation was 72407 of 99145 patients (73.0%). Patient and
hospital characteristics for those with EMS prenotification
compared with those without are provided in Table 1.
Among EMS-transported patients, EMS was more likely to
prenotify hospitals for patients who were younger, white,
male, and had a history of atrial fibrillation. Patients with a
history of previous stroke/TIA, diabetes mellitus, peripheral
vascular disease, hypertension, dyslipidemia, or heart fail-
ure were less likely to have EMS prenotification. Time from
symptom onset to hospital arrival was shorter in patients
with prenotification. EMS prenotification also tended to
occur for patients with higher NIHSS scores and those arriv-
ing during facility off-hours. Hospital characteristics also
differed among those patients with and without EMS
prenotification (Table 1).

Differences were observed in timing of evaluation, tim-
ing of treatment, and the portion of eligible patients treated
with tPA between EMS-arriving patients with and without
prenotification. Patients with prenotification underwent
more rapid evaluation and, when treated, more timely tPA
administration (Table 2). Among patients arriving within 3
hours of symptom onset, the median door-to–imaging times
were less (26 minutes versus 31 minutes, \( P<0.0001 \)) and the
portion of patients with door-to–imaging times within 25
minutes was higher with EMS prenotification compared with
patients without EMS prenotification (48.8% versus 40.5%,
\( P<0.0001 \)). With EMS prenotification, the onset-to–door
times were lower (113 minutes versus 150 minutes, \( P < 0.0001 \)), and more eligible patients were treated with tPA within 120 minutes of symptom onset (31.9% versus 29.5%, \( P < 0.0001 \)) compared with those patients without prenotification. There was a greater portion of eligible patients arriving within 2 hours who were treated with tPA within 3 hours compared with patients without EMS prenotification (73.0% versus 64.0%, absolute difference +9.0%, \( P < 0.0001 \)).

Adjustment for potential confounding variables and accounting for the correlation of data within hospitals demonstrates that EMS prenotification was independently associated with earlier imaging and more rapid tPA administration (Table 3). EMS prenotification was associated with improved timeliness in imaging among patients arriving within 3 hours (door-to–imaging time \( \leq 25 \) minutes) and improved timeliness of tPA administration by both door-to–needle times (door-to–needle time \( \leq 60 \) minutes) and onset-to–needle times (onset-to–needle time \( \leq 120 \) minutes). EMS prenotification was also independently associated with more eligible patients with acute ischemic stroke being treated with tPA, adjusted rates 71.8% versus 62.2% (absolute difference +9.6%, \( P < 0.0001 \)), with and without EMS prenotification (Table 3). After multivariate adjustment, EMS prenotification patients arriving
within 2 hours of symptom onset had greater odds of receiving treatment with intravenous tPA within 3 hours from symptom onset. Similar results were obtained using the multivariable GEE models (online-only Data Supplement Table I).

When the analyses were repeated with adjustment for NIHSS, using data from the 199154 patients with NIHSS documented, the results were similar, though differences in tPA treatment were more modest (Table 4). Among eligible patients arriving by 2 hours, patients with EMS prenotification were more likely to be treated with tPA within 3 hours (82.8% versus 79.2%, absolute difference +3.5%, P<0.0001). EMS prenotification was independently associated with more eligible patients with acute ischemic stroke being treated with tPA, adjusted rates 82.3% versus 78.1% (absolute difference +4.2%, P<0.0001), with and without EMS prenotification. Adjustment for potential confounding variables and accounting for the correlation of data within hospitals demonstrates that EMS prenotification was independently associated with earlier imaging, more rapid tPA administration, and more eligible patients treated with tPA, as shown in Table 5. Similar results were obtained using the multivariable GEE models (online-only Data Supplement Table II).

No significant association was found between EMS prenotification and complications from intravenous tPA, such as symptomatic intracranial hemorrhage ≤36 hours, or life-threatening systemic hemorrhage ≤36 hours, or any serious

Table 2. In-Hospital Evaluation and Treatment of Patients With Acute Ischemic Stroke With EMS Prenotification Compared With Patients Without EMS Prenotification

<table>
<thead>
<tr>
<th>Measure</th>
<th>EMS Prenotification</th>
<th>No EMS Prenotification</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door-to–imaging time, median, min (patients arriving ≤3 h)</td>
<td>76459</td>
<td>28220</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Door-to–imaging time ≤25 min, (in patients arriving ≤3 h), %</td>
<td>48.8%</td>
<td>40.5%</td>
<td>+8.3% (7.6–8.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, median, min (25th to 75th percentile)</td>
<td>230430</td>
<td>112580</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Door-to–needle time ≤60 min, %</td>
<td>30.9%</td>
<td>22.4%</td>
<td>+8.5% (8.2–8.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset-to–needle time, median, min (25th to 75th percentile)</td>
<td>76 (60–100)</td>
<td>80 (60–103)</td>
<td>−2 min</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset-to–needle time ≤120 min, %</td>
<td>31.9%</td>
<td>29.5%</td>
<td>+2.4% (2.1–3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tPA Rx rate (arrive by 2 h, treat by 3 h), n/n, %</td>
<td>22305/30541</td>
<td>7193/11244</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table displays crude rates and times. EMS indicates emergency medical services; RR, relative risk; CI, confidence interval; min, minutes; h, hours; tPA, tissue plasminogen activator; Rx, treatment.

Table 3. Unadjusted and Adjusted Rates, Times, and Relative Risks for Stroke Evaluation and Treatment in Patients With EMS Prenotification Compared With Patients Without EMS Prenotification

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unadjusted Rates and Times</th>
<th>Adjusted Rates and Times</th>
<th>Adjusted Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door-to–imaging time, median, min (patients arriving ≤3 h)</td>
<td>24.0</td>
<td>31.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time ≤25 min, (in patients arriving ≤3 h), %</td>
<td>48.5%</td>
<td>38.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time, median, min</td>
<td>39.5</td>
<td>54.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time ≤25 min</td>
<td>31.9%</td>
<td>21.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, median, min</td>
<td>78.2</td>
<td>83.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤60 min</td>
<td>24.5%</td>
<td>21.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset-to–needle time, median, min</td>
<td>140.0</td>
<td>145.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset-to–needle time ≤120 min</td>
<td>31.5%</td>
<td>28.0%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tPA Rx rate (arrive by 2 h, treat by 3 h)</td>
<td>65.9%</td>
<td>56.2%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Modified Poisson regression with robust variance estimators to account for clustering of patients within hospitals. Variables included in multivariable models were age, sex, race/ethnicity, prior medical history of atrial fibrillation/flutter, coronary artery disease/prior myocardial infarction, carotid stenosis, diabetes mellitus, hyperlipidemia, heart failure, hypertension, smoking status, prior stroke/transient ischemic attack, peripheral vascular disease, and prostatic heart valve, insurance status, arrival during on/off hours, hospital characteristics of bed size, geographic region, teaching status, average number of patients with ischemic stroke/transient ischemic attack annually, and average number of patients treated with tissue plasminogen activator annually. The adjusted times represent the geometric means. EMS indicates emergency medical services; CI, confidence interval; min, minutes; h, hours; tPA, tissue plasminogen activator; Rx, treatment.
tPA complication on unadjusted or adjusted analyses (Table 6). Similar results were found in the sensitivity analyses adjusting for NIHSS (data not shown).

Discussion

Our analysis supports the role of EMS prenotification as a potentially important but underused means to improving rapid triage, evaluation, and treatment of patients with acute ischemic stroke. Although previous studies have shown that EMS use may speed therapy in selected settings,8–12 our study expands these findings to the stroke patients from all regions of the country and diverse hospital settings. Among patients transported via EMS, we found prenotification to be independently associated with more patients undergoing timely evaluation, shorter onset-to-needle and door-to-needle times, and more eligible acute ischemic stroke patients being treated with tPA.

Despite the proven benefits of timely administration of tPA for acute ischemic stroke and national targets for timely evaluation and treatment, many hospitals still find difficulty in meeting these performance goals.5 Although delays from the time of stroke symptom onset to patient arrival (prehospital delay) remains a barrier to timely tPA administration, a substantial portion of patients arrive within a time window in which intravenous tPA could be administered.13 Identifying and implementing effective strategies to facilitate the rapid evaluation and treatment of patients with acute ischemic stroke is an important next step.

Table 4. In-Hospital Evaluation and Treatment of Acute Ischemic Stroke Patients With EMS Prenotification Compared With Patients Without EMS Prenotification Among Patients With NIHSS Documented (N=199,154)

<table>
<thead>
<tr>
<th>Measure</th>
<th>EMS Prenotification</th>
<th>No EMS Prenotification</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door-to–imaging time, n, median (25th to 75th percentile), min (in patients arriving ≤3 h)</td>
<td>54.983</td>
<td>17.838</td>
<td>−2 min</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time ≤25 min, (in patients arriving ≤3 h), %</td>
<td>54.8%</td>
<td>48.5%</td>
<td>+6.3% (5.4–7.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, n, median (25th to 75th percentile), min</td>
<td>132.374</td>
<td>54.462</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Door-to–needle time ≤60 min, %</td>
<td>32 (18–63)</td>
<td>41 (22–80)</td>
<td>−9 min</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤25 min, %</td>
<td>69.3%</td>
<td>60.5%</td>
<td>+8.8% (8.3–9.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, n, median (25th to 75th percentile), min</td>
<td>77 (59–99)</td>
<td>79 (60–101)</td>
<td>−2 min</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤60 min, %</td>
<td>27.7%</td>
<td>26.9%</td>
<td>+0.8% (0.4–2.0)</td>
<td>0.1787</td>
</tr>
<tr>
<td>Door-to–needle time ≤25 min, %</td>
<td>56.3%</td>
<td>47.3%</td>
<td>+9.0% (8.2–9.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, median (25th to 75th percentile), min</td>
<td>28.3</td>
<td>38.8</td>
<td>−9.4 min (7.8–11.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤25 min, %</td>
<td>43.2%</td>
<td>31.6%</td>
<td>+11.6% (9.8–12.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, median (25th to 75th percentile), min</td>
<td>76.8</td>
<td>81.2</td>
<td>−4.4 min (2.1–6.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤60 min, %</td>
<td>25.4%</td>
<td>21.9%</td>
<td>+3.5% (2.5–4.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤25 min, %</td>
<td>82.8%</td>
<td>79.2%</td>
<td>+3.6% (2.5–4.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Table displays crude rates and times.*

EMS, emergency medical services; NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; Rx, treatment.

Table 5. Unadjusted and Adjusted Rates, Times, and Relative Risks for Stroke Evaluation and Treatment in Patients With EMS Prenotification Compared With Those Without EMS Prenotification Among Patients With NIHSS Documented (N=199,154)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unadjusted Rates and Times</th>
<th>Adjusted Rates and Times</th>
<th>Adjusted Relative Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door-to–imaging time, median, (in patients arriving ≤3 h), min</td>
<td>19.8</td>
<td>24.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time ≤25 min (in patients arriving ≤3 h), %</td>
<td>56.3%</td>
<td>47.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time, median, min</td>
<td>28.3</td>
<td>38.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–imaging time ≤25 min, %</td>
<td>43.2%</td>
<td>31.6%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time, median, min</td>
<td>76.8</td>
<td>81.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to–needle time ≤60 min, %</td>
<td>25.4%</td>
<td>21.9%</td>
<td>0.0002</td>
</tr>
<tr>
<td>Onset-to–needle time, median, min</td>
<td>140.0</td>
<td>144.0</td>
<td>0.0006</td>
</tr>
<tr>
<td>Onset-to–needle time ≤120 min, %</td>
<td>32.2%</td>
<td>28.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tPA Rx rate (arrive by 2 h, treat by 3 h), n/n, %</td>
<td>19476/23,531</td>
<td>6017/77,594</td>
<td>82.8%</td>
</tr>
</tbody>
</table>

Modified Poisson regression with robust variance estimators to account for clustering of patients within hospitals. Variables included in multivariable models were National Institutes of Health Stroke Scale and the variables listed in Table 3.

EMS indicates emergency medical services; CI, confidence interval; RR, relative risk; tPA, tissue plasminogen activator; Rx, treatment.
stroke is critical. Prearrival notification is one such strategy, and prior studies have suggested that this approach may facilitate more timely stroke evaluate and care. These smaller studies generally found EMS prenotification was associated with faster imaging and imaging interpretation times and increased patient eligibility for tPA. Abdullah et al identified a study population of 118 patients arriving at the Massachusetts General Hospital emergency department by EMS within 6 hours of symptom onset, with an EMS prenotification rate of 37%. This analysis found significantly shorter door-to–imaging times and increased occurrence of thrombosis in the prenotification group compared with no prenotification. Multivariate linear regression modeling found that advance notification by EMS was associated with a 23% shorter door-to–imaging times. This is a smaller and diverse group of patients and demonstrate not just an association with improved imaging times but improved timeliness of tPA administration and more eligible patients treated with tPA compared with those patients arriving by EMS without prenotification.

This GWTG–Stroke study also demonstrates that EMS prenotification is generally underused in contemporary US practice. Our results suggest that improved rates of EMS use and prenotification for patients with ischemic stroke may improve the speed of patient evaluation, allow for more eligible patients to be treated with tPA, and facilitate more timely tPA administration. As the benefits of tPA are operative at 3 major levels. First, increasing patient stroke symptom recognition and rapid activation of EMS is important to address. Community education initiatives should be undertaken to inform the public of the outcome benefits associated with EMS use. Second, adequate training of EMS staff in the proper use of stroke screening instruments for timely identification of ischemic stroke together with hospital prenotification is vital. As the first form of medical contact, trained EMS personnel have the opportunity to stabilize the patient, prenotify the nearest hospital equipped to administer tPA in the appropriate circumstances, and provide rapid transport to this facility. Previous studies have suggested that such training should focus on defining the minimum thresholds and type of data required for activation of hospital-based stroke teams. Furthermore, standardized tools necessary for acute stroke detection in the ambulatory setting should be developed and implemented across the board.

The collective data support the need for targeted improvements in rates of EMS prenotification and awareness of the benefits of prenotification, as part of local, regional, and national initiatives to improve stroke care and outcomes. Increasing the portion of patients evaluated and treated with tPA in a timely fashion requires a systems approach that is appropriate at 3 major levels. First, increasing patient stroke symptom recognition and rapid activation of EMS is important to address. Community education initiatives should be undertaken to inform the public of the outcome benefits associated with EMS use. Second, adequate training of EMS staff in the proper use of stroke screening instruments for timely identification of ischemic stroke together with hospital prenotification is vital. As the first form of medical contact, trained EMS personnel have the opportunity to stabilize the patient, prenotify the nearest hospital equipped to administer tPA in the appropriate circumstances, and provide rapid transport to this facility. Previous studies have suggested that such training should focus on defining the minimum thresholds and type of data required for activation of hospital-based stroke teams. Furthermore, standardized tools necessary for acute stroke detection in the ambulatory setting should be developed and implemented across the board.

**Table 6. Complications of tPA Use in Patients With EMS Prenotification Compared With Patients Without EMS Prenotification: Unadjusted Rates and Adjusted Relative Risk**

<table>
<thead>
<tr>
<th>tPA Complication</th>
<th>EMS Prenotification</th>
<th>No EMS Prenotification</th>
<th>P Value</th>
<th>Adjusted Relative Risk</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic intracranial hemorrhage ≤36 h</td>
<td>5.8%</td>
<td>6.0%</td>
<td>0.4020</td>
<td>0.97</td>
<td>0.87–1.08</td>
<td>0.6095</td>
</tr>
<tr>
<td>Life-threatening or serious systemic hemorrhage ≤36 h</td>
<td>1.4%</td>
<td>1.3%</td>
<td>0.2705</td>
<td>1.11</td>
<td>0.88–1.39</td>
<td>0.3770</td>
</tr>
<tr>
<td>Other serious complications ≤36 h</td>
<td>2.1%</td>
<td>1.9%</td>
<td>0.1686</td>
<td>1.15</td>
<td>0.94–1.51</td>
<td>0.1741</td>
</tr>
<tr>
<td>Any serious complications</td>
<td>11.6%</td>
<td>11.5%</td>
<td>0.7793</td>
<td>1.02</td>
<td>0.95–1.10</td>
<td>0.5512</td>
</tr>
</tbody>
</table>

Adjusted for variables listed in Table 3. EMS indicates emergency medical services; CI, confidence interval.

**Limitations**

There are several limitations to this study that need to be acknowledged. First, although GWTG–Stroke covers >1000 US hospitals, participation is voluntary and could, in fact, select for centers with greater interest in quality improvement and, thus, better process performance than non-GWTG–Stroke centers. Second, as with all registries, the data presented here are dependent on the accuracy and completeness of abstraction from the medical records. In some patients, EMS prenotification may have taken place but not
been documented in the medical record. In other patients, specific stroke patient pretreatment may have been documented but not actually occurred. The assessment of EMS pretreatment was confined to present or absent and additional information that may have been communicated to hospitals such as prehospital stroke screening results and type of symptoms were not captured. We also do not have any data on the type of first responder, the level of training of the rendering prehospital providers, or characteristics of the EMS agencies. Additionally, participating hospitals are instructed to include all consecutive admissions for ischemic stroke; however, since these processes are not audited, the potential exists for selection bias. Although our analysis has identified a number of patient and hospital characteristics that may impact stroke care, there are likely other important influencing factors not captured. Residual measured and unmeasured confounding variables may have influenced some or all of the findings. NIHSS was not documented in 33.4% of patients; however, findings were similar in models with and without NIHSS, although the absolute difference in tPA treatment in eligible patients was smaller in models adjusting for NIHSS. As a result of the large sample size, some small differences in absolute terms and of uncertain clinical significance are still highly statistically significant. Finally, measures of stroke functional outcomes such as modified Rankin score at discharge or 90 days are not available in this study.

Conclusions

Among patients with acute ischemic stroke, transported by EMS to GWTG–Stroke participating hospitals, EMS pretreatment is independently associated with more timely imaging and administration of tPA, and a greater portion of eligible patients with acute ischemic stroke receiving tPA. Despite these benefits, EMS pretreatment occurred in only 23% of eligible patients with acute ischemic stroke arriving by EMS. These findings support the need for initiatives targeted at improving EMS pretreatment rates nationally as a mechanism for improving acute ischemic stroke quality of care and outcomes.

Disclosures

Dr Smith serves as a member of the GWTG Science Subcommittee and receives research support from the National Institutes of Health (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 serves as a member of the GWTG Science Subcommittee; as a scientific consultant regarding trial design and conduct to CoAxia, Concentric Medical, Talecris/Grifols, Ferrer, PhotoThera, BrainsGate, SYGNIS, and ev3; received lecture honoraria from Ferrer; and is an employee of the University of California, which holds a patent on retriever devices for stroke.

Dr Liang is a member of the Duke Clinical Research Institute, which serves as the AHA GWTG data coordinating center.

Dr Olson is a member of the Duke Clinical Research Institute, which serves as the AHA GWTG data coordinating center.

Dr Hernandez is a member of the Duke Clinical Research Institute, which serves as the AHA GWTG data coordinating center.

Dr Hernandez is a recipient of an AHA Pharmaceutical Roundtable grant (0675060N); has received a research grant from Johnson & Johnson; and has received honorarium from AstraZeneca and Amgen.

Dr Peterson has received research grants from Eli Lilly and Company, Johnson & Johnson, and Bristol-Myers Squibb, Sanofi-aventis, and the Merck/Schering-Plough partnership. Dr Peterson serves as principle investigator of the Data Analytic Center for GTWG.

Dr Schwamm serves as chair of the GWTG Steering Committee; 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 DIA34 clinical trial.

Dr Fonarow receives research support from the National Institutes of Health (significant) and is an employee of the University of California, which holds a patent on retriever devices for stroke (significant).

The other authors report no conflicts.

Role of the Sponsors: The industry sponsors had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; or the preparation, review, or approval of the manuscript.

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References


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Cheryl B. Lin, Eric D. Peterson, Eric E. Smith, Jeffrey L. Saver, Li Liang, Ying Xian, DaiWai M. Olson, Bimal R. Shah, Adrian F. Hernandez, Lee H. Schwamm and Gregg C. Fonarow

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Supplemental Table I: Unadjusted and Adjusted Odds Ratios for Stroke Evaluation and Treatment in Patients with EMS Pre-Notification Compared with Those without EMS Pre-Notification

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unadjusted</th>
<th></th>
<th>Adjusted</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI P-value</td>
<td>OR 95% CI P-value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Door-to-Imaging Time ( \leq 25 \text{ min} ) in patients arriving ( \leq 3\text{hr} )</td>
<td>1.53 1.44-1.63 &lt;0.0001</td>
<td>1.53 1.44-1.63 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Door-to-Imaging Time ( \leq 25 \text{ min} )</td>
<td>1.72 1.61-1.83 &lt;0.0001</td>
<td>1.70 1.60-1.80 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Door-to-Needle Time ( \leq 60 \text{ min} )</td>
<td>1.22 1.11-1.34 &lt;0.0001</td>
<td>1.20 1.10-1.31 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset-to-Needle Time ( \leq 120 \text{ min} )</td>
<td>1.18 1.11-1.27 &lt;0.0001</td>
<td>1.17 1.09-1.25 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tPA Rx Rate (arrive by 2 hr treat by 3hr)</td>
<td>1.56 1.44-1.69 &lt;0.0001</td>
<td>1.64 1.50-1.79 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Multivariable generalized estimating equation analyses. Variables included in multivariable models were age, gender, race/ethnicity, prior medical history of atrial fibrillation/flutter, coronary artery disease/prior myocardial infarction, carotid stenosis, diabetes mellitus, hyperlipidemia, heart failure, hypertension, smoking status, prior stroke/TIA, peripheral vascular disease, and prosthetic heart valve, insurance status, arrival during on/off hours, hospital characteristics of bed size, geographic region, teaching status, average number of ischemic stroke/TIA patients annually, and average number of patients treated with tPA annually. OR, odds ratio.
Supplemental Table II: Unadjusted and Adjusted Odds Ratios for Stroke Evaluation and Treatment in Patients with EMS Pre-Notification Compared with Those without EMS Pre-Notification for Patients with Complete NIHSS Data (N=199,154)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>P-value</td>
</tr>
<tr>
<td>Door-to-Imaging Time ≤25 min (in patients arriving ≤3hr)</td>
<td>1.44 1.35-1.53</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to-Imaging Time ≤25 min</td>
<td>1.65 1.53–1.77</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Door-to-Needle Time ≤60 min</td>
<td>1.22 1.10-1.35</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Onset-to-Needle Time ≤120 min</td>
<td>1.20 1.12-1.30</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tPA Rx Rate (arrive by 2 hr treat by 3hr)</td>
<td>1.35 1.24-1.47</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Multivariable generalized estimating equation analyses. Variables included in multivariable models were age, gender, race/ethnicity, prior medical history of atrial fibrillation/flutter, coronary artery disease/prior myocardial infarction, carotid stenosis, diabetes mellitus, hyperlipidemia, heart failure, hypertension, smoking status, prior stroke/TIA, peripheral vascular disease, and prosthetic heart valve, insurance status, arrival during on/off hours, NIHSS, hospital characteristics of bed size, geographic region, teaching status, average number of ischemic stroke/TIA patients annually, and average number of patients treated with tPA annually. OR, odds ratio