Improving Door-to-Needle Times
A Single Center Validation of the Target Stroke Hypothesis

Ilana M. Ruff, MD; Syed F. Ali, MD; Joshua N. Goldstein, MD; Michael Lev, MD; William A. Copen, MD; Joyce McIntyre, RN; Natalia S. Rost, MD; Lee H. Schwamm, MD

Background and Purpose—National guidelines recommend imaging within 25 minutes of emergency department arrival and intravenous tissue-type plasminogen activator within 60 minutes of emergency department arrival for patients with acute stroke. In 2007, we implemented a new institutional acute stroke care model to include 10 best practices and evaluated the effect of this intervention on improving door-to-computed tomography (CT) and door-to-needle (DTN) times at our hospital.

Methods—We compared patients who presented directly to our hospital with acute ischemic stroke in the preintervention (2003–2006) and postintervention (2008–2011) periods. We did not include 2007, the year that the new protocol was established. Predictors of DTN ≤60 minutes before and after the intervention were assessed using χ² for categorical variables, and t test and Wilcoxon signed-rank test for continuous variables.

Results—Among 2595 patients with acute stroke, 284 (11%) received intravenous tissue-type plasminogen activator. For patients arriving within an intravenous tissue-type plasminogen activator window, door-to-CT <25 improved from 26.7% pre intervention to 52.3% post intervention (P < 0.001). Similarly, the percentage of patients with DTN <60 doubled from 32.4% to 70.3% (P < 0.001). Patients with DTN ≤60 did not differ significantly with respect to demographics, comorbidities, or National Institutes of Health Stroke Scale score in comparison with those treated after 60 minutes.

Conclusions—Door-to-CT and DTN times improved dramatically after applying 10 best practices, all of which were later incorporated into the Target Stroke Guidelines created by the American Heart Association. The only factor that significantly affected DTN60 was the intervention itself, indicating that these best practices can result in improved DTN times. (Stroke. 2014;45:504-508.)

Key Words: stroke ■ thrombolytic therapy

Intravenous tissue-type plasminogen activator (tPA) can reduce disability after acute ischemic stroke (AIS), but this effect is highly time dependent. The opportunity to achieve functional independence is less with delays in time to treatment. The current American Heart Association (AHA) guideline recommends door-to-needle (DTN) times of <60 minutes. Rapid administration of intravenous tPA requires teamwork between the emergency department (ED), radiology, pharmacy, and neurology teams. Stroke teams and rapid triage pathways improve DTN times, but a recent study showed that even in hospitals participating in the Get with the Guidelines (GWTG)-Stroke, a DTN time of <60 minutes occurs in only 26.6% of patients.¹

In 2007, our hospital developed a new acute stroke protocol with 10 best practices to lower DTN times, all of which were later incorporated into the Target Stroke Initiative launched by the AHA and American Stroke Association in 2011.² We hypothesized that these system changes would significantly improve median ED door-to-computed tomography (DTCT) and DTN times.

ED and Intravenous tPA Protocol
The Massachusetts General Hospital (MGH) stroke protocol was modified in 2007 (Table 1). Emergency Medical Services personnel in Massachusetts are required to notify the ED of potential stroke patients, using the term stroke whenever possible. On ED arrival, patients are assessed at triage and sent to the highest acuity area of our ED, which is specifically designed to rapidly care for patients with critical illness. The ED team activates a group pager notifying 16 medical professionals, including physicians (acute stroke fellow and attending, ED-based neurology resident, neuroradiology fellow, and attending), technologists (ED-based computed tomography [CT] and MRI staff), research fellows, a pharmacist, nurses (operating room neuroendovascular nurse and nursing supervisor), and a quality tracking pager. ED physicians order laboratories and rapid imaging. The ED nurse draws super STAT laboratories, including platelets and a coagulation panel and CT technologists clear the scanner. Simultaneously, the patient is placed on a portable monitor and assessed by the in-house acute stroke fellow and neurology resident who confirm the patient’s history, evaluate the AHA exclusion criteria, and perform a brief examination including all components of the National Institutes of Health Stroke Scale (NIHSS). The

Methods

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Table 1. Target: Stroke Guidelines and MGH Door to Needle 60 Stroke Protocol Initiative

<table>
<thead>
<tr>
<th>MGH Stroke Protocol</th>
<th>Target Stroke Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. EMS encouraged to notify ED of possible stroke</td>
<td>1. Advance hospital notification by EMS</td>
</tr>
<tr>
<td>2. Triage prioritizes patients with stroke and sends them to the highest acuity area of the ED</td>
<td>2. Rapid Triage Protocol and Stroke Team Notification</td>
</tr>
<tr>
<td>3. ED2CT pager notifies physicians, radiology techs, nurses, and laboratory pharmacy</td>
<td>3. Single Call Activation System of Entire Stroke Team</td>
</tr>
<tr>
<td>5. CT techs and neuroradiologists are available for rapid imaging and evaluation</td>
<td>5. Rapid brain imaging</td>
</tr>
<tr>
<td>6. Laboratories sent super STAT for time critical diagnoses</td>
<td>6. Rapid laboratory testing</td>
</tr>
<tr>
<td>7. Pharmacist at bedside during entire code stroke and mixes intravenous tPA immediately if patient is eligible</td>
<td>7. Mixing rt-PA medication ahead of time for likely cases</td>
</tr>
<tr>
<td>8. Intravenous tPA stored in ED drug dispenser or in a hand-held tPA toolkit</td>
<td>8. Rapid access to intravenous tPA</td>
</tr>
<tr>
<td>9. Monthly case review at the acute stroke quality taskforce</td>
<td>9. Team-based approach with periodic review of data and goals</td>
</tr>
<tr>
<td>10. Weekly emails sent to the entire acute stroke team involved in intravenous tPA cases</td>
<td>10. Prompt data feedback after each case to team members</td>
</tr>
</tbody>
</table>

CT indicates computed tomography; ED, emergency department; EMS, Emergency Medical Services; MGH, Massachusetts General Hospital; rt-PA, recombinant tissue-type plasminogen activator; and tPA, tissue-type plasminogen activator.

Patient Population
We performed a retrospective analysis of a prospectively collected cohort using our hospital’s GWTG-Stroke Registry. All consecutive patients directly presenting to our ED with AIS from January 2003 to December 2011 were included. GWTG-Stroke is an ongoing voluntary, continuous registry, and performance improvement initiative. Trained hospital personnel identify patients with stroke through ED records, ward census lists, neurological consultations, and International Classification of Diseases, Ninth Revision discharge codes. The eligibility of each acute stroke is confirmed at chart review before abstraction. Patient data, including clinical and demographic information, testing and treatments, and quality measures and outcomes are entered into the GWTG-Stroke database using a Web-based patient management tool (PMT, outcomes, and quintiles). All patients were evaluated by a stroke neurologist at the bedside and images were reviewed by a neuroradiologist. The decision to give intravenous tPA was determined using the standard inclusion and exclusion criteria on our website (www.massgeneral.org/stroke) and based on the AHA guidelines and the National Institute of Neurological Disorders and Stroke intravenous tPA trial.4,5 Intravenous tPA was administered ≤4.5 hours after last known well (LKW) once the results of the ECASS (European Cooperative Acute Stroke Study) 3 trial were published and the AHA advisory update endorsed this practice.6,7 We obtained institution review board approval from the MGH to conduct this analysis.

Statistical Analysis
We compared patients who presented directly to our hospital with AIS in the preintervention (2003–2006) and postintervention (2008–2011) periods. We did not include 2007, as this was the year that the new protocol was established. For dichotomous variables (sex, race, and comorbidities), frequencies with percentages were calculated. Values for age were expressed as mean±SD and values for NIHSS, DTCT, LKW to intravenous tPA and DTN as median with interquartile ranges. Pearson χ² was used for categorical variables to compare baseline characteristics of the 2 groups. For continuous variables, we used independent sample t test for age and Wilcoxon rank-sum test for comparative analysis of NIHSS, DTCT, DTN, and LKW to intravenous tPA time. Statistical significance was set at a P value of <0.05 (2-tailed).

All variables were included in a univariate analysis that explored the factors associated with DTN ≤60 as compared with DTN >60 minutes. Results were tabulated and temporal changes shown by line chart. Statistical analyses were performed using the software SPSS (version 20.0).

Results

Patients Characteristics
From 2003 to 2011, a total of 4477 patients were admitted to MGH with a diagnosis of AIS. In this analysis, we included only the 2595 (58%) patients who presented directly to MGH ED; those patients transferred after initial evaluation elsewhere were excluded. Among these 2595 patients, 52.9% were men, 87.9% were whites, with a mean age of 70.1 years and median initial NIHSS of 4 (interquartile range, 2–11). Eleven percent (n=284) of the study cohort received intravenous tPA. Patients receiving intravenous tPA had a mean age of 72.1±15.2 years, 48.4% were men, and the median NIHSS was 13 (8–19). There were 1413 (60.4%) patients in the preintervention period (2003–2006) and 925 in the postintervention period (2008–2011). Compared with patients in the preintervention period, those in the postintervention period were older, more often white, and had more stroke risk factors, including hypertension, diabetes mellitus, and hyperlipidemia. The postintervention group was less likely to be active smokers. The median NIHSS was similar in both groups (Table 2). Among the subset of patients who presented within 3 hours of LKW, the only difference that remained was that the postintervention group had fewer active smokers (Table 3). In comparing patients with DTN ≤60 versus DTN >60, there were no significant differences between any patient demographic factors or comorbidities (Table in the online-only Data Supplement).
Outcomes

For all patients first presenting to the ED during the study period, median DTCT time was 68 (33–153) minutes; and for patients who ultimately received intravenous tPA, median DTCT was 24 (17–35) minutes and median DTN time was 58 (40–75) minutes. The new protocol was implemented in 2007. Median DTCT improved significantly when comparing the pre-intervention versus post-intervention in all patients (71 minutes versus 59 minutes; \( P < 0.001 \)), in those patients presenting within 3 hours of LKW (38 versus 24 minutes; \( P < 0.001 \)) and in those patients who received intravenous tPA (30 versus 18 minutes; \( P < 0.001 \); Figure). Similarly, median DTN time also improved significantly after the intervention (70 versus 47 minutes; \( P < 0.001 \)). In addition, we evaluated the percentage of patients who achieved the nationally recommended time targets for acute evaluation and treatment. Among all intravenous tPA-treated patients, the percentage achieving the targets doubled for both DTCT \( \leq 25 \) minutes (37.5% versus 75.4%; \( P < 0.001 \)) and DTN \( \leq 60 \) minutes (32.1% versus 70.3%; \( P < 0.001 \); Table 2). Similar results were seen in the cohort of tPA-treated patients presenting within 3 hours of LKW (Table 3). In a univariate analysis evaluating factors associated with improved DTN60, only calendar year was found to be significant (Table in the online-only Data Supplement).

Discussion

Implementing 10 best practice initiatives at our institution was associated with a dramatic improvement in the timeliness of...
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acute stroke care. These practices were based on reviewing the barriers we faced in achieving the national time targets established by the NINDS and stroke expert community. These 10 practices mirror those adopted by the AHA in the Target Stroke Initiative and provide evidence that these practices can be effectively applied. After the intervention, we found that of patients who received tPA, 75% had CT imaging within 25 minutes and 70% received tPA within 60 minutes of ED arrival. Our postintervention performance compares favorably with published national data from GWTG-Stroke.8 A hospital-level analysis of the data in that recent publication demonstrates that <2% of sites achieved a DTN of ≤60 minutes in >60% of their patients (source: unpublished supplementary analyses, courtesy of the authors). Despite trends that suggest gradual improvement in DTN times across the country, the rapid improvement in our timeliness of care is likely associated with the changes to our acute stroke protocol (Figure).

The purpose of initiatives like Target Stroke is to improve rapid assessment and treatment of patients with AIS. DTN times have been the standard in the cardiac literature for thrombolytic treatment of acute MI. In contrast to cardiac patients, there are additional challenges to meeting time targets for patients with acute stroke including the need for imaging to exclude hemorrhage and the importance of confirming a LKW time. This can be particularly challenging in patients with neglect or aphasia who arrive without a reliable witnessed time of onset. Hence, there are additional barriers to achieving rapid DTN times in patients with stroke that must be addressed.

In this study, both DTCT and DTN times were significantly shorter after the new protocol. Several critical factors contribute to the improved DTCT phase of care, including prehospital notification to the ED to prepare everyone for an incoming stroke, a hospital pager informing neuroradiologists and CT technologists to clear the scanner and prepare any necessary imaging, and a large multidisciplinary team that working together to evaluate patients quickly before imaging. Prior studies have demonstrated that prehospital notifications reduces DTCT and DTN times.4–11 In a small study, DTCT and DTN times were reduced even further by having prenotification from Emergency Medical Services directly to the neurologist rather than the ED.12 Investigators in Helsinki, Finland, recently reported median DTN times of 20 minutes. In their intervention, Emergency Medical Services personnel evaluated the patients en route to confirm LKW and documented an NIHSS and obtained consent for tPA in the ambulance, allowing them to bring patients directly to the CT scanner from the ambulance bay. They benefitted from a national central health record that could be accessed by the hospital before patient arrival, allowing for prescreening of the medical record and current medications.13 With stronger connections to first responders, DTCT times might be further decreased.

Another recent study evaluated the process of acute stroke workflow using value stream mapping analysis techniques and found that several factors cause increased DTN times: inefficient patient flow, serial rather than parallel processing of tasks, and laboratory delay. To address these barriers, a multi-pronged intervention was created that transported patients directly to CT, assigned specific tasks to the ED and stroke teams to eliminate duplication of work, and used point of care testing to remove laboratory delays. They found a significant reduction in DTCT and DTN times without an increase in symptomatic hemorrhage or worsened outcomes, confirming that this approach to improved workflow can safely reduce DTN times.14 Although urgent transport to imaging is critical, it is also important to avoid delays that can be associated with advanced imaging before thrombolysis decision making. It has been suggested that acquisition of advanced imaging may also affect DTN times. Although our patients often receive both CT angiography and MRI in the ED, they are given intravenous tPA immediately after their noncontrast head CT, before any advanced imaging. This likely contributed meaningfully to the improved timeliness of care.

Prior literature has shown that arrival in the ED sooner after symptom onset may delay tPA therapy because of a perception of having extra time to give tPA,8,15,16 although the likelihood of a good outcome clearly increases when intravenous tPA is given closer to symptom onset.17 This concept was confirmed by a recent study that looked at intravenous tPA administration in the 3- to 4.5-hour window. Patients who arrived within a 3-hour time window were often receiving their tPA within a 3- to 4.5-hour window and median DTN times were 20 minutes faster for patients arriving at 2 to 3.5 hours after symptom onset than for patients arriving 0 to 2 hours after symptom onset.16 This finding was replicated in the national GWTG-Stroke analysis showing that early arriving patients were less likely to achieve a DTN60 than those arriving more than 1 hour after symptom onset.1 In our study, despite having increased numbers of patients who arrived within 3 hours in the post- versus preintervention phases (34% versus 25%; P<0.0001), the DTN times were significantly shorter post implementation, suggesting that our intervention helped to address these disparities in tPA timeliness (Table 2). A recent study supports this finding, by showing that standardized protocols can eliminate the in-hospital delay initiated by the 3-hour effect.18

Overall, the importance of working together as a team cannot be overemphasized. Because the team includes members from multiple departments, the members will always be different, so feedback becomes essential to accomplishing rapid DTN times. In our institution, feedback is given to each member of the team through emails after every intravenous tPA case, documenting DTCT and DTN times and identifying opportunities for improvement by team members who reply to the emails with suggested solutions. In addition, we hold periodic DTN60 recognition events for teams that have accomplished the shortest DTN times, to improve collaboration and emphasize the importance of rapid evaluation. Prior studies have shown that feedback alone can reduce DTN times.19

Our study has several important limitations. This is a single center study at a tertiary care hospital, with sufficient patient volume and experienced stroke trained physicians. In addition, rapid specialist assessment is available at all times as there is 24-hour in-house stroke fellow and neurology resident coverage. Finally, postdischarge outcome data are not available, so we cannot evaluate whether reduced times translated into improved outcomes. It is likely that our experience would replicate those found in national cohorts, suggesting that rapid DTN times are associated with better outcomes.17,20
In conclusion, implementing a bundle of best practice interventions improved DTCT and DTN times at our hospital, doubling the number of patients who received imaging and intravenous tPA within the recommended national time targets. These best practices reflect the approach advocated by the AHA Target Stroke Initiative, and our data support the concept that implementation of the Target Stroke 10 best practices is not only feasible but also leads to faster treatment for patients with acute stroke.

Disclosures

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References

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**Supplemental Table:** Demographics and clinical characteristics of patients with acute ischemic stroke who received IV tPA within 60 minutes during a pre-intervention period (2003-2006) as compared to a post-intervention period (2008-2011).

<table>
<thead>
<tr>
<th></th>
<th>Pre-Intervention (n=37)</th>
<th>Post-Intervention (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>73.4 ± 14.3</td>
<td>71.6 ± 15.2</td>
<td>0.529</td>
</tr>
<tr>
<td><strong>Gender- Male</strong></td>
<td>54.1</td>
<td>50.0</td>
<td>0.673</td>
</tr>
<tr>
<td><strong>Race – White</strong></td>
<td>86.5</td>
<td>84.0</td>
<td>0.720</td>
</tr>
<tr>
<td><strong>Co-morbidities</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>HTN</td>
<td>78.4</td>
<td>69.0</td>
<td>0.280</td>
</tr>
<tr>
<td>DM</td>
<td>24.3</td>
<td>19.0</td>
<td>0.493</td>
</tr>
<tr>
<td>HL</td>
<td>37.8</td>
<td>42.0</td>
<td>0.660</td>
</tr>
<tr>
<td>CAD/Prior MI</td>
<td>32.4</td>
<td>23.0</td>
<td>0.261</td>
</tr>
<tr>
<td>A. fib</td>
<td>29.7</td>
<td>26.0</td>
<td>0.662</td>
</tr>
<tr>
<td>Smoking</td>
<td>16.2</td>
<td>11.0</td>
<td>0.411</td>
</tr>
<tr>
<td><strong>NIHSS</strong>*</td>
<td>16 (10 – 21)</td>
<td>13 (7 – 18)</td>
<td>0.085</td>
</tr>
<tr>
<td><strong>Door to CT</strong>*</td>
<td>25 (22 – 30)</td>
<td>17 (14 – 22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Door to CT ≤ 25</strong></td>
<td>54.1</td>
<td>84.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>LKW to IV tPA</strong>*</td>
<td>100 (84 - 148)</td>
<td>94 (70 - 137)</td>
<td>0.161</td>
</tr>
<tr>
<td><strong>Door to IV tPA</strong></td>
<td>51 (44 – 56)</td>
<td>39 (28 – 49)</td>
<td>&lt;0.0001</td>
</tr>
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