Strategies Used by Hospitals to Improve Speed of Tissue-Type Plasminogen Activator Treatment in Acute Ischemic Stroke

Ying Xian, MD, PhD; Eric E. Smith, MD, MPH; Xin Zhao, MS; Eric D. Peterson, MD, MPH; DaiWai M. Olson, PhD, RN; Adrian F. Hernandez, MD, MHS; Deepak L. Bhatt, MD, MPH; Jeffrey L. Saver, MD; Lee H. Schwamm, MD; Gregg C. Fonarow, MD

Background and Purpose—The benefits of intravenous tissue-type plasminogen activator in acute ischemic stroke are time dependent, and several strategies have been reported to be associated with more rapid door-to-needle (DTN) times. However, the extent to which hospitals are using these strategies and their association with DTN times have not been well studied.

Methods—We surveyed 304 Get With The Guidelines-Stroke hospitals joining Target: Stroke regarding their baseline use of strategies to reduce DTN times in the January 2008 to December 2009 time frame before the initiation of Target: Stroke and determined the association between hospital strategies and DTN times.

Results—Among 5460 patients receiving tissue-type plasminogen activator within 3 hours of symptom onset in surveyed hospitals, the median DTN time was 72 minutes (interquartile range, 55–94). Reported use of the different strategies varied considerably. Of 11 hospital strategies analyzed individually by multivariable analysis, 3 strategies were independently associated with shorter DTN times. These included rapid triage/stroke team notification (209/304 [69%] hospitals, 8.1-minute reduction in DTN time), single-call activation system (190/304 [63%] hospitals, 4.3 minutes), and tissue-type plasminogen activator stored in the emergency department (189/304 [62%] hospitals, 3.5 minutes). When analyzed incrementally, hospitals that used a greater number of strategies had shorter DTN times with 1.3 minutes (adjusted mean difference) saved for each strategy implemented (14 minutes if all strategies were used).

Conclusions—Although the majority of participating hospitals reported using some strategy to reduce delays in tissue-type plasminogen activator administration for acute ischemic stroke, the strategies applied vary considerably and those most strongly associated with shorter DTN times were applied relatively less frequently. (Stroke. 2014;45:1387-1395.)

Key Words: quality of health care ■ quality improvement ■ stroke

See related article, p 1243.

Intravenous tissue-type plasminogen activator (tPA) is currently the most effective treatment to improve outcomes for acute ischemic stroke. However, the benefits of tPA are highly time dependent. Pooled data from major tPA trials suggest that the therapeutic benefit is maximal when given early after stroke onset and declines rapidly during the next 4.5 hours. For every minute that treatment is delayed in a typical large vessel ischemic stroke, nearly 2 million neurons die. Therefore, rapid treatment is a critical factor in the outcomes of patients with acute stroke who are treated with intravenous tPA. Although the current guidelines of the American Heart Association/American Stroke Association (AHA/ASA) recommend the delivery of thrombolytic therapy within 60 minutes from hospital arrival (class I; level of evidence A), the door-to-needle (DTN) time for intravenous tPA administration vary widely in the United States. Even among hospitals in the AHA/ASA Get With The Guidelines-Stroke (GWTG-Stroke) quality improvement program, <30% of patients treated with intravenous tPA had a DTN time of the recommended ≤60 minutes in the United States. Therefore, there are substantial opportunities nationally to improve timely tPA administration for patients with acute ischemic stroke.
Experience with acute myocardial infarction and acute ischemic stroke system of care have suggested numerous hospital strategies for reducing treatment delays. However, the extent to which hospitals are using these strategies has not been well studied. More importantly, it is not clear which strategies are most effective. Therefore, we conducted a national survey of hospitals joining the AHA/ASA’s Target: Stroke Initiative. This study represents the first large national survey of hospitals regarding their DTN time strategies. Our specific aims were to assess baseline use of best practice strategies to reduce DTN times before the initiation of Target: Stroke and quantify the association of these hospital strategies with DTN times.

Methods

Target: Stroke Initiative

Target: Stroke builds on the success of GWTG-Stroke, Brain Attack Coalition, and Mission: Lifeline. Target: Stroke is a national quality improvement initiative by the AHA/ASA to improve the care of stroke. The initial goal of Target: Stroke is for participating hospitals to achieve DTN times within 60 minutes in ≥50% ischemic stroke treated with tPA. To facilitate more rapid integration of evidence into clinical practice, Target: Stroke provided participating hospitals with best practice strategies, supporting tools, and educational resources necessary to improve the timeline of administration of intravenous tPA to eligible patients with acute ischemic stroke. To identify best practice strategies for reducing DTN times, the AHA/ASA formed a multidisciplinary work group of expertise from stroke neurology, emergency medicine, nursing, quality improvement, emergency medical services (EMS), and hospital management to study this issue. With input from other national organizations as well as participating hospitals, the work group performed a systematic review of the English language literature on improving DTN times in acute ischemic stroke and time to treatment reduction strategies in acute myocardial infarction. Based on the literature review and expert consensus on local best practice, the work group identified best practice strategies that could be rapidly, feasibly, and cost effectively adopted by participating hospitals. Details of the Target: Stroke Initiative and Target: Stroke best practice strategies have been described in the literature.

As a condition of the Target: Stroke enrollment process, representatives from each participating hospital completed an online survey (available at http://www.strokesociety.org/targetstroke) of their baseline practice for intravenous tPA administration for patients with acute ischemic stroke. The survey questions were developed based on literature review and expert consensus to query hospitals on previous DTN time practice and further refined after pilot testing. The 11 practices hospitals were surveyed for were advance hospital notification by EMS, rapid triage protocol and stroke team notification, single-call activation system, access to stroke expertise 24x7, rapid acquisition and interpretation of brain imaging, rapid laboratory testing (including point-of-care testing if indicated), tPA administration protocols, mix tPA medication ahead of time, rapid access to intravenous tPA, team-based approach, and prompt data feedback. In addition, hospitals were surveyed whether trainees are involved in the acute stroke team as a routine component of acute stroke care. The survey was structured regarding use of the process or protocol all of the time, some of the time, or none of the time or yes/no. An AHA/ASA staff member was available to provide assistance and ensure accurate interpretation of the survey questionnaires.

Measures and Statistical Analysis

Using the survey data, we conducted a cross-sectional study of 350 GWTG-Stroke hospitals joining the Target: Stroke Initiative and assessed their baseline use of specific strategies for reducing DTN in the January 2008 and December 2009 time frame before the initiation of the Target: Stroke program. For descriptive purposes, we reported the frequency and percentages of hospitals responses for each strategy as well as DTN times among eligible patients who received intravenous tPA within 3 hours of symptom onset. Data on individual patients were obtained from GWTG-Stroke Registry. The design and conduct of the GWTG-Stroke Registry as well as the validity and reliability of GWTG-Stroke data collection have been previously reported.

Multivariable generalized linear regression models were performed to investigate the relationships between each hospital strategy and DTN times adjusting for baseline demographic and clinical characteristics. These variables included age, sex, race/ethnicity, medical history (atrial fibrillation, prosthetic heart valve, previous stroke or transient ischemic attack, coronary artery disease or prior myocardial infarction, carotid stenosis, diabetes mellitus, peripheral vascular disease, hypertension, smoking status, dyslipidemia, and heart failure), arrival mode, on-hour presentation (presenting to the emergency department [ED] between 7:00 am and 6:00 pm on any weekday), on-set-to-door times, and National Institutes of Health Stroke Scale. The effect of each individual strategy on DTN times was calculated as the adjusted mean difference between the DTN times of hospitals implementing the selected strategy and hospitals not implementing the strategy. Similar multivariable logistic regression analysis was performed to evaluate the association between hospital strategy and DTN times ≤60 minutes. All these analyses accounted for hospital-level clustering using a generalized estimating equations approach. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc). Outcome, a Quintiles Company, is the data collection coordination center for the AHA/ASA GWTG programs. The Duke Clinical Research Institute served as the data analysis center, and institutional review board approval was granted to analyze aggregate deidentified data for research purposes.

Results

Study Samples

Of the 350 GWTG-Stroke hospitals joining Target: Stroke and completing the survey by January 2011, 36 hospitals (10.3%) did not administer tPA during the study period and 1 hospital (0.3%) did not have any ischemic stroke admissions during the study period. We also excluded 3 hospitals (0.9%) with invalid DTN time and 6 hospitals (1.7%) with onset-to-needle time >3 hours to confine the study population to patients covered by the class I guideline recommendation present during the study period. Because DTN times were calculated as the difference between patient arrival time and tPA initiated time, in-hospital stroke was excluded from the analysis. After these exclusions, our analyses included 304 hospitals treating 5460 patients with ischemic stroke with intravenous tPA within 3 hours of symptom onset between January 2008 and December 2009 (before the initiation of Target: Stroke). Survey respondents represented a range of physicians, nurses, and hospital quality management and administration personnel (Table I in the online-only Data Supplement). A total of 50% hospitals were academic centers, and 48% were primary stroke centers. The median bed size was 343 (interquartile range [IQR], 231–481). Approximately 50% of hospitals had an ischemic stroke volume of >150 patients per year (median, 163; IQR, 106–247). The median tPA volume was 10 patients (IQR, 6–17) per year. Compared with GWTG-Stroke hospitals that did not participate in the Target: Stroke survey during the study period, Target: Stroke survey hospitals were more frequently larger, academic hospitals, primary stroke centers, with higher ischemic stroke volume, shorter baseline DTN times, and more experience with tPA administration (Table II in the online-only Data Supplement).

Hospital Strategies and DTN Times

Table 1 summarizes the strategies hospitals used at baseline. Reported use of the different strategies varied considerably.
The strategies least frequently used included advance hospital notification by EMS (52.3%), rapid triage protocol with stroke team notification (68.8%), single-call activation system all of the time (62.5%), trainees involved in the stroke team all of the time (26.0%), routine premixing of tPA (16.1%), and storing tPA in the ED (62.2%).

Among 304 Target: Stroke hospitals participating in the survey, the median DTN time was 79 minutes (IQR, 71–89).

Table 1. Hospitals Reporting Use of Strategies Before the Initiation of Target: Stroke and Associated DTN Times Among 5460 Patients Receiving Intravenous tPA Within 3 Hours of Symptom Onset

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Hospitals, n (%)</th>
<th>Median DTN Time (IQR), min</th>
<th>P Value</th>
<th>DTN Time ≤60 min</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advance hospital notification by emergency medical services</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>11 (3.6)</td>
<td>77 (59–94)</td>
<td>0.13</td>
<td>28.9%</td>
<td>0.12</td>
</tr>
<tr>
<td>Some of the time</td>
<td>129 (42.4)</td>
<td>73 (56–95)</td>
<td></td>
<td>32.5%</td>
<td></td>
</tr>
<tr>
<td>All of the time</td>
<td>159 (52.3)</td>
<td>72 (54–92)</td>
<td></td>
<td>35.2%</td>
<td></td>
</tr>
<tr>
<td>Rapid triage protocol and stroke team notification</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>None of the time</td>
<td>20 (6.6)</td>
<td>78 (64–102)</td>
<td></td>
<td>22.0%</td>
<td></td>
</tr>
<tr>
<td>Some of the time</td>
<td>71 (23.4)</td>
<td>78 (61–98)</td>
<td></td>
<td>25.0%</td>
<td></td>
</tr>
<tr>
<td>All of the time</td>
<td>209 (68.8)</td>
<td>70 (53–92)</td>
<td></td>
<td>36.2%</td>
<td></td>
</tr>
<tr>
<td>Single-call activation system</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>None of the time</td>
<td>76 (25.0)</td>
<td>80 (63–99)</td>
<td></td>
<td>22.8%</td>
<td></td>
</tr>
<tr>
<td>Some of the time</td>
<td>29 (9.5)</td>
<td>76 (59–95)</td>
<td></td>
<td>27.3%</td>
<td></td>
</tr>
<tr>
<td>All of the time</td>
<td>190 (62.5)</td>
<td>70 (53–91)</td>
<td></td>
<td>37.3%</td>
<td></td>
</tr>
<tr>
<td>Access to in-house stroke expertise 24×7</td>
<td></td>
<td></td>
<td>0.004</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>None of the time</td>
<td>16 (5.3)</td>
<td>78 (60–101)</td>
<td></td>
<td>25.8%</td>
<td></td>
</tr>
<tr>
<td>Some of the time</td>
<td>45 (14.8)</td>
<td>75 (59–94)</td>
<td></td>
<td>27.8%</td>
<td></td>
</tr>
<tr>
<td>All of the time</td>
<td>240 (79.0)</td>
<td>72 (54–93)</td>
<td></td>
<td>35.0%</td>
<td></td>
</tr>
<tr>
<td>Trainees (residents, students, fellows) involved in the stroke team</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>None of the time</td>
<td>143 (47.0)</td>
<td>75 (57–95)</td>
<td></td>
<td>35.9%</td>
<td></td>
</tr>
<tr>
<td>Some of the time</td>
<td>61 (20.1)</td>
<td>75 (56–97)</td>
<td></td>
<td>16.4%</td>
<td></td>
</tr>
<tr>
<td>All of the time</td>
<td>79 (26.0)</td>
<td>68 (51–89)</td>
<td></td>
<td>44.4%</td>
<td></td>
</tr>
<tr>
<td>Rapid brain imaging protocol</td>
<td></td>
<td></td>
<td>0.11</td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>No</td>
<td>25 (8.22)</td>
<td>74 (57–96)</td>
<td></td>
<td>30.2%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>279 (91.8)</td>
<td>72 (55–94)</td>
<td></td>
<td>34.0%</td>
<td></td>
</tr>
<tr>
<td>Rapid laboratory testing protocol</td>
<td></td>
<td></td>
<td>0.34</td>
<td></td>
<td>0.26</td>
</tr>
<tr>
<td>No</td>
<td>21 (6.9)</td>
<td>73 (58–96)</td>
<td></td>
<td>30.4%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>283 (93.1)</td>
<td>72 (55–94)</td>
<td></td>
<td>34.0%</td>
<td></td>
</tr>
<tr>
<td>tPA administration protocol</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>31 (10.2)</td>
<td>80 (63–101)</td>
<td></td>
<td>23.6%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>273 (89.8)</td>
<td>72 (55–93)</td>
<td></td>
<td>34.4%</td>
<td></td>
</tr>
<tr>
<td>Routine premixing of tPA ahead of time</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>255 (83.9)</td>
<td>74 (56–94)</td>
<td></td>
<td>32.1%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>49 (16.1)</td>
<td>66 (50–92)</td>
<td></td>
<td>41.4%</td>
<td></td>
</tr>
<tr>
<td>Team-based approach to stroke care</td>
<td></td>
<td></td>
<td>0.31</td>
<td></td>
<td>0.43</td>
</tr>
<tr>
<td>No</td>
<td>19 (6.3)</td>
<td>74 (57–100)</td>
<td></td>
<td>30.4%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>285 (93.8)</td>
<td>72 (55–94)</td>
<td></td>
<td>33.9%</td>
<td></td>
</tr>
<tr>
<td>tPA stored in emergency department</td>
<td></td>
<td></td>
<td>0.006</td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>No</td>
<td>115 (37.8)</td>
<td>74 (56–95)</td>
<td></td>
<td>31.2%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>189 (62.2)</td>
<td>71 (54–93)</td>
<td></td>
<td>35.3%</td>
<td></td>
</tr>
<tr>
<td>Regular feedback on DTN times provided</td>
<td></td>
<td></td>
<td>0.002</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>84 (27.6)</td>
<td>75 (58–95)</td>
<td></td>
<td>29.6%</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>220 (72.4)</td>
<td>72 (54–93)</td>
<td></td>
<td>35.1%</td>
<td></td>
</tr>
</tbody>
</table>

DTN indicates door-to-needle; IQR, interquartile range; and tPA, tissue-type plasminogen activator.
Among patients admitted to 304 Target: Stroke hospitals par-

≤odds of DTN times per each strategy) were independently associated with increased

gies used (odds ratio, 1.12; 95% confidence interval, 1.02–1.24

certainty, 1.04–1.80), and a greater number of strate-

ies involved in the stroke team all the time (odds ratio, 1.37; 95%

certainty, 1.02–1.71), trainees involved in the stroke team all of the time (Table 1). In

addition, hospitals that implemented tPA administration protoc-

ols, routinely premixed intravenous tPA, had tPA stored in

ED, and provided regular feedback on DTN times had shorter

DTN times than hospitals that did not implement such strategies. Similarly, the hospitals that used these strategies were more likely to reach the DTN goal within 60 minutes.

The majority of hospital strategies were associated with shorter DTN times in unadjusted analyses (Table 2). After multivariate adjustment, the most strongly associated hospital strategies were rapid triage protocol with stroke team notification, single-call activation, had access to in-house stroke expertise, and train-

ees involved in the stroke team all of the time (Table 1). In

addition, hospitals that implemented tPA administration proto-

cols, routinely premixed intravenous tPA, had tPA stored in

ED, and provided regular feedback on DTN times had shorter

DTN times than hospitals that did not implement such strategies. Similarly, the hospitals that used these strategies were more likely to reach the DTN goal within 60 minutes.

The measure DTN time reflects a complex clinical process which requires coordination across departments and disciplines to provide rapid and efficient care to patients with acute ischemic stroke. Although variation in this complex process is inevitable, some delays may be preventable through organizational change to effect timely triage, diagnosis, decision making, and treatment of patients with ischemic stroke. In this large national survey of hospitals regarding their strategies to reduce DTN time, we found that the speed of tPA treatment in many surveyed hospitals was significantly longer than the recommended national target of ≤60 minutes. In contrast, many centers in Europe have reported DTN time well <60 minutes including 50 minutes in Cologne, Germany; 38 minutes in Bergen, Norway; and 20 minutes in Helsinki, Finland. Although lack of experience may explain prolonged delay in treatment, a small previously inexperienced center can achieve shorter DTN times after organizational and logistical changes in deliver of stroke care. Although most participating US hospitals report using some strategies to improve the timeliness of tPA administration, use of each pre-

specified strategy varied substantially. In particular, reported use of rapid triage protocol and stroke team notification all of the time (68.8%), single-call activation system all of the time (62.5%), and storing tPA in the ED (62.2%) were relatively low in surveyed hospitals. However, these strategies were the ones most strongly associated with shorter DTN times in the multivariable analysis.

The time intervals were significantly shorter for patients admitted to hospitals in which rapid acute triage protocol and stroke team notification were used to facilitate the timely recognition and treatment of stroke (8.1-minute reduction

Discussion

Among patients admitted to 304 Target: Stroke hospitals par-

ticipating in this survey, only a minority of patients treated with

intravenous tPA had DTN times within 60 minutes. Although all hospitals reported use of some recommended strategies to improve the DTN times, many of the best practice strategies are not commonly used. This may account, in part, for the substantial delays to acute stroke treatment in the United States.

Furthermore, this study analyzed the association of hospital strategies with DTN times and found that rapid triage protocol with stroke team notification, single-call activation systems, and tPA stored in the ED were independently associated with more rapid tPA administration. In sequential analyses, incremental reductions in DTN times were observed for all 11 ana-

lyzed strategies, with the potential to reduce DTN time by as much as 14 minutes if all strategies were used.

The median DTN time was 72 minutes (IQR, 55–94), and

1849 of 5460 (33.9%) patients had DTN time ≤60 minutes.

The median DTN times were shorter at hospitals that used rapid triage protocol with stroke team notification, single-call activation, had access to in-house stroke expertise, and train-

ees involved in the stroke team all of the time (68.8%, 62.5%, 26.0%, and 62.2%, respectively). When all 11 strategies were used by only two thirds of the surveyed hospitals (68.8%,

62.5%, 26.0%, and 62.2%), hospitals that implemented a greater number of strategies also had shorter DTN times in unadjusted analyses (Table 2). After multivariable adjustment, the most strongly associated hospital strategies were rapid triage protocol with stroke team notification all the time (mean reduction in DTN time, 8.1 minutes), single-call activation system all the time (4.3 minutes), trainees involved in the stroke team all the time (4.6 minutes), and tPA being stored in ED (3.5 minutes). In general, these strategies were used by only two thirds of the surveyed hospitals (68.8%, 62.5%, 26.0%, and 62.2%, respectively). When all 11 strategies were analyzed incrementally (excluding trainees in the stroke team because it is not applicable to nonacademic centers), hos-

pitals that implemented a greater number of strategies also had shorter average DTN times. On average, 1.3 minutes could be saved for each strategy implemented. This represents a potential to reduce DTN time by as much as 14 minutes if all strategies were used. Similarly, when analyzing the proportion of patients with DTN times ≤60 minutes, tPA being stored in ED (odds ratio, 1.32; 95% confidence interval, 1.02–1.71), trainees involved in the stroke team all the time (odds ratio, 1.37; 95% confidence interval, 1.04–1.80), and a greater number of strategies used (odds ratio, 1.12; 95% confidence interval, 1.02–1.24 per each strategy) were independently associated with increased odds of DTN times ≤60 minutes (Table 3).
Table 2. Association Between Hospital Strategies and Door-to-Needle Times

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Unadjusted Mean Difference in DTN Time (95% CI), min</th>
<th>P Value</th>
<th>Adjusted Mean Difference in DTN Time (95% CI), min</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advance hospital notification by emergency medical services</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Some of the time</td>
<td>0.4 (−4.4 to 5.3)</td>
<td>0.86</td>
<td>2.1 (−3.8 to 7.9)</td>
<td>0.49</td>
</tr>
<tr>
<td>All of the time</td>
<td>−1.1 (−5.9 to 3.7)</td>
<td>0.66</td>
<td>−0.5 (−6.2 to 5.3)</td>
<td>0.87</td>
</tr>
<tr>
<td>Rapid triage protocol and stroke team notification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Some of the time</td>
<td>−2.4 (−6.8 to 2.1)</td>
<td>0.30</td>
<td>−7.0 (−13.6 to −0.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>All of the time</td>
<td>−8.8 (−13.0 to −4.7)</td>
<td>&lt;0.001</td>
<td>−8.1 (−14.1 to −2.1)</td>
<td>0.008</td>
</tr>
<tr>
<td>Single-call activation system</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Some of the time</td>
<td>−3.5 (−6.6 to −0.35)</td>
<td>0.029</td>
<td>−2.2 (−7.9 to 3.5)</td>
<td>0.45</td>
</tr>
<tr>
<td>All of the time</td>
<td>−8.1 (−10.1 to −6.1)</td>
<td>&lt;0.001</td>
<td>−4.3 (−7.8 to −0.7)</td>
<td>0.018</td>
</tr>
<tr>
<td>Access to in-house stroke expertise 24×7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Some of the time</td>
<td>−3.0 (−7.8 to 1.8)</td>
<td>0.22</td>
<td>1.7 (−8.8 to 12.3)</td>
<td>0.75</td>
</tr>
<tr>
<td>All of the time</td>
<td>−5.7 (−10.1 to −1.3)</td>
<td>0.011</td>
<td>0.9 (−9.1 to 11.0)</td>
<td>0.85</td>
</tr>
<tr>
<td>Trainees (residents, students, fellows) involved in the stroke team</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Some of the time</td>
<td>3.8 (0.9 to 8.5)</td>
<td>0.11</td>
<td>4.8 (0.6 to 9.0)</td>
<td>0.025</td>
</tr>
<tr>
<td>All of the time</td>
<td>−4.6 (−8.2 to −0.9)</td>
<td>0.014</td>
<td>−3.6 (−7.0 to −0.3)</td>
<td>0.035</td>
</tr>
<tr>
<td>Rapid brain imaging protocol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−3.0 (−6.8 to 0.8)</td>
<td>0.12</td>
<td>−3.8 (−11.1 to 3.4)</td>
<td>0.30</td>
</tr>
<tr>
<td>Rapid laboratory testing protocol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−1.9 (−5.6 to 1.8)</td>
<td>0.31</td>
<td>−0.9 (−6.7 to 4.9)</td>
<td>0.76</td>
</tr>
<tr>
<td>tPA administration protocol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−7.3 (−10.7 to −4.0)</td>
<td>&lt;0.001</td>
<td>−2.7 (−8.3 to 2.9)</td>
<td>0.35</td>
</tr>
<tr>
<td>Routine premixing of tPA ahead of time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−4.7 (−6.5 to −2.8)</td>
<td>&lt;0.001</td>
<td>−2.2 (−6.8 to 2.4)</td>
<td>0.36</td>
</tr>
<tr>
<td>Team-based approach to stroke care</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−2.6 (−7.8 to 2.5)</td>
<td>0.32</td>
<td>−3.7 (−16.4 to 9.0)</td>
<td>0.57</td>
</tr>
<tr>
<td>tPA stored in emergency department</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−2.0 (−3.6 to −0.5)</td>
<td>0.012</td>
<td>−3.5 (−6.7 to −0.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Regular feedback on DTN times provided</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>…</td>
<td>Reference</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>−2.4 (−4.2 to −0.6)</td>
<td>0.008</td>
<td>−1.4 (−5.0 to 2.1)</td>
<td>0.42</td>
</tr>
<tr>
<td>Total number of hospital strategies per 1 increase*</td>
<td>−1.9 (−2.4 to −1.4)</td>
<td>&lt;0.001</td>
<td>−1.3 (−2.4 to −0.3)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; DTN, door-to-needle; and tPA, tissue-type plasminogen activator.

*Excluding trainees (residents, students, fellows) involved in the stroke team because not all hospitals have training program.
Table 3. Association Between Hospital Strategies and Door-to-Needle Times ≤60 Minutes

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Unadjusted OR (95% CI)</th>
<th>P Value</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advance hospital notification by emergency medical services</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Some of the time</td>
<td>1.19 (0.81–1.74)</td>
<td>0.38</td>
<td>0.96 (0.67–1.37)</td>
<td>0.83</td>
</tr>
<tr>
<td>All of the time</td>
<td>1.34 (0.92–1.96)</td>
<td>0.13</td>
<td>1.07 (0.75–1.54)</td>
<td>0.71</td>
</tr>
<tr>
<td>Rapid triage protocol and stroke team notification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Some of the time</td>
<td>1.18 (0.81–1.73)</td>
<td>0.39</td>
<td>1.10 (0.59–2.04)</td>
<td>0.76</td>
</tr>
<tr>
<td>All of the time</td>
<td>2.01 (1.41–2.88)</td>
<td>&lt;0.001</td>
<td>1.41 (0.80–2.51)</td>
<td>0.24</td>
</tr>
<tr>
<td>Single-call activation system</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Some of the time</td>
<td>1.27 (0.98–1.65)</td>
<td>0.069</td>
<td>0.96 (0.59–1.56)</td>
<td>0.87</td>
</tr>
<tr>
<td>All of the time</td>
<td>2.02 (1.70–2.39)</td>
<td>&lt;0.001</td>
<td>1.32 (0.97–1.80)</td>
<td>0.08</td>
</tr>
<tr>
<td>Access to in-house stroke expertise 24×7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Some of the time</td>
<td>1.11 (0.75–1.64)</td>
<td>0.60</td>
<td>0.86 (0.32–2.25)</td>
<td>0.75</td>
</tr>
<tr>
<td>All of the time</td>
<td>1.55 (1.08–2.22)</td>
<td>0.017</td>
<td>1.04 (0.41–2.62)</td>
<td>0.93</td>
</tr>
<tr>
<td>Trainees (residents, students, fellows) involved in the stroke team</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the time</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Some of the time</td>
<td>0.76 (0.51–1.12)</td>
<td>0.16</td>
<td>0.66 (0.44–0.98)</td>
<td>0.041</td>
</tr>
<tr>
<td>All of the time</td>
<td>1.42 (1.08–1.87)</td>
<td>0.014</td>
<td>1.37 (1.04–1.80)</td>
<td>0.027</td>
</tr>
<tr>
<td>Rapid brain imaging protocol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.19 (0.88–1.60)</td>
<td>0.25</td>
<td>1.16 (0.73–1.84)</td>
<td>0.53</td>
</tr>
<tr>
<td>Rapid laboratory testing protocol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.18 (0.89–1.58)</td>
<td>0.26</td>
<td>0.96 (0.60–1.54)</td>
<td>0.88</td>
</tr>
<tr>
<td>tPA administration protocol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.70 (1.29–2.24)</td>
<td>&lt;0.001</td>
<td>1.48 (0.86–2.53)</td>
<td>0.16</td>
</tr>
<tr>
<td>Routine premixing of tPA ahead of time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.50 (1.31–1.72)</td>
<td>&lt;0.001</td>
<td>1.33 (0.93–1.91)</td>
<td>0.12</td>
</tr>
<tr>
<td>Team-based approach to stroke care</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.17 (0.79–1.75)</td>
<td>0.43</td>
<td>0.91 (0.38–2.15)</td>
<td>0.83</td>
</tr>
<tr>
<td>tPA stored in emergency department</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.20 (1.06–1.35)</td>
<td>0.003</td>
<td>1.32 (1.02–1.71)</td>
<td>0.03</td>
</tr>
<tr>
<td>Regular feedback on DTN times provided</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Reference</td>
<td>...</td>
<td>Reference</td>
<td>...</td>
</tr>
<tr>
<td>Yes</td>
<td>1.29 (1.12–1.48)</td>
<td>&lt;0.001</td>
<td>1.23 (0.93–1.64)</td>
<td>0.15</td>
</tr>
<tr>
<td>Total number of hospital strategies per 1 increase*</td>
<td>1.20 (1.14–1.25)</td>
<td>&lt;0.001</td>
<td>1.12 (1.02–1.24)</td>
<td>0.014</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; DTN, door-to-needle; OR, odds ratio; and tPA, tissue-type plasminogen activator. *Excluding trainees (residents, students, fellows) involved in the stroke team because not all hospitals have training program.
in DTN times), those in which the entire stroke team was activated with a single call from the ED that simultaneously alerts the entire stroke team (4.3 minutes), and those in which the tPA is readily available in the ED (3.5 minutes). Unlike some strategies that might require costly investment in new resources, these strategies could be rapidly implemented with existing resources, representing a potential immediate target for quality improvement in care of patients with stroke. In addition, the time intervals were shorter in hospitals with trainees involved in the stroke team (4.6 minutes). Although not all hospitals have a training program, this finding suggests that trainees can be integrated into an acute stroke team without significant delay in treatment.

Importantly, we found hospitals that had implemented a greater number of strategies also had a shorter DTN time. On average, 1.3 minutes would be saved for each of the 11 strategies implemented. Although the size of effect for individual strategies may seem modest, in aggregate, they exceed an absolute difference of 14 minutes in DTN times. With the median DTN times of 72 minutes in GWTG-Stroke in recent years, a 14-minute reduction would achieve the target of treatment within 60 minutes in the majority of patients, potentially saving thousands of patients per year from a lifetime of disability. Indeed, the 60-minute target itself might not be optimal and could probably be reduced even further given some centers can achieve DTN times of 20 minutes by systematically implementing multiple strategies. After the study period, in response to accumulating new evidence, Target: Stroke added as an additional best practice strategy—direct transfer of patients from EMS to the computed tomographic scanner. Because substantial reduction in treatment delays can rarely be achieved by a single strategy, but rather from changes to the whole stroke system of care, implementing the entire suite of strategies represents a promising approach to shortening DTN times further and reducing all possible delays in thrombolysis.

Based on literature review and expert consensus, the Target: Stroke initiative advocates the adoption of best practice strategies to reduce DTN times for intravenous tPA in acute ischemic stroke. Although some of these strategies were not independently associated with DTN times in our current analysis, our survey was not powered to detect modest impacts. All these best practice strategies have previously been reported to be effective in increasing the number of eligible patients treated or reported to reduce time to treatment in acute myocardial infarction and stroke. A variety of factors may have attenuated relationships between individual strategies and DTN times in this study. For instance, we have previously reported that faster treatment is associated with advance hospital notification by EMS in a patient-level analysis. However, EMS prenotification is more an EMS strategy than hospital strategy and not wholly under the control of the receiving hospital. As a result, the frequency of EMS prenotification might vary from patient to patient within the same hospital and is difficult to estimate in a hospital-level survey response. Because the Target: Stroke best strategies were published before hospitals completed the survey, hospital respondents may have reported what they should or planned to be doing, as opposed to actual practice. In addition, it may not have been possible to detect the influence of some strategies because of their already high adoption in surveyed hospitals (eg, ≈80% of hospitals have access to in-house stroke expertise at all times and >90% of hospitals implement brain imaging, laboratory testing, and tPA protocols and use team-based approach to stroke care). Residual measured or unmeasured confounding may also account for some of these findings. Furthermore, the use of multivariable logistic regression for DTN ≤60 minutes may be less sensitive in detecting effective strategies because DTN time is continuous and not dichotomous.

There are several limitations to this study. First, although several specific hospitals strategies are associated with a significant reduction in the DTN times, the cross-sectional design cannot establish causal relationship. Follow-up studies are planned to examine how implementation of key best practice strategies may have changed over the course of the initiative, and, more importantly, how timeliness of treatment may have changed over time after accounting for secular trends. Nonetheless, understanding how successful hospitals adopted these strategies at baseline can identify gaps in current practice and provide evidence for a collaborative national campaign tailored to overcome barriers in the system level. Second, data on use of strategies were self-reported and may have some subjectivity that cannot be avoided in survey-based research. Nevertheless, we extensively pilot-tested the survey instrument to ensure comprehensibility before the launch of the program. An AHA/ASA staff member was also available to provide assistance and ensure accurate interpretation of questionnaires during the survey. In addition, unlike a telephone survey which is often reported by a single respondent, our online survey was designed to be completed by the key personnel and encouraged to integrate input from other hospital team members. Furthermore, the baseline survey was administered as close as possible to the enrollment date to minimize recall bias inherent in survey research. Third, this study was cross-sectional using DTN times as a process measure, and no in-hospital or longitudinal outcomes were assessed. However, previous GWTG studies have demonstrated the benefit of rapid reperfusion therapy for clinical outcomes. Fourth, we confined the study population to patients covered by the class I guideline recommendation present during the study period. This approach potentially could remove less well-performing hospitals with patients who could have been treated within the 3-hour window. Nonetheless, the AHA/ASA did not publish the recommendation for expansion of treatment window until the end of May 2009, which was 6 months before the end of our study period. Although it has been increasingly adopted in clinical practice, there were relatively few patients treated with tPA after 3 hours during our study period. Last, although our survey included hospitals with a wide range of size, academic status, and geographic regions, these findings may not be generalized to rural hospitals, high-volume centers, and hospitals in other regions of the world. Furthermore, Target: Stroke is a voluntary program. Hospitals participate based on their level of interest in quality improvement in stroke care. Target: Stroke hospitals were more likely to have shorter DTN times than nonparticipating centers. Therefore, the generalizability of our findings to nonparticipating hospitals remains to
be established. It is likely that the hospitals in this survey use DTN time strategies more frequently than nonparticipating hospitals, further supporting the need for a national campaign to promote best practice strategies and improve the timeliness of tPA treatment in the United States.

Conclusions

Among hospitals participating in this study, DTN times vary substantially, with only one third of tPA-treated patients having DTN times within 60 minutes before the inception of Target: Stroke. The strategies most strongly associated with shorter DTN times were rapid triage protocol and stroke team notification, single-call activation system, and tPA being stored in the ED. Although most surveyed hospitals report use of certain strategies to improve the timeliness of tPA administration for acute ischemic stroke, relatively fewer hospitals implemented specific strategies that were most strongly associated with shorter DTN times. Future efforts are needed to facilitate the integration of evidence into clinical practice and disseminate the most effective strategies for improving timeliness of acute stroke thrombolysis.

Sources of Funding

Target: Stroke is an initiative provided by the American Heart Association/American Stroke Association.

Disclosures

Dr Peterson has received research grants from BMS/Schering Plough and serves as the principal investigator of the American Heart Association’s (AHA) Get With The Guidelines (GWTG) Analytical Center. Dr Hernandez has received research grants from Johnson & Johnson (Scios, Inc), Medtronic, Merck and honoraria from AstraZeneca, Geron, Medtronic, Novartis, and Sanofi-Aventis. Dr Hernandez has made available online detailed listings of financial disclosures (http://www.dcri.duke.edu/research/coi.jsp). Dr Bhatt serves on the Advisory Board of Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences and Board of Directors of Boston VA Research Institute, Society of Cardiovascular Patient Care. He also serves as a Chair of AHA GWTG Steering Committee and has received honoraria from American College of Cardiology (Editor, Clinical Trials, Cardiosource), Belvort Publications (Editor-in-Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), Harvard Clinical Research Institute (clinical trial steering committee), HMP Communications (Editor-in-Chief, Journal of Invasive Cardiology), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, Cardiology Today’s Intervention), WebMD (CME steering committees), and Data Monitoring Committees of Duke Clinical Research Institute, Harvard Clinical Research Institute, Mayo Clinic, and Population Health Research Institute. He has also received research grants from Amaryn, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, Roche, Sanofi Aventis, The Medicines Company and performed unfunded research for FlowCo, PLX Pharma, and Takeda. Dr Saver is a member of the GWTG Science Subcommittee; the University of California receives payments for Dr Saver’s service as a scientific consultant regarding trial design and conduct to Covidien, CoAxia, Grifols, Braintree, and St Jude Medical; 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.

References


Strategies Used by Hospitals to Improve Speed of Tissue-Type Plasminogen Activator Treatment in Acute Ischemic Stroke

Ying Xian, Eric E. Smith, Xin Zhao, Eric D. Peterson, DaiWai M. Olson, Adrian F. Hernandez, Deepak L. Bhatt, Jeffrey L. Saver, Lee H. Schwamm and Gregg C. Fonarow

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SUPPLEMENTAL MATERIAL

Supplemental Table I. Survey Respondents at Target: Stroke Hospitals (n=304)

<table>
<thead>
<tr>
<th>Professional or occupational group the person completing the survey*</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians</td>
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</tr>
<tr>
<td>ABPN-certified neurologian</td>
<td>12</td>
</tr>
<tr>
<td>Neurologist (not ABPN-certified in vascular neurology)</td>
<td>6</td>
</tr>
<tr>
<td>Hospitalist or other MD (internist, cardiologist, family medicine)</td>
<td>2</td>
</tr>
<tr>
<td>Nurses</td>
<td></td>
</tr>
<tr>
<td>Stroke advance practice nurse</td>
<td>66</td>
</tr>
<tr>
<td>Stroke unit nurse</td>
<td>13</td>
</tr>
<tr>
<td>Emergency medicine nurse</td>
<td>13</td>
</tr>
<tr>
<td>Stroke rehabilitation nurse</td>
<td>1</td>
</tr>
<tr>
<td>Nurse, other</td>
<td>72</td>
</tr>
<tr>
<td>Pharmacist/PharmD</td>
<td>1</td>
</tr>
<tr>
<td>Quality management and administration personnel</td>
<td></td>
</tr>
<tr>
<td>Emergency medicine quality management</td>
<td>2</td>
</tr>
<tr>
<td>Hospital quality management</td>
<td>43</td>
</tr>
<tr>
<td>Hospital administration</td>
<td>15</td>
</tr>
<tr>
<td>Other</td>
<td>125</td>
</tr>
</tbody>
</table>

ABPN, American Board of Psychiatry and Neurology

* Survey may be completed by more than 1 respondent from the hospital team. Therefore, the total number of survey respondents is greater than the total number of hospitals.
Supplemental Table II. Characteristics of GWTG Stroke Hospitals participating in Target: Stroke and Nonparticipating Hospitals

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Target Stroke Hospitals (N=304)</th>
<th>Nonparticipating Hospitals (N=1,079)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of beds, median (IQR)</td>
<td>343 (231-481)</td>
<td>249 (144-379)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Annual ischemic stroke volume, median (IQR)</td>
<td>163 (106-247)</td>
<td>99 (49-168)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Annual intravenous tPA cases, median (IQR)</td>
<td>10 (6-17)</td>
<td>5 (2-10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Academic hospital</td>
<td>152 (50.0%)</td>
<td>395 (36.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary stroke center</td>
<td>147 (48.4%)</td>
<td>317 (29.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td>West</td>
<td>55 (18.1%)</td>
<td>197 (18.3)</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>105 (34.5)</td>
<td>364 (33.7)</td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>69 (22.7)</td>
<td>251 (23.3)</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>75 (24.7)</td>
<td>267 (24.8)</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>17 (5.6)</td>
<td>168 (15.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Door-to-needle time, min (hospital-level)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>79 (71-89)</td>
<td>83 (74-93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Door-to-needle time, min (patient-level)</td>
<td><strong>N=5,460 patients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>72 (55-94)</td>
<td>78 (59-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≤60 min</td>
<td>33.9% (1,849/5,460)</td>
<td>27.1% (5,496/20,298)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IQR, interquartile range