Advancing Stroke Systems of Care to Improve Outcomes
Update on Target: Stroke Phase II

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Acute Ischemic Stroke Reperfusion Therapy

- The benefits of acute ischemic stroke treatment both with intravenous tissue plasminogen activator (tPA) or endovascular therapy are highly time dependent.

- Shorter onset to treatment times are associated with improved functional outcomes, lower complication rates, and in some studies lower mortality.

- Because of the importance of rapid treatment, AHA/ASA guidelines recommend a door-to-needle (DTN) time of ≤60 minutes for IV tPA.

- Yet prior studies indicated fewer than 30% of IV tPA treated acute ischemic stroke patients in the United States were meeting this goal.

In a Typical Acute Ischemic Stroke, Every Minute Until Reperfusion the Brain Loses:

- 1.9 million neurons
- 14 billion synapses
- 7.5 miles myelinated fibers

-- Saver, Stroke 2006
Effect of Intravenous tPA is Time Dependent

**Trials – Pooled RCTs**

![Graph showing the common odds ratio (95% CI) versus treatment delay (hours).](image)

**Practice – National GWTG-Stroke**

![Graph showing predicted probability versus onset to treatment (OTT) in minutes.](image)

mRS 0-1 rate

Stroke 2016;47:2373-2379
Circulation 2017;135:128–139
AHA/ASA Guideline Recommendations

EDs should establish standard operating procedures and protocols to triage stroke patients expeditiously (Class I, Level of Evidence B).

Standard procedures and protocols should be established for benchmarking time to evaluate and treat eligible stroke patients with rt-PA expeditiously (Class I, Level of Evidence B).

Target treatment with rt-PA should be within 1 hour of the patient’s arrival in the ED (Class I, Level of Evidence A).

Comprehensive overview of nursing and interdisciplinary care of the acute ischemic stroke patient: a scientific statement from the American Heart Association. Stroke 2009;40;2911-2944
Substantial Opportunity to Improve Timeliness of IV tPA in Ischemic Stroke

Target: Stroke

- Target: Stroke was initiated by the AHA/ASA as a national collaborative comprising a broad alliance of hospitals and clinicians.

- The goal of Target: Stroke was for GWTG participating hospitals to treat at least 50% of tPA treated acute ischemic stroke patients within 60 minutes of hospital arrival.

- An expert working group performed a literature review to identify 10 key evidence-based strategies associated with timely tPA administration that could be most rapidly and feasibly adopted by hospitals.

Target: Stroke 10 Key Best Practice Strategies

1. Hospital pre-notification by Emergency Medical Services
2. Rapid triage protocol and stroke team notification
3. Single call/paging activation system for entire stroke team
4. Use of a stroke toolkit containing clinical decision support, stroke-specific order sets, guidelines, hospital-specific algorithms, critical pathways, NIH Stroke Scale and other stroke tools
5. Rapid acquisition and interpretation of brain imaging
6. Rapid Laboratory Testing (including point-of-care testing) if indicated
7. Pre-mixing tPA medication ahead of time for high likelihood candidates
8. Rapid access to intravenous tPA in the ED/brain imaging area
9. Team-based approach
10. Rapid data feedback to stroke team on each patient’s DTN time and other performance data

Customizable Implementation Tools

● Patient time-trackers
● Guideline based algorithms
● tPA checklist
● Standardized order sets
● Dosing charts
● Clinical pathways
● Evidence-based protocols
● EMS tools
● Patient educational materials
● Other tools

Target: Stroke tools: www.targetstroke.org
Clinical tools library: heart.org/strokeclinicaltools.

Selection of the Study Population

1,587,230 Patients with Acute Ischemic Stroke

1,487,761 Excluded
  - In-Hospital Strokes (n=30,897)
  - Transferred In (n=174,002)
  - Not Treated with IV tPA (n=1,278,602)
  - tPA at Outside Hospital (n=4,260)

99,469 Patients Treated with IV tPA at Participating Hospital

21,500 Excluded
  - Experimental Protocol (n=458)
  - Time(s) Missing (n=4,421)
  - Treated >3 Hours Post Onset (n=16,621)

6,800 Excluded
  - Hospitals Not Participating During Both Pre- and Post-Target: Stroke Periods (n=6,800)

71,169 Patients Included in the Primary Analysis

Hospitals n=1030

Primary Analysis:
Patients with OTT times ≤3 hours (Class I in guidelines)

Sensitivity Analysis:
Patients with OTT times ≤4.5 hours (Class IIA in guidelines)

N=83,220

Time Trend in the Proportion of Patients with DTN Times within 60 Minutes
Pre- and Post-Target: Stroke

(P<0.0001 for comparison of the two slopes)
The percentage of patients with DTN times ≤60 minutes increased from 29.6% immediately prior to the start of Target: Stroke in Quarter 4 of 2009 to 53.3% in Quarter 3 of 2013 (P<0.0001).

The median DTN time was 74 minutes in Quarter 4 of 2009 immediately prior to initiation of Target: Stroke and declined to 59 minutes by Quarter 3 of 2013 (absolute difference 15 minutes, P<0.0001).

In 2009, prior to initiation of Target: Stroke, 15.6% of hospitals had DTN times ≤60 minutes in 50% or more of tPA treated stroke patients whereas in 2013, this benchmark was being met by 46.7% of participating hospitals (P<0.0001).
The Target: Stroke intervention was also associated with an increase in tPA use.

- tPA use in eligible patients arriving by 2 hours and treated by 3 hours: 64.7% pre- vs. 85.2% post-intervention, P<0.0001
- tPA use in eligible patients arriving by 3.5 hours and treated by 4.5 hours: 22.5% pre- vs. 63.9% post-intervention, P<0.0001
- tPA use among all acute ischemic stroke patients: 5.7% pre- vs. 8.1% post-intervention, P<0.0001

No evidence for unintended consequences with the intervention with tPA use being avoided in patients who may have less favorable DTN times.

Clinical Outcomes Pre- and Post-Target: Stroke in Patients in Patients with Onset to Treatment Time within 4.5 Hours

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre-Target: Stroke (n=29,986)</th>
<th>Post-Target: Stroke (n=53,234)</th>
<th>P Value</th>
<th>Unadjusted Odds Ratios (95% CI)</th>
<th>P Value</th>
<th>Adjusted Odds Ratios (95% CI)*</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-Hospital Mortality</td>
<td>9.95%</td>
<td>8.08%</td>
<td>&lt;0.0001</td>
<td>0.79 (0.75-0.84)</td>
<td>&lt;0.0001</td>
<td>0.90 (0.84-0.95)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Discharge Home</td>
<td>37.6%</td>
<td>43.3%</td>
<td>&lt;0.0001</td>
<td>1.25 (1.20-1.29)</td>
<td>&lt;0.0001</td>
<td>1.13 (1.08-1.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ambulatory Status Independent</td>
<td>42.2%</td>
<td>45.9%</td>
<td>&lt;0.0001</td>
<td>1.16 (1.10-1.22)</td>
<td>&lt;0.0001</td>
<td>1.02 (0.96-1.09)</td>
<td>0.4538</td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>5.74%</td>
<td>4.74%</td>
<td>&lt;0.0001</td>
<td>0.81 (0.75-0.88)</td>
<td>&lt;0.0001</td>
<td>0.84 (0.78-0.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any tPA Complications</td>
<td>6.75%</td>
<td>5.54%</td>
<td>&lt;0.0001</td>
<td>0.80 (0.75-0.86)</td>
<td>&lt;0.0001</td>
<td>0.84 (0.78-0.91)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Adjusted for patient characteristics including age, sex, race, medical history of atrial fibrillation, prosthetic heart valve, previous stroke/transient ischemic attack, coronary heart disease or prior myocardial infarction, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, and current smoking, stroke severity (NIHSS), arrival time during regular work hours, arrival mode, onset-to-arrival time; hospital characteristics of hospital size, region, teaching status, certified primary stroke center, annual volume of tPA, and annual stroke discharge.

National Impact of Target: Stroke:

1. Care: 18,238 more patients treated with tPA
2. Clinical Outcomes: 977 additional lives saved
3. Quality of Life: 5,883 patients reduced their long-term disability
Trends in Door-to-Thrombolysis Time in the Safe Implementation of Stroke Thrombolysis Registry

750 clinical centers in >40 countries involving n=45,079 tPA patients enrolled between 2002-2011

Stroke. 2015;46:1275-1280
What were the winning strategies that helped drive the improvement?

29.6% Q4 2009

53.3% Q3 2013

Fonarow GC et al. JAMA. 2014; 311(16):1632-40
Target: Stroke Phase II Survey

Use of Strategies to Improve Door-to-Needle Times With Tissue-Type Plasminogen Activator in Acute Ischemic Stroke in Clinical Practice

Findings from Target: Stroke

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Background—The implementation of Target: Stroke Phase I, the first stage of the American Heart Association’s national quality improvement initiative to accelerate door-to-needle (DTN) times, was associated with an average 15-minute reduction in DTN times. Target: Stroke phase II was launched in April 2014 with a goal of promoting further reduction in treatment times for tissue-type plasminogen activator (tPA) administration.

Methods and Results—We conducted a second survey of Get With The Guidelines—Stroke hospitals regarding strategies used to reduce delays after Target: Stroke and quantify their association with DTN times. A total of 16901 ischemic stroke patients were treated with intravenous tPA within 4.5 hours of symptom onset from 888 surveyed hospitals between June 2014 and April 2015. The patient-level median DTN time was 56 minutes (interquartile range, 42–75), with 59.3% of patients receiving intravenous tPA within 60 minutes and 30.4% within 45 minutes after hospital arrival. Most hospitals reported routinely using a majority of Target: Stroke key practice strategies, although direct transport of patients to computed tomographic/magnetic resonance imaging scanner, premix of tPA ahead of time, initiation of tPA in brain imaging suite, and prompt data feedback to emergency medical services providers were used less frequently. Overall, we identified 16 strategies associated with significant reductions in DTN times. Combined, a total of 20 minutes (95% confidence intervals 15–25 minutes) could be saved if all strategies were implemented.

Conclusions—Get With The Guidelines—Stroke hospitals have initiated a majority of Target: Stroke–recommended strategies to reduce DTN times in acute ischemic stroke. Nevertheless, certain strategies were infrequently practiced and represent a potential immediate target for further improvements. (Circ Cardiovasc Qual Outcomes. 2017;10:e003227. DOI: 10.1161/CIRCOUTCOMES.116.003227.)
Frequency of Hospital Strategies Used

- Advanced hospital notification by EMS*: 95%
- Stroke tools†: 97%
- Rapid triage protocol and stroke team notification*: 100%
- Single-call activation system*: 100%
- Transport of patients by EMS directly to the CT/MRI scanner first*: 40%
- Rapid brain imaging†: 95%
- Rapid central laboratory testing†: 88%
- Pre-mix of tPA ahead of time*: 25%
- tPA stored in emergency department†: 70%
- Initiation of IV-tPA bolus while patient is still in the brain imaging suite*: 0%
- A team-based approach to stroke care†: 99%
- Prompt patient-specific data feedback to the ED staff and stroke team*: 95%
- Prompt patient-specific data feedback to EMS providers*: 60%

*Percent of the time (median). †Yes.

## Hospital Strategies and DTN Times

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Hospital Use of Strategy % of the Time</th>
<th>Unadjusted Differences in DTN Times (95% CI)</th>
<th>Adjusted Differences in DTN Times (95% CI)</th>
<th>P Values for Adjusted Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMS prehospital stroke-screening tool</td>
<td>Median (IQR) 95 (75 to 100) Mean (SD) 80 (29)</td>
<td>−1.0 (−1.6 to −0.3)</td>
<td>−0.9 (−1.5 to −0.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>EMS triage to primary or comprehensive stroke center</td>
<td>100 (85 to 100)</td>
<td>−0.3 (−1.0 to 0.4)</td>
<td>−0.3 (−1.0 to 0.4)</td>
<td>0.38</td>
</tr>
<tr>
<td>Advanced hospital notification by EMS</td>
<td>95 (75 to 100)</td>
<td>−0.7 (−1.4 to −0.1)</td>
<td>−0.5 (−1.3 to −0.3)</td>
<td>0.30</td>
</tr>
<tr>
<td>Rapid triage protocol and stroke team notification</td>
<td>100 (90 to 100)</td>
<td>−2.6 (−4.0 to −1.3)</td>
<td>−2.5 (−3.9 to −1.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Single-call activation system</td>
<td>100 (100 to 100)</td>
<td>−1.1 (−1.9 to −0.3)</td>
<td>−1.1 (−1.9 to −0.3)</td>
<td>0.006</td>
</tr>
<tr>
<td>A timer or clock attached to a chart, clip board, or patient’s bed to track time</td>
<td>0 (0 to 5)</td>
<td>−0.6 (−1.1 to 0.0)</td>
<td>−0.6 (−1.2 to −0.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Transport of patients by EMS directly to the CT/MRI scanner</td>
<td>40 (0 to 95)</td>
<td>−0.8 (−1.2 to −0.3)</td>
<td>−0.7 (−1.1 to −0.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>Written informed consent is not required before tPA administration</td>
<td>100 (25 to 100)</td>
<td>−0.8 (−1.3 to −0.3)</td>
<td>−0.8 (−1.3 to −0.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>INR and platelet results are not required before tPA administration</td>
<td>80 (10 to 100)</td>
<td>−1.2 (−1.7 to −0.8)</td>
<td>−1.2 (−1.6 to −0.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interpretation of brain imaging is performed immediately by stroke team members</td>
<td>95 (15 to 100)</td>
<td>−1.7 (−2.2 to −1.3)</td>
<td>−1.6 (−2.0 to −1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treatment decision made by neurologist attending or trainee after in-person evaluation</td>
<td>75 (20 to 100)</td>
<td>−1.5 (−1.9 to −1.0)</td>
<td>−1.2 (−1.7 to −0.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treatment decision made by neurologist attending or trainee after telephone only evaluation</td>
<td>25 (0 to 75)</td>
<td>0.4 (−0.2 to 0.9)</td>
<td>0.3 (−0.3 to 0.8)</td>
<td>0.31</td>
</tr>
<tr>
<td>Treatment decision made by ED physician, without input from neurologist or trainee</td>
<td>0 (0 to 10)</td>
<td>0.1 (−0.6 to 0.8)</td>
<td>0.0 (−0.6 to 0.8)</td>
<td>0.87</td>
</tr>
<tr>
<td>Trainees (residents and fellows) are involved in the stroke team and perform the initial assessment</td>
<td>0 (0 to 100)</td>
<td>−1.1 (−1.6 to −0.6)</td>
<td>−1.1 (−1.5 to −0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Premix of tPA ahead of time</td>
<td>25 (0 to 90)</td>
<td>−1.2 (−1.7 to −0.7)</td>
<td>−1.1 (−1.6 to −0.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Initiation of IV-tPA bolus while patient is still in the brain imaging suite</td>
<td>0 (0 to 5)</td>
<td>−3.5 (−4.2 to −2.8)</td>
<td>−3.4 (−4.1 to −2.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prompt patient-specific data feedback to the ED staff and stroke team</td>
<td>95 (70 to 100)</td>
<td>−1.7 (−2.3 to −1.0)</td>
<td>−1.6 (−2.3 to −1.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prompt patient-specific data feedback to EMS providers</td>
<td>60 (15 to 95)</td>
<td>−1.2 (−1.7 to −0.7)</td>
<td>−1.0 (−1.5 to −0.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Hospital Strategies and DTN Times

• We identified 16 strategies associated with significant reductions in DTN times

• On average, 1.25 minutes could be saved for each strategy implemented

• This represents a potential to reduce DTN times by as much as 20 minutes (95% CI 15-25 minutes) if all strategies were used

• At the patient level, a reduction of 20 minutes in DTN times would save 36 million neurons, reduce the risk of mortality and sICH, and increase the chance of functional independency

• At the national level, a reduction of 20 minutes could bring the median DTN times towards 30 minutes

Target: Stroke Phase II

- **National Goal:**
  - Achieve DTN times within 60 minutes for 75% of eligible patients
  - Achieve DTN times within 45 minutes for 50% of eligible patients

- **Additional Hospital Recognition**
  - Target: Stroke Honor Roll: existing criteria
  - Target: Stroke Honor Roll Elite: DTN ≤ 60 minutes in 75% of eligible patients
  - Target: Stroke Honor Roll Elite-Plus: DTN ≤ 60 minutes in 75% of eligible patients and DTN ≤ 45 minutes in 50% of patients

- **Additional Target: Stroke Resources**
  - Updated time tracker and new tools
  - Additional strategies (transfer patient directly to CT, timer or clock at bedside) and evidence
  - New educational resources
Target: Stroke Phase II 12 Key Best Practice Strategies

1. Hospital pre-notification by Emergency Medical Services
2. Rapid triage protocol and stroke team notification
3. Single call/paging activation system for entire stroke team
4. Use of a stroke toolkit containing clinical decision support, stroke-specific order sets, guidelines, hospital-specific algorithms, critical pathways, NIH Stroke Scale and other stroke tools
5. Timer or clock attached to chart, clipboard, or bed
6. Transfer directly to CT/MRI scanner
7. Rapid acquisition and interpretation of brain imaging
8. Rapid Laboratory Testing (including point-of-care testing) if indicated
9. Pre-mixing tPA medication ahead of time for high likelihood candidates
10. Rapid access to intravenous tPA in the ED/brain imaging area
11. Team-based approach
12. Rapid data feedback to stroke team on each patient’s DTN time and other performance data

Conclusions

- Findings from Target: Stroke support the favorable impact of applying performance improvement techniques: identifying best practices, clinical decision support, guideline-driven care improvement tools, educational outreach, collaborative support, performance profiling, feedback, and recognition.

- Programs to facilitate rapid administration of tPA such as Target: Stroke have substantially improved care and outcomes and should be applied globally.

- Significant progress is being made toward the Target: Stroke Phase II goals.

- Nevertheless, ongoing quality improvement efforts will be required to meet the goals of ≥75% of patients with DTN times ≤60 minutes and ≥50% of patients with DTN times ≤ 45 minutes.
Acknowledgements

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• DCRI