

The ‘Golden Hour’ Treatment of Acute Ischemic Stroke

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DATA ON THE INCIDENCE OF STROKE, collected by the American Heart Association, indicate that in the United States there is a stroke about every 40 seconds and a person dies of stroke about every four minutes. At the moment, there are three to four million Americans who are stroke survivors. Each year, there are roughly 795,000 new strokes in the United States. The death rate is approximately 30% of all stroke victims.

A CONCEPTUAL FRAMEWORK FOR EARLIER TREATMENT OF STROKE

Studies of cerebral blood flow and metabolism show that flow in brain region supplied by an occluded artery is variably reduced depending in part on the distance of the region from the stroke epicenter, and that flow in much of these regions is sufficient to maintain viability for some period of time as evidenced by correlative measurements of local oxygen and glucose metabolism. The brain regions that are threatened but viable are termed the “ischemic penumbra” and the time this penumbra could remain viable is termed the ‘therapeutic time window’ The more profound the reduction in blood flow the briefer this window becomes.¹

Saver calculated that in patients experiencing a typical large vessel ischemic stroke, 1.9 million neurons, 14 billion synapses and 7.9 miles of myelinated fibers are destroyed each minute. Compared with the normal rate of neuronal loss in aging brain, the ischemic brain ages 3.6 years each hour without treatment.²

CLINICAL DATA IN SUPPORT OF EARLIER TREATMENT TIMES

Results of acute ischemic stroke treatment trials have taught us that in order to maximize therapeutic benefit we must treat our patients early; the earlier the better. In the landmark NINDS study those who were treated in zero to 90 minutes had lesser disability at three months than those treated between 91-180 minutes. More specifically, treatment with rtPA initiated within 90 minutes of symptom onset was associated with an odds ratio of 2.11 (95% confidence interval, 1.33 to 3.55) for favor-

able outcome at three months as compared with placebo. In comparison, the odds ratio for good outcome at three months for treatment with rtPA initiated within 90 to 180 minutes was 1.69 (95% confidence interval, 1.09 to 2.62).³ Results of NINDS study were closely matched by at least one subsequent large clinical trial.⁴

Lansberg et al looked at the pooled data set of the first six major randomized acute stroke trials of intravenous tissue plasminogen activator with a goal to identify the **number needed to benefit (NNB)** and **number needed to harm (NNH)**. They found that NNB was 3.6 for patients treated between zero and 90 minutes, 4.3 for treatment between 91 and 180 minutes, 5.9 for treatment between 181 and 270 minutes, and 19.3 for treatment between 271 and 360 minutes. The NNH estimates for the corresponding time intervals were 65, 38, 30, and 14. The analysis clearly showed that earlier treatment was linked to a greater chance of benefit and a reduced chance of harm. It also showed that treatment up to 4.5 hours resulted in more benefit than harm.⁵

EMERGING CONCEPT OF THE GOLDEN HOUR

Prehospital delay continues to contribute the largest proportion of delay in treatment.⁶ Lack of awareness of stroke symptoms is a key component of that delay. The CDC analyzed data from an optional module of the 2005 Behavioral Risk Factor Surveillance System (BRFSS) survey that was used in 13 states and the District of Columbia (DC). The findings were as follows: All five stroke warning symptoms were identified by 43.6% of respondents; 18.6% were aware of all stroke warning symptoms and knew that sudden chest pain is not a stroke warning sign; 38.1% were aware of all stroke warning symptoms and would first call 9-1-1 if they thought that someone was having a heart attack or stroke, and 16.4% were aware of all five stroke warning symptoms, knew that sudden chest pain is not a stroke warning symptom, and would call 9-1-1 if they thought that someone was having a heart attack or stroke. Awareness of all

five stroke warning symptoms and calling 9-1-1 was higher among whites (41.3%), women (41.5%), and persons at higher education levels (47.6% for persons with a college degree or more) than among blacks and Hispanics (29.5% and 26.8%, respectively), men (34.5%), and persons at lower education levels (22.5% for those who had not received a high school diploma).⁷

Patients receiving treatment within the first 60 minutes of symptom onset, termed the Golden Hour, have the greatest opportunity to benefit from recanalization therapy.

An analysis of data from hospitals participating in the American Heart Association and American Stroke Association Get With the Guidelines Stroke initiative found that 30,220 patients (28.3%) arrived in emergency room within 60 minutes of stroke symptom onset, 33,585 (31.7%) arrived between 61-180 minutes and 42,846(40.1%) patients arrived >180 minutes. Compared with patients arriving at 61-180 minutes, golden hour patients received thrombolytic therapy more frequently (27.1% vs. 12.9%), but experienced a significantly longer **door to needle time (DTN)** – 90.6 vs. 76.7 minutes. Only 18.3% of golden hour patients received thrombolytic therapy in less than 60 minutes from arrival.⁸ An inverse relationship was found between time remaining in the treatment window and time to treatment i.e., those with the greatest amount of time left to treat had the longest DTN time while those who had the least amount of time left had the shortest DTN times.

GWTG-Stroke data indicate that patients arriving within 60 minutes of stroke onset accounted for one in eight of all ischemic stroke patients at GWTG hospitals. Projected nationally, these numbers translate to more than 55,000 patients presenting to acute care hospitals within the first 60 minutes of ischemic stroke onset.

Since early time of presentation is critical to early start of therapy, a public health priority is to increase even further the proportion of acute ischemic stroke patients presenting within the first 60 minutes after onset. The two most powerful

predictors of early arrival are 1) stroke severity on NIH stroke scale and 2) arrival by ambulance rather than private vehicle.

GTWG-stroke hospitals currently constitute only 23% of US hospitals. The treatment numbers are less robust in non-participating hospitals. In the California Acute Stroke Pilot Registry, of 374 patients with ischemic stroke, 88 (23.5%) arrived at the emergency department within three hours of symptom onset, of whom only 16 (4.3%) received thrombolytic treatment. The authors derived hypothetical treatment rates for thrombolysis based on observed rates of eligibility and treatment. If all patients with known onset times had called 911 immediately, they calculated the overall rate of thrombolytic treatment within three hours would have increased from 4.3 to 28.6%. If all patients with known time of onset had arrived within one hour and been rapidly assessed, 57% could have received treatment.⁹

MEASURES THAT MAY REDUCE TREATMENT TIMES AND A NATIONAL PROGRAM TARGETING IMPROVEMENT

With compelling evidence that our efforts to reduce stroke related disability and improve outcome in many stroke patients is intimately tied to early intravenous therapy, let's look at what measures seem to work.

It all must start with Community education with focus on awareness of stroke symptoms, knowledge of stroke risk factors and utilization of emergency response system – 911.¹⁰

A national quality improvement initiative of the American Heart Association and American Stroke Association to improve the care of acute stroke is underway. Termed Target: Stroke, the goal is to achieve a door to needle time within 60 minutes in at least 50% of ischemic stroke patients.

The following measures are based on American Stroke Association sponsored Target: Stroke campaign's 'Best Practice Strategies':

- Advance hospital notification by EMS.
- Rapid ED triage protocol and stroke team notification

- Single call activation system – A single call should activate the entire stroke team
- Stroke tools – A Stroke Toolkit containing clinical decision support, stroke specific order sets, and other stroke tools should be available in the ED and utilized for each patient
- Rapid acquisition and interpretation of brain imaging – Scanner clearance as soon as ED is made aware of incoming patient, It is essential to initiate a CT scan (or MRI) within 25 minutes of arrival and complete interpretation of the scan within 45 minutes of arrival to exclude intracranial hemorrhage prior to administration of IV rt-tPA
- Rapid laboratory testing. Recent studies suggest it is not necessary to wait for INR results of patients in whom coagulopathy is not suspected
- Mix the tPA medication ahead of time. Genentech has a stated policy of replacing the drug free of charge if it is mixed but not given in time-critical emergency situations like acute stroke
- tPA should be readily available in the ED or CT scanner (if scanner is located away from the ED). Dosing charts and standardized order sets will facilitate timely administration
- Team based approach – Collaboration in developing treatment pathways among physicians, nurses, pharmacists, laboratory administrators, department of neurology and radiology has been shown to be effective in reducing time to treatment in stroke
- Continuous data collection to drive system improvement. Accurately measuring and tracking the hospital's door to needle times equips the stroke team to identify areas for improvement and take appropriate action. A data monitoring and feedback system includes Get With The Guidelines® – Stroke Patient Management Tool which creates a process for providing timely feedback and comparisons to national averages.

CONCLUSION

In summary, the last decade of stroke research has highlighted the importance of rapid treatment of acute stroke. Improving treatment times is possible and can be accomplished through a variety of system interventions.

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