Stroke: Part 1

These summaries reflect initial care of stroke victims and the opportunity for emergency medical services (EMS) agencies to provide essential early care, which can improve outcomes in this important patient group. The next report in this series will emphasize new interventions that are changing the approach to stroke care.

Koton S, Schneider AL, Rosamond WD, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. *JAMA*. 2014;312:259-268.

Sacco RL, Dong C. Declining stroke incidence and improving survival in US communities: evidence for success and future challenges. *JAMA*. 2014;312:237-238.

Stroke affects approximately 800,000 Americans each year. For 600,000 of these patients, a first stroke is experienced. Stroke remains the fourth leading cause of death and is the main cause of adult disability in the United States. Many adults fear the disability associated with stroke more than death. Worldwide, stroke is the second leading cause of death, causing 9.5% of total deaths each year with a greater burden in developing countries. Overall, stroke mortality has declined over the past decade, chiefly in Western countries. Several studies have documented a decrease in stroke incidence. These favorable trends are likely caused by better vascular risk factor control and improvements in acute stroke treatment at many institutions including specialized stroke centers. Historically, however, in the United States, there are persistent racial, ethnic, sex, and regional disparities in age-adjusted stroke mortality.

The study of Koton and coworkers, which took place from 1987 to 2011, reported a 7% incident stroke rate in over 1,000 participants with an overall rate of 3.56 strokes per 1,000 person years. This trial, the Atherosclerosis Risk in Communities (ARIC) trial, confirmed the greater incidence of stroke among men compared with women and among blacks compared with whites. Important new results show a substantial and similar decrease in stroke incidence per 10 years among men, women, whites, and blacks with an overall absolute decline of 0.93 per 1,000 person years for each 10-year interval. The decline in stroke incidence among blacks is encouraging because this population has had greater stroke risk in multiple studies including previous reports from ARIC. However, a decline in stroke incidence was evident only among participants aged 65 years or older.

A number of factors may explain these results. First, there is a documented increase in the prevalence of use of cholesterol-lowering medications (from 3.8% to 12.9%) and a coinciding reduction in median low-density lipoprotein cholesterol levels. The use of cholesterol-lowering medications has been associated with a lower risk of incident stroke. Second, antihypertensive medication use has increased from 29.5% at the first visit to 43.4% in the most recent follow-up of the ARIC study population. The use of antihypertensives was increased predominantly among patients older than 65 years and not among those aged 55 to 64 years. Third, there is a decreased prevalence of current smoking when patients are compared in this longitudinal study.

The study also showed that the overall mortality after stroke decreased over time (absolute decrease of 8.09 per 100 strokes after 10 years), mostly because of the decline of stroke mortality in the group younger than 65 years (absolute decrease of 12.2 per 100 strokes after 10 years). This decrease in mortality was consistent across sex and race subgroups. The use of cholesterol-lowering medications was associated with lower mortality, whereas higher mortality hazards were associated with diabetes and current smoking.

Despite the strengths of this report, concerns remain. For example, body mass and diabetes prevalence increased in the entire ARIC cohort, and there was no adjustment for behaviors such as physical activity, diet, and alcohol consumption. Increased rates in obesity, diabetes, and lack of physical activity could be an explanation for the lack of decline in stroke incidence in the middle-aged and younger population (younger than 65 years). Thus, it may be difficult to sustain the improvement seen here.

Aging and changing demographics of the population will lead to a substantial increase in the prevalence of stroke. By 2030, it is estimated that 4% of the US population will have had a stroke leading to a projected additional 3.4 million people with stroke in 2030 and an estimated total annual cost of over $240 billion by 2030. Continued efforts to prevent, provide acute management, and rehabilitate patients with stroke are essential.

Fonarow GC, Zhao X, Smith EE, et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. *JAMA*. 2014;311:1632-1640.

Grotta JC. tPA for stroke: important progress in achieving faster treatment. *JAMA*. 2014;311:1615-1617.

Saver JL, Fonarow GC, Smith EE, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. *JAMA*. 2013;309:2480-2488.

Ferrari J, Knoflach M, Kiechl S, et al. Stroke thrombolysis: having more time translates into delayed

therapy: data from the Austrian Stroke Unit Registry. *Stroke.* 2010;41:2001-2004.

Lees KR, Bluhmki E, von Kummer R, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet*. **2010;375:1695-1703.**

Intravenous tissue plasminogen activator (tPA) is the level 1A treatment for acute ischemic stroke. Several prospective trials comparing tPA with standard treatment in pooled analyses confirm the relationship of treatment success with time from symptom onset to the initiation of therapy. In a recent analysis of Get With The Guidelines database that included more than 58,000 patients with acute stroke treated with intravenous tPA, early treatment was associated with better functional outcome, lower hemorrhagic complication rates, and lower mortality rates. For each 1,000 treated patients, giving tPA 15 minutes earlier resulted in 18 more patients with improved ambulation at discharge (8 fully independent ambulation), 13 more patients discharged to a more independent environment (7 to home), and 4 fewer patients dying prior to discharge.

Despite two decades of efforts to streamline systems of care including the formation of designated stroke centers, placement of computed tomographic (CT) scanners in emergency departments, creation of stroke teams, and recognition that a dedicated neurologic emergency department pathway can speed treatment, only approximately 5% of stroke patients are treated with tPA. Most stroke patients are treated beyond 2 hours from symptom onset when tPA is less effective. The main reason is the lack of public recognition of stroke symptoms and the failure of patients to quickly seek care at a nearby institution or activate EMS. Another important reason within the control of physicians and other health care personnel is the inherent delay caused by emergency department triage, registration, evaluation, testing, and treatment. The median door-to-needle times for tPA administration in stroke center emergency departments in the United States has exceeded 60 minutes, the national benchmark, with little improvement since the drug was first approved in the United States in 1996. In fact, data from Europe and the United States indicate that the earlier the patients present to the emergency department with acute stroke, the longer the door-to-needle time is.

Fonarow and coworkers report a quality initiative designed to reduce door-to-needle times for tPA administration. In a large registry study comparing over 27,000 patients treated with tPA at over 1,000 US hospitals from 2003 to 2009 to nearly 44,000 patients treated from 2010 to 2013, the median door-to-needle time decreased to 67 minutes from 77 minutes before intervention. Clinical outcomes improved with in-hospital all-cause mortality reduced to 8.25% versus 9.93% before intervention and symptomatic hemorrhage rates reduced to 4.68% versus 5.68% before intervention. Among patients with ischemic stroke, 8.1% received tPA versus 5.7% before intervention.

Although the work of Fonarow and coworkers is commendable given the large data sets analyzed, consistent data input in this before-and-after analysis may limit the applicability of results. As Grotta points out in an excellent commentary, further analysis will be helpful in identifying specific factors in the quality improvement program, which were most important in contributing to the improvement in outcomes seen.

There are 2 broad ways to increase the rate of tPA use for the treatment of acute ischemic stroke: raising public awareness and speeding up the acute care process (prehospital and hospital care). Public education focuses not only on recognizing stroke symptoms but also patient behavior once stroke symptoms are recognized (calling an ambulance instead of taking aspirin, waiting for symptoms to improve, and so on). The ultimate recognized goal is treatment with tPA within the "golden hour" (the first 60 minutes after onset of stroke symptoms, not the first 60 minutes after arriving to the emergency room) when this therapy appears to have greatest benefit.

As more patients receive tPA within the "golden hour," the number of patients who will benefit from the treatment will increase. According to a meta-analysis of the large tPA trials in the United States and Europe, the number needed to treat to achieve an excellent outcome (defined as return to prestroke functioning) is 4.5 patients for the first 90 minutes, 9 patients for the second 90 minutes, and 14 patients for the third 90 minutes. However, the impact of establishing and maintaining stroke care models (especially if not regulated and rationed) remains unclear. This cost impact can potentially affect both the payers who will support a stroke care network and the hospital and EMS organizations that will implement acute stroke care. Because of the small number of patients receiving contemporary high-efficacy treatment, carefully constructed cost-effectiveness studies will be essential.

Walter S, Kostopoulos P, Haass A, et al. Diagnosis and treatment of patients with stroke in a mobile stroke unit versus in hospital: a randomised controlled trial. *Lancet Neurol.* 2012;11:397-404.

Ebinger M, Kunz A, Wendt M, et al. Effects of golden hour thrombolysis: A Prehospital Acute Neurological Treatment and Optimization of Medical Care in Stroke (PHANTOM-S) substudy. *JAMA Neurol.* 2015;72:25-30.

Padrick MM, Chapman Smith SN, McMurry TL, et al. NIH stroke scale assessment via iPad-based mobile telestroke during ambulance transport is feasible—Pilot data from Improving Treatment with Rapid Evaluation of Acute Stroke via Mobile Telemedicine (iTREAT) study.
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The Germans are leaders in the stroke community in bringing stroke care to patients. The German strategy is based on a