FROM THE INTERNATIONAL STROKE CONFERENCE

'Golden Hour' Arrival Ups Odds of Getting tPA

BY ROBERT FINN

SAN DIEGO — Patients with ischemic stroke who arrive within 1 hour of symptom onset at a hospital participating in the Get With the Guidelines-Stroke program were significantly more likely to receive thrombolytic therapy, according to a study presented at the International Stroke Conference.

Only 28% of the 106,924 patients studied arrived within that "golden hour," said lead investigator and vascular neurologist Jeffrey L. Saver of the University of California, Los Angeles. Of those, 27% eventually received intravenous tissue plasminogen activator (tPA), compared with 13% of the patients who arrived 1-3 hours after symptom onset.

Data from prior studies suggested that 25%-30% of golden-hour patients would be eligible for tPA treatment. "We're actually doing pretty well at these hospitals," Dr. Saver said at a news briefing at the conference sponsored by the American Heart Association, which also sponsored the study.

Rapid treatment requires a "cultural revolution," according to Dr. Saver. "We are changing our training techniques for the new generation of physicians who are going to be interventionally minded stroke physicians. Every stroke is a treatable emergency, and it is the stroke team member's responsibility to get treatment done as soon as possible. We tell our residents, 'Push the gurney yourself to the CT scanner. Don't wait for the critical care transport nurse. Run the bloods yourself over to the lab. Run and get the tPA [from the pharmacy].' "

The study was retrospective and used data collected between 2003 and 2007 from 905 hospitals. All participating hospitals were part of the Get With the Guidelines-Stroke (GWTG-S) program, and hospital staffs were thus among the most educated on the need for the rapid treatment of people with stroke.

In the golden-hour patients, the average time to thrombolytic treatment—the "door-to-needle" (DTN) time—was 91 minutes. The average DTN for later arriving patients was significantly shorter at 77 minutes, but still longer than the recommended 60-minute target DTN time.

"We do have some room for improvement," Dr. Saver said. "It's a natural tendency when a patient gets to the hospital early for physicians to take time to make a more considered and deliberate decision. Unfortunately, deliberation comes at the expense of brain when you treat stroke. …Time is brain. Every minute that your patient is not treated, 2 million nerve cells die. We know that every 10 minutes in which [tPA] delivery is delayed, one less patient benefits from treatment."

In Dr. Saver's view, two factors account for the smaller proportion of late-arriving patients who receive tPA. First, some of them arrive too late for the hospital to complete all the tests before 3 hours have elapsed from the onset of symptoms. tPA is approved only for patients who can be treated within that time limit.

Second, late-arriving patients are more likely to have neurologic deficits that are predicted to be moderate rather than severe. Therefore, a fewer late-arriving patients would be expected to benefit from thrombolytic therapy. It's difficult to tease out the relative contributions of those two factors, Dr. Saver said.

Dr. Saver disclosed relationships with Concentric Medical, CoAxia, Talecris Biotherapeutics, E.E. Smith, Mitsubishi, and Boehringer Ingelheim. ■

Rosuvastatin Cuts Risk of Stroke in Half: JUPITER Trial

BY ROBERT FINN

SAN DIEGO — Patients with normal lipid levels but elevated C-reactive protein showed a 48% reduction in the risk of stroke when taking rosuvastatin, according to a study presented, at the International Stroke Conference.

These results came from a planned additional analysis of JUPITER (Justification for Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin). Investigators presented the main results of this trial, demonstrating a reduction in overall cardiovascular mortality, at the American Heart Association meeting in November 2008. The AHA also sponsored the stroke conference.

Investigators randomized 17,802 patients to receive either 20 mg/day rosuvastatin or placebo, and they followed the patients for up to 4.5 years. During that time 33 patients in the rosuvastatin group and 64 patients in the placebo group experienced a stroke, corresponding to a statistically significant reduction of 48% in relative risk.

The Kaplan-Meier survival analysis reported here revealed that the placebo and rosuvastatin groups began diverging within the first year of the trial. By 4.5 years, about 2% of the placebo group and about 1% of the rosuvastatin patients had a stroke, for a 1% absolute difference in those patients who were followed for that long.

This difference in absolute risk implies that about 100 patients would have to be treated with rosuvastatin in order to prevent one stroke.

"This wouldn't be very large if the focus was only on preventing stroke," Robert J. Glynn, Ph.D., Sc.D., said at a news conference. "But look at the composite primary outcome. The really striking result here is that the benefit for stroke is almost spot on the benefit for myocardial infarction. And the number needed to treat overall in the population is 25 to prevent a primary vascular event. So you can't view stroke in isolation when making a treatment decision." Dr. Glynn is a biostatistician at the Harvard School of Public Health, Boston, and one of the co-authors of the study.

Subgroup analyses showed significant reductions in relative risk for men but not women, for patients with a BMI of 29.9 kg/m^2 or below, for patients with hypertension, and for those whose Framingham risk scores were above 10, regardless of age or smoking status.

The investigators also found significant risk reductions among patients whose C-reactive protein levels were 5 mg/L or above, for patients with LDL cholesterol above 100 mg/dL, for those with low HDL cholesterol, and for those with triglyceride levels below 150 mg/dL.

Dr. Cheryl Bushnell of Wake Forest University, Winston-Salem, N.C., commented that "C-reactive protein is elevated generally in people who are obese and do not exercise. Are we going to tell these people to do anything differently based on elevated C-reactive protein? If so, we'll be treating a lot of extra people who may not have otherwise been treated. There's a really important discussion that has to happen in terms of the risks and benefits of treatment, as well as the cost of giving C-reactive protein tests."

Dr. Glynn received grant support for this study from AstraZeneca, which manufactures rosuvastatin (Crestor). ■

In Midlife, Fivefold More Silent Cerebral Infarcts Than Strokes

BY DOUG BRUNK

SAN DIEGO — Silent cerebral infarction occurs in midlife more than five times as often as clinical stroke, according to an analysis of data from the Framingham Heart Study.

"Silent cerebral infarcts have been referred to as 'silent' because patients and/or clinicians may not recognize them when they occur, but silent infarcts are associated with a higher risk of cognitive impairment and clinical stroke," Dr. Jose Rafael Romero said in an interview at the International Stroke Conference. "Given that hypertension is the main risk factor associated with higher risk of silent cerebral infarcts [SCIs], and is a modifiable risk factor, early surveillance and treatment should be emphasized. Our study supports the recommendation by several guidelines for early treatment of hypertension and surveillance."

Dr. Romero, of the department of neurology at Boston University, and his colleagues studied 1,485 participants in the original Framingham cohort and their offspring. They were free of stroke or transient ischemic attacks and had undergone two brain MRI scans at least 1 year apart, in 1999-2003 and 2004-2006. SCI was defined as a lesion greater than 3 mm with hyperintense signal on T_2-weighted images and cerebrospinal fluid signal intensity on subtraction images, separate from the circle of Willis vessels and perivascular spaces. Clinical stroke was determined by prospective ongoing surveillance using standard protocols. The mean age of the patients at baseline was 63 years, 46% were women, and 40% had hypertension.

'Silent infarcts are associated with a higher risk of cognitive impairment and clinical stroke.'

DR. ROMERO

Over a mean follow-up of 5 years, SCI was observed in 8.7% of study participants while clinical stroke occurred in 1.7% of study participants. The majority of SCIs (83%) were single incident in nature.

An age-stratified analysis revealed that the incidence of SCI was more than five times that of clinical stroke among those younger than 65 years of age (4.8% vs. 0.9%, respectively). The incidence of both SCI and stroke increased among those aged 65-74 years (13% vs. 2.8%, respectively) and those aged 75 years and older (16.9% vs. 3.2%).

"Our study adds to what is known about incident SCI by including younger persons," Dr. Romero said, because the Framingham Heart Study participants are nearly a decade younger than those of prior studies of silent infarcts. "Hypertension appears to be the main stroke risk factor associated with a higher risk of incident SCI." A significant link between hypertension and higher risk of incident SCI was observed in those older than 65 years (odds ratio 1.75).

A key limitation of the study is that the participants were primarily of European descent, Dr. Romero said at the conference, which was sponsored by the American Heart Association.

The study was supported by grants from the National Institutes of Health. ■