Stroke Guidelines Called 'Hopelessly Outdated'

BY CHRISTINE KILGORE
Contributing Writer

Current guidelines on the use of thrombolytic therapy for acute ischemic stroke are "hopelessly outdated," Louis R. Caplan, M.D., said in an editorial that accompanied several reports of patient outcomes studies published in the Journal of the American Medical Association.

The guidelines, which are nearly a decade old, exclude from thrombolytic therapy patients who may indeed benefit from it and do not consider the major advances in diagnostic technology that have occurred over the past 2 decades, said Dr. Caplan, chief of the division of cerebrovascular diseases at Beth Israel Deaconess Medical Center in Boston.

The results of two recent studies on outcomes after thrombolysis are "an important reminder" that few patients with ischemic stroke receive thrombolytic therapy, according to Dr. Caplan (JAMA 2004;292:1883-5).

On the other hand, this treatment "is not a panacea and may actually cause intracerebral hemorrhage or death" in some patients, said Dr. Caplan, who is also professor of neurology at Harvard Medical School, Boston.

In a study by the German Stroke Registers Study Group on predictors of in-hospital mortality after thrombolysis, only 3% of almost 60,000 patients presenting with acute stroke received intravenous tissue plasminogen activator (tPA). Of treated patients, 10% died during hospitalization.

In the second study, more than half (51%) of 216 patients treated with alteplase in London, Ont., failed to improve significantly after treatment when the published guidelines were followed.

The guidelines for thrombolytic therapy do not consider the major advances in diagnostic technology that have occurred over the past 2 decades.

Neither study reported causative vascular lesions, or the extent of infarction before or after treatment—information that can be identified with modern imaging techniques, Dr. Caplan noted.

"If the present guidelines continue to be followed, as in the [two studies], physicians will never know which patients with what degree of infarction and with what vascular lesions and at-risk tissue will benefit from thrombolysis," he said.

Nor will physicians know "whether intravenous, intraarterial, or combined intravenous and intraarterial [therapies] are best and in what circumstances," Dr. Caplan said. "Clinicians also will not know how alteplase compares with other promising newer thrombolytic agents and, possibly, with other therapies."

In the German study—a prospective, observational cohort study conducted at 225 community and academic hospitals throughout Germany—investigators reported that the factors predicting in-hospital death after thrombolytic therapy were decreased level of consciousness (an odds ratio of 3.5) and older age (an adjusted odds ratio of 1.6 for each 10-year increment of age). Each factor independently increased the risk of death, said Peter U. Heuschmann, M.D., of the University of Münster (Germany), and his associates (JAMA 2004;292:1831-8).

The overall rate of symptomatic intracranial hemorrhage was 7% and increased with age. One or more serious complications occurred in 27% of all patients and 84% of those who died after treatment.

In the Ontario study—a prospective study of acute stroke patients who received alteplase at a university hospital over 4 years—investigators reported that a lack of improvement at 24 hours was associated with poor outcome and death at 3 months. At 3 months, 20% of patients had died.

They identified three factors—elevated baseline glucose level (144 mg/dL), cortical involvement, and time to thrombolytic therapy—that predicted a lack of improvement at 24 hours. For each 5-minute increase in the time that elapsed from symptom onset to treatment, the chance of no improvement increased by 5%, said Gustavo Saposnik, M.D., of the London Health Sciences Centre, and his associates (JAMA 2004;292:1839-44).

In his editorial, Dr. Caplan said that although earlier treatment is better, studies show that the mandated 3-hour time window for thrombolytic therapy may not be appropriate.

"Patients with stroke do not become poor candidates for alteplase when the clock strikes 4 hours," he said.

Dr. Caplan cautioned against "cookbook guidelines" and explained that treatment decisions must utilize modern diagnostic technology and be individually focused on "each given patient with a given lesion and a known extent of infarction."

There is also an urgent need for more qualified stroke centers, more experienced stroke clinicians, and new ways to get patients to the centers quickly, he said. ■

MRI Equals CT in Confirming Acute Intracerebral Hemorrhage

BY CHRISTINE KILGORE
Contributing Writer

Magnetic resonance imaging is superior to CT for detection of chronic brain hemorrhage and is its equal in confirming suspected acute intracerebral hemorrhage, judging from the findings of a prospective, multicenter study.

Many stroke centers currently obtain both MRI and CT in initial evaluations of suspected brain hemorrhage, a practice that is costly in both time and money. Given the new findings, MRI "may be acceptable as the sole imaging technique for acute stroke at centers with expertise," reported Chelsea S. Kidwell, M.D., of the UCLA Stroke Center, and associates.

The findings of the Hemorrhage and Early MRI Evaluation (HEME) study also suggest that gradient recalled echo (GRE) MRI—in addition to detecting hyperacute and chronic hemorrhage—may be able to detect regions of hemorrhagic transformation of an acute ischemic stroke that are not evident on CT (JAMA 2004;292:1823-30).

The study was performed between 2000 and 2003 at two stroke centers. Patients in the study had a mean age of 75 years. Patients presenting with focal stroke symptoms within 6 hours of onset underwent brain GRE MRI followed by noncontrast CT. Scans were read by four blinded readers.

The findings complement another recently published study performed by the German Stroke Competence Network, which suggested that MRI is as accurate as CT for the detection of hyperacute hemorrhage (Stroke 2004;35:502-6).

In fact, when preliminary results of this other study became available, the HEME investigators performed an interim analysis of their own data and found that MRI was detecting acute hemorrhages not seen on CT. They stopped their own study early, after 200 patients were enrolled, to expedite their analysis.

The panel detected hemorrhage of any type in 71 patients with MRI and in 29 patients with CT. Acute hemorrhage specifically was diagnosed in 25 patients on both MRI and CT.

In four additional patients, however, acute hemorrhage was identified on the MRI but not on the corresponding CT. The panel interpreted each of these cases as hemorrhagic transformation of an ischemic infarct.

In three patients, regions interpreted as acute hemorrhage on CT were interpreted as chronic hemorrhage on MRI. In one patient, subarachnoid hemorrhage was diagnosed on CT but not on MRI. And in 49 patients, chronic hemorrhage, most often microbleeds, was seen on MRI but not on CT.

The investigators noted that it is unclear whether evidence of hemorrhagic transformation on MRI conveys a higher risk of symptomatic hemorrhage with thrombolytic treatment. The role of microbleeds in determining patient eligibility for thrombolytic therapy is also unknown, the investigators said.

An important caveat to the role of MRI, they noted, is that with small hemorrhages, blood that appears as acute on CT may appear as chronic on GRE MRI. "A noncontrast CT may be required to confirm the diagnosis in these cases," they said. ■

Many Stroke Patients May Not Respond to Aspirin

BY PEGGY PECK
Contributing Writer

VANCOUVER, B.C. — Results of a small prospective study suggest that almost half of patients hospitalized for treatment of ischemic stroke or transient ischemic attack (TIA) are "aspirin resistant."

But some stroke experts are not convinced, citing a lack of evidence that the results of the platelet function analyzer (PFA-100) assay used in the study are a true measure of antiplatelet function.

Of 59 patients tested, 47% had aspirin resistance, which was defined as a clotting time of 171 seconds or less, Mark J. Alberts, M.D., reported at the Fifth World Stroke Congress, sponsored by the International Stroke Society.

In an earlier study of outpatients, Dr. Alberts, professor of neurology at Northwestern University, Chicago, reported that 37% of such patients were aspirin resistant. That study, first reported at the American Stroke Association meeting in 2003, was recently published (Stroke 2004;35:175-8).

In the later study, the 59 patients had a mean age of 64 years and had been taking aspirin for at least 3 days prior to an acute event (stroke or TIA). PFA-100 testing was done at the time of hospital diagnosis, before any loading dose of antiplatelet therapy was administered. The PFA-100 device measures the clotting time of a blood sample that is pumped through a collagen-coated membrane, a test design that mimics the behavior of circulating blood. The device, about the size of a drip coffee maker, costs about $15,000 and produces results in about 5 minutes at a cost of $15-$20 per assay, he said.

Overall, 63% of patients were taking 325 mg/day of aspirin and 37% were using baby aspirin (81 mg). Aspirin resistance was seen in 73% of patients taking low-dose aspirin and in 32% of those taking high-dose aspirin, a significant difference. Patients using enteric-coated aspirin also were more likely than others to show resistance.

The results suggest that "dose-adjusted therapy is where the field is headed. …'One size fits all' therapy doesn't work for aspirin," Dr. Alberts said.

Ralph L. Sacco, M.D., director of the stroke and critical care division at Columbia University, New York, said in an interview that Dr. Alberts' findings were "thought-provoking, but I don't know how an abnormal finding on PFA correlates with clinical outcomes." ■