

# Antiplatelets Tied to Intracranial Hemorrhage

BY RICHARD HYER

FROM THE ANNUAL MEETING OF THE  
CENTRAL SURGICAL ASSOCIATION

CHICAGO — Increasing rates of traumatic intracranial hemorrhage in elderly patients appeared to be linked with the use of antiplatelet agents in a retrospective study of two different time periods.

The rise in traumatic intracranial hemorrhage (TICH) occurred without significant increases in diagnosis of atrial fibrillation or in warfarin (Coumadin) use, and overall mortality remained unchanged, Dr. Jeffrey J. Siracuse said at the meeting.

“Increased life expectancy and the rising prevalence of risk factors have led to [the use of] increased atrial fibrillation nationwide,” said Dr. Siracuse of Beth Israel Deaconess Medical Center, Boston. “Patients with atrial fibrillation are at high risk for stroke and may also be at high risk for bleeding complications.” They often are treated with anticoagulants based on their CHADS<sub>2</sub> scores, which are used to estimate risk of throm-

boembolism in cases of atrial fibrillation, he said. This scoring system emphasizes warfarin prophylaxis. However, these patients also are likely to be taking antiplatelet agents.

The review of the hospital’s trauma registry database of 5,371 subjects examined records for all 526 patients admitted with intracranial hemorrhage during 1999-2000 (139 patients) and 2007-2008 (387 patients). Intracranial hemorrhages were considered traumatic if they were secondary to an identified external injury.

Patient records were reviewed for pre-existing anticoagulation, international normalized ratio (INR), mechanism of trauma, atrial fibrillation, mortality, and length of stay in the hospital or ICU. CHADS<sub>2</sub> scores were recorded for both groups.

In both time periods, the mean age of patients was 77 years, and half were male. The principal cause of trauma in both groups was a simple fall from the standing position. In the 1999-2000 group, 6.2% of all trauma admissions

were TICH patients, but this number doubled to 12.3% in the 2007-2008 group, a significant difference.

The study found little increase in warfarin use in either group over the two periods. However, the use of “strong antiplatelet agents, specifically clopidogrel and Aggrenox, increased fivefold between the two periods,” said Dr. Siracuse. He also said that in the earlier period, 27% of TICH patients were on aspirin, but by the later period, 48% were on aspirin, a significant difference.

The prevalence of atrial fibrillation in patients with TICH did not increase (20% vs. 23%), nor did the average CHADS<sub>2</sub> scores for all trauma patients with atrial fibrillation taking warfarin (2.4 vs. 2.3, a nonsignificant difference).

“Those figures suggested that we had in our area a mature, well-served population where anticoagulation for atrial fibrillation was fully implemented before the development and widespread use of the CHADS<sub>2</sub> scoring system,” said Dr. Siracuse.

Overall, the mortality of patients with

TICH was unchanged between the two periods (12.4% vs. 12.2%), and patients showed no difference in the mean numbers of either hospital- or ICU-free days.

“We did not see a large increase, as we thought we would, in atrial fibrillation or in Coumadin use in our TICH population. This could perhaps reflect [the fact] that Massachusetts has the highest patient/physician primary care patient ratio in the country,” said Dr. Siracuse. He said this suggested that medical conditions were identified early and treated aggressively.

The vast majority of patients were injured by simple falls from standing, he said, and many patients on anticoagulation because of high risk for thromboembolism were also at high risk for falls. Therefore, he concluded, increasing rates of TICH appeared to be associated with the use of strong antiplatelet agents rather than with increased warfarin use.

Dr. Siracuse reported no relevant financial interests. The study was sponsored by Beth Israel Deaconess. ■

## IV Thrombolysis Effective in Very Elderly Stroke Patients

BY MITCHEL L. ZOLER

FROM THE INTERNATIONAL STROKE CONFERENCE

SAN ANTONIO — Intravenous infusion of a thrombolytic drug helped octogenarian ischemic stroke patients as much as it did middle-aged adults with stroke in a meta-analysis of data collected from more than 1,700 very elderly patients.

Octogenarian stroke patients “show significant benefit” from intravenous treatment with recombinant tissue plasminogen activator (rt-PA) and no excess harm compared with younger patients, Dr. Kennedy R. Lees said at the conference. The results showed “no diminution of efficacy with age. We have consistent evidence to disregard age when treating ischemic stroke patients with rt-PA,” he said.

Furthermore stroke patients aged at least 75 years are also, in general, the best candidates for rt-PA treatment, according to data from a second independent report at the conference.

Analysis of 1,774 adult ischemic stroke patients who presented to the emergency department at the University of Cincinnati in 2005 showed that the percentage of patients eligible for acute treatment with intravenous rt-PA reached the highest level, 10%, in patients 85 or older; 75- to 84-year-old patients comprised the subgroup with the next highest percentage of good rt-PA candidates, 9%. These rates compared with an 8% eligibility level for all adult stroke patients in the study, Dr. Dawn O. Kleindorfer said of the second report.

“We were surprised to see eligibility increase with age. It’s because as patients get older they have more severe strokes,” said Dr. Kleindorfer, director of the division of vascular neurology at the University of Cincinnati.

Strokes too mild to warrant rt-PA treatment made many younger adults ineligible for intravenous treatment, the analysis showed.

Despite this new evidence of the appropriateness, efficacy, and safety of rt-PA in patients aged 75 and older, this demographic subgroup stands out as undertreated with intravenous thrombolytics.

“There is a bias at the bedside of a 90-year-old patient,” Dr. Kleindorfer said in an interview. The evi-

dence suggests that physicians weigh factors differently for very old patients. ... In the United States, we place no upper age limit [on rt-PA treatment of stroke patients], but I think there still is inherent tentativeness for treating extremely elderly patients.”

To assess the efficacy of rt-PA in octogenarians, Dr. Lees and his associates used data collected in the Virtual International Stroke Trials Archive (VISTA), a compilation of data from more than 20 stroke trials that involved more than 15,000 patients (Stroke 2007;38:1905-10).

VISTA contained data for nearly 10,000 patients who were enrolled in neuroprotection trials and had a stroke during 1998-2007. Narrowing the database down to ischemic stroke patients with complete follow-up assessment by a modified Rankin scale score yielded nearly 6,000 patients, including almost 1,200 patients who were older than 80. The total group included 1,703 patients who received intravenous rt-PA and 4,114 who didn’t receive intravenous thrombolysis.

Among the octogenarians, treatment with intravenous rt-PA led to a statistically significant 34% improvement in outcomes in an analysis that adjusted for age and baseline NIH Stroke Scale score. This relative benefit closely matched the 42% benefit from rt-PA seen in patients younger than 80, said Dr. Lees, professor of cerebrovascular medicine at the University of Glasgow (Scotland).

To analyze rt-PA eligibility, Dr. Kleindorfer and her associates used data from 1,774 adults with ischemic strokes who presented to the emergency department at the University of Cincinnati during 2005. Their average age was 70, and 142 patients (8%) were judged eligible for intravenous rt-PA treatment based on Dr. Kleindorfer’s retrospective review of the patients’ records. Seventy-two of the rt-PA-eligible patients actually received the drug.

Among the more than 1,600 patients judged ineligible for rt-PA treatment, the most common reason, in 77%,

was that their time at presentation exceeded the 3-hour time window for intravenous rt-PA treatment that existed in 2005. (The American Stroke Association last year issued guidelines that expanded the rt-PA treatment window to 4.5 hours after stroke symptom onset). Two other common reasons for ineligibility for rt-PA were a mild stroke with an NIH Stroke Scale score of less than 5, which applied to 58% of the patients, and blood pressures that were too high, in 15% of patients. (The percentages add up to more than 100% because some patients had two or more reasons for not being eligible.)

The extent of patient eligibility and the actual rate at which eligible patients received rt-PA varied significantly by age (see chart). The overall pattern of increased eligibility for rt-PA with increased age, and decreased treatment with rt-PA with increased age were

### Rt-PA Eligibility, Use in Stroke Varies by Age

Patient age in years	Eligible for IV rt-PA	Received IV rt-PA
18-44 (n = 90)	3%	67%
45-54 (n = 197)	7%	36%
55-64 (n = 305)	7%	57%
65-74 (n = 372)	8%	67%
75-84 (n = 507)	9%	49%
85 or more (n = 303)	10%	35%

Note: Data from 1,774 stroke patients seen at the ED of the University of Cincinnati in 2005.

Source: Dr. Kleindorfer

both statistically significant, Dr. Kleindorfer said. The analysis also showed that patients aged 75 or older had a significantly higher rate of an international normalized ratio above 1.6, a legitimate reason for rt-PA ineligibility. But those patients also had a significantly higher rate of more severe strokes that qualified them for rt-PA treatment.

Dr. Lees said he has received honoraria from Boehringer Ingelheim Corp. and from Thrombogenics Inc. Dr. Kleindorfer said she has served on the speakers bureaus for Boehringer Ingelheim and Genentech Inc. ■