Data Awaited on PFO Closure for Migraine Relief

Physicians remain concerned about safety and efficacy in the face of patient demand and positive data.

BY DAMIAN McNAMARA
Miami Bureau

SCOTTSDALE, ARIZ. — Existing data suggest that a subset of migraine patients may benefit from closure of their patent foramen ovale, Dr. David W. Dodick said during a symposium sponsored by the American Headache Society.

However, any clinical decision of the merits of surgical closure of a patent foramen ovale for patients with migraine should await the results of a number of ongoing safety and efficacy trials, he stressed.

Closures are being done with regularity as a treatment for migraines in the United States and Europe despite the lack of safety and efficacy data. "This [procedure] is gathering momentum, to say the least. We have a responsibility to know the data and give patients proper and appropriate advice," said Dr. Dodick, professor of neurology at Mayo Clinic Arizona. "This is something patients will come into your office wanting to talk about, if they haven't already."

Physicians are in a tough spot between patient demand and a dearth of data to support patent foramen ovale (PFO) closure for migraine relief, he acknowledged.

Some research indicates an association between a PFO and migraines with aura, particularly in patients with a large left-to-right shunt. In one study, patients with migraine with aura were three times more likely to have a PFO than those who experienced migraines without aura (Neurology 1999;53:2213-4).

The main take-home message for now remains that PFO appears to be more prevalent in patients whose migraines involve aura, Dr. Dodick said.

A left-to-right shunt is also more common among migraine-with-aura patients. In addition, both large atrial shunts and large PFOs are dominantly inherited and might therefore share a genetic origin (Heart 2004;90:1315-20).

One of the large, prospective trials underway is the Migraine Intervention with STARFlex Technology (MIST) study. Patients with migraine with aura will be assessed by a cardiologist and then randomized to closure or no closure.

Although results are not finalized, enrollment data show 60% of 370 participants having a right-to-left shunt (versus 27% of the general population) and 38% having a large PFO (versus 7% of the general population).

Updates and an animation that shows a possible role of PFO in migraine can be viewed on www.migraine-mist.org.

PFO closure might effectively treat migraine in a subgroup of patients, Dr. Dodick proposed. A number of studies suggest that closure eliminates migraines in about one-third of migraineurs, reduces frequency in another third, and does not alter attacks in another third of patients.

"Are there factors that will reliably predict which patients will benefit? If these studies are positive, how will we know that a patient in front of us in the future will benefit significantly from this invasive procedure?" he asked.

Many headache specialists are taking a conservative stance. "While many patients have disabling migraines, many people think migraines are not life threatening. They are life altering but not life threatening," Dr. Dodick. "And the surgery is invasive." There is an overall peri-interventional adverse-event rate of about 6% (Catheter Cardiovasc. Interv. 2004;62:512-6).

Some physicians do not believe PFO closure will make a difference. They oppose the prospective, controlled trials underway in the United States and Canada. However, Dr. Dodick said, "like it or not, the studies are being done—which I think is good." ■

Higher Statin Dose Lowers Stroke Risk

BY BRUCE JANCIN
Denver Bureau

DALLAS — Intensive statin therapy appears to further decrease the risk of cerebrovascular events beyond the already significant reduction achieved with standard-dose statins, Dr. Jessica L. Mega reported at the annual scientific sessions of the American Heart Association.

She presented a metaanalysis of three major randomized trials of intensive- versus moderate-dose statins featuring rates of stroke and transient ischemic attacks as a predefined end point. In these three studies totaling nearly 19,000 randomized patients, the cerebrovascular event (CVE) rate was 3.5% with standard-dose statin therapy and 2.9% with high-dose statins. That works out to a 17% relative reduction in the risk of CVEs overall and a 21% decrease in the relative risk of stroke with intensive compared with moderate-dose statin therapy.

At least six other studies have shown that standard-dose statins reduce the incidence of CVEs compared with placebo, added Dr. Mega of Massachusetts General Hospital, Boston.

The observed stroke prevention benefit with intensive statin therapy didn't appear to be the result of the greater degree of LDL lowering achieved with these drugs. Indeed, patients who experienced a CVE had LDL levels similar to those who did not. This is consistent with epidemiologic studies that have failed to find a consistent link between cholesterol levels and risk of CVEs, she noted.

A clue as to the mechanism of benefit comes from the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT) trial, in which 4,162 patients were randomized to 40 mg/day of pravastatin or 80 mg/day of atorvastatin. In that study, patients who experienced a CVE had significantly higher C-reactive protein levels 30 days into treatment than did those who did not experience a CVE, by a margin of 2.7 mg/L vs. 1.9 mg/L. The day-30 CRP level was an independent predictor of stroke or transient ischemic attack even after adjustment for age, prior CVE, diabetes, and atrial fibrillation. This finding reinforces the link between inflammation and CVEs. It seems likely that the anti-inflammatory and vascular-stabilizing properties of the statins account for the reduction in strokes, Dr. Mega continued.

In addition to PROVE-IT, the trials included in Dr. Mega's metaanalysis were the 10,001-patient Treating to New Targets (atorvastatin 10 mg/day vs. 80 mg/day) and the 4,497-subject Aggrastat to Zocor (simvastatin 20 mg/day vs. 80 mg/day). ■

Stroke Outcomes in The Elderly Improve With Early Heparin

Early intravenous heparin improves 90-day outcomes after nonlacunar stroke, Dr. Massimo Camerlingo and colleagues concluded.

Dr. Camerlingo of Ospedali Riuniti, Bergamo, Italy, and associates randomized 418 stroke patents (mean age 71 years) to either saline or heparin initiated within 3 hours of stroke; 208 received heparin and 210 received saline. The therapies were continued for 5 days, at which time both groups received 100 mg/day oral aspirin or other anticoagulants to obtain prothrombin times of 2.0-3.0 (Stroke 2005;36:2415-20).

Compared with those receiving intravenous saline, patients who got unfractionated heparin within 3 hours of their stroke were significantly more likely to be independent 3 months later (39% vs. 29%). There were fewer deaths (35 vs. 46) but more symptomatic brain hemorrhages (13 vs. 3) and fatal brain hemorrhages (7 vs. 1) in the heparin group.

—Michele G. Sullivan

Depression Intensifies the Risk of Stroke in Elderly Patients

BY MITCHEL L. ZOLER
Philadelphia Bureau

DALLAS — Depression boosted the risk for stroke in a study of more than 4,000 elderly people followed for 10 years.

People with the highest depression scores at baseline had twice the incidence of a cerebrovascular event or transient ischemic attack during follow-up, compared with people who had no depression, Dr. Abraham A. Ariyo reported at the annual scientific sessions of the American Heart Association.

The finding that depression is a risk factor for stroke follows a prior analysis of the same group of people showing that depression boosted the risk for coronary artery disease, said Dr. Ariyo, director of HeartMasters in Dallas.

The Cardiovascular Health Study Collaborative Research Group enrolled 4,483 men and women aged 65 or older who were completely free of any clinical sign of cardiovascular disease at baseline. The study also excluded patients who were treated with an antidepressant. All participants were assessed for depression using a modified version of the Center for Epidemiologic Studies Depression Scale.

The participants were categorized into quartiles based on their scores. Those with a score of zero had no depression. The next quartile included people with a score of 1-5, followed by quartiles with scores of 6-10, 11-15, and 16 and over.

In 10.3 years of follow-up, 533 people had a stroke, and an additional 1,359 died.

In a multivariate analysis that controlled for baseline differences in age, gender, race, marital status, income, education diabetes, serum cholesterol, and activity of daily living, the incidence of stroke was related to depression scores. Compared with people who had a score of zero, those with a score of 1-5 had 19% more strokes, those with a score of 6-10 had 57% more strokes, those with a score of 11-15 had 78% more strokes, and people with a score of 16-30 had twice as many strokes. The increased stroke rates seen in patients with depression scores of six or higher were significantly different from the rate for people with no depression.

An analysis of death rates showed a similar pattern. People with scores of 6-10 had a 27% higher death rate; those with scores of 11-15 had a 73% higher mortality; and those with scores of 16 or more had 86% more deaths.

Several mechanisms may explain how depression affects stroke rates and mortality, Dr. Ariyo said. Depressed people are less physically active and engage in more unsafe behaviors, such as smoking. They also have increased levels of circulating platelets, fibrinogen, and other factors that raise thrombogenicity. In addition, depression also boosts serum levels of steroids, free fatty acids, and other factors that are proinflammatory and proatherogenic. ■