

Stroke Risk in Atrial Fib Patients Jumps at Age 85

BY BRUCE JANCIN
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COLORADO SPRINGS — The stroke risk without warfarin therapy in atrial fibrillation patients aged 85 years and older who have no other stroke risk factors is more than double that of patients aged 75-84 years, according to new data from the ATRIA study.

Moreover, the absolute reduction in stroke risk achieved with warfarin in the 85-plus age group appears to be substantially greater than in younger atrial fibrillation (AF) patients, study investigator Dr. Daniel E. Singer reported at a conference sponsored by the American Heart Association.

These findings from the National Institutes of Health-sponsored Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study indicate a need to revisit current national guidelines, which allow aspirin rather than warfarin for AF patients aged 75 years and up with no stroke risk factors other than their advanced age.

"These data suggest that looking at old people with just a single age cutoff at 75 misses the fact that those who are age 85 and older are at considerably heightened risk. The risk in the rapidly growing oldest old population shouldn't be confused with that of the younger old population age 75-84. Those 85 and up should be considered strong candidates for warfarin," said Dr. Singer, profes-



sor of medicine and epidemiology at Harvard Medical School and chief of the clinical epidemiology unit at Massachusetts General Hospital, both in Boston.

Dr. Singer also is the principal investigator in ATRIA, a study to assess the impact of warfarin in usual care that has enrolled 13,559 northern California patients with nonvalvular AF. In effect, ATRIA is a real-world post-marketing study of a 60-year-old drug.

The 4,330 ATRIA participants who had no additional stroke risk factors at baseline have accumulated 16,000 person-years of follow-up. During that period, those aged 75-84 years who were not on warfarin had a 1.41% annual stroke rate, compared with a 3.31% annual rate among the patients aged 85 and up with no other stroke risk factors who were not on warfarin.

Those aged 75-84 years who were on warfarin had a 0.53% annual stroke rate, while those aged 85 years and older had a 0.86% event rate on warfarin, indicating a substantially greater absolute benefit for warfarin in the oldest group. The caveat, he stressed in an interview, is that ATRIA was not a randomized trial, so the main focus should be on the core stroke risk off warfarin—impressively greater in patients aged 85 and older.

As for the dark side of warfarin therapy, the intracranial hemorrhage rate in patients aged 85 years and older with no stroke risk factors other than age was

0.60%/year on warfarin and 0.58%/year in those not taking the anticoagulant.

"When you get into these older age groups, the intracranial hemorrhage rate is quite substantial. But the fact is, it's high on or off warfarin," he observed.

The widely used CHADS2 stroke risk scoring system for AF patients awards one point each for congestive heart failure, hypertension, age over 75 years, and diabetes, and two points for a history of stroke. The ATRIA findings suggest that age 85 years or greater ought to receive more weight—perhaps two points—although this has to be viewed as a tentative conclusion, because ATRIA is the first study to show a substantially greater stroke risk in the oldest old, Dr. Singer stressed.

Surveys indicate roughly 60% of AF patients in North America received warfarin; the rate drops off sharply at age 85 years.

The landmark randomized, placebo-controlled clinical trials have established that warfarin reduces stroke risk in AF by 68% across the board. That's based on intention-to-treat analysis. In reality, many patients who had strokes in the trials had stopped taking the drug or were clearly underanticoagulated.

"The relative risk reduction on treatment probably approaches 80%, which is very much what you'd expect to find if you were reversing the entire effect of atrial fibrillation," Dr. Singer said.

There was considerable hope in the 1990s for aspirin as a safer alternative, but its impact proved to be quite small. And aspirin turned out to be particularly poor at preventing severe or fatal strokes, he said.

Atrial Arrhythmias Double Deaths in Congenital Heart Disease

BY BRUCE JANCIN
Denver Bureau

CHICAGO — Adults with congenital heart disease who develop atrial fibrillation or another atrial arrhythmia have more than twice the subsequent mortality and triple the hospitalization rate of those without atrial arrhythmias, Dr. Ariane J. Marelli reported at the annual meeting of the American College of Cardiology.

With more and more congenital heart disease patients today surviving decades longer than was typical in the past, health care systems will need to be ready to deal with a growing burden of atrial arrhythmia-related disease, including stroke, heart failure, and need for hospital-based interventions, added Dr. Marelli of McGill University, Montreal.

She presented a population-based study of all 38,430 adult congenital heart disease (ACHD) patients in a Quebec-wide administrative registry during 1983-2005. After a 5-year washout period designed to exclude patients with atrial arrhythmias secondary to pulmonary hypertension or heart failure, all patients free of atrial arrhythmias at the start of 1988 were followed through 2005.

In 2005, the prevalence of atrial arrhythmia was 15% in the overall group. However, among those with transposition of the great arteries, univentricular heart, or Ebstein anomaly, the preva-

lence of atrial arrhythmia was 25%-30%.

In contrast, the rate was 20% in patients with atrial septal defects, 15% in those with tetralogy of Fallot, and less than 10% in patients with other forms of ACHD.

Among patients with severe ACHD—that is, those with univentricular heart, atrioventricular canal defects, tetralogy of Fallot, truncus arteriosus, or transposition of the great arteries—the lifetime risk of atrial arrhythmia was 60%. It was 43% in those who had other forms of ACHD.

A 20-year-old Quebec ACHD patient without atrial arrhythmia at baseline had a 7% risk of developing such an arrhythmia during the next 20 years. That's comparable with the 20-year risk in a 55-year-old without congenital heart disease, which has been reported at 7%-10% in various studies.

"Tim Garson [a pediatric cardiologist who is executive vice president and provost at the University of Virginia, Charlottesville] used to say, 'We have young patients with old hearts.' I think this is an illustration of that fact," Dr. Marelli observed.

A 55-year-old ACHD patient in the Quebec study had a 20-year risk of atrial arrhythmia of 38%.

Dr. Marelli and her coinvestigators matched 12,768 ACHD patients with atrial arrhythmias by age, gender, calendar time, and disease severity to an equal

number of ACHD controls free of atrial arrhythmia.

The crude mortality rate was 55/1,000 in the atrial arrhythmia group, compared with 9/1,000 among controls.

The crude hospitalization rate was 5.1 days/1,000 person-days in ACHD patients with atrial arrhythmia versus 0.8 days/1,000 person-days in ACHD controls.

After adjustment for potential confounders, this translated into a 2.1-fold increased mortality risk and 3.2-fold greater hospitalization risk in the atrial arrhythmia group.

Audience members noted that until now, ventricular arrhythmias in ACHD have gotten the vast majority of the re-

search attention. They expressed gratitude to the Montreal group for conducting the most thorough study to date on the impact of atrial arrhythmias in ACHD patients.

They were particularly eager to learn whether Dr. Marelli and her coworkers have come up with a way to risk-stratify ACHD patients with atrial arrhythmias to guide anticoagulation and other preventive therapies.

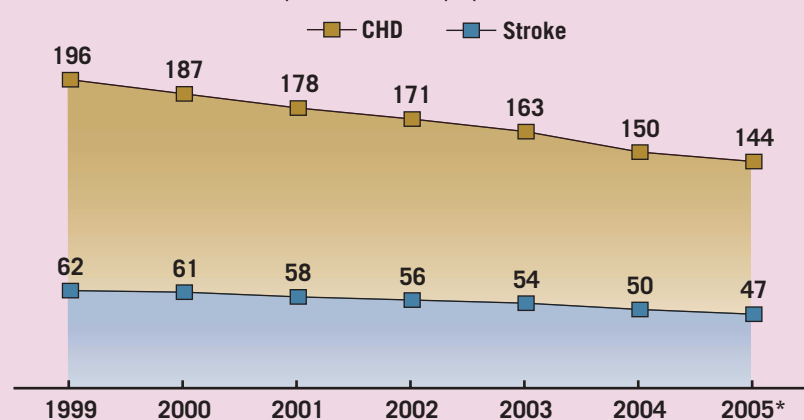
Dr. Marelli replied that she, too, sees this as a pressing need.

She and her colleagues tried applying the widely used CHADS-2 risk scoring system but found it just does not work in an ACHD population.

There was a 2.1-fold increased mortality risk and 3.2-fold greater hospitalization risk in the ACHD patients with atrial arrhythmias.

DATA WATCH

Age-Adjusted Mortality For Congenital Heart Disease and Stroke Is Declining (per 100,000 population)



*Preliminary data.
Source: American Heart Association