Framingham Score Predicts Raloxifene's Stroke Risk

BY DAMIAN McNAMARA
Miami Bureau

ORLANDO — The Framingham stroke risk score can predict a high-risk postmenopausal woman's likelihood of a future cerebrovascular event with raloxifene use, according to new analysis of data from the Raloxifene Use for the Heart (RUTH) study.

Investigators in 26 countries enrolled 10,101 women at risk for a major coronary event in RUTH. A total of 5,031 women had documented coronary heart disease and the remaining 5,070 had multiple coronary heart disease risk factors (Am. J. Cardiol. 2002;90:1204-10). Although overall stroke risk was not significantly different between women randomized to raloxifene versus placebo, a higher number of fatal stroke events occurred in the treatment group, 59, compared with 39 in the placebo group during a mean of 5.6 years follow-up (N. Engl. J. Med. 2006:355:125-37).

Investigators launched a second study to see how this increased risk associated with raloxifene (hazard ratio, 1.49; absolute risk increase, 0.7 per 1,000 woman-years) would apply to women stratified by baseline Framingham stroke scale score.

David Cox, Ph.D., and his associates retrospectively calculated 10-year cumulative risk. He presented findings at the annual meeting of the North American Menopause Society. Eli Lilly & Co. supported the study, and Dr. Cox is a clinical research scientist for the company.

Not surprisingly, risks appeared to congregate in the third and fourth highest quartiles of Framingham score risk. However, there were no significant differences between treatment groups in either all strokes or nonfatal strokes, regardless of baseline Framingham score.

Regarding fatal stroke, Dr. Cox said, "after 2 years, you start to see a split between placebo and raloxifene for risk of fatal stroke by Framingham stroke risk score in RUTH. We think the pattern and data would suggest most of the excess risk was among those in the upper half of risk." Specifically, women who scored a 13 or greater on the Framingham tool at baseline (the median) were at increased risk of stroke death, compared with women who scored lower.

A meeting attendee asked at what age raloxifene should no longer be considered, offering 70 years as an example. "Even at age 70, she might not have enough risk factors," Dr. Cox said. "But it depends on the risk factor." For example, he said, "atrial fibrillation would put her over the 13 score."

Dr. Cox and his colleagues also retrospectively assessed application of the Framingham risk score to 7,705 postmenopausal women with osteoporosis randomized to raloxifene or placebo in the Multiple Outcomes of Raloxifene Evaluation (MORE) study (JAMA 2002;287:847-57). In this study, raloxifene was not associated with an increase in rate of all strokes (hazard ratio, 0.71) or stroke death (HR, 0.57). He noted that the MORE population was generally lower risk than women in RUTH, with baseline Framingham scores of less than 13 in 80%.

Raloxifene's effect on the stroke death rate might differ by baseline stroke risk, Dr. Cox said. Assessing cumulative stroke risk may help target raloxifene treatment to postmenopausal women with the most favorable risk-benefit profile. ■

Behavioral Screening Effective For HSV-2 in Young Women

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Behavioral and demographic factors were more predictive of herpes simplex virus type 2 than were clinical symptoms in a study of 127 adolescents, approximately one-third of whom were infected with the disease.

Data from population-based studies have shown that herpes simplex virus type 2 (HSV-2) most often is acquired by women between the ages of 20 and 29 years, but many of them have no clinical symptoms, said Dr. Kenneth Fife of Indiana University, Indianapolis.

To determine the demographic and behavioral factors associated with HSV-2 infection in young women, Dr. Fife and his colleagues collected data for 4-6 years from 127 adolescents aged 14-18 years at baseline. The researchers presented their results in a poster at the jointly held annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy and the Infectious Diseases Society of America.

Of the study population, 92% were black and 7% were white; 33% were antibody positive for HSV-2 at baseline. Only three participants had a history of clinically diagnosed herpes when they entered the study, and the participants underwent quarterly screening for incident STDs. Each participant kept a detailed behavioral diary for two 12-week periods each year and collected weekly vaginal swab samples during these 12-week periods. At the conclusion of the study, the average age of the participants was 21 years.

"Only increasing age, increased time since sexual debut, and an increased number of lifetime sexual partners were significantly correlated with a positive HSV-2 test," Dr. Fife noted. The odds ratios for these factors were 1.36, 1.17, and 1.09, respectively.

The researchers found no significant association between a positive test result and recorded clinical symptoms of genital pain or discharge.

Of 121 participants for whom complete behavioral data were available, 67 had previous sera available for HSV-2 antibody testing, and 17 (25%) of these women seroconverted from negative to positive during the course of the study.

The DNA testing for HSV-2 in the study population is ongoing, but preliminary results from 13 women with positive results on PCR tests showed that most of the participants shed virus from the genital tract and most had several positive DNA tests over a single 12-week period.

The study was limited by the use of self-reports, but the results suggest that HSV-2 control programs should include young women because they shed virus frequently despite a lack of clinical symptoms, and early signs of infection may go unrecognized, Dr. Fife said.

The study was supported by a grant to Dr. Fife from GlaxoSmithKline and funding from the National Institutes of Health. ■

One-Year Follow-Up: Nonsurgical Approach Beneficial in SUI

BY DOUG BRUNK
San Diego Bureau

LAS VEGAS — A nonsurgical approach to treating stress urinary incontinence that strengthens transurethral collagen by denaturing it with heat provided measurable durable improvement at 12 months, according to preliminary results from a multicenter clinical trial.

The study involved the use of the Renessa System, which was approved by the Food and Drug Administration in 2005 for the treatment of stress urinary incontinence (SUI) caused by hypermobility in women who have failed conservative care and are not candidates for surgical therapy.

"We have limited treatment options to offer women with stress urinary incontinence," lead investigator Dr. Denise M. Elser said in an interview after the study was presented during a poster session at a congress sponsored by the AAGL.

"Pelvic muscle exercises are safe but don't work for everyone, and in practical terms, our patients are rarely compliant in the long run. Not all patients want surgery, whether it's due to cost, time off work, or fear of anesthesia and a procedure. There are no FDA-approved medications available to us to use for treating SUI. Renessa offers a safe option that will allow more than half of patients improvement or cure of their incontinence," said Dr. Elser, who disclosed that she has been a paid consultant to Novasys Medical Inc., the manufacturer of the Rensessa System.

The system includes a small probe that the physician passes through the natural opening of the urethra. The probe heats multiple small treatment sites in the submucosa of the bladder neck and upper urethra, denaturing collagen in the tissue. Previous studies of the system have assessed its safety and initial success rates, but the current study is designed to evaluate patients at baseline and at 3, 6, 12, 18, 24, and 36 months following treatment.

Study participants included 136 women with stress urinary incontinence at 13 physician offices or ambulatory surgery centers in the United States who had failed prior conservative treatment. Their average age was 47 years and they received pretreatment oral antibiotic and local periurethral lidocaine injection.

The Renessa device was placed in the bladder and radiofrequency energy "was delivered in nine 1-minute increments, resulting in collagen denaturation of 36 circumferential sites from the bladder neck to the proximal urethral submucosa," according to the poster.

At each time point, patients answered questions on the Incontinence Quality of Life (I-QOL), the Urogenital Distress Inventory (UDI-6), the Patient Global Impression of Improvement (PGI-I) surveys, and underwent a 1-hour in-office stress pad weight test.

At baseline the mean number of leaks per day was 2.9; the mean I-QOL score was 51.3 and the mean UDI-6 score was 52.7.

The researchers reported their 12-month results as intention to treat analysis because 63 of the 136 patients did not report for the 12-month follow-up visit. This was done "in an attempt to present the final analysis as comprehensively as possible and to account for those lost to follow-up," said Dr. Elser, a gynecologist who practices in Oak Lawn, Ill.

At 12 months, the mean number of leaks had dropped to 1.9 per day and 69% of patients reported a greater than 50% reduction in leaked volume on the stress pad weight test (a median reduction of 15.2 g from a baseline of 39.34 g).

The stress pad test also indicated that 45% of women were dry. Of these, 29% had no leaks and 16% had less than one gram of leakage.

The mean I-QOL and UDI-6 scores improved from baseline by 11.8 and 14.1 points, respectively. Results from the PGI-I indicated that 50% of patients deemed their incontinence to be "little," "much," or "very much" improved from baseline. No serious adverse events were reported at any time point.

Dr. Elser acknowledged that the number of patients completing the 12-month evaluation was a limitation of the study but the intent to treat analysis attempted to compensate for this.

The study was funded by Novasys Medical. ■