Genetics Factor Into Fracture Susceptibility, per Twin Study

BY PATRICE WENDLING
Chicago Bureau

The genetic influence on fracture susceptibility depends on the type of fracture and age at the time of the event, results from a large Swedish twin study suggest.

In addition, the heritability of osteoporotic fractures is stronger than has been previously estimated, especially for early-occurring osteoporotic fractures, according to the study's lead author, Karl Michaëlsson, M.D., Ph.D., of the Uppsala (Sweden) University Hospital and associates.

The effect of genes was seen most clearly in hip fractures; 48% of the variance in liability to these fractures was attributed to genetic factors.

The investigators identified 33,432 twins born from 1896 to 1944 included in the Swedish Twin Registry, currently the largest twin registry in the world.

Among them, 24,598 agreed to take part in the study.

Computer-assisted telephone interviews and the Swedish Inpatient Registry were used to identify 6,021 twins with any fracture, 3,599 with osteoporotic fractures, and 1,055 with a hip fracture after the age of 50 years.

Just 16% of the overall age-adjusted fracture variance and 27% of the osteoporotic age-adjusted fracture variance were explained by genetic variation (Arch. Intern. Med. 2005;165:1825-30).

The strongest genetic influence was evident for hip fractures. Nearly half (48%) of the variance in liability to these fractures was attributable to genetic factors.

There was a tendency toward lower heritability estimates of fractures among the men, but it was not statistically significant.

If the first hip fracture within a twin pair occurred before age 69 years, 68% of the variance of liability was explained by genetic factors. If the first hip fracture happened between ages 69 and 79 years, 47% of the variance was attributable to genetic variation. After age 79 years, that figure fell to 3%.

The same pattern of attenuated heredity estimates with increasing age also was evident for the other fracture categories.

"A search for genes and gene-environment interactions that affect early osteoporotic fracture risk is likely to be fruitful, but fracture-prevention efforts at older ages should be focused on lifestyle habits," the authors report.

Finally, they suggest that an assessment of osteoporotic fracture risk by clinical examination may be recommended for relatives of patients with hip fractures before age 80 years. ■

Risedronate Lowers Hip Fracture Risk in Men Following Stroke

BY SHERRY BOSCHERT
San Francisco Bureau

The bisphosphonate risedronate significantly reduced the risk of hip fracture in elderly men with a history of stroke, in the first randomized, double-blind study on this topic.

Risedronate sodium, an inhibitor of bone resorption, previously was shown to decrease the risk of nonvertebral fractures in postmenopausal women with osteoporosis and of hip fractures in women who had a stroke.

The current study randomized 280 consecutive ambulatory men aged 65 years or older with a previous stroke to a daily dosage of 2.5 mg risedronate or placebo for 18 months. By the study's end, 10 patients in the placebo group and 2 in the risedronate group had sustained hip fractures, representing an 80% reduction in risk of fracture in the risedronate group, reported Dr. Yoshihiro Sato of Mitate Hospital, Tagawa, Japan, and his associates (Arch. Intern. Med. 2005;165:1743-8).

The investigators estimated that 16 elderly men who had previous strokes would need to be treated with risedronate to prevent one hip fracture.

All of the hip fractures were on the patient's hemiplegic side. In addition to hip fractures, wrist or ankle fractures occurred in two patients in the risedronate group, and six patients in the placebo group sustained other fractures—two at the proximal femur, two at the ribs, one at the proximal humerus, and one at the pelvis.

Bone mineral density on the hemiplegic side increased by 2.5% in men in the risedronate group, compared with baseline measurements, but decreased by 3.5% in men in the placebo group, compared with baseline, a significant difference.

On the nonhemiplegic side, bone density increased by more than 3% in the risedronate group and decreased by 2% in the placebo group. Bone density was significantly lower on the hemiplegic side in both groups. A key marker of bone resorption—urinary deoxypyridinoline—decreased by 59% in the risedronate group and by 37% in the placebo group. Bone resorption typically increases during the first year after a stroke in both men and women, studies have shown.

Patients in the current study were advised to take risedronate with water 30-60 minutes before breakfast and not to take any other drugs that could affect bone or calcium metabolism. Patients were asked to return pills not taken, which were counted to check adherence to therapy. A single physician who was blinded to treatment assignment did the follow-up assessments of all patients, evaluating them every 4 weeks for falls or possible hip fractures and performing hematologic and biochemical tests.

Six patients in the risedronate group and seven in the placebo group dropped out of the study or were lost to follow-up, illness, or death. ■

Casual Sun Exposure May Not Guarantee Adequate Serum Levels of Vitamin D

BY KERRI WACHTER
Senior Writer

NASHVILLE, TENN. — Physicians may need to rethink their advice to patients to get some casual sun to ensure vitamin D sufficiency, according to new data presented at the annual meeting of the American Society for Bone and Mineral Research.

In a study of young adults in Hawaii, abundant sun exposure did not guarantee adequate serum levels of vitamin D, said Dr. Neil C. Binkley of the osteoporosis clinical center and research program at the University of Wisconsin in Madison.

The highest levels of 25(OH)D_3 were close in the Hawaii and Wisconsin groups. Levels in the Hawaii group were unrelated to sun exposure or skin color.

"This suggests that some individuals—for an unclear reason or reasons—do not achieve a high circulating D_3 concentration despite abundant sun exposure," he said. "It seems logical that the clinical approach that many of us take to recommend casual sun exposure for patients is certainly not a guarantee of vitamin D adequacy."

Initially, individuals with abundant sun exposure were studied in order to identify the upper limit of the normal range of 25-hydroxy vitamin D_3 (25[OH]D_3).

The investigators recruited 100 young adults, most of whom were surfers, from the Honolulu area in March 2005.

Participants were required to have had 3 or more hours of sun exposure per day, 5 or more days per week, for the previous 3 months. Information about sun exposure, sunscreen use, and dietary vitamin D intake was obtained by questionnaire. Skin color was measured by reflectance colorimetry.

Forty-one percent of the cohort used no sunscreen. On average, participants were exposed to the sun for about 4 hours per day, or 28 hours weekly.

This estimate included hours exposed to the sun with sunscreen.

As part of the self-questionnaire, respondents were asked to fill in areas of skin coverage on human figures. The researchers were then able to calculate that the group had an average of 10.6 hours per week of whole-body sun exposure.

A group of 174 healthy controls were recruited from the University of Wisconsin between January and April of 2005. No data were obtained from this group regarding sun exposure, sunscreen use, and dietary vitamin D.

The two groups were similar in terms of average age, 24, and average body mass index, 23. There were slightly more men in the Hawaii cohort (67% vs. 46%).

Serum 25(OH)D_3 was measured by a precise high-performance liquid chromatography assay.

Results correlated well with those obtained by tandem mass spectroscopy.

Using a cutoff of 30 ng/mL to define inadequate vitamin D status—a point of some contention among researchers—86% of the Wisconsin cohort was vitamin D inadequate. And "somewhat surprisingly, 51% of the Hawaii cohort was below this arbitrary cutoff."

The mean concentration of serum 25(OH)D_3 was 31.4 ng/mL in the Hawaii cohort, compared with 18.3 ng/mL in the Wisconsin cohort.

The highest levels of 25(OH)D_3 were almost identical in the Hawaii and Wisconsin groups (62.0 ng/mL vs. 62.3 ng/mL). Levels of 25(OH)D_3 in the Hawaii group were unrelated to hours of sun exposure or skin color.

Among those in the Hawaii cohort, the 10 participants with the lowest serum 25(OH)D_3 levels were similar to the rest of the cohort in terms of parathyroid hormone levels, age, body mass index, serum chemistries, multivitamin use, and number of hours of sun exposure without sunscreen.

They did have a lower average number of hours per week of whole-body sun exposure (6 hours).

Serum vitamin D_3 levels were also measured in a random subset of 20 individuals in the Hawaii cohort. "Despite abundant sun exposure, some of these individuals do not maintain a high serum concentration of D_3," Dr. Binkley said.

The individuals with the highest 25(OH)D_3 levels in both cohorts had levels slightly higher than 60 ng/mL.

This suggests that the upper limit for normal 25(OH)D_3 levels is 60-80 ng/mL, which is consistent with published reports, Dr. Binkley said.

The results are limited by the self-reporting of sun exposure. ■