Low BMD Tied to Risk of Less-Severe Hip Fractures

BY KERRI WACHTER
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PHILADELPHIA — The increased risk of hip fracture in women with lower bone mineral density mainly reflects an increased risk of nonsevere fracture rather than severe fracture, Jane A. Cauley, Dr.P.H., reported at the annual meeting of the American Society for Bone and Mineral Research.

Dr. Cauley, a professor of epidemiology at the University of Pittsburgh, looked for differences in risk factors for severe and nonsevere hip fractures using data from the longitudinal Study of Osteoporotic Fractures, involving 9,704 women aged 65 years and older.

The women were contacted every 4 months by postcard to determine if a hip fracture had occurred. The average follow-up period was 10.5 years.

Preoperative hip radiographs were obtained for 462 women—249 with femoral neck fractures and 213 with intertrochanteric fractures.

The fractures were rated by a single radiologist using the Garden and Kyle systems.

Most hip fractures were classified as severe. Of the femoral neck fractures, 70% were displaced. Of the intertrochanteric fractures, 72% were unstable.

For femoral neck hip fracture, women who went on to have undisplaced fractures had a femoral neck BMD about 7% lower than did women who had a displaced fracture. Among women in the lowest tertile for femoral neck BMD, 58% had displaced fractures, compared with 83% of women in the highest tertile for BMD.

Although lower femoral neck BMD was associated with a greater risk of both types of fracture, a one-standard-deviation decrease in BMD was associated with a more than threefold increased risk of having an undisplaced fracture. There was only an 86% increase in having a displaced fracture.

For intertrochanteric hip fracture, women who went on to have stable fractures had an intertrochanteric BMD about 7% lower than did women who had an unstable fracture. Among women in the lowest tertile for intertrochanteric BMD, 62% had unstable intertrochanteric fractures compared with about 80% of women with higher BMD, said Dr. Cauley.

Again, while low intertrochanteric BMD was associated with an increased risk of both types of intertrochanteric fractures, women with lower BMD had a threefold increase in the risk of having a stable intertrochanteric fracture, compared with an almost twofold increased risk of having an unstable fracture.

One standard deviation decrease in walking speed was a risk factor for femoral neck displaced and undisplaced fractures. A greater height at the age of 25 and steroid and alcohol use were associated with an increased risk for a femoral neck displaced factor.

Dr. Cauley disclosed that she has received research grants from Pfizer Inc., Novartis Pharmaceuticals Corp., Merck & Co, and Eli Lilly & Co. She also has received consulting fees from Novartis. ■

JOINT DECISIONS

An 81-year-old man presented with severe proximal muscle pain, reduced mobility, and a history of frequent falls as well as knee osteoarthritis, hypertension, and a vertebral wedge collapse nearly 2 decades earlier. Clinical examination revealed ankle swelling and left knee synovitis, as well as bilateral quadriceps muscle wasting and grade 4 or 5 muscle power.

Scintigraphy showed the Lone Ranger sign, with increased uptake in the skull and around the eyes and reduced soft tissue activity. Laboratory evaluations identified and elevated calcium level, at 4.02 mmol/L, and an elevated alkaline phosphate level, at 782 U/L, which suggested severe bone disease.

Diagnosis

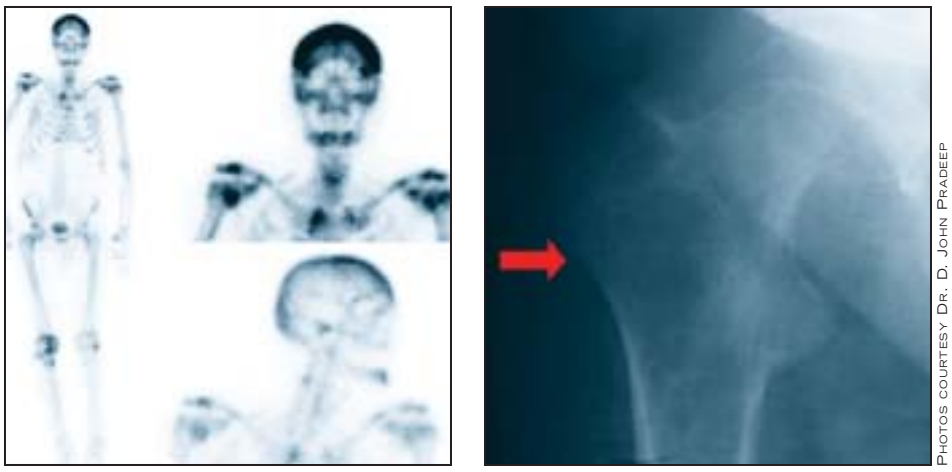
The diagnosis, based on scintigraphy and other radiographic investigations, was long-standing parathyroid bone disease complicating primary hyperparathyroidism (Ann. Rheum. Dis. 2006;65:1244).

The scintigraphic findings were characterized as a superscan, in which there is diffuse increased skeletal uptake relating to increased bone turnover and which can appear to be a negative or normal scan. This appearance is more common in metastatic cancer and is quite unusual in hyperparathyroid bone disease, according to Dr. D. John Pradeep of Norfolk and Norwich University Hospital, Norwich, England.

Hyperparathyroidism itself today is usually detected quite early, and a presentation such as this, with extensive bone disease, is quite rare, Dr. Pradeep said in an interview. Aside from the scintigraphic findings, hyperparathyroidism also is characterized by x-ray findings of brown tumors, which are small lytic lesions of the hip.

Further diagnostic evaluation of this patient using ultrasound and Tc-99m sestamibi scanning identified a mass by the left upper pole of the thyroid. The tumor was removed by minimally invasive parathyroidectomy, and histologically was found to be a benign adenoma.

—Nancy Walsh



PHOTOS COURTESY DR. D. JOHN PRADEEP

Lone Ranger sign from excessive cranial uptake and reduced soft tissue background activity is visible in all scintigraphy views (left). A brown tumor is shown (right).

Increased BMD

Bisphosphonate *from page 1*

The trial was funded by Novartis; Dr. Black disclosed a significant financial relationship with Novartis.

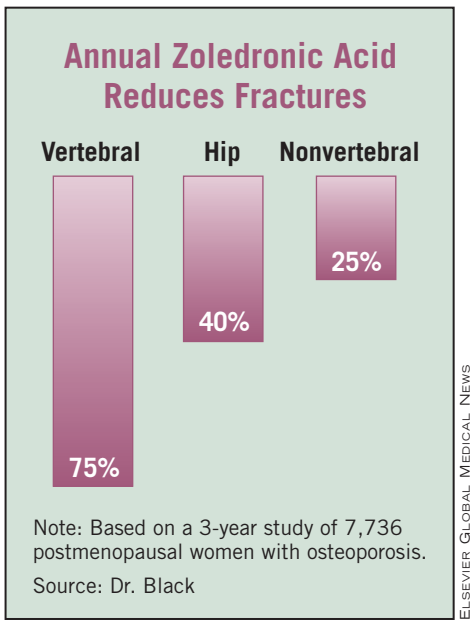
In the trial, women randomized to the treatment group received an annual infusion of zoledronic acid (5 mg). All women received calcium (1,000 mg-1,500 mg/day) and vitamin D (400 IU-1,200 IU/day).

Women were included in the trial if they were aged 65-89 years (mean age, 73 years) with either a femoral neck T score of –2.5 or less or prevalent vertebral fracture and a femoral neck T score of –1.5 or less.

Women were recruited into two groups based on their osteoporosis treatment history. A total of 6,084 women were not currently taking an osteoporosis drug and had minimal prior therapy; 1,652 women were currently taking a selective estrogen-receptor modulator, calcitonin, or hormone therapy for osteoporosis at baseline.

Primary end points included new morphologic vertebral fractures in women not currently taking an osteoporosis drug and hip fractures in both those undergoing and those not undergoing treatment at baseline. Secondary end points included nonvertebral fractures, change in bone mineral density (BMD) measured by dual-energy x-ray absorptiometry, changes in biochemical markers of bone metabolism, and changes in bone density and size determined by quantitative CT. Safety end points included evaluation of adverse events, assessment of bone histology by histomorphometry, and postdose monitoring for acute changes in renal laboratory values.

A total of 3,875 women were randomized to zoledronic acid (3,045 in stratum I and 830 in stratum II), while 3,861 were randomized to placebo (3,039 in stratum I and 822 in stratum II). Dr. Black presented data from the trial start-up to March 31, 2006 (the study was scheduled to end in June 2006). Mean follow-up was 2 years and 8 months. Retention was 84%.



ELSEVIER GLOBAL MEDICAL NEWS

Overall, 3.8% of women receiving treatment had morphometric vertebral fractures at 3 years, compared with 12.8% of women on placebo, representing a 70% reduction. During the first 2 years, there was a 71% reduction, and during the first year, there was a 60% reduction.

"There was a 40% reduction in the risk of hip fractures [at 3 years] that was also highly statistically significant," said Dr. Black. Clinical vertebral fractures were reduced by 75% and nonvertebral fractures were reduced by 25% in treated women, compared with those on placebo. Lumbar spine BMD was increased by 7% and total hip BMD was increased by 6% in treated women, compared with those on placebo.

In addition, bone markers were measured in a subsample of 605 women (300 on zoledronic acid and 305 on placebo). There was a decline in beta C-telopeptide of type 1 collagen (β-CTX), a bone resorption marker, following the first infusion. "The values remain relatively constant over the 36 months of the study," said Dr. Black.

The mean β-CTX values for women on zoledronic acid remained within the premenopausal reference range. There was no progressive decline in β-CTX levels over 3 years.

Additional sampling was performed just after the third infusion at 24 months to determine in more detail how β-CTX levels responded to zoledronic acid infusion. "There is an immediate decline in β-CTX values within 10 days after the infusion. But then the levels begin to increase fairly linearly over the course of that third year," said Dr. Black.

Likewise, there was a decline in bone-specific alkaline phosphatase values following the first infusion of zoledronic acid, but the values remained fairly constant with no progressive decline following subsequent infusions. These values were also within the reference range for premenopausal women.

Osteonecrosis, defined as exposed bone in the mouth for longer than 6 weeks, occurred in three patients—two on placebo and one on zoledronic acid. All three cases healed with antibiotic treatment. ■