

# Age, Frailty Shouldn't Deter Bisphosphonate Tx

*An analysis showed a reduced risk of new vertebral fractures among elderly women with osteoporosis.*

BY DIANA MAHONEY  
New England Bureau

HARROGATE, ENGLAND — Age and frailty should not deter physicians from offering very elderly osteoporotic patients antiresorptive therapy, despite age-associated increases in comorbid conditions, said Steven Boonen, M.D.

The results of a pooled analysis from three randomized, double-blind controlled trials showed a significantly reduced risk of new vertebral fractures among 704 osteoporotic women aged 80 and older who received bisphosphonate therapy, compared with age and disease-matched patients randomized to placebo treatment, Dr. Boonen reported in a presentation at the annual conference of the National Osteoporosis Society.

"To the best of our knowledge, this study is the first to document a benefit of antiresorptive treatment in addition to that afforded by calcium and vitamin D in a population of women aged 80 and older with osteoporosis," said Dr. Boonen of Leuven (Belgium) University Center for Metabolic Bone Disease, the study's principal investi-

gator. "The findings tell us that, even in the very old, reducing bone resorption rates remains an effective treatment strategy."

The three studies each looked at 3-year fracture end points and included women aged 80-100 years with documented osteoporosis. In each study, the women randomized to bisphosphonate therapy were prescribed 5 mg/day of risedronate (Actonel) for up to 3 years, and control group patients were given a placebo pill for the same duration. All participants received 1,000 mg calcium supplementation per day and, if baseline levels were low, up to 500 U of vitamin D per day.

At 1 year, the risedronate groups had a new vertebral fracture rate of 2.5%, compared with 10.9% for the control groups. At 3 years, the new vertebral fracture rates for the bisphosphonate and placebo groups were 18.2% and 24.6%, respectively, "representing a 44% reduction in risk for the women who took risedronate," Dr. Boonen said.

The rates of nonvertebral fractures were not significantly different between the two groups, he said. At 3 years, the risedronate patients had a 14% risk, compared with

the placebo group's 16.2% risk. The studies also showed risedronate to have a safety profile similar to that of placebo.

The early efficacy of the risedronate therapy was consistent across the three trials, Dr. Boonen said. The treatment was well tolerated, even among the oldest women in the study population, "despite the fact that evaluation of baseline characteristics showed these patients to have a higher prevalence of gastrointestinal diseases than younger patients."

The findings are of particular relevance, considering the aging of the population. "The prevalence of vertebral deformities in women increases markedly between the ages of 50 and 90, and epidemiological data suggest that half or more of women aged 80 and older have vertebral fractures," he said. "Our findings suggest that adding [bisphosphonate] treatment to calcium and vitamin D could significantly decrease the incidence of vertebral fractures in elderly women with osteoporosis and thus reduce the public health burden associated with these fractures."

The hope is that these data will help increase the number of "very old" patients with osteoporotic fractures who are deemed eligible for and who receive treatment. "Despite the debilitating effects of osteoporotic fractures and the availability of therapies to reduce fracture recurrence, only a small percentage of women with osteoporotic fractures receive treatment, and this percentage decreases with age," Dr. Boonen said.

"Clinicians may presume that it is too late to alter the course of disease in its late stage, but these results tell us that is not so."

Because each of the antiresorptive therapies used to treat osteoporosis has unique characteristics and side-effect profiles, the observations made in this study cannot be generalized to include other bisphosphonates, he cautioned.

Dr. Boonen disclosed that he has received research grants from Procter and Gamble Pharmaceuticals but has no other financial relationship with it or any other company that markets bisphosphonates. ■

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## Low Albumin, T3 May Mark Increased Vertebral Fracture Risk

BY DIANA MAHONEY  
New England Bureau

HARROGATE, ENGLAND — Low serum albumin and T3 levels are independently predictive of vertebral fractures in women older than 50 years, a 10-year prospective study has shown.

Because albumin and T3 deficiencies are considered markers of frailty and sickness, the findings suggest that chronic poor health may itself be a risk factor for vertebral fracture, said Judith Finigan, principal investigator and research nurse in the bone metabolism group at the University of Sheffield (England).

To identify predictors of fracture in women between ages 50 and 85, the Sheffield investigators acquired baseline bone mineral density (BMD) measures and medical and lifestyle information from a population-based group of 375 women. They also collected fasting blood samples for measuring serum calcium, alkaline phosphatase, parathyroid hormone, creatinine, phosphate, albumin, and thyroid hormones.

All of the participants had spinal radiographs taken at baseline and at years 2, 5, 7, and 10, which were reviewed for incident vertebral fractures by a single radiologist. Nonvertebral fractures were confirmed by radiologist reports.

Cox regression analysis showed that numerous risk factors—including age; BMD at the lumbar spine, hip, or total body; years of estrogen exposure; and prevalent vertebral fracture—predicted fractures overall.

Low serum T3, low serum albumin, and low body fat were specifically predictive of vertebral fractures but not nonvertebral fractures.

These measures remained significantly predictive, even after adjusting for age, Ms. Finigan reported at the annual conference of the National Osteoporosis Society. Neither TSH nor T4 predicted fracture, she noted.

The age-adjusted relative risks per standard deviation decrease for T3, albumin, and body fat were 1.71, 1.74, and 1.55, respectively. "T3 and albumin also predicted vertebral fracture independently of spine or hip BMD," Ms. Finigan said.

In a separate analysis of a larger cohort, the investigators examined the relationship between serum albumin and vertebral fractures in postmenopausal women from the placebo arms of the Hip Intervention Program (HIP) trial and the Vertebral Efficacy with Risedronate Therapy (VERT) trial.

At 3 years, 381 of 2,720 subjects had experienced one or more incident vertebral fractures. Analysis showed a 1.23 relative risk of vertebral fracture for each standard deviation decrease in serum albumin, after adjusting for femoral neck BMD, weight, and age. As in the smaller study, low serum albumin was not associated with an increased risk of incident nonvertebral fractures in the larger population.

The findings of the second analysis "confirm the association between low baseline albumin levels and incident vertebral fractures," she said.

Serum albumin and thyroid hormone measurements are recommended as part of a routine evaluation for osteoporosis in postmenopausal women. Patients with deficiencies in these may be candidates for antiresorptive treatment to reduce their risk of vertebral fractures, Ms. Finigan concluded. ■

## Disuse Fractures Are Possible When Immobile Elders Are Moved

BY NORRA MACREADY  
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LAS VEGAS — Elderly patients in long-term care have a real but underrecognized risk of minimal-trauma fractures, Violeta Galabova, M.D., warned at the annual meeting of the American Geriatrics Society.

Osteoporosis associated with disuse, although not extensively studied, is thought to be the primary mechanism behind the fractures, which often occur as the patient is being moved. "It's very important to teach nursing staff proper transfer techniques," said Dr. Galabova, a fellow in geriatric medicine at the University of Pennsylvania, Philadelphia.

People who are confined to bed or wheelchair for 6 months or more are especially vulnerable, particularly if they've already sustained a previous fracture. Other risk factors include use of predisposing medications such as steroids, and poor nutritional status, as reflected in a body mass index less than 20 kg/m<sup>2</sup> or a serum albumin level below 3 g/dL. These patients should be watched carefully and might benefit from supplemental calcium and vitamin D, as well as treatment with bisphosphonates, Dr. Galabova told this newspaper.

She described three patients whose cases illustrate how these fractures may become apparent.

The first was a 101-year-old woman who had been wheelchair bound for several years. During a routine examination 3 years ago, her doctor noted swelling of her left leg and diagnosed a spontaneous fracture of the left tibial-fibular segment, which occurred without any identifiable precipitating event. Over the next few years, the patient developed two more lower-extremity fractures.

The second patient was a 93-year-old bed-bound woman who had a history of a hip fracture and seizures. Since admission to a nursing home, she sustained a fracture of the right femur and the left humerus, both during routine transfers from a wheelchair to bed.

In the third case, a 79-year-old man with a history of Parkinson's disease and a right total hip arthroplasty was able to get around with a walker until he fell and sustained a subarachnoid hemorrhage that left him confined to bed. Six months after his fall, he complained of pain in his right thigh while being adjusted in bed by a member of the nursing home staff, and was diagnosed with a spiral periprosthetic fracture of the right femur.

It may be premature to recommend routine preventive measures for all nursing home patients, but people with risk factors for disuse fractures deserve close watching, Dr. Galabova said. ■