# Primary Care Physicians Doing More to Manage Osteoporosis

BY KERRI WACHTER
*Senior Writer*

PHILADELPHIA — More physicians are using bone mineral density measurements and biochemical marker testing to identify and treat osteoporosis, according to data from a national survey.

More than 200,000 postmenopausal, nonosteoporotic women were enrolled in the National Osteoporosis Risk Assessment (NORA) in September 1997. In conjunction with the study, 2,836 referring primary care physicians completed a baseline survey in 1998 that tested their knowledge of osteoporosis screening and treatment. In 2006, 808 of these providers responded to a follow-up survey designed to assess changes in their practice patterns and knowledge of the condition, Dr. Paul D. Miller reported in a poster at the annual meeting of the American Society for Bone and Mineral Research.

The number of physicians who reported frequent use of bone mineral density (BMD) measurements to screen for, diagnose, or monitor osteoporosis more than doubled between 1998 and 2006—from 35% to 87%. More impressively, the number of physicians who reported sometimes or often using biochemical marker testing to screen for, diagnose, or monitor osteoporosis almost tripled—from 19% to 54%, wrote Dr. Miller, medical director of the Colorado Center for Bone Research and a professor at the University of Colorado Health Sciences Center in Denver.

In the same period, the percentage of physicians who knew that a bone mineral density T score of –2.5 or less was the threshold indicating the presence of osteoporosis almost doubled, from 34% to 67%.

However, the percentage of physicians who knew the threshold value requiring pharmacologic intervention (T score of –2.5 or less [according to the World Health Organization] or a T score of –2.0 or less with no risk factors [according to the National Osteoporosis Foundation]) remained the same at 60%.

In terms of changes in treatment, the use of hormone therapy dropped sixfold (67% vs. 11%) from 1998 to 2006. In contrast, bisphosphonate use jumped from 15% to 59%.

Dr. Miller reported that he has received funding and consulting fees from F. Hoffmann–La Roche Ltd. and GlaxoSmithKline.

In a separate analysis of data from NORA, Dr. Ethel S. Siris and her colleagues found that most of the women in the study had a repeat BMD measurement within 6 years of baseline.

As part of NORA, the women had their BMD measured at the heel, forearm, or finger at baseline. At 1, 3, and 6 years, the women were asked about repeat measurements.

Within 3 years of baseline, 29% of the women had a repeat BMD, while 58% had one within 6 years, Dr. Siris of the Toni Stabile Osteoporosis Center at Columbia University Medical Center in New York wrote in a poster.

Women were more likely to have repeat BMD measurements within 6 years of baseline if they were taking an osteoporosis medication (odds ratio 3.22), had talked with their physician about their baseline BMD results (OR 1.41), were taking corticosteroids (OR 1.25), were taking thyroid medication (OR 1.16), or weighed less than 127 pounds (OR 1.14) following multivariate adjustment.

Interestingly, women with a baseline T score of –2.5 or lower were less likely to have a repeat BMD (adjusted OR 0.86), while women with a baseline T score between –1.0 and –2.49 were slightly more likely (adjusted OR 1.12).

This study received funding from Merck & Co. Dr. Siris reported receiving consulting fees from Merck & Co., Procter & Gamble, Eli Lilly and Company, and Pfizer Inc. ■

# *Low BMD Linked to Myocardial Ischemia*

BY MITCHEL L. ZOLER
*Philadelphia Bureau*

CHICAGO — Low bone-mineral density was associated with exercise-induced myocardial ischemia in a retrospective analysis of more than 1,000 patients.

These are the first study results to show a link between bone mineral density (BMD) and exercise-induced ischemia using exercise echocardiography, Dr. Aaron M. From and his associates said in a poster presented at the annual scientific sessions of the American Heart Association.

Results from prior studies had linked low BMD and an increased risk of stroke, atherosclerosis, and cardiovascular death, said Dr. From, a physician at the Mayo Clinic in Rochester, Minn.

The latest analysis included all patients who underwent dual energy x-ray absorptiometry of the femoral neck at the Mayo Clinic between August 1998 and October 2003 who also had an exercise echocardiography examination for any indication sometime soon after undergoing the bone scan procedure.

The researchers identified 1,142 patients who fulfilled these criteria. All of the patients were referred for both studies by their physicians.

The group included a total of 643 patients with low BMD, including 126 with osteoporosis and 517 with osteopenia. The remaining 499 patients had BMDs in the normal range. The most common reason for the exercise echo examination was chest pain/dyspnea, in 57% of the patients; 6% had known coronary artery disease.

The analysis showed that patients with the lowest BMD (a T score of –4 to –3) had the shortest exercise duration, 5.8 minutes, while patients with the highest T scores (+1 to +2) had the longest exercise duration, 8.9 minutes.

In a multivariate analysis that controlled for baseline clinical and demographic differences, the risk of having exercise-induced ischemia rose by 22% for every one-point decrease in T score (representing one standard-deviation decrease in T score) a statistically significant difference, Dr. From and his associates reported in the poster. ■

# Denosumab Therapy Appears to Improve Bone Strength

BY KERRI WACHTER
*Senior Writer*

PHILADELPHIA — The investigative osteoporosis therapy denosumab appears to improve several measures of bone geometry, which are factors in bone strength, according to data presented at the annual meeting of the American Society for Bone and Mineral Research.

In a post hoc analysis of phase II trial data, researchers found that denosumab therapy was associated with increased bone cross-sectional areas, cortical thickness, and measures of bending strength and stability against high compressive stresses. "These positive changes in structural geometry support the likelihood that treatment improves the mechanical strength of the proximal femur," said Dr. Thomas J. Beck, professor of radiology at Johns Hopkins University, Baltimore.

Denosumab is a fully human monoclonal antibody that binds to the receptor activator of nuclear factor kappa B ligand, the primary mediator of osteoclast differentiation, activation, and survival. Denosumab binds to this protein, inhibiting osteoclast differentiation, activation, and survival.

In the phase II study, denosumab therapy was shown to increase bone mineral density (N. Engl. J. Med. 2006;354:821-31) and presumably bone mechanical strength as well.

Bone strength can be altered by changes in bone geometry—the amount and distribution of bone—or by changes in the composition of bone tissue.

**Indicators of increased bone strength in patients treated with denosumab included greater cortical thickness and lower change in buckling ratio.**

The trial data included 39 patients on 60 mg of denosumab every 6 months, 39 subjects on placebo, and 38 patients on open-label alendronate (70 mg once weekly).

The study was funded in part by Amgen Inc. Dr. Beck disclosed that he has significant financial relationships with Merck & Co. Inc., Amgen Inc., and Hologic Inc.

The researchers used hip structural analysis to calculate bone cross-sectional area, section modulus (an indicator of bending strength), estimated cortical thickness, and buckling ratio (an estimate of cortical stability in buckling or against high compressive stresses) from dual-energy x-ray absorptiometry hip scans at baseline and at 12 and 24 months.

Hip structural analysis is an investigational technique used to assess bone geometry in cross-sections of three regions of the proximal femur: across the femoral neck at its narrowest point, in the intertrochanteric region (along the bisector of the neck-shaft angle), and across the shaft (2 cm distal to the midpoint of the lesser trochanter).

For the femoral neck at 24 months, the percent change in bone mineral density (BMD) from baseline was significantly greater for denosumab than for placebo. The percent change in cross-sectional area was similar for denosumab and alendronate, according to Dr. Beck.

The percent changes in section modulus and estimated cortical thickness were significantly greater for denosumab than for placebo, and the percent change in buckling ratio was significantly lower for denosumab than for placebo (a positive result, indicating increased strength).

Dr. Beck added that for the intertrochanteric region at 24 months, the percent change in BMD from baseline was significantly greater among patients receiving denosumab therapy than for those given placebo. The percent change in cross-sectional area was significantly greater for denosumab than for alendronate, he reported.

The percent change in section modulus was significantly greater for denosumab than for placebo. The percent change in estimated cortical thickness was significantly greater for denosumab than for placebo, and the percent change in buckling ratio was significantly lower for denosumab than for placebo.

For the shaft at 24 months, the percent change in BMD from baseline was significantly greater for denosumab than for placebo. The percent change in cross-sectional area was significantly greater for denosumab than for alendronate, according to Dr. Beck.

The percent changes in section modulus and estimated cortical thickness were significantly greater for denosumab than for alendronate, and the percent change in buckling ratio was significantly lower for denosumab than for alendronate. ■