Software Simplifies Fracture Risk Prediction

BY MICHAEL VLESSIDES

KANANASKIS, ALTA. — An investigational computer program considers more than just bone mineral density in determining fracture risk, summarizing its findings in a color-coded representation of the patient.

Developed by rheumatologist William Bensen, the Bone DESTINY software program predicts fractures more reliably than do bone mineral density (BMD) assessments alone. Using the Bone DESTINY program achieves prediction accuracy comparable with that attained by following the guidelines developed by Osteoporosis Canada (Can. Assoc. Radiol. J. 2005;56:178-88).

Bone DESTINY software is free to physicians but has not been released for general use yet. Its development has been funded by Dr. Bensen and McMaster University, Hamilton, Ont.

Bone DESTINY begins with bone density, then factors in age, steroid use, propensity to fall, history of previous falls, body mass index, and previous fragility fractures, said Dr. Maggie Larché, a rheumatologist at McMaster.

"These data are plugged into a handheld computer, which then generates a graphic with a color-coded representation of the patient's risk." The program produces an accompanying text report.

In the first of two studies presented at the annual meeting of the Canadian Rheumatology Association, Dr. Larché and her colleagues at McMaster studied the predictive value of the software program in 14,812 postmenopausal women at least 60 years old. For each patient, treatment recommendations were produced based on BMD alone, Osteoporosis Canada guidelines, or Bone DESTINY results.

Among 7,049 patients aged 60-69 years, BMD analysis alone recommended treatment in 19%. By comparison, 20% were recommended for treatment according to OC guidelines, and 28% according to the software. In 5,252 patients aged 70-79 years, 29% were recommended for treatment based on BMD alone, 43% according to Bone DESTINY, and 51% according to OC guidelines. In 2,511 patients at least 80 years old, 47%, 72%, and 77% would be recommended for treatment according to BMD, OC guidelines, and Bone DESTINY results, respectively.

A second study compared predictive values of the three methods in 572 men and 3,914 women (aged 50 years and older) who had suffered at least one previous fragility fracture.

For all age groups, both Bone DESTINY and OC guidelines recommended treatment in 80% of the women to prevent another fracture; 35% of the women would have received treatment based on BMD alone, Dr. Larché reported.

The most significant difference, however, was observed in men, in whom Bone DESTINY recommended treatment in 73%, compared with 26% by BMD alone and 41% by OC guidelines.

Dr. Larché reported receiving honoraria and/or speakers fees from Amgen, Abbott, BMS, Pfizer, Schering, and GSK. ■

Use of Some Glitazones Linked To Increased Bone Fragility

BY MITCHEL L. ZOLER

NEW YORK — Treatment with a thiazolidinedione, either pioglitazone or rosiglitazone, was linked to an increased rate of bone fractures, particularly in women, in several recent reports.

The evidence to date is suggestive enough to prompt caution in the treatment of patients with a thiazolidinedione (TZD), Dr. Robert G. Josse said at a meeting sponsored by the American Diabetes Association.

The idea that treatment with pioglitazone (Actos) or rosiglitazone (Avandia) may cause osteoporosis and produce an increased rate of bone fractures is biologically plausible, and has been suggested in the results from adverse-event reports from large, randomized, controlled trials; from a pair of small, randomized, controlled studies that specifically used bone density as an end point; and in two observational studies, said Dr. Josse, medical director of the department of medicine at the osteoporosis center at St. Michael's Hospital in Toronto.

A meta-analysis published in January compiled adverse-event data from 10 randomized, controlled studies with a total of more than 13,000 patients, and also reviewed two observational studies with a total of more than 31,000 patients (CMAJ 2009;180:32-9). In the 10 randomized trials, patients treated with a TZD had a statistically significant 45% increased risk for bone fracture, compared with patients in the control groups. When the analysis broke the study population down by sex, a statistically significant 2.2-fold increased fracture risk was seen in women treated with a TZD, but absolutely no increased risk was seen in men. Additional analysis by sex showed that, in women, TZD treatment was linked with significant reductions of bone mineral density in the lumbar spine and hip. The two observational studies also showed a significant link between TZD use and fracture risk in women, but not in men.

The two short-term, randomized studies included a study with 50 healthy postmenopausal women without osteoporosis or diabetes who were randomized to treatment with 8 mg rosiglitazone daily or placebo for 14 weeks. Despite the brief period of treatment, the women in the rosiglitazone-treated group had a statistically significant reduction in their total hip bone mineral density, compared with the placebo group (J. Clin. Endrocrinol. Metab. 2007;92:1305-10). A second study, published last May, randomized 30 postmenopausal women with polycystic ovary syndrome but without diabetes to treatment with either 30 mg pioglitazone daily or placebo. After 16 weeks, the women treated with pioglitazone had significantly lower lumbar spine and femoral neck density, compared with the controls (J. Clin. Endrocrinol. Metab. 2008;93:1696-701). The TZD-treated women also showed significantly decreased blood levels of bone-turnover hormones and enzymes.

Dr. Josse reported receiving research support from, and serving on the speakers bureau and advisory panel for Amgen Inc., Eli Lilly & Co., Procter & Gamble Co., and Sanofi-Aventis. ■

Improved MRI, CT Compete to Assess Bone Quality

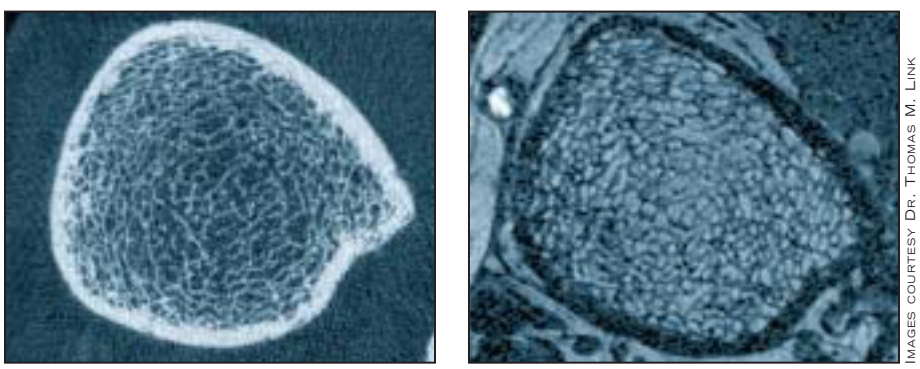
BY SHERRY BOSCHERT

SAN FRANCISCO — High-resolution MRI, multidetector CT, and high-resolution peripheral quantitative CT each may be useful in assessing bone quality, according to recent data.

The three imaging modalities can produce significantly different absolute numbers compared with each other when assessing trabecular or cortical bone structure, yet all correlate reasonably well with micro-CT as a standard of reference, Dr. Thomas M. Link said at a conference sponsored by the International Society for Magnetic Resonance in Medicine.

Trabecular and cortical bone structure are key components of bone quality, an important component of bone strength according to the National Institutes of Health (JAMA 2001;285:785-95).

In one randomized, double-blind study, for example, 51 postmenopausal women with osteopenia were treated with alendronate or placebo and followed over a 2-year period by 3T MRI of the radius, tibia, and femur; high-resolution peripheral quantitative CT (hr-pQCT) of the radius and tibia; and dual x-ray absorptiometry measures of bone mineral density. Both high-resolution MRI (hrMRI), and hr-pQCT results for trabecular bone showed moderate but significant correlation with bone density as a reference, even though there was a twofold to fourfold difference between hrMRI and hr-pQCT in parameter values such as trabecular number, thickness, or separation (J. Bone Miner. Res. 2008;23:463-74).



IMAGES COURTESY DR. THOMAS M. LINK

The trabecular and cortical bone architecture in the distal tibia is shown in high-resolution peripheral quantitative CT (left) and high-resolution 3T MRI (right).

For corticol bone imaging, a newer area of research, two 2008 studies using hr-pQCT showed substantial differences between postmenopausal women with hip or wrist fractures, compared with fracture-free women, said Dr. Link, professor of radiology at the University of California, San Francisco.

Experimentally, hrMRI and hr-pQCT are being used to assess cortical bone porosity, which affects bone stability. One recent study using hr-pQCT found significant differences among normal premenopausal women, normal postmenopausal women, and postmenopausal women with renal osteodystrophy. MRI or hr-pQCT provide high spatial resolution and produce no (or relatively little) radiation, compared with high-radiation exposure from multidetector CT. Multidetector CT allows imaging of more central skeletal sites, he said.

The hr-pQCT scanners image only peripheral sites, whereas hrMRI covers larger areas of the radius, tibia, and possibly the femur.

The CT techniques provide measures of bone densitometry. Although hrMRI gives no densitometric data, some studies suggest it may be used to analyze bone marrow composition through spectroscopy in order to assess bone stability. The three techniques appear to have similar rates of reproducibility.

MRI and hr-pQCT are expensive and prone to motion artifacts. Multidetector CT is available and requires less time for a scan. But postimage processing is challenging for MRI and CT.

Dr. Link reported receiving research funding and support from Merck & Co., which markets medication to treat osteoporosis. ■