Note Forearm Bone Density in Prostate Ca Patients

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Checking bone mineral density in the forearm as well as the spine and hip in 181 men taking androgen deprivation therapy identified more patients with bone loss than did using densitometry on the spine and hip alone, according to data from a recent study.

Dual-energy x-ray absorptiometry (DXA) scans of the hip and spine have been the accepted standard for osteoporosis screening in men taking androgen deprivation therapy for prostate cancer. The therapy is well known to cause bone loss, Dr. Paul R. Sieber and his associates said.

Interpreting lumbar spine DXA results in these patients can be problematic, so the researchers started adding routine DXA scans of the distal third of the radius to the hip and spine scans of patients using androgen deprivation therapy. They compared results using just the hip and spine scans with results using those plus the forearm scan. The patients had a mean age of 77 years; duration of therapy was up to 10 years.

With the central DXA scans alone, 30 patients (17%) were classified as normal (T score of –1.0 or better), 101 (56%) were osteopenic (T score of –1.0 to –2.5), and 50 (28%) were considered to have osteoporosis (T score less than –2.5). The percentages were rounded.

Adding in the results of the peripheral scan moved seven patients (23% of the normal group) out of the normal range and increased the numbers of osteopenic and osteoporotic patients, the researchers said in a poster presentation at the annual meeting of the International Society for Clinical Densitometry.

With the central plus peripheral DXA scan results, 23 patients (13%) had normal bone density, 93 (52%) were classified as osteopenic, and 65 (36%) had osteoporosis, said Dr. Sieber, of Urological Associates of Lancaster, Penn.

Nine DXA scans of the hip and 42 scans of the spine were uninterpretable, underscoring the need for forearm bone density measurements when screening these patients.

He did not disclose any potential relationships with DXA scan providers or manufacturers, or with companies that make osteoporosis treatments. ■

Watch for Risks to Bone Health in Continuous Androgen Deprivation

BY NEIL OSTERWEIL
Contributing Writer

CHICAGO — Six or more months of continuous androgen deprivation therapy was associated with significantly increased risk of fragility fractures and type 2 diabetes in an observational study of nearly 20,000 men aged 66 years and older with prostate cancer, reported investigators at the annual meeting of the American Society of Clinical Oncology.

Continuous androgen deprivation was not associated with elevated risk for either acute myocardial infarction or hypercholesterolemia, however. There was actually a slight decrease in risk for dyslipidemia, and nonsignificant trends toward lower rates of AMI and sudden cardiac death, said Dr. Shabbir M.H. Alibhai.

Concern about adverse effects of androgen deprivation therapy on bone is based on four retrospective studies and a case-control study showing an increase risk for both fragility fractures and nonfragility fractures with its use, according to Dr. Alibhai, a research scientist in the department of medicine at Princess Margaret Hospital and the University of Toronto.

A large prospective study by Dr. Nancy L. Keating and her coauthors at Brigham and Women's Hospital in Boston showed use of a gonadotropin-releasing hormone agonist was associated with a 44% increased risk of incident diabetes, 16% increase each in risk of coronary heart disease and sudden cardiac death, and an 11% rise in risk of MI (J. Clin. Oncol. 2006 20;24:4448-56).

"These findings are worrisome, but at the same time, there are some limitations that must be kept in mind," said Dr. Alibhai. "The findings are not entirely consistent among studies. Some studies suggested, for example, increased rate of fatal myocardial infarction, but no overall increased rate of myocardial infarction. And another study suggested that while androgen deprivation increased the risk of MI, diabetes, and hypertension, paradoxically, it did not seem to in that cohort."

Dr. Alibhai and his colleagues looked at data on 19,709 men in Ontario (Canada), who had continuous androgen deprivation therapy for at least 6 months or had undergone bilateral orchiectomy, and an identical number of controls. The treated patients were matched by age and prior prostate cancer therapy to other men who did not receive androgen deprivation.

The primary end points were fragility fractures, incident diabetes, incident dyslipidemia, acute MI, and sudden cardiac death. Secondary outcomes were any fracture, heart failure, stroke, use of diagnostic cardiac catheterization, and cardiac revascularization with either angioplasty or coronary artery bypass graft surgery.

The investigators found in a time-to-event analysis that after a mean of 6.47 years, use of androgen deprivation was associated with a hazard ratio for fragility fractures of 1.65 (*P* less than .001), and a 1.26 hazard ratio for incident diabetes (*P* less than .001).

In contrast, there was a 14% lower risk for incident dyslipidemia (HR 0.86, *P* less than .001), and nonsignificant trends toward lower MI risk (HR 0.92, $P = .059$) and time to sudden cardiac death (HR 0.96, $P = .53$).

In analysis of secondary outcomes, androgen deprivation was significantly associated with higher risk of any fracture (HR 1.46) and lower risk for stroke (HR 0.88), cardiac catheterization (HR 0.88), and cardiac revascularization (HR 0.87).

Dr. Alibhai acknowledged that the study was limited by its restriction to men 66 years and older, possible undercoding of some comorbidities or minor fractures, lack of information on tumor stage or grade, the fact that the outcomes of dyslipidemia were not validated, and that propensity analysis lessens but does not eliminate the potential for confounding.

"In men who are age 66 [years] or older, on continuous androgen deprivation for at least 6 months," Dr. Alibhai said in his conclusion, "this therapy was associated with an increased risk of fragility fracture—of course as well as any fracture—a decreased risk of dyslipidemia … and no appreciable impact on myocardial infarction. And, if anything, there was a slight decrease in acute myocardial infarction in this cohort, which goes against the previously published studies to date."

The study was supported by the Toronto General and Toronto Western Hospital Foundation and the National Cancer Institute of Canada. Dr. Alibhai reported no financial conflict of interest. ■

Atorvastatin Tied to Fewer Cardiac Events in Diabetics

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — All statins may not be created equal as far as diabetes patients are concerned, according to a recent study.

In patients with diabetes initiating statin therapy for the first time, those who took atorvastatin experienced 12% fewer cardiovascular events than those who took simvastatin, said Joshua Benner, Pharm.D., Sc.D., of IMS Health Care, Falls Church, Va. He spoke at the annual scientific sessions of the American Diabetes Association in place of the study's first author, Dr. Joanne M. Foody of Harvard Medical School, Boston.

The observational, comparative-effectiveness study used a large managed-care database including patient information from 92 health care plans in the United States, In all, the investigators identified 12,304 patients with diabetes initiating statin therapy with simvastatin and 33,772 initiating statin therapy with atorvastatin.

The researchers included only adult patients who were continuously enrolled in their health plan for 1 year prior to their first statin prescription and for at least 30 days after. Patients had to be taking either 10 mg or 20 mg of atorvastatin or 20 mg or 40 mg of simvastatin. The simvastatin group was followed for a mean of 591 days, and the atorvastatin group was followed for a mean of 556 days.

Among patients taking atorvastatin, the unadjusted rate of cardiovascular events requiring hospitalization was 3.35 per 100 person-years, significantly lower than the rate for simvastatin, which was 4.45 per 100 person-years.

After adjustment for age, gender, type of health plan, payer type, geographic region, calendar year of statin initiation, physician specialty, comorbidities, concomitant therapies, and prior health care cost, the hazard ratio for atorvastatin was 0.88 relative to simvastatin, indicating a 12% reduction in cardiovascular risk.

Atorvastatin and simvastatin were the two most commonly prescribed statins in the United States during the study period, which ran from January 2003 to September 2005, said Dr. Benner. "The comparison between these two statins is especially important given the recent trends in their utilization, where simvastatin recently became generic and is now preferred by many payers in the United States."

Patients taking atorvastatin persisted with that prescription for a mean of 219 days, significantly longer than the 153 days for the patients taking simvastatin. Although the investigators did not compile data on adverse events, Dr. Benner said that this difference in persistence times suggests that there were fewer dose-limiting or a treatment-limiting side effects among those taking atorvastatin.

Future studies are needed to determine whether differences in "persistence, achieved LDL levels, or other factors may have contributed to the improved outcomes in diabetes patients taking atorvastatin," he said.

The researchers have not yet concluded that atorvastatin's greater efficacy justifies its higher cost. "That's where a number of analyses are headed, because this raises the important policy question of what is the clinical and economic value of a marginal increase in effectiveness."

Dr. Benner said the IMS Health Group conducts research and consulting projects supported by manufacturers of numerous lipid-lowering drugs. ■