Imaging Shows Gender Differences in Bone Aging

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NASHVILLE, TENN. — Three-dimensional, high-resolution peripheral quantitative computed tomography has revealed significant differences in the way that trabecular bone microstructure changes with age in men and women.

The technique allows for in vivo assessment of bone density and trabecular microstructure, Sundeep Khosla, M.D., said at the annual meeting of the American Society for Bone and Mineral Research.

He and his associates at the Mayo Clinic, Rochester, Minn., imaged 278 men and 324 women, aged 21-97 years. The nondominant wrist was scanned to obtain 116 views at the distal end of the radius.

The slice thickness was 89 μm.

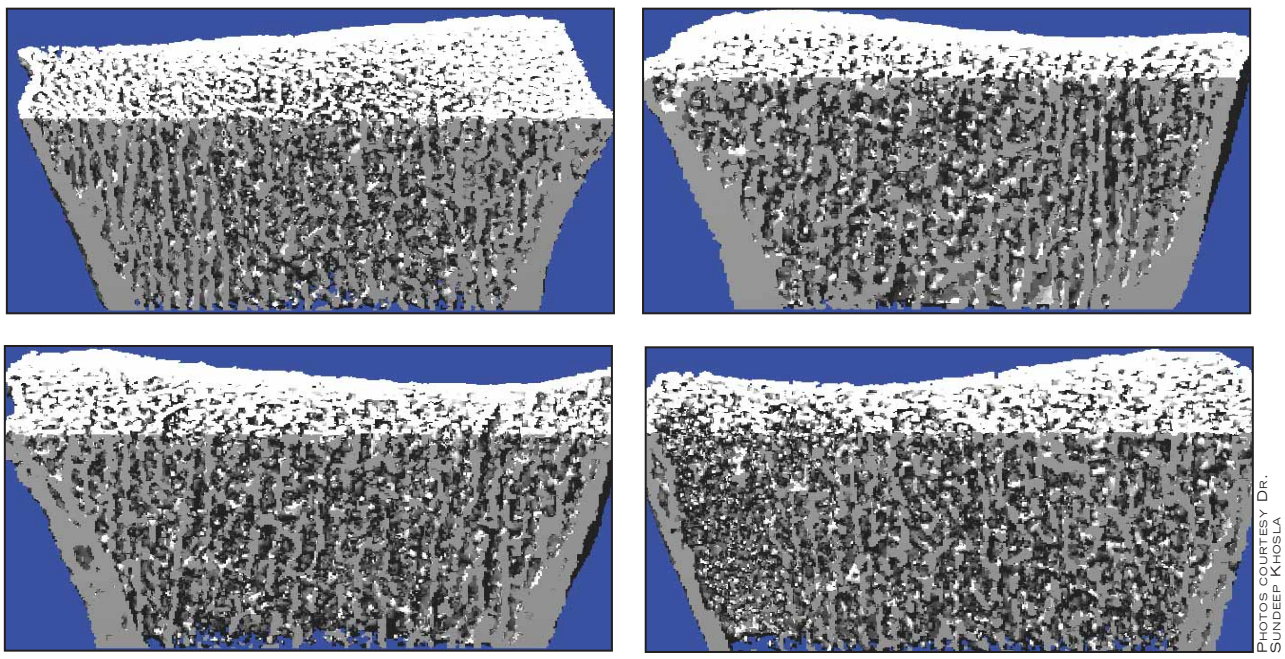
Differences in the structure of trabecular bone in men and women are evident in young adulthood. Compared with young women, young men have indices of trabecular structure that predict stronger bones and greater resistance to fractures—higher bone volume/tissue volume (BV/TV) and thicker trabeculae, he said.

Over their lifetimes, men and women have similar reductions in BV/TV, but "the structural basis for this parallel decrease in BV/TV seems to be quite different in women and men," Dr. Khosla said.

In women aged 20-49 years, trabecular number remains stable, then declines at about the same rate as seen in men aged 50 years and older. Men show no long-term net change in trabecular numbers, because decreases from age 50 on are offset by increases from ages 20 to 49.

Trabecular separation increases by 24% over men's lifetimes, but most of this change occurs after age 50. "Trabeculae actually tend to get closer together in men between the ages of 20 and 50, and then separation increases." The net effect is that there isn't much change, he said.

Trabecular thickness goes down more than twice as much in men than in women over their lifetimes. "Trabecular thickness goes down fairly linearly over life in women. But in men there is a much more dramatic decrease in trabecular thickness from about age 20 to age 50, and then it looks like it doesn't decrease further," he said. "In women, aging is associated with loss of trabeculae, whereas in men the primary mechanism of the decrease in BV/TV appears to be trabecular thinning."



PHOTOS COURTESY DR. SUNDEEP KHOSLA

Differences in trabecular structure are shown here in two 24-year-olds, male (top left) and female (top right), a 73-year-old man (botton left) and a 71-year-old female.

"Losing trabeculae is much more detrimental to bone strength than is thinning trabeculae," Dr. Khosla noted. A 10% drop in BV/TV due to a reduction in trabecular number results in a twofold to fivefold greater loss of bone strength than the same drop in BV/TV caused by a reduction in trabecular thickness.

In a separate study, investigators used MRI-based virtual bone biopsy (VBB) to track trabecular microarchitecture changes in two groups of postmenopausal women aged 45-55 years—one receiving hormone therapy and the other not receiving the therapy.

A 20-patient treatment group received hormone therapy (0.05 mg/day estradiol transdermal patch); a 27-patient control group did not. All women received supplemental calcium (1,500 mg/day), said Glenn A. Ladinsky, M.D., of the University of Pennsylvania, Philadelphia.

In the control group, VBBs collected at the distal radius and the distal tibia showed conversion from trabecular plate to rod structure, indicating a reduction in bone strength during the 24-month study. Platelike trabecular architecture was preserved in patients who received hormone therapy. There was a 3%-4% reduction in bone mineral density in the control group, as measured by DXA. No changes in BMD were noted in the therapy group.

Dr. Ladinsky is a part owner of MicroMRI Inc., which developed the MRI-based VBB technology. The study was funded in part by Novartis Inc. ■

Sex Hormone Suppression Boosts Effect of PTH in Men

NASHVILLE, TENN. — Suppression of androgens or estrogens increases bone turnover and bone loss in men, according to data presented at the annual meeting of the American Society for Bone and Mineral Research.

A total of 58 men, aged 20-45 years, were assigned to receive combinations of gonadotropin-releasing hormone (GnRH), an aromatase inhibitor, and hormone add-back therapy for 6 weeks, depending on their hormonal status, said Benjamin Z. Leder, M.D., of Massachusetts General Hospital in Boston.

Men in group 1 (16) received a GnRH analog, 3.6-mg goserelin acetate, given subcutaneously every 3 weeks, as well as an aromatase inhibitor, 5-mg anastrozole, given daily. Men in group 2 (12) also received the GnRH analog and aromatase inhibitor, but testosterone was replaced with a testosterone gel (AndroGel), at 5 g daily. Men in group 3 (14) received the GnRH analog and aromatase inhibitor, but estradiol was replaced with an estradiol transdermal patch, applied twice weekly. Men in group 4 (16) received the GnRH analog, aromatase inhibitor, testosterone gel, and estradiol patch. These men were sufficient in both testosterone and estradiol and served as a control group.

All the men underwent 18-hour infusions of parathyroid hormone (PTH) (1-34) at a dose of 0.55 U/kg per hour at baseline and at 6 weeks. Serum levels of the bone turnover markers cross-linked N-telopeptides (NTx) of type I collagen and osteocalcin were measured every 6 hours during the PTH infusions.

Resorption of bone by osteoclasts results in the production of NTx of type I collagen. NTx is specific to bone and is found in serum and urine as a stable end product of bone degradation.

Mean NTx levels measured prior to PTH infusion did not change between baseline and week 6 in the control group, but NTx levels increased by 24% in group 1, by 16% in group 2, and by 11% in group 3. Serum NTx levels increased during PTH infusion in all groups at all time points.

Serum osteocalcin levels decreased in all groups at all time points during PTH infusion. No differences in serum osteocalcin levels were observed between baseline and week 6 in any of the four groups. ■

Bone Mineralization Reduced in Women With Idiopathic Osteoporosis

Women with idiopathic osteoporosis appear to have a low mineralization in trabecular bone, which suggests that alterations in the mineralization processes could be responsible for bone fragility, Jochen G. Hofstätter, M.D., reported at the annual meeting of the American Society for Bone and Mineral Research.

Dr. Hofstätter and his associates assessed bone mineral density distribution using quantitative backscattered electron imaging, and bone biopsies were collected from nine premenopausal women with idiopathic osteoporosis. Bone mineral density distribution was also evaluated for 15 healthy, age-matched women.

Quantitative backscattered electron imaging is a relatively new technique for studying mineralization patterns, said Dr. Hofstätter of the Ludwig Boltzmann Institute of Osteology in Vienna. The sample is scanned using an electron microscope. The quantity of electrons backscattered from a given surface is proportional to the mean atomic number of the measured material, allowing researchers to identify and quantify minerals present in bone.

To determine the bone mineral density distribution, the researchers measured the mean calcium content, the typical calcium content, the variation of calcium content, and the percentage of low-mineralized matrix.

There were significantly lower levels of mean calcium content (–3.1%) and typical calcium content (–2.7%) among the women with idiopathic osteoporosis, compared with those in the control group.

This is "an interesting finding with respect to the [low] bone turnover situation reported in these patients. One would expect exactly the opposite," Dr. Hofstätter noted. Low bone turnover typically permits prolonged secondary mineralization in a larger number of bone pockets, resulting in higher mineral content.

There were no significant differences between the two groups in terms of the variation of calcium content and the percentage of low mineralized matrix.

The lower degree of mineralization in women with idiopathic osteoporosis, combined with low bone turnover, suggests that there are differences in their mineralization processes, Dr. Hofstätter said. These changes may be the result of alterations in the extracellular matrix and may in turn contribute to increased fragility. ■