Ancient Bones Shed Light on Modern Fractures

BY ALISON PALKHIVALA
Contributing Writer

MONTREAL — The decreased reliance on brute force and manual labor for human survival during the past few thousand years has taken a toll on bone density, anthropologist Christopher B. Ruff, Ph.D., said at the 17th Scientific Meeting of the International Bone and Mineral Society.

This conclusion comes from a review of archaeological samples of human long bones, reported Dr. Ruff of the center for functional anatomy and evolution, Johns Hopkins University, Baltimore. The modern human genus essentially originated about 2 million years ago. Using cross sections of long bones as a measurement of bone strength reveals that, between 2 million and 8,000 years ago, bone strength relative to body size in humans steadily diminished. Extrapolating the trend to modern times reveals modern humans have bone strength about 30% below what would be expected if the trend had continued. "There are many different possible explanations for this, but my preferred explanation is an environmental one relating to mechanical loading and muscle activity effects," said Dr. Ruff. Over time but especially in the past few thousand years, modern advances have meant brute force and manual labor are less important for survival. This trend demonstrates how important mechanical loading is for bone strength. The price, of course, is today's increased incidence of osteoporotic fractures.

The observed 30% decrease in bone strength seems to be due to advances that made it less necessary for humans to rely on brute force to survive.

Archaeological samples also shed light on normal growth and developmental patterns in bone. "Patterns of growth and development are very ancient," said Dr. Ruff. Computed tomography of the bones of 31 children of various ages who died more than a million years ago reveals a pattern of periosteal expansion, followed, around adolescence, by endosteal expansion and then contraction. Studies of modern tennis players who began practicing the sport at different ages reveal that the same pattern of bone growth persists today.

In addition to revealing these patterns of bone growth, archaeological samples also allow for identifying differences between males and females. For instance, marked endosteal contraction occurs in late adolescence in the female femur but is less apparent in the upper limbs; endosteal contraction occurs equally in upper and lower limbs in men. Both systemic factors, such as hormones, and mechanical factors, such as differences in body size, account for these differences, said Dr. Ruff.

Comparing humans to other species reveals an important difference: Although primates, who use all four limbs for locomotion, have similar bone strength in their upper and lower limbs, bipedal humans have stronger lower limbs than upper limbs. This difference starts to develop after about 1 year of age, because humans are generally quadrupedal in their first year of life. Recognizing this helps archaeologists identify when humans first relied primarily on their lower limbs for locomotion. It also reveals that differences between child and adult skeletons and the growth patterns that lead from one to the other have been maintained for at least 2 million years.

During the past 2 million years, patterns of bone growth and development have remained remarkably stable in humans, allowing for the use of archaeological samples to better understand the bones of modern man. "Archaeological samples tend to be more homogeneous genetically and environmentally, so you get a cleaner signal," said Dr. Ruff. "They are [from] very similar populations with similar diets, similar activity levels. Skeletal material is available for all ages, as opposed to autopsy samples, where it's very difficult to find younger individuals, and [archaeological samples] can serve as a useful baseline for comparison with really modern samples."

There are disadvantages to using archaeological samples, however. These include the need to rely on cross-sectional study designs, the potential bias inherent in only being able to study the skeletons that have survived this long, and the inability to reliably determine the sex of the skeletons of humans who died before adolescence or in old age. ■

Six-Item Clinical Index Predicts Fractures in High-Risk Women

BY DIANA MAHONEY
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A new assessment index based on six easily accessible variables effectively predicts the risk of nonvertebral fractures in postmenopausal osteoporotic women, a study has shown.

Because of its efficacy and clinical convenience, the new tool can be used to help in the identification and management of high-risk patients, reported lead investigator Dr. Christian Roux of Université de Paris Descartes, and colleagues.

The effect of a given osteoporosis treatment on nonvertebral fracture risk is a potential determinant of treatment choice. As such, the assessment of nonvertebral fracture risk in postmenopausal women with osteoporosis has important management implications, the authors wrote. Because risk assessment in this population can be difficult, in that multiple variables such as type and mechanism of fracture can impact an individual's risk profile, the investigators sought to identify significant predictive factors from which to develop a clinical useful fracture-risk-assessment tool.

Toward this end, they analyzed 3 years of follow-up data from 2,546 postmenopausal osteoporotic women who had been in the placebo groups of three multicenter, randomized controlled trials of the biphosphonate risendronate.

At baseline, the mean age of the study participants was 72 years, the mean femoral T score was –2.5, and 60% and 53% had prevalent vertebral and nonvertebral fractures, respectively.

All of the participants received 1,000 mg of calcium daily and up to 500 IU of vitamin D daily if baseline serum hydroxyvitamin D was less than 16 ng/mL (Ann. Rheum. Dis. 2007;66:931-35).

During the 3-year follow up, 222 nonvertebral fractures were observed in 206 patients. Of 14 variables included in logistic regression analysis of the fracture group, 6 emerged as independent predictors of nonvertebral fracture risk: age, height, prior nonvertebral fracture, number of prevalent vertebral fractures, femoral neck T score, and serum 25-hydroxyvitamin D, the authors reported.

With respect to vitamin D, "In the 48 patients who had a baseline serum hydroxyvitamin D less than 16 ng/mL, the incidence of nonvertebral fractures was 14.58%," compared with 8.25% among the patients whose baseline measure was 16 ng/mL or higher, the authors wrote.

"Although patients received supplements of calcium and vitamin D, the low baseline level of 25-hydroxyvitamin D was still a significant risk factor for fracture, which may be related to a long-term effect of sarcopenia due to vitamin D deficiency," they stated.

Based on the odds ratios for fracture associated with each of these variables, the investigators calculated fracture-risk index values for intervals within each variable, adjusting the minimal possible index contribution for each variable to zero (see index value chart).

For example, the risk index value for patients younger than 65 years is 0, while the index value for patients 80 years or older is 0.8.

The area under the receiver operating characteristic (ROC) curve for the final model based on the six predictors was 0.66. To minimize the absolute difference between sensitivity and specificity in the ROC curve, the investigators selected a cut-off value of 0.086 (or 8.6% nonvertebral fracture risk at baseline) for the predicted probability of nonvertebral fracture.

According to the model, patients with an index value of 2.1 or higher belong to a subgroup at high risk for nonvertebral fracture, the authors wrote.

In the 998 women from the original study population with an index value of at least 2.1, "the incidence of nonvertebral fractures was 13.2%, 1.5 times higher than the average of the population," they noted.

One of the study's primary limitations is the lack of information on falls, which was not available.

This "ignored parameter" can be of crucial importance in explaining the fractures and may be useful in explaining the low value of the ROC curve, according to the researchers.

Still, the study findings suggest that "among osteoporotic women, a proportion of patients with a high risk of nonvertebral fractures can be selected and an index is a convenient tool for this selection in clinical practice," the authors concluded. ■

Nonvertebral Fracture Risk Index

	Index Value		Index Value
Age (yr)		**Height (cm)**	
<65	0	<147	0
65 to <70	0.2	147 to <153	0.2
70 to <75	0.4	153 to <161	0.4
75 to <80	0.6	161 to <167	0.5
≥80	0.8	≥167	0.7
Femoral T Score		**Vitamin D (ng/mL)**	
<–3.8	0.8	≥90	0
–3.8 to <–3.0	0.6	70 to <90	0.2
–3.0 to <–2.2	0.4	50 to <70	0.4
–2.2 to <–1.4	0.2	30 to <50	0.6
≥–1.4	0	<30	0.8
# of Prevalent Vertebral Fractures		**Prevalent Nonvertebral Fractures**	
0	0	Yes	0.4
1	0.1		
2 to 6	0.4		
≥7	1.1		

Notes: Patients with an index value ≥2.1 belong to a subgroup at high risk for nonvertebral fracture. Based on data from 222 nonvertebral fractures in 206 patients.
Source: Dr. Roux

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