Premenopausal Women with Distal Radius Fractures Have Deteriorated Trabecular Bone Density and Morphology Compared to Non-Fracture Controls

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Introduction:

Osteoporosis and fragility fractures are major public health issues with significant social and economic costs. Measurement of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is currently the gold standard for the diagnosis of osteoporosis, and low bone density is widely accepted as a major risk factor for fragility fracture. Yet, up to 50% of those who suffer a fracture do not have osteoporosis by BMD testing.1,2,3 Thus, recent efforts have focused on more sophisticated imaging technology to more accurately assess the determinants of bone strength and fracture risk.

Although the majority of bone loss occurs after menopause, recent population-based studies have found that women experienced a significant decline in trabecular bone mass and architecture before menopause.4-6 Thus, an alternative approach to treating women already at high risk for fractures would identify premenopausal women with signs of skeletal fragility and initiate lifestyle and/or pharmacologic interventions to prevent further deterioration and reduce future fracture burden. We hypothesize that pre-menopausal women with fractures of the distal radius will have similar BMD but altered micro-architecture when compared to controls with no history of fracture. To address this hypothesis we compared trabecular and cortical bone microarchitecture assessed by high resolution peripheral quantitative computed tomography (HR-pQCT) at the distal radius and distal tibia in premenopausal women with fractures of the distal radius to non-fracture controls. In addition, we compared BMD by DXA in pre-menopausal women with fractures of the distal radius to non-fracture controls.

Methods:

Subjects: We enrolled premenopausal women under the age of 45. Women were eligible for inclusion as fracture cases if they had a fracture of the distal radius within the prior 3 months. Control subjects had no history of fractures in adulthood. Subjects were excluded if they were pregnant, had endocrinopathies, history of eating disorder or metabolic bone disease. Exposure to glucocorticoids, immunosuppressive medications, or osteoporosis medications also constituted exclusion criteria.

Fracture treatment and classification: Non-displaced fractures were treated with casting until union. Displaced fractures were offered surgical treatment at the discretion of the treating surgeon. Thirty-five fractures were reviewed and the fractures were classified according to the AO fracture classification by a fellowship trained orthopaedic hand surgeon.

HR-pQCT of the distal radius and tibia: Trabecular and cortical bone density and microarchitecture at the distal radius and tibia were assessed using high resolution peripheral quantitative computed tomography (HR-pQCT, XtremeCT, Scanco Medical AG, Basserdorf, Switzerland). Scans were acquired at 82 μm isotropic voxel size; 110 CT slices were acquired, thus delivering a 3D representation of approximately 9 mm in the axial direction. The first CT slice was acquired 9.5 mm and 22.5 mm proximal to the reference line for the distal radius and tibia. Using semi-automated software, trabecular (Dtrab, mg/cm³) and cortical bone density (Dcort, mg/cm³), and morphology, including cortical thickness (Ct, Th, mm), trabecular thickness (Tb, Th, mm), number (Tb, N, mm⁻¹), and separation (Tb, Sp, mm) were assessed. Other outcomes variables in our analysis included trabecular bone volume fraction (BV/TV, %) and distribution of trabecular separation (Tb, Sp, SD, mm). BMD by DXA: Areal BMD (g/cm²) of the hip, spine and forearm was measured by dual-energy X-ray absorptiometry (QDR4500, Hologic, Inc., Waltham, MA) in the array (fan beam mode).

Statistical Analysis: BMD and trabecular and cortical bone micro-architecture were compared between pre-menopausal women with and without distal radius fractures using two-tailed student’s t-test, with P < 0.05 considered statistically significant.

Results:

28 fracture patients (FX) and 82 controls (CONT) were enrolled. Subjects did not differ with regard to age, race or body mass index (BMI). The average time between fracture and scan acquisition was 55 ± 42.4 days. FX and CONT subjects were similar in their demographic characteristics and medical conditions (Table 1). Among FX, 19 injuries were sustained from a fall from a standing height and 9 were the result of high energy sports. According to the AO classification, there were 9 A fractures (A1 n=4, A2 n=4, a3 n=1), 1 type B fractures (B1 n=1, B2 n=0, B3 n=0) and 18 type C fractures (C1 n=6, C2 n=7, C3 n=5). Eighteen fractures were treated with casting and 10 fractures underwent operative fixation.

Cortical and trabecular microarchitecture differed between groups both at the distal radius and distal tibia. At the distal radius total density was 8% lower in FX than CONT (p=0.03) and 12% lower at the distal tibia (p=0.003). FX had lower trabecular density (-10%, p=0.02) and trabecular thickness (-8%, p=0.01) than CONT. Trabecular bone volume fraction at the radius was lower in FX (-10%, p=0.02). There was also more stress to lower cortical thickness, cortical area and periosteal perimeter although values did not reach statistical significance. At the distal tibia, total density (-12%, p=0.01), trabecular density (-14%, p<0.001) and cortical density (-9%, p=0.01) were lower in FX than CONT. FX also had lower cortical thickness (-11%, p=0.01), and trabecular thickness (-13%, p=0.001) than CONT. BMD was similar between groups at the hip, spine and forearm.

Discussion:

We found that premenopausal women with distal radius fractures have similar BMD, but deteriorated trabecular and cortical bone architecture compared to non-fracture controls. These findings suggests that HR-pQCT detects differences in bony architecture that are not measured by DXA scans alone. To date, the use of this imaging modality in the premenopausal patient population has been limited, and despite the potential of identifying the early stages of skeletal fragility, we are not aware of any studies examining bone geometry and microarchitecture in premenopausal fracture patients.

Study limitations include our focus on fractures of the distal radius. Although spine and hip fractures are associated with greater morbidity and may have shown greater differences in bone microarchitecture parameters, we focused on the distal radius because these are among the most common injuries in young adults and the second most common fragility fracture in postmenopausal women. Also, adult distal radius fractures typically occur at an earlier age than fractures of the hip or spine, offering a unique opportunity to initiate treatment for underlying abnormalities in bone structure and metabolism. These fractures are thus an important cohort to study in the setting of osteoporosis and fracture risk. Our study’s strength lies in that it is the first to our knowledge to compare bony microarchitecture in premenopausal women with and without fractures. We also limited the number of potential confounders by applying strict inclusion and exclusion criteria.

In conclusion, we found that premenopausal women with fractures have similar BMD but altered micro-architecture when compared to controls with no history of fracture. Changes affected trabecular and cortical parameters alike. Although our cross sectional study does not allow the possibility of predicting future fractures, it suggests that fractures at a younger age may be important risk factors for subsequent fragility fractures. Future work identifying patients at risk of osteoporosis before menopause will expand on our findings and provide opportunities to initiate early treatment and prevention efforts.

Significance:

Osteoporosis and fragility fractures present a significant burden to our aging society. Identification of patients at risk for osteoporosis before menopause would provide a unique opportunity to initiate early treatment and prevention efforts in order to decrease future fractures.