Deterioration of Trabecular and Cortical Microarchitecture and Reduced Bone Stiffness at Distal Radius and Tibia in Postmenopausal Women with Vertebral Fractures

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Introduction: Vertebral fractures, which directly result from collapse of weakened vertebral bodies, are also reflective of extensive deterioration of trabecular and cortical microarchitecture at peripheral skeletal sites [1-3]. At distal radius and distal tibia, postmenopausal women with vertebral fractures have fewer and more widely spaced trabeculae, and thinner cortices compared with women without fractures. Studies segmenting plate- and rod-like trabeculae in the trabecular network suggest that increased bone fragility in postmenopausal women is associated with disrupted trabecular plate microarchitecture, the predominant component of trabecular bone strength [4-6]. However, it is unknown whether women with vertebral fractures have such deficiencies in trabecular plate and rod microarchitecture. This study aims to characterize explicitly the alterations of trabecular and cortical microarchitecture and bone stiffness at distal radius and distal tibia in postmenopausal women with vertebral fractures.

Methods: Postmenopausal women with a history of low trauma vertebral fractures (n=45) and controls with no history of fracture and normal spine x-rays (n=45) had areal bone mineral density (aBMD) of lumbar spine, total hip, femoral neck, 1/3 radius, ultradistal radius measured by dual-energy x-ray absorptiometry. Microarchitecture of distal radius and tibia were imaged by high-resolution peripheral quantitative computed tomography (HR-pQCT). We applied an automatic segmentation algorithm to divide the trabecular and cortical compartments [7], which were subjected to individual trabecula segmentation (ITS)-based trabecular plate and rod morphological analysis [6, 8] and a customized cortical evaluation script [9, 10], respectively. Finite element analysis estimated whole bone and trabecular bone stiffness.

Results: The fracture group and the control group were similar in age (70±8 and 70±7 yrs), race (82% and 84% Caucasian, respectively), and body mass index (28±10 and 27±6). Mean aBMD T-scores of the fracture group were 0.5-0.75 SD lower (p<0.05) than controls at total hip, femoral neck, and ultradistal radius, but did not differ at lumbar spine and 1/3 radius (Figure 1). The prevalence of osteoporosis and osteopenia in this cohort were 45% and 47%, respectively. Marked differences in trabecular and cortical microarchitecture were observed between the two groups (Figure 2). At distal tibia, trabecular microarchitecture of the fracture subjects was characterized by preferentially lower trabecular plate bone volume, number, and connectivity over rod-related parameters, in addition to decreased axially aligned trabeculae and lower plate-rod ratio. At distal radius, both trabecular plate and rod microarchitecture showed significantly lower volume, number, and connectivity. Additionally, differences in trabecular plate and rod sizes were observed. Differences in trabecular plate volume, number, connectivity, and axial trabecular bone volume remained significant after adjustment for
aBMD, but trabecular rod parameters did not. Compared to controls, women with vertebral fractures had lower cortical thickness, smaller cortical area, and larger trabecular area. Cortical porosity and pore size did not differ. Group differences in trabecular microarchitecture appeared greater at the radius than at the tibia, whereas differences in cortical microarchitecture were more pronounced at the tibia. Whole bone stiffness and trabecular bone stiffness were reduced in women with vertebral fractures by 18% and 22%, respectively at the radius, and by 19% and 16% at the tibia.

**Discussion:** Postmenopausal women with vertebral fractures showed deterioration of both trabecular and cortical microarchitecture at distal radius and tibia. ITS analysis in the vertebral fracture subjects detected major depletion of trabecular plates, loss of axially aligned trabeculae, and trend to convert into more rod-like trabecular network. Trabecular microarchitecture at distal radius tended to be more severely affected than tibia, which is consistent with the finding that the association of microarchitecture of distal radius with stiffness at the spine was stronger than associations between the tibia parameters and the spine [11]. Moreover, the thinner cortex and expanded trabecular and total bone area suggested more endocortical bone resorption in women with vertebral fractures. These results suggest that this pattern of bone quality deterioration contributes to bone fragility and increased susceptibility to vertebral fractures in postmenopausal women.

**Significance:** This study characterizes explicitly the alterations of trabecular and cortical microarchitecture and bone stiffness at distal radius and distal tibia in postmenopausal women with vertebral fractures.
Figure 1. Comparison of aBMD T-scores between women with vertebral fractures and controls. LS, lumbar spine; TH, total hip; FN, femoral neck; 1/3R, 1/3 radius; UDR, ultradistal radius. (* p<0.05, ** p<0.01)
Figure 2. Difference in ITS, cortical, and FEA parameters between women with vertebral fractures and controls. pBV/TV, plate bone volume fraction; rBV/TV, rod bone volume fraction; aBV/TV, axial bone volume fraction; P-R ratio, plate-rod volume ratio; pTb.N, trabecular plate number; rTb.N, trabecular rod number; pTb.Th, trabecular plate thickness; rTb.Th, trabecular rod thickness; pTb.S, trabecular plate surface area; rTb.l, trabecular rod length; P-P Junc. D, plate-plate junction density; P-R Junc.D, plate-rod junction density; R-R Junc.D, rod-rod junction density; Tt.Ar, total area; Tb.Ar, trabecular area; Ct.Ar, cortical area; Ct.Th, cortical thickness; Ct.Po, cortical porosity; Ct.Po.Dm, cortical pore diameter. (* p<0.05, ** p<0.01, *** p<0.001, fracture vs. control difference; * p<0.05, distal radius differs from distal tibia in fracture vs. control difference)