M459
See Sunday Plenary Number S459

M460
Relationships Between Leptin, FTH, Vitamin D and Bone Metabolism Markers in Patients with Hip Fracture, A. A. Fisher, E. K. Southerland, S. L. Gold, W. Srikusumaprasert, M. W. Dancey, P. N. Smith. 1. Department of Geriatric Medicine, The Canberra Hospital, Australian National University, The Canberra Hospital, Woden, ACT, Australia, 2. Department of Orthopaedic Surgery, The Canberra Hospital, Australian National University, The Canberra Hospital, Woden, ACT, Australia.

The relationship between leptin and bone metabolism is controversial. The study aim was to investigate leptin-related interactions in older patients with hip fracture (HF), a population not previously studied.

In 297 consecutive patients (mean age 82.1 ± 7.9 years; 75.8% women) with low-energy trauma HF (118/83 cervical/rochantic) serum concentrations of leptin, 25-hydroxyvitamin D (25[OH]D), parathyroid hormone (PTH), calcium, phosphorus, magnesium, osteocalcin (OC), bone-specific alkaline phosphatase (BAP) and urine excretion (normalized for urinary creatinine) of free deoxyxyrouridinol (DDP) and N-terminal cross-linked telopeptide of type I collagen (NTx) were measured and clinical data collected prospectively.

Elevated PTH (> 65 pmol/L) was present in 35.5%, 25(OH)D insufficiency (< 50 nmol/L) in 81.6%, excessive bone resorption (increased DPD and/or NTx) at 14.7% and low bone formation (low OC and/or BAP) in 59.2%. Leptin (log-transformed) was significantly and positively correlated with OC (r = 0.18; p < 0.006) and negatively with NTx (r = 0.17; p = 0.013) and DPD (r = 0.14; p = 0.031). In both central and trochanteric HF groups, leptin was positively associated with OC, but the association with DPD was significant only in trochanteric HF (r = 0.30; p < 0.009). Trochanteric compared to cervical HF had higher levels of leptin, FTH (7.9 ± 6.5 vs. 5.9 ± 3.4 pmol/L; p = 0.006), but the concentrations of leptin, 25(OH)D and bone turnover markers were similar. Only in cervical HF patients were leptin and PTH positively correlated (r = 0.26; p = 0.003) and 25(OH)D levels were negatively and significantly correlated with NTx (r = 0.35; p = 0.016). DPD (r = 0.31; p = 0.002) and BAP (r = 0.24; p = 0.012). Other bone metabolism parameters were not associated with leptin in neither group.

These findings suggest that in HF patients there exists a complex relationship between leptin and calcitropic factors, that serum leptin may independently contribute to bone resorption, it is likely to exert different effects on cortical and trabecular bone compartments.

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M461

Age-related skeletal deterioration results not only in decreased bone mass but also bone quality. Inadequate modeling responses and/or incomplete infilling of resorption cavities following bone fatigue contribute to this decline in bone mechanical properties. Using the rat ulna fatigue model, we hypothesized that older adult rats would show less periosteal bone formation and resorption space infilling when compared with younger adult rats following mechanical loading. With IACUC approval, 28 male F344 rats (14, 5 month-old, 14, 12 month-old) were obtained from the National Institute on Aging (Bethesda, MD). Right tibia of each age formed the experimental group and the remaining were used for bone strain calibration. Right forelimbs were cyclically loaded in vivo using a piezoelectric actuator and strain gages. The tibiae were bonded to a plate using cyanoacrylate. The rats were subjected to 30% of the maximum force of the control group. The resorption space (RS), periosteal bone area (PA), and bone mineral density of the tibiae were measured at 0, 1, 3, 5 and 10 million cycles at 1 Hz. The tibiae were embedded in acrylic and sectioned perpendicular to the bone surface. The sections were stained with hematoxylin and eosin for histomorphometric analysis. The results showed that the young rats had significantly greater bone formation and less resorption compared to the older rats. The periosteal bone area and bone mineral density were also greater in the young rats. These findings suggest that the rate of bone turnover is affected by age and that mechanical loading may have a greater effect on the bone response in younger rats. These findings are consistent with the hypothesis that age-related changes in bone metabolism may contribute to the decline in bone mechanical properties.

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M462

Spaceflight challenges the skeletal health of astronauts by exposure to radiation in microgravity. Hamilton et al. (2006) showed that irradiation to bone dose decreases bone mass in growing mice 4 to 6 weeks after exposure to 2 Gy vs. controls, does cause musculoskeletal disease. We hypothesized that radiation and disuse share cellular and molecular mechanisms to cause rapid bone loss in the adult. To define dose (1-2 Gy) and time dependence (1 or 10 d) of irradiation-induced bone resorption, C57Bl/6J mice were exposed to 10 Gy or 100 mGy whole-body x-rays. After a washout period, mice were irradiated with 10 Gy, and bone loss was assessed by dual X-ray absorptiometry (DXA) and microCT. In the first study, mice were hindlimb unloaded (HU) or normally loaded (NL). 7 d later, half the mice from each group were irradiated with 2 Gy d 45 d later.

In the second study, mice were repeated irradiated and analyzed 2 Gy d 15 d later. Mice were analyzed 2 Gy d 30 d later. MicroCT showed decreased trabecular bone thickness and trabecular number. Histomorphometric analysis showed decreased trabecular bone volume. The results suggest that irradiation-induced bone resorption is not affected by muscle function and that irradiation-induced bone resorption is not affected by muscle function.

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