Effects of Protein Supplementation During Weight Loss on Bone Mineral Density and Bone Marrow Adipose Tissue in the Lumbar Spine: A Randomized Controlled Trial

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Disclosures: None

INTRODUCTION: Reduction of bone mineral density (BMD) in the lumbar spine is a concern for older adults attempting to lose weight for the treatment of obesity and related comorbidities. In addition to BMD, bone marrow adipose tissue (BMAT) changes with weight fluctuation and may play a role in fracture risk. Randomized controlled trial data from 187 low-functioning older adults with obesity (mean±SD: 71.6±4 years; BMI 34.3±4.2 kg/m²; 65% female) were collected to analyze the effects of protein supplementation on BMD and BMAT during weight loss (NCT03819478).

METHODS: A 6-month weight loss (WL) intervention consisting of caloric restriction and moderate-intensity treadmill walking (3 days/week) with a 12month follow up was conducted (IRB00038668; Figure 1) where participants were randomized into one of three groups: 50 g/d of supplemental protein (6m PRO; n = 62) or carbohydrate (CHO; n = 62) during the active WL intervention period, or 50 g/d of supplemental protein throughout the 18-month intervention and follow up period (18-m PRO; n = 63). Dual-energy computed tomography (DECT) scans were collected at baseline, 6-, and 18-months and analyzed using QCTProTM (Figure 2) to extract volumetric BMD (vBMD) and BMAT from the L1-L4 vertebrae. Analysis of covariance adjusted for age, sex, race, and baseline bone measure was used to assess changes in vBMD and BMAT at 6- and 18-month timepoints. The protein supplement groups were pooled at the 6-month time point to create one PRO group as both groups received the same intervention for months 0-6. Associations between lumbar vBMD, BMAT, and weight changes at 6- and 18-months were tested using linear regression, adjusting for age, sex and race.

RESULTS: There was no difference in weight loss between groups at 6-months (mean ±SD: -8.4 ± 4.7 kg, 18-m PRO; -8.4 ± 5.0 kg, 6-m PRO; -7.0 ± 5.2 kg, CHO) or 18-months (-5.3±5.6, -4.9±5.4, and -4.6±5.3 kg, respectively). The protein supplement group had higher protein intakes at both 6-months (1.3±0.4). vs 0.8 ± 0.2 g/kg body weight/d; p<0.01) and 18-months (1.0 ± 0.4 g/kg/d for 18-m PRO vs 0.8 ± 0.3 g/kg/d for the 6-m PRO and CHO groups; p<0.01). Average lumbar vBMD (L1-L4) increased for all groups at 6-months (4.6±2.0% CHO, 5.2±1.9% PRO), however only remained slightly elevated in the 6-m PRO group (0.8±2.1%) at 18-months (Figure 3), while both the CHO group (-0.2±2.0%) and 18-m PRO group (-1.9±2.2%) saw decreases from baseline. Similarly, both the CHO and PRO groups saw increases in BMAT at 6-months (7.3±4.0% and 6.3±3.8%, respectively) and decreases at 18-months (-0.2±3.7% CHO, -10.2±3.8% 6-m PRO, -5.4±3.9% 18-m PRO; Figure 3). Changes in vBMD were negatively associated with changes in BMAT and weight at 6-months ($\beta \pm SE$; -0.6 \pm 0.2, p<0.01; -0.3 \pm 0.1, p<0.01, respectively), but not at 18-months (-0.5 \pm 0.3, p=0.08; -0.04 \pm 0.1, p=0.67, respectively). Changes in weight were not associated with 6-month change in BMAT (-0.2±0.3, p=0.5), but were negatively associated with 18-month BMAT changes (-0.8±0.3, p<0.01).

DISCUSSION: Differences between lumbar metrics of BMD were minimal, with similar trends seen for all treatment groups. Increases in vBMD at the 6month timepoint may be due to the aerobic exercise component of the intervention increasing physical activity in all groups of previously sedentary older adults. Greater increases in BMD were associated with decreased BMAT at 6-months, however this association was lost at 18-months, Interestingly, greater decreases in weight were also associated with increases in BMD at 6-months. These changes in weight were not associated with BMD changes at 18-months, but instead with BMAT where greater decreases in weight from baseline resulted in higher BMAT.

SIGNIFICANCE/CLINICAL RELEVANCE: With population age increasing and obesity rates still on the rise, it is imperative to find ways of combating obesity related comorbidity and complications without sacrificing skeletal health. Results from this trial suggest that protein intake during weight loss likely does not influence vertebral quality, and that BMD is most heavily decreased during active weight loss and might drive changes in BMAT independent of changes in weight in the short term.

ACKNOWLEDGEMENTS: Funding provided by the National Institute on Aging (K25 AG058804; R01 AG050656).

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