Effect of Protein Supplementation During Weight Loss on Bone Mineral Density, Cortical Thickness, and Bone Strength of the Hip in Older Adults with Obesity: A Randomized Controlled Trial

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INTRODUCTION: Weight loss (WL) to treat obesity is controversial in older age as it can exacerbate bone loss. We conducted a double-blind, randomized controlled trial in 187 low-functioning older adults with obesity (mean±SD: 71.0±4.3 years; BMI 34.2±4.1 kg/m^2; 34% men) to assess the effect of protein supplementation during WL on hip volumetric bone mineral density (vBMD), cortical thickness, and bone strength (NCT03819478).

METHODS: Participants were enrolled in a 6-month WL intervention (caloric restriction and moderate-intensity treadmill walking 3days/week) followed by 12 months of follow-up and randomized to one of 3 groups (IRB00038668; **Figure 1**): 50 g/d of supplemental protein (PRO; n=62) or carbohydrate (CHO; n=62) for the 6-month WL period, or 50 g/d of supplemental PRO for the 18-month WL plus follow-up period (n=63). Computed tomography (CT) scans at baseline, 6 months, and 18 months were analyzed to assess vBMD and cortical thickness of the hip, and bone strength was assessed via finite element modeling of a sideways fall (**Figure 2**). Bone changes over 6 and 18 months were examined using analysis of covariance, adjusting for age, sex, race, and baseline bone measure. The two protein supplement groups were pooled at the 6-month timepoint as both groups received the same intervention for months 0-6. Spearman's correlations of WL vs bone changes at 18 months adjusted for age, race, and sex were also examined.

RESULTS: Weight loss did not differ by group at 6 months (mean±SD: -8.4±4.7, -8.4±5.0, -7.0±5.2 kg for 18-m PRO, 6-m PRO and 6-m CHO) or at 18 months (-5.3±5.6, -4.9±5.4, and -4.6±5.3 kg, respectively). As expected, protein intake at 6 months was higher in the protein supplement groups compared to the CHO group (1.3±0.4 vs. 0.8±0.2; p<0.01). Protein intake at 18 months was higher in the 18-m PRO group compared to the 6-m PRO and 6-m CHO groups (1.0±0.4 vs 0.8±0.3 and 0.8±0.3 g/kg body weight/d, respectively; p<0.01). Total hip trabecular vBMD changes did not differ by group (**Figure 3**), but there was higher vBMD gain with protein supplementation at 6 months (adjusted mean±SE: 1.6±1.1 vs. 0.3±1.1 mg/cm^3) and attenuated vBMD loss in the 18-m PRO group at 18 months (0.0±1.4 vs -1.8±1.4 and -0.9±1.3 mg/cm^3 for 6-m PRO and 6-m CHO, respectively). Similar trends were observed for femoral neck, trochanter, and intertrochanter trabecular vBMD. Cortical thickness improved ~0.5% over 6 months (0.01±0.02 mm all groups), and ~2% over 18 months (18-m PRO: 0.03±0.02 mm; 6-m CHO & PRO: 0.02±0.02 mm). Similar increases were observed in cortical vBMD of the total hip, femoral neck, trochanter, and intertrochanter. Hip bone strength increased 3.2±1.6% over 6 months in participants randomized to protein vs. carbohydrate supplementation (0.10±0.07 vs. -0.02±0.08 kN; p=0.03). While group differences were not significant at 18 months, the average bone strength increased 2.4% in the 18-m PRO group (0.09±0.11 kN) and 1% in the 6-m PRO group (0.03±0.11 kN), but decreased -1% in the 6-m CHO group (-0.02±0.10 kN). The amount of weight change was not significantly associated with changes in cortical vBMD, cortical thickness, or bone strength, but greater weight loss was associated with more trabecular vBMD loss at the total hip at 18 months (ρ=0.22, p=0.03).

DISCUSSION: In low-functioning older adults with obesity in a weight loss trial, trends suggest protein supplementation for 18 months (during active WL and the year after) better preserved trabecular vBMD of the hip compared to protein or carbohydrate supplementation for the 6-month WL phase. Six-month gains in hip bone strength were significantly higher in the participants randomized to protein vs. carbohydrate supplementation. The 18-m PRO participants continuing protein supplementation for the year after WL (during the 12-month follow-up period) appeared to maintain hip bone strength gains ~2.4 times better than participants on protein supplementation for 6 months. Further, protein supplementation in both groups appeared to protect against the overall loss of bone strength observed in the WL controls consuming the carbohydrate supplement. The observed gains in hip cortical thickness and vBMD may possibly be due to the exercise component of the intervention increasing physical activity and musculoskeletal loading in this previously sedentary population.

SIGNIFICANCE/CLINICAL RELEVANCE: More than one-third of older adults have obesity, but intentional WL is controversial in this population due to the association with bone loss and fracture risk. This randomized controlled trial demonstrating the effectiveness of protein supplementation in mitigating bone loss in an intentional WL intervention has the potential to inform obesity treatment guidelines for older adults.

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IMAGES:

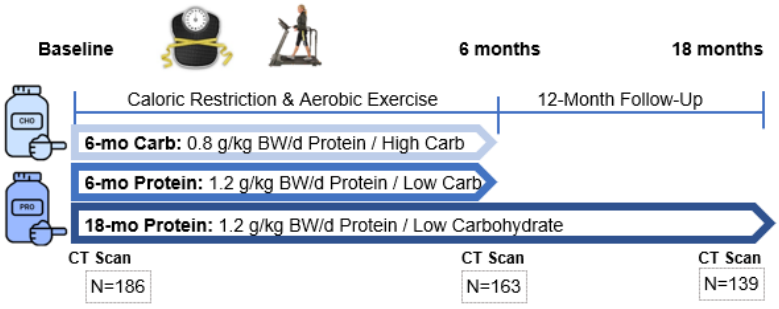

Figure 1. Intervention Design and CT Scan Data Collection Timeline.

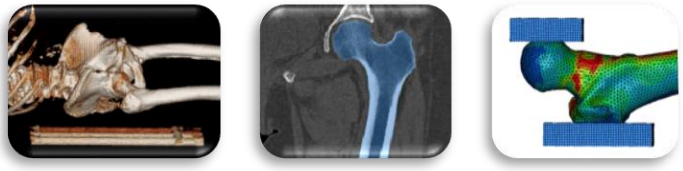

Figure 2. CT scans with a calibration phantom to measure vBMD and cortical thickness. Subject-specific finite element simulations of a sideways fall to measure hip bone strength.

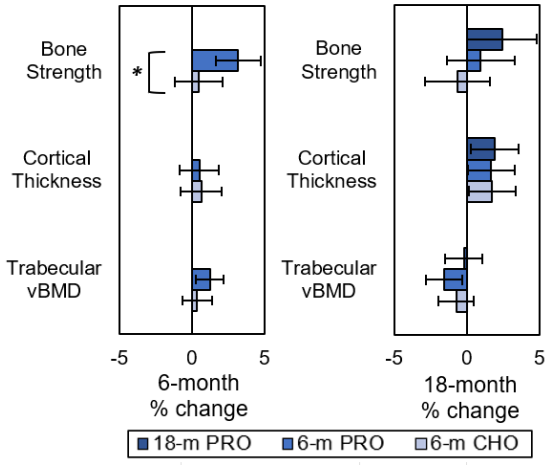

Figure 3. Hip bone changes over 6 and 18 months by treatment group. The 6-m and 18-m PRO groups are pooled at the 6-month timepoint as both of the protein supplementation groups received the same intervention for months 0-6.