

## **Levothyroxine Use and Bone Loss in Euthyroid Older Adults: A Longitudinal Analysis From Baltimore Longitudinal Study of Aging**

### **PURPOSE**

Levothyroxine (LT4) is the second most commonly prescribed medication in older adults. Frank hyperthyroidism accelerates bone turnover and even subclinical hyperthyroid has been associated with increased fracture risk. Data indicates that a significant proportion of thyroid hormone prescriptions may be given to older adults without hypothyroidism raising concerns about subsequent relative excess of thyroid hormone even when treatment is targeted to reference range goals. In this study we aimed to determine whether LT4 use and higher thyroid hormone levels within the reference range are associated with higher bone loss over time in older adults.

### **METHODS AND MATERIALS**

Using the Baltimore Longitudinal Study of Aging a prospective observational cohort of community-dwelling older adults, participants age 65 and older at the baseline visit with at least 2 visits with thyroid function tests within the reference ranges at all visits were included. We employed propensity score matching (1:5), to match LT4 users with non-users according to relevant baseline characteristics: age, gender, BMI, race, history of alcohol intake, smoking, multi-pharmacy, and baseline serum TSH. Dual-Energy X-ray Absorptiometry were used to measure bone density and mass at each visit. Linear mixed-effects models and an interaction term of time interval between each visit and participant's first visit were used to estimate longitudinal relationships between exposure and outcomes. Stratified analyses were performed according to tertiles of average serum free thyroxine (FT4) level.

### **RESULTS**

The cohort included 81 euthyroid LT4 users (32 males, 49 females) and 364 non-users (148 males, 216 females), with a median age of 73 and thyrotropin levels of 2.35 at the index visit. LT4 use was found to be associated with greater longitudinal loss of total body bone mass (beta: -6.53; 95% CI: (-10.39, -2.67);  $p < 0.001$ ) and total body bone density (beta: -0.0014; 95% CI: (-0.002, -0.0006);  $p < 0.001$ ) over a median follow-up of 6.3 years (IQR: 4.0, 10.4). This association was stronger with increasing tertile of average FT4.

### **CONCLUSIONS**

Longitudinal loss of bone mass and density was greater among euthyroid LT4 users. The more pronounced effects at higher levels of FT4 suggest that LT4 use may be associated with a relative excess of thyroid hormone in some older adults on therapy, even with TSH levels within the reference range.

### **CLINICAL RELEVANCE/APPLICATIONS**

Even when adjusted to current treatment targets, bone loss may be an iatrogenic effect of levothyroxine use in older adults.