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Low Thyroid Stimulating Hormone Levels Are Associated with Low Bone Mineral Density in Femoral Neck in Elderly Women

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Background and Aims. To determine the relationship between thyroid stimulating hormone (TSH) and bone mineral density (BMD) in elderly women.

Methods. This is a retrospective cross-sectional population cohort study of women aged ≥65 years. All 1097 subjects had no overt thyroid dysfunction, 47 had subclinical hyperthyroidism and 100 had subclinical hypothyroidism. Overall, 167 had normal BMD, 594 had osteopenia and 336 had osteoporosis.

Results. The femoral neck (FN) BMD was lower in women with lower TSH, with a high prevalance of osteoporosis and osteopenia ($p = 0.036$).The prevalence of osteoporosis and osteopenia was significantly low in the lowest quartile compared with the third quartile ($p = 0.023$) and the fourth quartile ($p = 0.002$), and the second low quartile, compared with the fourth quartile ($p = 0.028$). The differences were not significant among subclinical hyperthyroid, subclinical hypothyroid and euthyroid women. Low TSH was related to low BMDs at FN by multiple logistic regression analysis corrected for age and BMI. TSH in the lower two quartiles were independently related to osteoporosis (OR: 1.960, $p = 0.023$ and OR: 1.800, $p = 0.037$) and osteopenia (OR: 2.108, $p = 0.005$ and OR: 1.723, $p = 0.030$). Low TSH quartile (β: 0.007, $p = 0.013$) predicting low BMDs at FN.

Conclusion. Low TSH was independently related to decreased BMDs at FN in elderly women without overt thyroid dysfunction.

Key Words: Bone mineral density, Elderly women, Osteoporosis, Thyroid stimulating hormone.

Introduction

Thyroid dysfunction and osteoporosis are both common disorders in elderly women. Overt hyperthyroidism (1) and hypothyroidism (2) have long been recognized as risk factors for low BMD and osteoporotic fractures. However, the relationship between biochemical defined subclinical thyroid dysfunction and fracture risk or BMD remain controversial. Subclinical thyroid dysfunction is much more common than overt dysfunction, especially in older adults (3,4). Subclinical hypothyroidism [elevated TSH and normal free thyroxine (FT4)] has been reported to have a prevalence of up to 15% and subclinical hyperthyroidism (low TSH with normal FT4) in up to 1.5% in those aged 65 years or older (5). Serum TSH increases with increasing age in older individuals (6).

The evidence for the association between TSH and bone health status has been increasing and suggests that subclinical thyroid dysfunction might also be an important risk factor for low BMD and fragility fractures. Some studies have demonstrated that TSH has a direct action on bone cells (7,8). Although there have been reports suggesting that TSH concentrations were associated with BMD or fracture risk (9–14), other reports have shown discrepant results (15–18).

In the present study, we aimed to test the hypothesis that subclinical thyroid disease with low or elevated levels of serum TSH and normal free T4 may increase the risk of low BMD in women aged 65 years or older.

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Materials and Methods

Participants

A cohort of 1126 women aged ≥65 years were recruited from all consecutive visitors at the Nanjing Medical University Affiliated Nanjing Hospital (Nanjing First Hospital) between September 2012 and August 2015.

Exclusion criteria were history of thyroid dysfunction or surgery, parathyroid disease, medication for thyroid disease, osteoporosis, any hormonal treatment, and other disorders that affect BMD.

The study was approved by the Medical Ethics Committee of Nanjing Medical University Affiliated Nanjing Hospital (Nanjing First Hospital) and written informed consent was obtained from all participants.

Thyroid Function

Thyroid function was assessed by measurement of TSH (reference range: 0.5−5.0 uIU/mL), FT4 (reference range: 0.61−1.22 ng/dL) and FT3 (reference range: 2.5−3.9 pg/mL) using standard immunoassay (Centaur XP, Siemens, Germany). Subclinical hyperthyroidism was defined as a TSH level <0.5 mIU/L with FT4 level within normal range, and subclinical hypothyroidism was defined as a TSH level >5.0 mIU/L with FT4 level within normal range. When the TSH level was between 0.5 and 5.0 mIU/L with FT4 level within normal range, this was defined as euthyroidism. Quartiles of TSH were calculated for statistical analysis whereas TSH quartiles defined as 1, 2, 3 and 4 when TSH <25th percentile, 25th−50th percentile, 51th−75th percentile and >75th percentile.

Bone Mineral Density

BMD was measured at the lumbar spine (LS) (L1−L4) and the femoral neck (FN) by dual-energy X-ray absorptiometry (GE, LUNAR Prodigy, Madison, WI). The results were expressed as BMD in grams per square centimeter (g/cm^2). Osteoporosis was defined as a BMD ≤ −2.5 SD below the young adult mean (T-score). T-score values between −1 and −2.5 were defined as osteopenia. Normal BMD was defined as a T-score not less than −1.

Statistical Analysis

Continuous variables with normal distributions are reported as mean ± SD, and with non-normally distributions are reported as the median and interquartile range. Categorical variables are reported as numbers and frequencies. TSH was geometrically distributed; therefore, logTSH was calculated before comparison of means. As the age was not normally distributed, ANOVA was used to compare means among different groups. The relationship between TSH and osteoporosis, and osteopenia was analyzed using ANOVA and χ^2. Multiple regression analysis (OR, 95% CI) was performed with osteoporosis or osteopenia as a dependent variable and the lower TSH values (lowest quartile and the second lower quartile) as independent variables adjusted for age and BMI. Multivariate linear regression was used including BMDs as a continuous dependent variable. All statistical analyses were performed using SPSS 17.0 (IBM Corp.); $p < 0.05$ was considered statistically significant for all analyses.

Results

Ten women with overt hyperthyroidism and 19 women with overt hypothyroidism were excluded from the analysis. Of the remaining 1097 women analyzed, the mean age was 71 (range 67−76 years), height 1.58 ± 0.05 m, weight 61 ± 10 kg, body mass index (BMI) 24.5 ± 3.6 kg/m^2. Forty seven women had subclinical hyperthyroidism, 100 had subclinical hypothyroidism and 950 were euthyroid. There were 336 women with osteoporosis, 594 with osteopenia, and 167 with normal BMD.

As expected, logTSH was correlated inversely with FT4 ($r = -0.262$, $p < 0.001$). The correlation of BMD at LS with logTSH ($r = 0.054$, $p = 0.077$) or FT4 ($r = -0.037$, $p = 0.223$) did not reach statistical significance. The correlation of BMD at FN with logTSH was statistically significant ($r = 0.089$, $p = 0.003$), but not with FT4 ($r = -0.039$, $p = 0.195$).

Thyroid Function in Relation to BMD

Women were divided into subgroups as defined earlier: euthyroid, subclinical hyperthyroidism and subclinical hypothyroidism. Comparison of BMDs with the prevalence of osteoporosis and osteopenia did not show a significant difference between groups ($\chi^2 = 7.56$, df = 4, $p = 0.109$, Table 1).

Table 2 shows quartiles for TSH in the 1097 elderly women without overt thyroid dysfunction. When BMDs were compared between quartiles of TSH concentration, no difference was identified at LS BMD (ANOVA, F = 1.476, $p = 0.219$). There was, however, a significant difference at the FN BMD (ANOVA, F = 3.992, $p = 0.008$; Table 2). Further post-hoc (Least-Significant Difference) analysis indicated the lowest quartile differed significantly from the highest two quartiles. The percentage of osteoporosis and osteopenia were higher in the lowest TSH quartile (Figure 1). Further analysis showed the prevalence of osteoporosis and osteopenia were significantly higher in the lowest TSH quartile (<25th), compared with the third TSH quartile (51th−75th, $X^2 = 5.46$, df = 1, $p = 0.023$) and the fourth TSH quartile (>75th,