Effect of thyrotropin suppressive therapy on lumbar bone mineral density in patients with differentiated thyroid cancer: a retrospective cohort study

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Background: To investigate the effect of thyrotropin (TSH) suppressive therapy on lumbar bone mineral density (BMD) in patients with differentiated thyroid cancer (DTC) after operation.

Methods: We retrospectively analyzed 70 DTC patients at intermediate or high risk of recurrence, including 17 males, 30 premenopausal females, and 23 postmenopausal females. All patients were treated with oral ¹³¹I to clear any residual thyroid and L-thyroxine tablets to suppress TSH after surgery. The baseline and follow-up lumbar BMD were measured. The anthropometric and biochemical parameters, the doses of calcium supplement, and levothyroxine were collected.

Results: Lumbar BMD in the postmenopausal female group was markedly decreased (regression coefficient: −0.201; P<0.001) compared to the male group and premenopausal female group (both: P>0.05). Further comparisons between groups found that premenopausal women had a monthly lumbar BMD reduction of 0.001 g/cm² more than men, but the difference was not statistically significant (P=0.515). In contrast, postmenopausal women had a monthly lumbar BMD reduction of 0.004 g/cm² more than men and 0.003 g/cm² more than postmenopausal controls (P=0.017 and P<0.001, respectively). Lumbar BMD decreased significantly with the increasing duration of TSH suppression in both the calcium supplement group and the non-calcium supplement group (both: P<0.05), but there was no statistical difference between the two groups (P=0.534).

Conclusions: The longer the duration of TSH suppression in DTC patients after operation, the more significant the decrease of BMD, especially in postmenopausal women. Furthermore, calcium supplementation did not significantly improve lumbar BMD.

Keywords: Thyroid neoplasms; thyrotropin (TSH); bone density; postmenopause

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Introduction

Thyroid cancer is the most common endocrine malignant tumor, and differentiated thyroid cancer (DTC) is the most prevalent type of thyroid cancer, which can account for over 90% of all thyroid cancers (1-3). The management of DTC includes risk assessment, surgical management, radioiodine (RAI) remnant ablation and therapy, and thyrotropin (TSH) suppression therapy using levothyroxine (4,5). After ¹³¹I treatment following surgery, TSH suppressive therapy should be given to the patients promptly to reduce the
recurrence rate of DTC. The therapeutic value of TSH suppressive therapy for DTC has been proved (4,6,7).

It is well known that the metabolism, development, and reconstruction of bone are affected by the thyroid hormone. It was reported that lower TSH levels, even within the normal range, negatively affect the BMD (8). Furthermore, thyroid dysfunction has been known to represent a risk factor for bone disease (9,10). Both hyperthyroidism and subclinical hyperthyroidism were reported to affect bone metabolism resulting in decreased bone mineral density (BMD) and increased risk of fracture (10). TSH suppressive therapy leads to changes in the internal environment of patients, and sustained subclinical hyperthyroidism interferes with bone metabolism (11).

There are many studies on the effect of TSH suppressive therapy on BMD of patients with DTC, but the conclusions are divergent (12-22). Multiple studies have shown that TSH suppressive therapy can increase the risk of osteoporosis in patients with DTC (13-17). At the same time, many studies have demonstrated that TSH suppressive therapy does not reduce the BMD of the lumbar spine in patients with DTC (18-22). However, in some of the above studies, only female DTC patients or only female patients were included in the BMD test (13,15-19,22). Only two trials studied the effect of a calcium supplement or vitamin D supplement on BMD in DTC patients (14,17). A meta-analysis by Yoon et al. [2019] confirmed that, in postmenopausal women with DTC (instead of premenopausal women and men), there might be a link between chronic TSH suppression therapy and lower BMD in the spine and total hip (23). However, a meta-analysis by Wang et al. [2020] suggested that there was no significant difference in the lumbar BMD between the patients with DTC after TSH-suppressive therapy and the control groups (24). These two meta-analyses produced inconsistent results. Additionally, these results need to be interpreted with caution. Heterogeneity was observed in the above two meta-analyses results, and the results did not take into account the interactions among age, body mass index (BMI), and calcium supplementation.

Therefore, we designed this retrospective study to evaluate the effect of TSH suppressive therapy on lumbar BMD in DTC patients after surgery and RAI therapy, and to analyze whether this effect has a population difference. Another objective of this study was to evaluate whether calcium supplements can help improve BMD. We present the following article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-50/rc).

Methods

Patients

This was a retrospective cohort study. Patients who were scheduled to receive \textsuperscript{131}I treatment to remove residual thyroid tissue or as part of routine follow-up after DTC operation in our nuclear medicine discipline between October 2013 and September 2019 were eligible for the study. All patients took \textsuperscript{131}I solution after the surgery for thyroid ablation. After treatment, the patients took levothyroxine tablets to suppress TSH to an initial target level. For DTC patients at high-risk of recurrence, it is recommended by the American Thyroid Association (ATA) guidelines to suppress the initial TSH to below 0.1 mIU/L (2,25). For DTC patients at intermediate-risk of recurrence, it is recommended by the ATA guidelines to suppress the initial TSH to 0.1–0.5 mIU/L (2,25). All the included patients met the following criteria: (I) intermediate or high risk of recurrence after total or subtotal removal of DTC; (II) good treatment compliance, regular administration of levothyroxine in a timely manner, and achieved the initial TSH target during the initial treatment (the first year); and (III) the baseline BMD was measured after surgery, and the patients were followed up regularly to receive the BMD tests. The risk stratification after surgery was done according to the 2009 ATA guidelines. Intermediate-risk of recurrence met one of the following criteria: (I) microscopic invasion of the tumor into the perithyroidal soft tissues at initial surgery; (II) cervical lymph node metastases or \textsuperscript{131}I uptake outside the thyroid bed on the whole-body RAI scan done after thyroid remnant ablation; or (III) a tumor with aggressive histology or vascular invasion. High-risk of recurrence met one of the following criteria: (I) macroscopic tumor invasion; (II) incomplete tumor resection; (III) distant metastases; or (IV) thyroglobulinemia out of proportion to what is seen on the posttreatment scan (25).

A patient was excluded if they had or were any of the following: (I) hypoparathyroidism, serum level of parathyroid hormone (PTH) <16 pg/mL; (II) hypocalcemia, serum level of calcium <2.11 mmol/L; (III) bone metastasis; (IV) taking steroids; (V) treated with medications for osteoporosis; (VI) taking steroid hormones or steroid-modulating medications or (VII) missing or incomplete data.

This study was conducted following the principles of the Declaration of Helsinki (as revised in 2013) and was approved...
by the ethics committee of the Third Affiliated Hospital of Soochow University [approval No. (2020) WD-018]. Written informed consent was obtained from the patients.

**Study methods**

The anthropometric and biochemical parameters, the dose of calcium supplement and L-thyroxine, and the lumbar BMD score of the included patients were collected. Anthropometric parameters such as height and weight were measured while the patients were dressed in lightweight clothing. BMI was calculated using the following formula: weight in kilograms divided by the square of the height in meters (kg/m$^2$).

The concentrations of serum calcium and serum 25-hydroxyvitamin D were measured using an automated biochemical analyzer (Beckman Coulter AU5831, USA). The serum level of PTH was measured based on a chemiluminescence immunoassay (Siemens ADVIA Centaur, Germany). Concentrations of serum free T3 (FT3), serum free T4 (FT4), and TSH were evaluated with the radioimmunoassay method (Cobas 8000, Switzerland).

BMD was determined by DXA (dual-energy X-ray absorptiometry, Hologic, Discovery, WI, USA) and was performed on the lumbar spine (L1–L4) area. All DXA scans were performed by trained and certified DXA technicians. The BMD values were measured in g/cm$^2$. BMD of the lumbar spine was measured at the time of initial $^{131}$I admission (baseline) and during the follow-up period. If there were multiple BMD follow-ups during the TSH suppression period, the data from the final follow up was used for the statistical analysis.

The postmenopausal female controls (n=21) were randomly selected among participants that had more than two health check-up records, including BMD test, in the Third Affiliated Hospital of Soochow University. Participants who had any history of thyroid disease, diabetes, kidney disease, heart failure, or any other major medical conditions were excluded. All of the postmenopausal female controls had not taken any medications known to affect bone metabolism except calcium supplements. We also collected data on the BMI, serum levels of calcium, PTH, FT3, FT4, TSH, and BMD score of the postmenopausal controls.

**Statistical analysis**

Continuous variables were expressed as mean ± SD or median (Q1–Q3), while categorical variables were expressed as frequency (%). Non-paired Student's $t$-test or Mann-Whitney nonparametric test was used to compare continuous variables. Pearson chi-square test and Fisher exact test were used to analyze categorical variables.

We analyzed the trend of lumbar BMD after TSH suppression using linear regression. Afterwards, we used the generalized additive mixed model (GAMM) to examine the changes of BMD with the duration of TSH suppression or the duration of follow-up in different population groups and different calcium supplement groups. GAMM eliminated the influence of individual differences on the results of repeated measurements by introducing random effects into the statistical analysis (26). The linear relationship between lumbar BMD change and duration of TSH suppression or duration of follow-up was determined. The results were then adjusted for potential confounding factors such as age, BMI, risk of recurrence, calcium supplement, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D. All analyses were performed by using R, version 3.4.3 (https://www.r-project.org/). P<0.05 was considered statistically significant, and all statistical tests were two-tailed.

**Results**

**Analysis of the baseline status of enrolled patients**

Initially, 144 patients with postoperative DTC were eligible for the study, among which 74 patients were excluded, including 66 patients who only had one BMD test, 4 patients with hypoparathyroidism, and 4 patients with hypocalcemia. Eventually, 70 patients were included in the study (Figure 1). The patients were divided into the male group (17 cases), the premenopausal female group (30 cases), and the postmenopausal female group (23 cases). There was no significant difference in BMI, risk of recurrence, the proportion of patients who used calcium supplements, the number of BMD tests, suppression time, serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D among the three groups (P>0.05). However, there was a significant difference in age, the dose of L-thyroxine, and BMD of the lumbar spine among the three groups (P<0.001; Table 1).

**Changes of lumbar BMD with a duration of TSH suppression in the general population**

After adjusting for age, BMI, risk of recurrence, calcium
supplement, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D, the overall BMD value of all patients in the study decreased significantly with the increasing duration of TSH suppression (regression coefficient: −0.142; P<0.001) (Figure 2).

**Changes of lumbar BMD with suppression time in different population groups**

**Changes of lumbar BMD with suppression time among the male, premenopausal, and postmenopausal female groups**

After adjusting for age, BMI, risk of recurrence, calcium supplement, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D, the changes of BMD of the lumbar spine in the male and premenopausal female groups were not significant (regression coefficient: 0.058 and −0.051; P value: 0.483 and 0.308, respectively). However, the BMD of the lumbar spine in postmenopausal females showed a significant downward trend (regression coefficient: −0.201; P<0.001). We found that the decrease of lumbar BMD in the premenopausal female group was 0.001 g/cm² more than that of the male group per month, but there was no statistical significance (P=0.515). In contrast, the decrease of lumbar BMD in the postmenopausal female group was 0.004 g/cm² more than that of the male group per month, which was statistically significant (P=0.017). We further analyzed the interaction between different population groups and calcium supplementation. The results showed that there was no interaction between diverse populations and calcium supplementation (P>0.05) (Figure 3).

**Changes of lumbar BMD with the duration of follow-up between postmenopausal patients and postmenopausal controls**

There was no significant difference in age, BMI, calcium supplement, serum level of PTH, calcium, and BMD of the lumbar spine between the two groups (P>0.05). However, there was a significant difference in the serum level of TSH, FT3, and FT4, and the duration of follow-up between the two groups (P<0.001; Table 2). After adjusting for age, BMI, calcium supplement, and the serum level of TSH, FT3, FT4, PTH, and calcium, the changes of BMD of the lumbar spine in the postmenopausal controls were not significant (regression coefficient: 0.014; P=0.457). However, the BMD of the lumbar spine in postmenopausal patients showed a significant downward trend (regression coefficient: −0.365; P<0.001). The decrease of lumbar BMD in the postmenopausal women patient group was 0.003 g/cm² more than that in the postmenopausal control group per
Table 1 Comparison of general data among different populations

<table>
<thead>
<tr>
<th>Group</th>
<th>Male</th>
<th>Premenopausal female</th>
<th>Postmenopausal female</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>17</td>
<td>30</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.9±13.2</td>
<td>42.1±8.4</td>
<td>57.2±7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.4±2.6</td>
<td>24.0±3.0</td>
<td>24.8±4.0</td>
<td>0.055</td>
</tr>
<tr>
<td>Risk of recurrence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>16 (94.1)</td>
<td>22 (73.3)</td>
<td>15 (65.2)</td>
<td>0.100</td>
</tr>
<tr>
<td>High</td>
<td>1 (5.9)</td>
<td>8 (26.7)</td>
<td>8 (34.8)</td>
<td></td>
</tr>
<tr>
<td>Calcium supplement</td>
<td>4 (23.5)</td>
<td>7 (23.3)</td>
<td>11 (47.8)</td>
<td>0.118</td>
</tr>
<tr>
<td>Dose of L-thyroxine (µg)</td>
<td>136.8±28.5</td>
<td>113.3±15.0</td>
<td>110.9±18.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TSH (µIU/mL)*</td>
<td>0.06 (0.04–0.24)</td>
<td>0.08 (0.03–0.14)</td>
<td>0.06 (0.02–0.10)</td>
<td>0.452</td>
</tr>
<tr>
<td>FT3 (pmol/L)*</td>
<td>6.18 (5.69–6.29)</td>
<td>5.44 (5.00–6.37)</td>
<td>5.94 (5.50–6.38)</td>
<td>0.298</td>
</tr>
<tr>
<td>FT4 (pmol/L)*</td>
<td>27.20 (25.11–29.10)</td>
<td>25.08 (23.02–27.23)</td>
<td>25.89 (23.54–29.47)</td>
<td>0.155</td>
</tr>
<tr>
<td>PTH (pg/mL)</td>
<td>32.87±12.97</td>
<td>33.15±13.71</td>
<td>40.67±17.05</td>
<td>0.134</td>
</tr>
<tr>
<td>Ca (mmol/L)</td>
<td>2.58±0.19</td>
<td>2.46±0.14</td>
<td>2.52±0.19</td>
<td>0.071</td>
</tr>
<tr>
<td>25-hydroxyvitamin D (ng/mL)</td>
<td>15.37±6.41</td>
<td>14.31±5.07</td>
<td>13.68±6.37</td>
<td>0.668</td>
</tr>
<tr>
<td>Number of BMD*</td>
<td>2 (2–2)</td>
<td>2 (2–2)</td>
<td>2 (2–2)</td>
<td>0.621</td>
</tr>
<tr>
<td>Suppression time (month)*</td>
<td>6.3 (5.9–8.2)</td>
<td>7.1 (5.9–9.5)</td>
<td>7.2 (5.8–10.7)</td>
<td>0.544</td>
</tr>
<tr>
<td>Baseline BMD (g/cm²)</td>
<td>0.99±0.127</td>
<td>1.02±0.099</td>
<td>0.89±0.111</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Last BMD (g/cm²)</td>
<td>1.00±0.130</td>
<td>1.04±0.119</td>
<td>0.88±0.111</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results in the table: mean ± SD/n (%). *, median (Q1–Q3). BMI, body mass index; TSH, thyrotropin; FT3, free T3; FT4, free T4; PTH, parathyroid hormone; Ca, calcium; BMD, bone mineral density.

Figure 2 Curve fitting of lumbar BMD with a duration of TSH suppression (month) in all patients. After adjusting for age, BMI, risk of recurrence, calcium supplement, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D. BMD, bone mineral density; TSH, thyrotropin; BMI, body mass index; FT3, free T3; FT4, free T4; PTH, parathyroid hormone.

Figure 3 Curve fitting of lumbar BMD with a duration of TSH suppression (month) among the male, premenopausal, and postmenopausal women groups. After adjusting for age, BMI, risk of recurrence, calcium supplement, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D. BMD, bone mineral density; TSH, thyrotropin; BMI, body mass index; FT3, free T3; FT4, free T4; PTH, parathyroid hormone.
Table 2 Comparison of general data between postmenopausal patients and postmenopausal controls

<table>
<thead>
<tr>
<th>Group</th>
<th>Premenopausal controls</th>
<th>Postmenopausal patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.0±9.4</td>
<td>57.2±7.0</td>
<td>0.058</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.3±3.6</td>
<td>24.8±4.0</td>
<td>0.193</td>
</tr>
<tr>
<td>Calcium supplement</td>
<td>6 (28.571)</td>
<td>11 (47.826)</td>
<td>0.190</td>
</tr>
<tr>
<td>TSH (µIU/mL)*</td>
<td>2.35 (1.28–3.30)</td>
<td>0.06 (0.02–0.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FT3 (pmol/L)*</td>
<td>4.60 (4.28–4.94)</td>
<td>5.94 (5.50–6.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FT4 (pmol/L)*</td>
<td>15.73 (14.57–18.07)</td>
<td>25.89 (23.54–29.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PTH (pg/mL)</td>
<td>39.21±14.65</td>
<td>40.67±17.05</td>
<td>0.832</td>
</tr>
<tr>
<td>Ca (mmol/L)</td>
<td>2.50±0.17</td>
<td>2.52±0.19</td>
<td>0.809</td>
</tr>
<tr>
<td>Duration of follow-up (month)*</td>
<td>24.4 (16.9–37.7)</td>
<td>7.2 (5.8–10.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline BMD (g/cm²)</td>
<td>0.827±0.122</td>
<td>0.896±0.111</td>
<td>0.055</td>
</tr>
<tr>
<td>Last BMD (g/cm²)</td>
<td>0.822±0.110</td>
<td>0.881±0.111</td>
<td>0.083</td>
</tr>
</tbody>
</table>

Results in the table: mean ± SD/n (%). *, median (Q1–Q3). BMI, body mass index; TSH, thyrotropin; FT3, free T3; FT4, free T4; PTH, parathyroid hormone; Ca, calcium; BMD, bone mineral density.

Figure 4 Curve fitting of lumbar BMD with a duration of follow-up (months) in postmenopausal patients and postmenopausal controls. After adjusting for factors of age, BMI, calcium supplement, and the serum level of TSH, FT3, FT4, PTH, and calcium. BMD, bone mineral density; BMI, body mass index; TSH, thyrotropin; FT3, free T3; FT4, free T4; PTH, parathyroid hormone.

Changes of BMD with a duration of TSH suppression in different calcium supplement groups

According to whether they took a calcium supplement or not, 70 patients were divided into the calcium supplement group (22 cases; 1,000 mg/day) and the non-calcium supplement group (48 cases). In both the calcium supplement group and the non-supplement group, the BMD of the lumbar spine decreased significantly with the increase of suppression time (regression coefficient: −0.121 and −0.147; P=0.027 and P<0.001, respectively). After adjusting for the factors of age, BMI, population grouping, risk of recurrence, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D, changes of BMD of the lumbar spine with time in different calcium supplementation groups had no statistically significant difference (P=0.534). We further analyzed the interaction between population grouping and calcium supplement intake, and the results showed that there was no interaction between the two factors (P>0.05) (Figure 5).
Followed up with 126 patients after a study showed that the trabecular bone microstructure was more prone to the deterioration. Our results were similar to those of the above studies, suggesting that BMD is more likely to decrease in postmenopausal women with DTC after TSH suppressive therapy. The study of De Mingo et al. [2018] showed that the trabecular bone fraction of postmenopausal women with DTC receiving TSH suppressive therapy was lower compared with that of premenopausal patients, suggesting that the bone microstructure was more prone to the deterioration. The study of Mohammadi et al. [2007] indicated that, in postmenopausal women with DTC, the bone mass decrease was more likely to occur in the early stage of TSH suppressive therapy. These conclusions suggest that we should intervene in postmenopausal women as early as possible. We should carry out osteoporosis education as soon as possible, increase the frequency of follow-up, and give anti-osteoporosis therapy as quickly as necessary.

We also found that, for the included patients in the study, a calcium supplement did not seem to improve BMD in the lumbar spine. As is well known, a calcium supplement is essential for the treatment of osteoporosis. In 1996, the study of Kung et al. [1996] showed that a calcium supplement could improve bone mass reduction in postmenopausal women who received TSH suppressive therapy after a DTC operation. Our results do not entirely agree with the above conclusions. However, there are differences between our experimental design and the research of Kung et al. [1996]. The main difference was that the patients included in our study were at intermediate or high risk of recurrence after total or subtotal DTC resection, whereas in the study of Kung et al. [1996], there was no strict requirement for risk stratification. Moreover, the mean age of patients in the study of Kung et al. [1996] was 63.4±7 years, which was higher than the mean age of postmenopausal women in our study (57.2±7 years). In addition, only 23 postmenopausal women were included in our study. Among these 23 patients, 11 were supplemented with calcium, and 12 were not supplemented with calcium. Therefore, all of these factors may lead to different conclusions between our work and the study of Kung et al. [1996]. Our results suggest that, for the selected patients in

Figure 5 Curve fitting of lumbar BMD with a duration of TSH suppression (month) in different calcium supplement groups. Notes: After adjusting for factors of age, BMI, population grouping, risk of recurrence, the dose of L-thyroxine, and the serum level of TSH, FT3, FT4, PTH, calcium, and 25-hydroxyvitamin D. BMD, bone mineral density; TSH, thyrotropin; BMI, body mass index; FT3, free T3; FT4, free T4; PTH, parathyroid hormone.

**Discussion**

TSH can affect bone metabolism and BMD in various ways. TSH receptor (TSHR) exists in osteoblasts and osteoclasts. TSH can combine with TSHR to form a ligand-receptor complex, which directly affects bone reconstruction. TSH can also directly affect osteoclasts and osteoblasts. Takada et al. reported that TSH can suppress the formation and survival of osteoclasts through JNK/c-jun and NF-kB signaling pathways of RANK-L, thus affecting the function of osteoclasts. TSH affects the formation of osteoclasts by inhibiting the TNF-α response and suppresses the differentiation of osteoclasts by down-regulating Wnt and VEGF signals. TSH can affect osteoblasts by suppressing the expression of type 1 collagen in Runx-2 and transcription factors, thus inhibiting bone absorption and bone formation. All of these suggest the importance of TSH in bone metabolism. Subclinical hyperthyroidism caused by long-term TSH suppressive therapy will break the dynamic balance between osteoblasts and osteoclasts and will interfere with the process of bone metabolism. Furthermore, with the increase of treatment time, the bone density of some patients will be affected. This can partially explain our first conclusion. We found that the overall BMD value of all patients in the study decreased significantly with the increasing duration of TSH suppression, and this reduction was not affected by age and BMI.

Kim et al. [2015] followed up with 126 patients after a DTC operation. They found that TSH suppressive therapy accelerated bone loss, predominantly in postmenopausal women and exclusively during the early post-thyroidectomy period. Similarly, Kung et al. [1996] followed up with 46 postmenopausal DTC patients for 2 years and found that TSH suppressive therapy was associated with a bone mass reduction. Our results were similar to those of the above studies, suggesting that BMD is more likely to decrease in postmenopausal women with DTC after TSH suppressive therapy. The study of De Mingo et al. [2018] showed that the trabecular bone fraction of postmenopausal women with DTC receiving TSH suppressive therapy was lower compared with that of premenopausal patients, suggesting that the bone microstructure was more prone to the deterioration. The study of Mohammadi et al. [2007] indicated that, in postmenopausal women with DTC, the bone mass decrease was more likely to occur in the early stage of TSH suppressive therapy. These conclusions suggest that we should intervene in postmenopausal women as early as possible. We should carry out osteoporosis education as soon as possible, increase the frequency of follow-up, and give anti-osteoporosis therapy as quickly as necessary.
Our study had some limitations. We only studied the BMD of the lumbar spine, while the BMD data of the hip and the femoral neck were not included. Moreover, for osteoporosis, it would be more meaningful if some morphological markers of vertebral fractures were also added to the study. Also, the BMD measured by DXA is not a sensitive marker to indicate the change of bone strength. Some studies have shown that the BMD measured by DXA is relatively slow compared with the change of disease, and thus cannot reflect the trivial changes effectively and in a timely manner (33,34). Furthermore, the number of patients in our group was limited. When we analyzed the subgroups, the number of patients in each subgroup was relatively small, which might affect the accuracy of the results. Finally, our median follow-up time would have benefited from being longer. It is possible that BMD changes in male and premenopausal females were not significant in short follow-up time.

Conclusions
The lumbar BMD of DTC patients decreased significantly after operation and ¹³¹I therapy, especially in postmenopausal women. During the period of TSH suppression, calcium supplementation alone seems not to be sufficient enough to improve bone health estimated by lumbar BMD.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.ameresgroups.com/article/view/10.21037/gs-22-50/rc


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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted following the principles of the Declaration of Helsinki (as revised in 2013) and was approved by the ethics committee of the Third Affiliated Hospital of Soochow University [approval No. (2020) WD-018]. Written informed consent was obtained from the patients.

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