# High Prevalence of Radiological Vertebral Fractures in Women on Thyroid-Stimulating Hormone–Suppressive Therapy for Thyroid Carcinoma

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**Context:** Bone loss and nonvertebral fractures have been reported in patients with differentiated thyroid carcinoma (DTC) undergoing thyroid-stimulating hormone (TSH) suppressive therapy. Radiological vertebral fractures (VFs) are an early and clinically crucial marker of bone fragility.

**Objective and Design:** A cross-sectional study to evaluate the prevalence and determinants of radiological VFs in women receiving L-thyroxine (L-T4) therapy for DTC.

**Patients and Interventions:** A total of 179 consecutive women (median age, 59 years; n = 178 postmenopausal) who had undergone thyroidectomy for DTC and were currently receiving L-T4 were evaluated for radiological VFs and bone mineral density (BMD). There were three TSH target levels [<0.5 mU/L, group 1 (n = 83); 0.5 to 1.0 mU/L, group 2 (n = 50); >1.0 mU/L, group 3 (n = 46)].

**Results:** VFs were found in 51 patients (28.5%), with significantly ($P < 0.001$) higher prevalence in group 1 (44.6%) as compared with group 2 (24.0%) and group 3 (4.3%). VF prevalence was not significantly different among patients in group 1 with normal BMD, osteopenia, or osteoporosis, whereas in groups 2 and 3, VFs were more frequent in patients with osteoporosis than in those with either osteopenia or normal BMD. In the whole population, VFs were significantly and independently associated with TSH level <1.0 mU/L; densitometric diagnosis of osteoporosis at lumbar spine, femoral neck, or total hip; age of patients; and duration of L-T4 therapy.

**Conclusion:** The prevalence of VFs was high in women with DTC who were undergoing long-term, suppressive L-T4 therapy. (*J Clin Endocrinol Metab* 103: 956–964, 2018)

Thyroid hormones have physiological stimulatory effects on bone remodeling and bone mineralization, and normal euthyroid status during childhood and adolescence is required for acquisition of peak bone mass (1). However, when thyroid hormone levels increase, bone remodeling is excessively stimulated, with consequent bone loss, decrease in bone mineral density (BMD), and increase in fracture risk (2). Interestingly, an increased risk of fragility fractures has been reported even in patients exposed to mild excess of thyroid hormones, because it occurs during over-replacement of primary and central hypothyroidism (3–5).

Differentiated thyroid cancer (DTC) arising from thyroid follicular epithelial cells accounts for the vast

majority of thyroid cancers. Papillary thyroid cancer is found in about 85% of cases, compared with about 12% in cases with follicular histology, including conventional and oncocytic (Hürthle cell) carcinomas; and <3% being poorly differentiated tumors (6). DTC expresses TSH receptor on the cell membrane and TSH stimulates cell growth rate (7). Suppression of TSH by supraphysiologic doses of L-thyroxine (L-T4) is commonly used to treat patients with DTC with the aim of decreasing the recurrence risk (8–10). However, the consequent, chronic subclinical hyperthyroidism may be responsible for undesired effects, such as atrial fibrillation, major cardiovascular events, and osteoporosis (11).

Several studies and meta-analyses have reported an association between subclinical thyroid hormone excess and risk of fractures, mainly in postmenopausal women (4, 12–18). However, most of the data on fracture risk in these patients with subclinical hyperthyroidism were based on a retrospective historical assessment of the prevalence of clinical fractures, whereas data on vertebral fractures (VFs) are scanty (12). Indeed, VFs are the most common complication of osteoporosis (19) and are associated with decreased survival (20) and impaired quality of life (21). Moreover, in patients with DTC who may have secondary localization at the bone level, the finding of a VF raises the issue of differential diagnosis between osteoporosis and bone metastasis (22). Because only about one-third of VFs are clinically recognized (19), the radiological and morphometric approach has emerged as the method of choice for evaluating the true prevalence and incidence of these fractures in population and clinical studies (23). To our knowledge, this approach has not been used to investigate the VF risk in patients with DTC who are receiving TSH suppressive therapy.

In this cross-sectional study, we evaluated the prevalence and determinants of radiological VFs in patients with DTC who were undergoing L-T4 therapy with different serum TSH target levels.

## Study population and protocol

A total of 179 women (median age, 59 years; range, 42 to 82 years) attending outpatient endocrine clinics in the period from 2012 to 2017 were consecutively enrolled in this cross-sectional study (Supplemental Table 1). All but one of the women were postmenopausal. The inclusion criteria were as follows: (1) female sex, (2) histological diagnosis of DTC, (3) treatment with L-T4 for at least 1 year before study entry, (4) serum TSH values stable since the time of first tumor restaging after thyroid surgery with or without radioactive iodine (RAI) therapy, and (5) availability to be studied for BMD and VFs. The following were the exclusion criteria: (1) bone metastases,

(2) treatment with drugs that could cause secondary osteoporosis (24), and (3) treatment with anti-osteoporotic drugs (except for calcium and vitamin D). The clinical data were collected from a questionnaire administered at the study entry and from the information available in the clinical files. Staging of DTC was assessed according to American Joint Committee on Cancer criteria TNM system (10).

At the study entry, 144 of 179 patients were receiving treatment with vitamin D3 (combined with calcium in 75 patients), and serum 25-hydroxyvitamin D was measured in each patient within 3 months before the enrollment. Information on family history of osteoporosis and fractures was collected for each patient.

L-T4 treatment was performed according to clinical judgment and international guidelines available at the time of patient evaluation in the endocrine clinics (9, 10). During the follow-up after surgery and RAI therapy, serum TSH and free thyroxine (FT4) values were measured every 4 to 6 months for the first 5 years and then, for patients with longer follow-up, every 12 months. For the purpose of the study, we considered the last available biochemical data before the study entry. Based on serum TSH values during L-T4 therapy, patients were subdivided in three groups: group 1 (n = 83 cases; TSH values <0.5 mU/L), group 2 (n = 50 cases; TSH values between 0.5 and 1.0 mU/L), group 3 (n = 46 cases; TSH values >1.0 mU/L). Per inclusion criteria, all patients had stable TSH values within each group for the whole period of follow-up. The primary end point was the evaluation of VFs in patients with suppressed TSH values (group 1) as compared with those with higher serum TSH values (groups 2 and 3). The secondary end points were evaluation of the relationship between VFs and duration of L-T4 therapy, and of the relationship between VFs and BMD at different skeletal sites.

The protocol was approved by local ethics committee and the patients gave the informed consent to the study.

## Assessment of VFs and BMD

VFs were assessed by a quantitative morphometric approach using spine radiographs (25). Using a translucent digitizer and a cursor, six points were marked on each vertebral body to describe the vertebral shape. Anterior (Ha), middle (Hm), and posterior (Hp) vertebral heights were measured and height ratios (Hp/Hm, Hp/Ha, Hm/Ha) were calculated for each vertebral body from T5 to L4; the fractures were defined as mild, moderate, or severe on the basis of a height ratio decrease of 20% to 25%, 26% to 40%, and >40%, respectively. The analyses were performed by three experienced physicians (G.M., A.M.F., and S.F.). The intraobserver and interobserver coefficients of variation

were between 1% and 4% and 3% and 6%, respectively, in relation to the skeletal site (lumbar vs thoracic) and severity (mild vs severe) of VFs.

BMD was measured by dual-energy X-ray absorptiometry (DXA) at the total hip, femoral neck, and lumbar spine (QDR-4500W; Hologic, Waltham, MA). DXA results were expressed as a T-score comparing the results with those obtained in a sex-matched white population at the peak of bone mass (26). A T-score $\leq -2.5$ standard deviations at either skeletal site was defined as osteoporosis, whereas osteopenia was defined as a T-score between $-1.0$ and $-2.5$ standard deviations. Lumbar vertebrae affected by artifacts or involved by fractures were excluded from the BMD analysis. The coefficients of variation in the DXA measurements for BMD, bone mineral content, and area were 0.614%, 2.981%, and 2.89%, respectively.

## Biochemical assays

Fasting blood samples were collected for measurement of serum FT4 and TSH. Serum concentrations of TSH (reference range, 0.35 to 4.2 mIU/L; analytical sensitivity 0.004 mIU/L; intra- and interassay coefficients of variation, 2.5% and 5.7%, respectively) and of FT4 (reference range, 8.0 to 18.0 pg/mL analytical sensitivity 1.0 pg/mL; intra-assay and interassay coefficients of variation, 2.4% and 6.8%, respectively) were measured using a fully automated Architect i2000 analyzer (Abbott Diagnostics, Abbott Park, IL) based on chemiluminescent magnetic immunoassay. Serum 25-hydroxyvitamin D was measured by RIA (DiaSorin, Saluggia, Italy). The sensitivity of the test was 1.5 ng/mL and the intra-assay coefficient of variation ranged from 8.6% to 12.5%. Hypovitaminosis D was defined as values of 25-hydroxyvitamin D <30 ng/mL.

## Statistical analysis

Data were presented as median and range, unless otherwise stated. $\chi^2$ (or Fisher exact test, when necessary), Kruskall-Wallis, and Mann-Whitney nonparametric tests were used to compare categorical and quantitative data. Multivariate logistic regression was implemented to evaluate relationship between covariates and VFs in the whole population of enrolled patients. $P < 0.05$ was considered statistically significant.

## Results

### Whole population

#### Clinical characteristics

Clinical characteristics of the patients are listed in Supplemental Table 1. Papillary thyroid carcinoma was the most frequent tumor histotype (57%) and most patients had an intrathyroidal tumor without invasion of extraglandular structures (T1-T2, 78.8%) and/or without lymph node localization (N0, 85.5%) and distant metastases (M0, 96.0%). The median duration of L-T4 therapy was 5.0 years (range, 1 to 45 years) and the median L-T4 dose at the time of study entry was 100 μg/d (range, 50 to 175 μg/d; Supplemental Table 1).

Osteopenia and osteoporosis were found in 88 (49.2%) and 52 (29.1%) patients, respectively. Fifty-one patients (28.5%) had VFs, which were moderate to severe in 20 patients (11.2%) and/or multiple in 15 patients (8.4%)(Supplemental Table 1).

### Determinants of VFs

Patients with fractures had received RAI therapy more frequently; had lower serum TSH and higher serum FT4 values; were treated with a higher daily dose of L-T4 and for a longer time; had lower BMD T-score at the lumbar spine and femoral neck, and more frequently had osteopenia and osteoporosis, as compared with patients who did not have fractures (Table 1). Moreover, patients with fractures were less frequently treated with vitamin D3 plus calcium and more frequently treated with vitamin D alone, as compared with patients without VFs (Table 1). Stratifying the patients for tertiles of duration of L-T4 therapy, prevalence of VFs increased significantly after 6 years of therapy (Fig. 1).

Multivariate logistic regression analysis showed that VFs were significantly and independently associated with TSH levels <1.0 mU/L, densitometric diagnosis of osteoporosis at either skeletal site (lumbar spine, femoral neck, or total hip), age, and duration of L-T4 therapy (Table 2).

### Groups stratified based on TSH values

#### Clinical characteristics

Patients in group 1 had more advanced TNM stage of DTC, had received more frequent RAI therapy, were treated with a higher daily dose of L-T4 and for a longer period of time, and had higher serum FT4 values than patients in groups 2 and 3 (Supplemental Table 2). Moreover, patients in groups 1 and 2 were significantly younger than patients in group 3 (Supplemental Table 2).

Patients in group 1 had a lower BMD T-score at the femoral neck and total hip as compared with patients in groups 2 and 3, without a statistically significant difference in lumbar spine BMD T-score (Supplemental Table 2). The prevalence of osteoporosis was higher in group-1 patients than those in groups 2 and 3, and there were no significant differences between groups 2 and 3 (Supplemental Table 2).

**Table 1.  Demographic and Clinical Features of Women With VFs as Compared With Those Who Did Not Have VFs**

|  | No VF | VF | P Value[a] |
|---|---|---|---|
| Patients, No. | 128 | 51 |  |
| Age, y | 60 (42–79) | 63 (47–82) | 0.159 |
| RAI therapy, No. (%) | 83 (64.8) | 49 (96.1) | <0.001 |
| Duration of L-T4 therapy, y | 5 (1–26) | 6 (1–45) | 0.006 |
| L-T4 dose, μg/d | 100 (50–175) | 125 (50–175) | 0.02 |
| Serum TSH, mU/L | 0.80 (0.005–1.60) | 0.15 (0.004–1.20) | <0.001 |
| Serum FT4, pg/mL | 11.0 (8.50–16.8) | 13.0 (9.00–17.00) | <0.001 |
| Serum 25OH-vitamin D, ng/mL | 27 (7–54) | 30 (11–46) | 0.43 |
| Treatment of hypovitaminosis D, No. (%) |  |  | 0.01 |
| No therapy | 24 (18.8) | 11 (21.6) |  |
| Vitamin D3 alone | 42 (32.8) | 27 (52.9) |  |
| Vitamin D3 plus calcium | 62 (48.4) | 13 (25.5) |  |
| Family history of osteoporosis or fractures, No. (%) | 56 (43.8) | 29 (56.9) | 0.11 |
| LS BMD T-score | −1.10 (−3.60 to +2.80) | −1.90 (−3.40 to +2.30) | 0.001 |
| FN BMD T-score | −1.00 (−3.40 to +2.30) | −1.55 (−2.70 to +1.00) | 0.02 |
| TH BMD T-score | −0.90 (−2.90 to +3.40) | −0.50 (−2.20 to +0.20) | 0.99 |
| BMD categories, No. (%) |  |  | <0.001 |
| Normal | 34 (26.6) | 5 (9.8) |  |
| Osteopenia | 68 (53.1) | 20 (39.2) |  |
| Osteoporosis | 26 (20.3) | 26 (51.0) |  |

Data are given as median (range) unless otherwise indicated.

Abbreviations: 25OH-vitamin D, 25-hydroxyvitamin D; FN, femoral neck; LS, lumbar spine; TH, total hip.

[a]Comparisons were performed by nonparametric tests.

### Determinants of VFs

Patients in group 1 had a higher prevalence of total (44.6%), moderate/severe (18.1%), and multiple (14.5%) VFs as compared with patients in groups 2 and 3 (Fig. 2). Moreover, patients in group 2 had a higher prevalence of total VFs than patients in group 3 (24.0% vs 4.3%; $P$ = 0.008; Fig. 2). The differences in total VFs among the three groups were statistically significant regardless of BMD values (Fig. 3). Moreover, in group 1, the prevalence of total VFs was not significantly different

($P$ = 0.13) among patients with normal BMD (30.8%), osteopenia (37.1%), or osteoporosis (57.1%), whereas VFs were more frequent in patients with osteoporosis (62.5%) than with either osteopenia (18.8%) or normal BMD (10.0%) in group 2 ($P$ = 0.02; Fig. 3). In the presence of osteoporosis, the prevalence of VFs was not significantly different between groups 1 and 2 (57.1% vs 62.5%; $P$ = 0.78; Fig. 3).

No significant differences in prevalence of VFs were found among FT4 tertiles within each TSH group (Fig. 4).
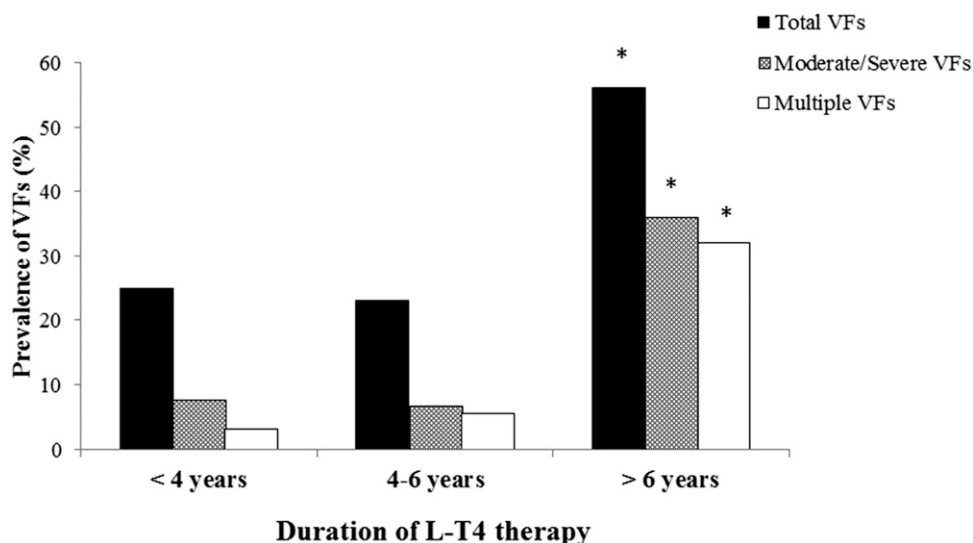


**Figure 1.** Prevalence of VFs in 179 women with DTC who were stratified for tertiles of duration of L-thyroxine (L-T4) therapy.*$P$ < 0.05 for third tertile vs first and second tertiles.

**Table 2.    Results of Multivariate Logistic Regression Analysis, Using Total VFs as the Dependent Variable**

|  | Odds Ratio | 95% CI | P Value |
|---|---|---|---|
| Age | 1.08 | 1.02–1.14 | 0.01 |
| Osteoporosis | 3.64 | 1.01–13.25 | 0.05 |
| L-T4 dose | 0.97 | 0.96–1.01 | 0.06 |
| Duration of L-T4 therapy | 1.12 | 1.02–1.23 | 0.02 |
| TSH <0.5 mU/L | 25.04 | 2.62–238.88 | 0.005 |
| TSH 0.5–1.0 mU/L | 10.38 | 1.67–64.45 | 0.01 |
| Serum FT4 value | 0.99 | 0.77–1.26 | 0.92 |
| RAI therapy | 3.35 | 0.59–18.97 | 0.17 |
| Treatment with vitamin D3 plus calcium | 0.65 | 0.42–1.02 | 0.06 |

Abbreviation: CI, confidence interval.

## Discussion

In this cross-sectional study, radiological VFs were found in about one-third of women with DTC who were undergoing postsurgical L-T4 therapy and correlated with duration of treatment, degree of TSH suppression, and age of patients. Interestingly, VFs were found even in patients with normal BMD, mainly when the TSH level was <0.5 mU/L.

The effects of thyroid hormone on bone metabolism are well established, ranging from impaired skeletal development in childhood hypothyroidism to an increased risk for osteoporosis in hyperthyroidism (27). The pathogenesis of bone damage due to thyroid hormone excess is multifactorial, including shortening of the bone remodeling cycle and acceleration of bone turnover (1). Indeed, thyroid hormones indirectly promote osteoclast formation and activation by inducing the expression of cytokines, prostaglandins, and the receptor activator of nuclear factor-$\kappa$ B ligand (28). Moreover, there is experimental evidence that TSH may exert direct effects on bone turnover with a specific inhibitory effect on bone resorption (29, 30). Therefore, effects on bone metabolism that were previously ascribed solely to high thyroid hormone levels could also be attributed to suppressed TSH levels (31). It has been hypothesized that low TSH values may contribute to bone loss in patients with hyperthyroidism, especially when the thyroid hormone excess is mild, such as in subclinical hyperthyroidism characterized by a low or undetectable concentration of serum TSH with free triiodothyronine and FT4 levels within laboratory reference ranges (32).

Exogenous subclinical hyperthyroidism is therapeutically induced by supraphysiologic doses of L-T4 in patients with DTC after thyroidectomy and RAI therapy to prevent tumor recurrence and eventually improve patient survival (9, 10). Several studies have reported an increase in bone turnover and decrease in BMD due to TSH suppressive therapy, especially in postmenopausal women and older men (11). Data on fractures in this clinical setting are scanty and produced by retrospective historical and questionnaire-based studies mostly focused on nonvertebral fractures (13–18). The effect of TSH suppressive therapy on VFs is still largely unknown because previous studies only looked at clinical VFs (14, 15), which represent a minority of the vertebral osteoporotic events, in heterogeneous populations including patients with exogenous and endogenous subclinical hyperthyroidism (12). It is noteworthy that VFs, even if mild, single, and asymptomatic, are always a hallmark of skeletal fragility predisposing patients to develop incident fragility fractures (33–36). Therefore, a radiological and morphometric analysis is mandatory to identify patients with VFs (23).

This was a clinical study evaluating the prevalence and determinants of radiological VFs in patients receiving chronic L-T4 therapy for DTC. When TSH was suppressed due to supraphysiologic dose of L-T4, VFs were
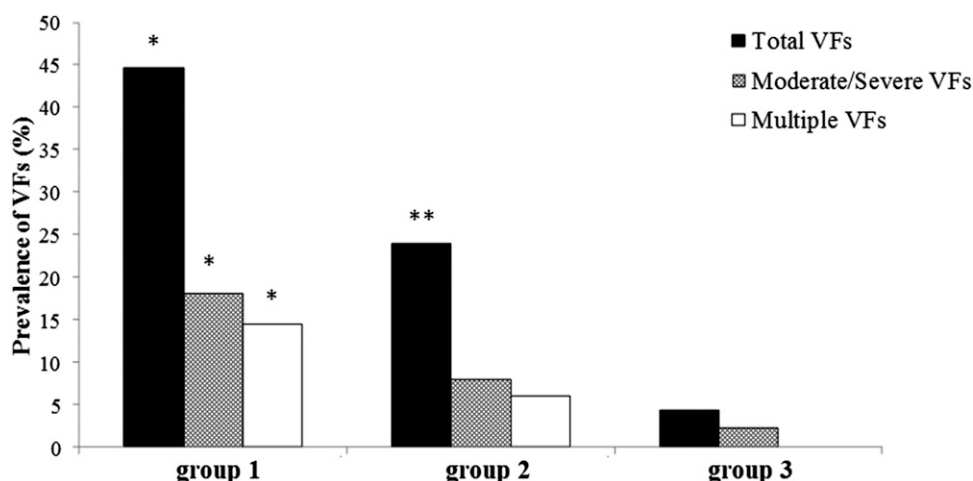


**Figure 2.** Prevalence of total, moderate/severe, and multiple VFs in patients stratified for serum TSH values (<0.5 mU/L, group 1; 0.5 to 1.0 mU/L, group 2; >1.0 mU/L, group 3). *P < 0.05 vs groups 2 and 3; **P < 0.05 vs group 3.
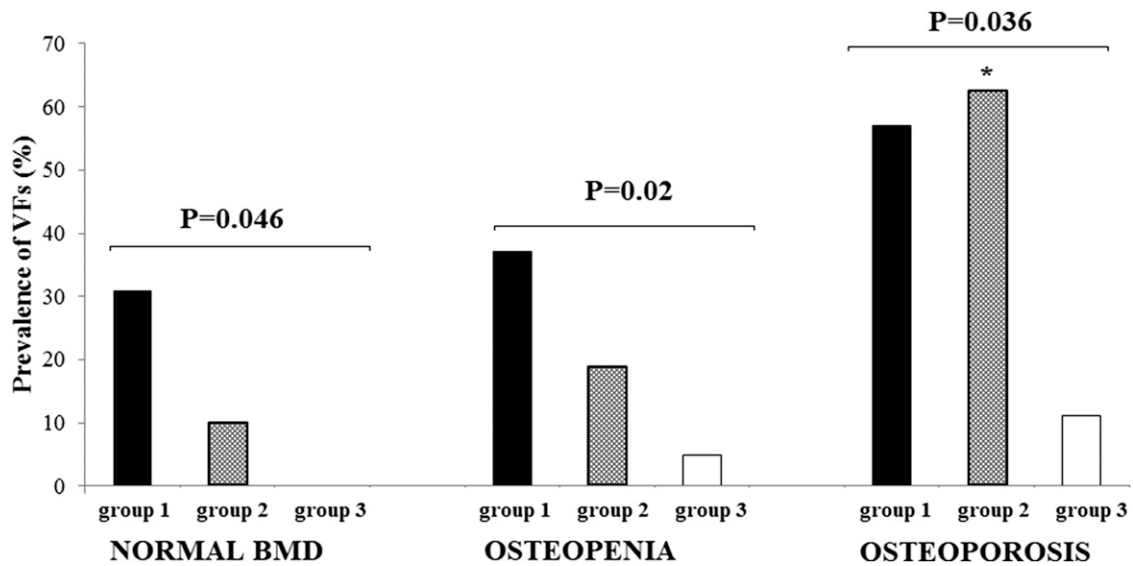
**Figure 3.** Prevalence of VFs in patients stratified for BMD categories (*i.e.*, normal BMD, osteopenia, and osteoporosis) and TSH values, as described in the text and the Fig. 2 legend. *$P < 0.05$ vs osteopenia and normal BMD.

found in about 40% of cases. This prevalence was comparable and even higher than that reported in other well-known forms of secondary osteoporosis (37–39), providing additional evidence that exogenous subclinical hyperthyroidism may cause skeletal fragility and fractures. Interestingly, VFs were moderate to severe in approximately one-half on patients who had fractures and multiple in approximately one-third, suggesting that these fractures may be also clinically relevant for their potential impact on quality of life and survival (20, 21). When TSH values were between 0.5 and 1.0 mU/L, about 25% of the women developed VFs, and the VF prevalence increased to >50% in the presence of densitometric diagnosis of osteoporosis. Interestingly, in these women, as

well as in those with suppressed TSH values, the prevalence of VFs was not influenced by serum FT4 values. These results are in agreement with previous observations in untreated, euthyroid, postmenopausal women with low-normal TSH values and concomitant low BMD (40), consistent with the hypothesis that low TSH levels *per se*, regardless of thyroid function or L-T4 therapy, may influence skeletal health and risk of fractures.

In several forms of drug-induced osteoporosis, fragility fractures are an early complication of the treatment (24, 41–43). In this series of patients with DTC who were undergoing L-T4 suppressive therapy, prevalence of VFs increased significantly only after 5 years of treatment. This finding is in agreement with results of a previous
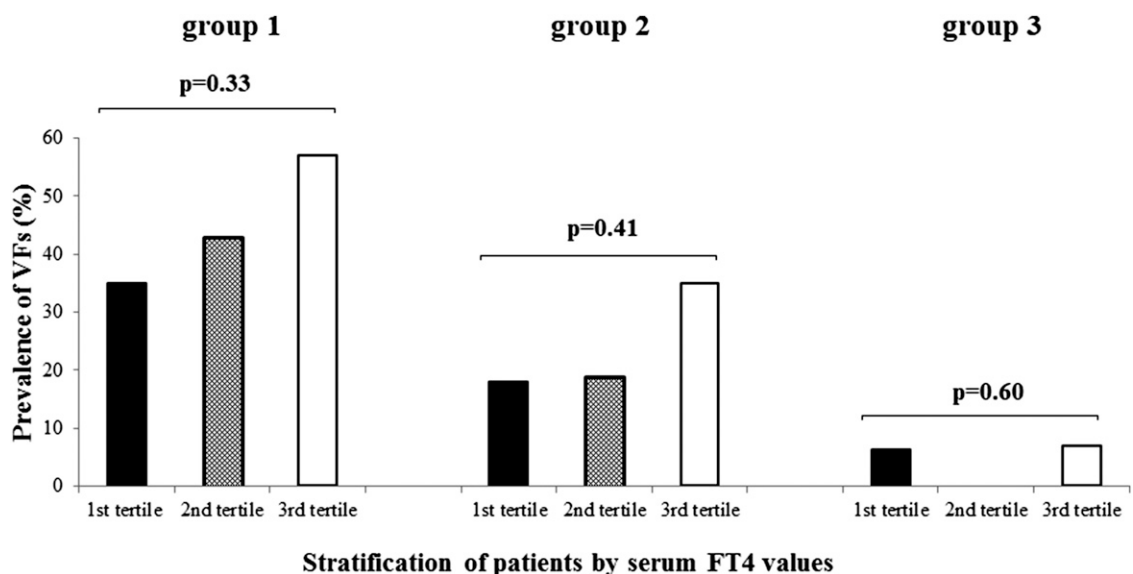


**Figure 4.** Prevalence of VFs in patients stratified for serum FT4 values within each therapeutic group defined in the text and the Fig. 2 legend.

population-based study in which a strong association was found between hip fracture and long-standing exposure to low TSH values (44). And the finding is reassuring about the skeletal safety of L-T4 suppressive therapy when used for a few years after thyroidectomy and RAI therapy in patients with DTC who have an intermediate risk of recurrence (10).

Previous studies did not clarify whether BMD could be a reliable marker of skeletal fragility in patients with DTC. In our patients, densitometric diagnosis of osteoporosis was an independent predictor of VFs, as demonstrated in women with postmenopausal osteoporosis (45). However, VFs also frequently occurred in patients with normal BMD, mainly when TSH was suppressed as an effect of L-T4 therapy. This finding is consistent with the concept that the skeletal damage induced by altered bone turnover caused by subclinical hyperthyroidism may not be always detected by DXA scan (46). This already has been demonstrated in other forms of secondary osteoporosis in which bone quality is generally affected more than bone quantity (41, 42, 47). The mechanisms responsible for the impairment in bone quality caused by subclinical hyperthyroidism are unknown. We could speculate that, whereas thyroid hormone excess causes predominantly an increase in bone resorption, suppressed TSH values may also inhibit bone formation (48), determining an uncoupled bone turnover responsible for a severe deterioration of bone microstructure that cannot be completely captured by DXA (48, 49). Previous studies have reported that TSH suppressive therapy may cause abnormalities in trabecular bone microstructure, as detected by trabecular bone score measurement (49) and peripheral high-resolution quantitative computed tomography (50); the current study demonstrated the actualization of this, thus far, theoretical risk.

These previous findings, along with the results of our study, may raise concerns and uncertainty in choosing the L-T4 dose and TSH targets in patients with DTC patients. The current guidelines suggest using DXA measurement of BMD to guide therapeutic-decision-making and stratify the fracture risk(10). Our study findings confirm that patients with osteoporosis are at high risk of VFs, but they also provide evidence that even patients with normal BMD may experience fracture when exposed to long-term suppression of TSH values.

The prevention and treatment of bone loss induced by thyroid hormone excess is still a matter of controversy, because the effects of bisphosphonates on BMD were shown to be variable (51, 52) and data on fractures are still lacking (53). Our study did not address this specific issue, because women treated with bone-active drugs were not enrolled. However, we found lower prevalence of VFs in women treated with vitamin D3 plus calcium as compared with either those treated with vitamin D3 alone or those who were untreated, which is consistent with the concept that vitamin D in combination with calcium may be more effective than vitamin D alone in preventing fractures (54).

There are some limitations to our study to be acknowledged and discussed. The cross-sectional design did not allow us to determine the onset of VFs during L-T4 therapy, as well as subsequent VF risk after decreasing L-T4 doses. However, the results deriving from the association analysis suggest that VFs may not be an early complication of L-T4 therapy and reduction of the L-T4 dose restoring TSH levels to >1 mU/L may normalize the fracture risk. The assignment of patients to different L-T4 regimens (i.e., TSH suppressive vs replacement therapies) was not randomized but based on clinical judgment and current guidelines (9, 10), and this approach allowed us to provide information on fracture risk induced by L-T4 therapy in real-life clinical practice. Another concern is that TSH measured on a single occasion may not reflect the overall suppression of TSH over time. To partly address this shortcoming, we enrolled patients with stable L-T4 therapy and TSH values during the years after thyroid surgery and RAI therapy. Finally, we did not enroll a sex- and age-matched group of patients without diagnosis of thyroid cancer for comparison with our study groups. However, we have previously demonstrated that in 263 postmenopausal women with hormone receptor-positive early breast cancer, the prevalence of VFs was only 18.9% in aromatase inhibitor-naive patients and increased to 31.2% only in those assessed during aromatase inhibitor therapy; these data apparently are lower than those reported here for women with DTC who were receiving TSH suppressive therapy (42)

The aforementioned limitations notwithstanding, the results of this study may provide some practical insights into the management of DTC. In current guidelines, DXA BMD is the only skeletal parameter considered among the factors influencing the indication of the optimal TSH target levels during L-T4 therapy (10, 55). Conversely, our study supports the importance of a first-line morphometric evaluation of VFs in all patients in whom a TSH-suppressive regimen is started, because VFs can occur even when BMD is normal. Moreover, the current guidelines recommend maintaining TSH values at the lowest end of the normal range when the risk of DTC recurrence is low (10). In this regard, concerns may arise from our study about the potential risk of VFs when TSH values are between 0.5 and 1.0 mU/L in patients with DTC who have a densitometric diagnosis of osteoporosis. Therefore, before opting for a moderate suppression of

TSH in patients at low risk for DTC, based on our results, a second-line morphometric study is recommended when DXA BMD results indicate a patient is in the osteoporotic range. Finally, based on the high prevalence of VFs, morphometric evaluation should also be considered the method of choice for the evaluation of skeletal health during the follow-up of patients with DTC who are undergoing long-term suppressive TSH treatment.

In conclusion, the results of study showed, in women with DTC who were undergoing long-term suppressive L-T4 therapy, a high prevalence of VFs, likely due to an impairment of bone quality. Vertebral morphometry at baseline and during follow-up should be performed in patients with DTC whose TSH levels are suppressed.

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