Ten-year estimated risk for bone fracture in women with differentiated thyroid cancer under TSH-suppressive levo-thyroxine therapy

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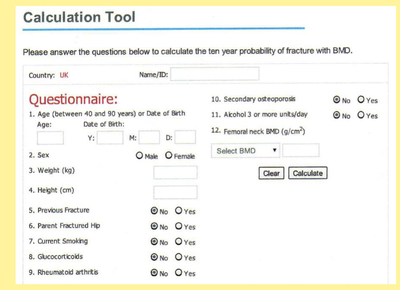
Background

After thyroidectomy (Tx) and radioiodine (RAI) therapy patients with differentiated thyroid cancer (DTC) are indefinitely treated with L-thyroxine (L-T4) to suppress TSH levels. Osteporosis is a debated consequence of hyperthyroxinemia.

Aim

The aim of this study was to evaluate bone mineral density (BMD) and the fracture risk assessment tool (FRAX) in a cohort of DTC women

Methods



FRAX tool calculate 10-year probability hip fracture (HF) and major osteoporotic fracture (MOF) in subjects aged from 40 to 90 yrs.

DXA was performed with Hologic instruments at L2- L4 and femoral sites.

Esaote equipment was used for neck sonography. Thyroid hormones, TSH, hyroglobulin, TgAb were available in all subjects.

Subjects

Seventy-four women with DTC diagnosed (stage 1-4; n=63 PCT, n=10 FvPTC, n=1 FTC) and treated (Tx 95%, RAI 73%) at the age of 51.9±12.0 yrs, were studied. Except for 4 Hispanic and 2 Asian women, all were Italian. L-T4 was started 78 months (median; range 12-229 mo) before Tx for goiter in 11% of patients. Baseline BMD measured by DXA of the lumbar spine and FRAX score calculated on femoral neck BMD were evaluated 3.0 yrs (median; range <1.0 - 27 yrs) after diagnosis. The age at this time was 56.5 ± 9.9 yrs (median 56 yrs; range 40-80 yrs) and 78% of patients were postmenopausal. BMD and FRAX evaluations were repeated after 5.0 yrs (median; range 2-14 yrs). Some clinical data are reported in table 1.

Table 1

	Baseline	2nd evaluation	Significance
Age (yrs; mean ± SD)	56.5 ± 9.9	61.5 ± 9.8	P<0.0001
BMI (kg/m²; mean ± SD)	26.0 ± 5.3	26.1 ± 5.0	NS
Menopausal state (%)	78	85	NS
Disease free for DTC recurrence (%)	99	99	NS
Subject with diseases involving bone (%) (1)	19	22	NS
Calcium/vitamin D supplementation (%)	24	62	P<0.0001
Under bone resorption inhibitor drugs (%)	22	32	NS

(1) primary hyperparathyroidism, thyrotoxicosis, malabsorption, rheumatoid arthritis; other

Table 2

	Baseline	2nd evaluation	Significance
TSH (mIU/l)	0.66 ± 1.22 (0.16)	0.23 ± 0.32 (0.07)	P=0.001
f-T4 (pg/ml)	15.9 ± 2.7 (16.1)	16.0 ± 2.6 (16.0)	NS
Time on L-T4 (months)	70.9 ± 70.7 (48)	140.7 ± 115.8 (124)	P<0.0001
BMD (gr/cm squared)	0.923 ± 0.167 (0.906)	0.938 ± 0.163 (0.933)	NS
HF (%)	1.2 ± 2.0 (0.6)	1.9 ± 3.2 (1.1)	P<0.0001
MOF (%)	5.0 ± 4.1 (3.9)	6.8 ± 6.3 (5.3)	P<0.001

Results are reported as mean ± SD, with medians in brackets.

Results

L-T4 dosages were 813.6 ± 208.8 µg/week and 782.1 ±184.4 µg/week at the baseline and 2nd evaluation, respectively (P=0.1, NS). Adequate TSH concentrations under moderate hyperthyroxinemia were more often observed on follow-up than on baseline evaluation, without significant changes in BMD (L2-L4) (table 2). Significant age-related changes in FRAX were found from the baseline to the 2nd evaluation (table 2, figure 1), with the probability of HF increasing more than that of MOF. A significant inverse correlation emerged between L-T4 dosage and HF/MOF probability, both at the baseline and the 2nd evaluation (figure 2). No correlation was noted between HF/MOF changes and length L-T4 therapy, f-T4 and TSH levels

Figure 1

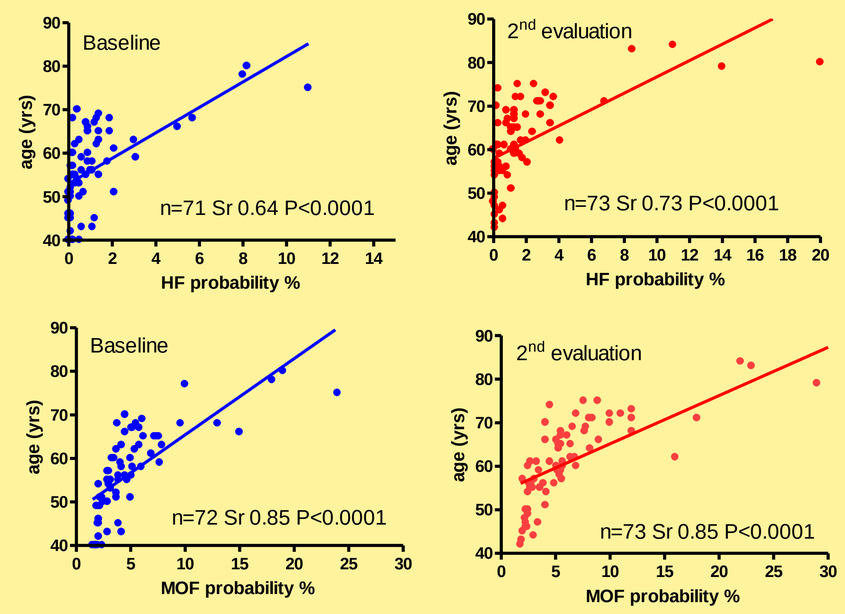
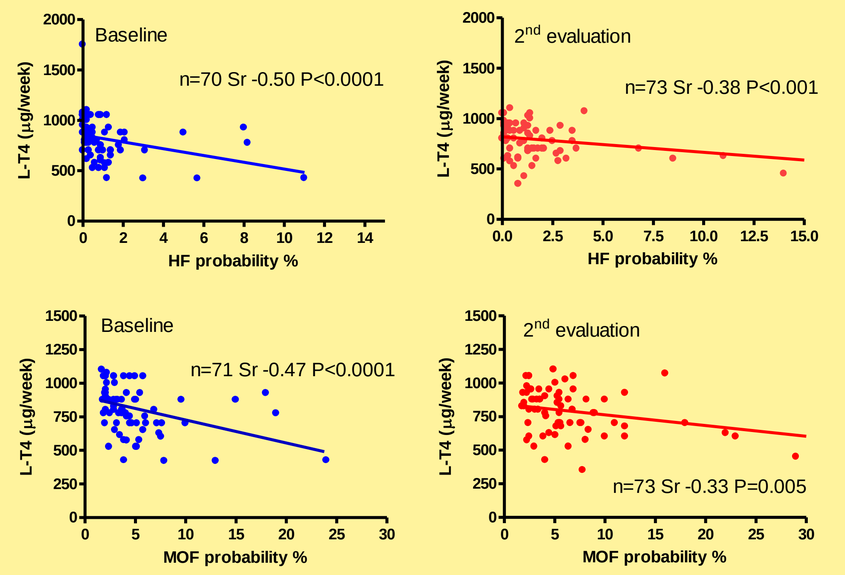


Figure 2



Conclusion

In conclusion, FRAX increase seems to be an age-related multi-factorial phenomenon. In DTC women, lumbar BMD does not change as much as FRAX. The absence of positive correlations between L-T4 dosage, length of therapy or f-T4 levels and FRAX does not allow us to attribute an increased fracture risk to DTC women with therapeutically well-controlled disease. A larger population of DTC patients and a longer period of observation may yield more conclusive data.