The effect of TSH suppression therapy on the cortical bone geometry in the patients with differentiated thyroid cancer

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Introduction & Objective

- Subclinical hyperthyroidism has been reported to increase the fracture risk. However, the effect of thyroid stimulating hormone (TSH) suppressive therapy on bone geometry in the hip area of patients with differentiated thyroid carcinoma (DTC) is still unclear.
- The aim of this study was to investigate the effect of TSH suppression on bone geometry in the hip area of pre- and postmenopausal women with DTC.

Subjects and Methods

- We conducted a retrospective cohort study including 99 women with DTC (25 pre- and 74 postmenopausal) who had received TSH suppressive therapy for at least 3 years and 297 control subjects (75 and 222, respectively) matched for sex and age.
- BMD in the spine and hip area and bone geometry at the proximal femur measured by DXA were compared between patients and controls.
- The association between thyroid hormone and bone parameters was investigated.
- All analyses of bone parameters were adjusted for age, BMI, and serum calcium levels.

Results

Subjects characteristics in the patient and control groups

	Premenopausal				Postmenopausal			
	Patient group (n=25)	Control group (n=75)	GEE analyses 95% CI	*p*	Patient group (n=74)	Control group (n=222)	GEE analyses 95% CI	*p*
Age (year)[a]	45.8 ± 3.1	45.8 ± 3.0			61.4 ± 7.6	61.4 ± 7.6		
BMI (kg/m^2)	22.6 ± 2.6	22.1 ± 2.8	-0.60 to 1.60	0.415	24.4 ± 3.5	23.0 ± 2.5	0.61 to 2.20	0.001*
Duration of DTC (years)	3.8 ± 1.2				5.2 ± 3.4			
Creatinine (mg/dL)	0.7 ± 0.1	0.7 ± 0.1	-0.07 to 0.03	0.512	0.7 ± 0.2	0.7 ± 0.1	-0.03 to 0.05	0.598
Total Calcium (mg/dL)	8.3 ± 0.8	8.7 ± 0.3	-0.72 to -0.10	0.009*	8.6 ± 0.6	9.0 ± 0.4	-0.54 to -0.24	< 0.001*
Phosphate (mg/dL)	3.7 ± 0.8	3.6 ± 0.6	-0.25 to 0.44	0.577	4.0 ± 0.6	3.8 ± 0.7	0.08 to 0.39	0.003*
25(OH)D (ng/mL)[b]	26.6 ± 3.2	16.7 ± 1.7	3.57 to 16.19	0.002*	29.1 ± 2.8	22.5 ± 1.3	0.52 to 12.64	0.033*
Dose of LT4 (μg/day)								
At evaluation	136.5 ± 20.1				133.5 ± 33.5			
Three-year average[c]	150.3 ± 17.2				141.7 ± 30.1			
TSH (mIU/L)[d]								
At evaluation	0.07 (0.09)	2.19 (1.56)	-3.54 to -2.55	< 0.001*	0.10 (0.14)	2.41 (1.71)	-3.47 to -2.74	< 0.001*
Three-year average[c]	0.11 (0.15)				0.14 (0.17)			
Free T4 (ng/dL)								
At evaluation	1.67 ± 0.27	1.09 ± 0.11	0.475 to 0.683	< 0.001*	1.74 ± 0.32	1.09 ± 0.14	0.57 to 0.72	< 0.001*
Three-year average[c]	1.76 ± 0.27				1.75 ± 0.28			

[a]Age was at the Dual-energy X-ray absorptiometry (DXA) evaluation
[b]Data were available in 13 and 45 premenopausal patients and controls, and in 33 and 111 postmenopausal patients and controls
[c]The average value during three years prior to the DXA evaluation
[d]Log-transformed variables were used in statistical analyses.
*$p < 0.05$

The comparison of bone parameters between patient and control group

	Premenopausal				Postmenopausal			
	Patient group (n=25)	Control group (n=75)	GEE analyses[a] 95% CI	*p*	Patient group (n=74)	Control group (n=222)	GEE analyses[a] 95% CI	*p*
BMD								
FN Z- or T-score[b]	0.08 ± 0.86	-0.25 ± 0.84	0.003 to 0.685	0.048*	-0.97 ± 0.91	-0.90 ± 0.85	-0.389 to 0.105	0.260
TH Z- or T-score[b]	0.42 ± 0.83	0.42 ± 0.73	-0.413 to 0.549	0.782	-0.47 ± 0.96	-0.26 ± 0.88	-0.568 to -0.028	0.031*
LS Z- or T-score[b]	0.29 ± 0.99	0.05 ± 0.94	-0.198 to 0.792	0.240	-0.84 ± 1.22	-0.70 ± 1.16	-0.565 to 0.079	0.139
FN BMD (g/cm^2)	0.93 ± 0.10	0.90 ± 0.09	-0.009 to 0.069	0.138	0.82 ± 0.11	0.83 ± 0.10	-0.052 to 0.006	0.116
TH BMD (g/cm^2)	0.98 ± 0.10	0.96 ± 0.08	-0.033 to 0.057	0.596	0.88 ± 0.12	0.91 ± 0.11	-0.064 to 0.002	0.063
LS BMD (g/cm^2)	1.21 ± 0.11	1.18 ± 0.12	-0.036 to 0.084	0.439	1.04 ± 0.14	1.07 ± 0.14	-0.081 to -0.004	0.030*
Geometry at proximal femur								
HAL (cm)	102.3 ± 4.3	101.3 ± 5.0	-2.03 to 2.63	0.802	100.8 ± 4.7	100.7 ± 5.1	-1.54 to 0.93	0.631
CSMI (cm^4)	9717 ± 2039	9184 ± 1704	-66.1 to 1312.2	0.076	7911 ± 1824	8072 ± 1776	-1097.1 to -76.2	0.028*
CSA (cm^2)	140.5 ± 12.9	134.5 ± 13.8	0.75 to 11.80	0.026*	120.5 ± 16.6	123.6 ± 17.0	-11.31 to -0.96	0.020*
CT, neck (cm)	5.4 ± 1.5	5.0 ± 1.3	-0.29 to 1.17	0.235	4.9 ± 1.3	5.1 ± 1.6	-0.72 to -0.01	0.045*
CT, shaft (cm)	5.0 ± 0.9	4.8 ± 0.9	-0.14 to 0.76	0.179	4.8 ± 0.9	4.8 ± 1.1	-0.36 to 0.14	0.402
Section modulus (cm^3)	560.0 ± 98.3	566.7 ± 79.6	-4.81 to 71.09	0.087	481.0 ± 94.6	498.7 ± 95.9	-64.53 to -11.88	0.004*
Buckling ratio	3.3 ± 1.2	3.5 ± 0.9	-0.70 to 0.44	0.656	3.7 ± 1.2	3.4 ± 1.1	-0.05 to 0.52	0.111

FN, femoral neck; TH total hip; LS, lumbar spine; HAL, hip axis length; CSMI, cross-sectional moment of inertia; CSA, cross-sectional area; CT, cortical thickness.
[a]GEE analyses was adjusted for age, BMI and total calcium.
[b]Z-score was compared in premenopausal women and T-score was compared in postmenopausal women.
*$p < 0.05$

Multivariable linear regression analysis between serum free T4 levels and bone parameters in patient group

Dependent variable	Premenopausal B	Premenopausal *p*	Postmenopausal B	Postmenopausal *p*
BMD				
FN Z- or T-score	1.307	0.038*	0.187	0.521
TH Z- or T-score	1.056	0.094	0.054	0.871
LS Z- or T-score	-0.072	0.920	0.067	0.874
FN BMD (g/cm^2)	0.086	0.273	0.022	0.512
TH BMD (g/cm^2)	0.119	0.121	0.005	0.901
LS BMD (g/cm^2)	-0.066	0.452	0.009	0.854
Geometry at proximal femur				
HAL (cm)	-4.230	0.219	-0.079	0.964
CSMI (cm^4)	578.9	0.704	-1483.6	0.022*
CSA (cm^2)	-3.768	0.159	-0.089	0.505
CT, neck (cm)	1.822	0.130	0.178	0.712
CT, shaft (cm)	0.067	0.922	-0.126	0.699
Section modulus (cm^3)	37.25	0.614	-74.43	0.021*
Buckling ratio	-1.405	0.144	-0.132	0.775

*$p < 0.05$

The comparison of bone parameters between patient with free T4 level > 1.79 and control subjects

	Premenopausal				Postmenopausal			
	Patient group (n=8)	Control group (n=24)	GEE analyses[a] 95% CI	*p*	Patient group (n=29)	Control group (n=87)	GEE analyses[a] 95% CI	*p*
BMD								
FN Z- or T-score[b]	0.60 ± 0.73	-0.24 ± 0.68	0.393 to 1.185	<0.001*	-0.93 ± 1.05	-0.79 ± 0.83	-0.771 to 0.118	0.150
TH Z- or T-score[b]	0.69 ± 0.64	0.47 ± 0.69	-0.914 to 0.468	0.572	-0.47 ± 1.07	-0.15 ± 0.90	-0.980 to -0.076	0.022*
LS Z- or T-score[b]	0.52 ± 0.92	0.18 ± 0.78	-0.035 to 0.835	0.071	-0.80 ± 1.18	-0.56 ± 1.21	-0.915 to -0.016	0.042*
FN BMD (g/cm^2)	0.94 ± 0.11	0.90 ± 0.08	-0.011 to 0.092	0.124	0.82 ± 0.12	0.85 ± 0.10	-0.101 to 0.002	0.061
TH BMD (g/cm^2)	1.00 ± 0.09	0.96 ± 0.07	-0.021 to 0.083	0.246	0.88 ± 0.13	0.92 ± 0.11	-0.117 to -0.009	0.021*
LS BMD (g/cm^2)	1.18 ± 0.11	1.19 ± 0.09	-0.048 to 0.052	0.935	1.05 ± 0.13	1.09 ± 0.15	-0.120 to -0.018	0.008*
Geometry at proximal femur								
HAL (cm)	100.7 ± 3.7	102.2 ± 4.0	-4.85 to 1.76	0.360	100.3 ± 5.0	101.1 ± 4.9	-3.72 to 0.19	0.076
CSMI (cm^4)	9117 ± 1660	9385 ± 1599	-1013.1 to 836.5	0.852	7195 ± 1138	8262 ± 1885	-2324.9 to -1042.2	<0.001*
CSA (cm^2)	140.5 ± 13.1	135.0 ± 13.6	-1.27 to 13.72	0.103	117.2 ± 15.8	125.8 ± 18.2	-21.89 to -5.84	0.001*
CT, neck (cm)	5.8 ± 1.6	4.8 ± 1.5	-0.21 to 2.09	0.111	4.6 ± 1.2	5.1 ± 1.5	-1.17 to -0.08	0.025*
CT, shaft (cm)	5.0 ± 0.9	4.8 ± 0.8	-0.46 to 0.92	0.515	4.6 ± 0.9	4.8 ± 1.0	-0.62 to -0.02	0.049*
Section modulus (cm^3)	582.7 ± 83.6	577.3 ± 76.4	-32.56 to 56.84	0.595	448.6 ± 66.7	508.7 ± 103.5	-131.10 to -57.60	<0.001*
Buckling ratio	3.0 ± 1.1	3.6 ± 0.9	-1.26 to 0.07	0.081	3.8 ± 1.2	3.4 ± 1.0	-0.14 to 0.88	0.153

[a]GEE analyses was adjusted for age, BMI and total calcium.
[b]Z-score was compared in premenopausal women and T-score was compared in postmenopausal women.
*$p < 0.05$

The comparison of bone parameters between patient with free T4 level ≤ 1.79 and control subjects

	Premenopausal				Postmenopausal			
	Patient group (n=17)	Control group (n=51)	GEE analyses[a] 95% CI	*p*	Patient group (n=44)	Control group (n=132)	GEE analyses[a] 95% CI	*p*
BMD								
FN Z- or T-score[b]	-0.17 ± 0.83	-0.25 ± 0.91	-0.384 to 0.494	0.807	-1.01 ± 0.83	-0.96 ± 0.86	-0.308 to 0.229	0.774
TH Z- or T-score[b]	0.29 ± 0.89	0.39 ± 0.76	-0.480 to 0.799	0.625	-0.45 ± 0.90	-0.32 ± 0.87	-0.455 to 0.174	0.383
LS Z- or T-score[b]	0.19 ± 1.03	-0.01 ± 1.01	-0.522 to 0.973	0.555	-0.87 ± 1.27	-0.77 ± 1.13	-0.533 to 0.323	0.631
FN BMD (g/cm^2)	0.93 ± 0.10	0.90 ± 0.10	-0.036 to 0.072	0.446	0.81 ± 0.10	0.83 ± 0.10	-0.039 to 0.025	0.658
TH BMD (g/cm^2)	0.97 ± 0.10	0.97 ± 0.09	-0.071 to 0.057	0.833	0.89 ± 0.11	0.90 ± 0.11	-0.047 to 0.030	0.661
LS BMD (g/cm^2)	1.23 ± 0.11	1.18 ± 0.13	-0.056 to 0.126	0.449	1.04 ± 0.15	1.06 ± 0.14	-0.077 to 0.028	0.365
Geometry at proximal femur								
HAL (cm)	103.0 ± 4.4	100.9 ± 5.4	-1.36 to 4.42	0.300	101.0 ± 4.4	100.5 ± 5.3	-1.04 to 1.91	0.561
CSMI (cm^4)	9999 ± 2183	9090 ± 1758	190.2 to 2102.4	0.019*	8353 ± 2054	7964 ± 1706	-515.1 to 740.5	0.725
CSA (cm^2)	140.5 ± 13.3	134.3 ± 14.1	-2.16 to 14.31	0.148	122.6 ± 17.1	122.3 ± 16.1	-7.15 to 5.11	0.745
CT, neck (cm)	5.2 ± 1.5	5.0 ± 1.2	-0.71 to 1.14	0.648	5.0 ± 1.3	5.1 ± 1.6	-0.72 to 0.23	0.310
CT, shaft (cm)	5.0 ± 0.9	4.7 ± 0.9	-0.35 to 0.84	0.423	4.8 ± 0.9	4.8 ± 1.2	-0.36 to 0.33	0.929
Section modulus (cm^3)	608.1 ± 105.9	561.6 ± 81.4	-7.92 to 107.87	0.091	500.9 ± 105.3	492.9 ± 91.3	-33.97 to 27.75	0.844
Buckling ratio	3.5 ± 1.3	3.4 ± 0.9	-0.66 to 0.97	0.704	3.7 ± 1.3	3.4 ± 1.1	-0.16 to 0.55	0.288

[a]GEE analyses was adjusted for age, BMI and total calcium.
[b]Z-score was compared in premenopausal women and T-score was compared in postmenopausal women.
*$p < 0.05$

Summary

- In premenopausal subjects, bone parameters were not deteriorated by TSH suppression.
- In postmenopausal subjects, DTC patients showed poor bone geometry at the femoral neck than those of control subjects, whereas their femoral neck BMD was comparable with controls.
- The alteration of femoral neck bone geometry became more prominent in the postmenopausal patients with free T4 levels > 1.79 ng/dL.

Conclusion

TSH suppression decreased bone strength in postmenopausal DTC patients by altering bone geometry rather than BMD in the hip area, especially the proximal femur.

17 ECE
1-GP-27
Thyroid cancer & Thyroid
Jae Hoon Moon
DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY