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Treatment of subclinical hyperthyroidism: effect on body composition

Diana Boj Carceller[1], Alejandro Sanz París[1], Enrique Sánchez Oriz[2], Rafael García-Foncillas López[2], Pilar Calmarza Calmarza[3], Vicente Blay Cortes[4] and M.ª Dolores Abós Olivares[5]

[1]Hospital Universitario Miguel Servet, Department of Endocrinology & Nutrition. [2]Department of Biostadistics and Public Health, University of Zaragoza. [3]Hospital Universitario Miguel Servet, Service of Clinical Biochemistry. [4]Hospital General de la Defensa Orad y Gajías, Department of Endocrinology. [5]Hospital Universitario Miguel Servet, Department of Nuclear Medicine. Spain.

Abstract

Background: **subclinical hyperthyroidism (SHT) is associated with harmful effects on cardiovascular system, bone metabolism and progression to clinical hyperthyroidism.**

Loss of weight is a common fact in patients with clinical hyperthyroidism and of particular relevance in elderly patients.

Objective: **to assess changes in body composition after radioiodine therapy for SHT due to toxic nodular goiter.**

Subjects and methods: **prospective controlled cohort study. Patients with persistent SHT due to toxic nodular goiter were purposed to receive treatment with radioiodine (treatment group) or to delay treatment until the study was over (control group). All treated patients received 555 MBq of ^{131}I.**

Body composition (lean mass, fat mass and bone mineral content) was determined by dual-energy X-ray absorptiometry (DEXA) at baseline and 12 months after.

Results: **twenty-nine patients were studied (age 69.5 ± 11.5; 75.9% women; BMI 27.1 ± 5.7 kg/m^2; serum thyrotropin (TSH) 0.20 ± 0.21 μUI/mL; serum free thyroxine (T4) 1.01 ± 0.19 ng/dL), 17 belonging to the treatment group and 12 to the control group.**

Study groups were comparable, although there was a trend for the treatment group to have more fat mass.

No longitudinal changes in body composition were noted in either group, except for a trend to gain fat mass. However, when individuals with age > 65 years were selected, only patients who received radioiodine therapy showed a significant increase in body weight (from 64.1 ± 10.0 to 66.9 ± 9.2 kg), BMI (from 27.3 ± 4.8 to 28.7 ± 4.5 kg/m^2), fat mass (from 26.1 ± 8.5 to 27.8 ± 7.9 kg), lean mass (from 36.3 ± 0.4 to 37.4 ± 0.4 kg) and skeletal muscle mass index (SMI) (from 6.0 ± 0.6 to 6.3 ± 0.6 kg/m^2).

Correspondence: Diana Boj-Carceller.
Hospital Universitario Miguel Servet,
Department of Endocrinology & Nutrition.
Paseo Isabel La Católica, 1-3, 50009, Zaragoza, Spain.
E-mail: dbojcarc@gmail.com

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TRATAMIENTO DEL HIPERTIROIDISMO SUBCLÍNICO: EFECTO SOBRE LA COMPOSICIÓN CORPORAL

Resumen

Introducción: **el hipertiroidismo subclínico (HS) se asocia a efectos deletéreos sobre el sistema cardiovascular, el metabolismo óseo y puede progresar a hipertiroidismo clínico. La pérdida de peso es habitual en los pacientes con hipertiroidismo clínico y adquiere especial relevancia en los sujetos añosos.**

Objetivo: **evaluar los cambios en la composición corporal después del tratamiento del HS por bocio nodular con radioyodo.**

Sujetos y métodos: **estudio de cohortes prospectivo controlado. A los pacientes con HS persistente debido a bocio nodular tóxico se les ofreció la opción de recibir tratamiento con radioyodo (grupo tratamiento) o retrasar dicho tratamiento hasta que el estudio hubiera acabado (grupo control). Al final, todos los pacientes recibieron 555 MBq de ^{131}I.**

La composición corporal (masa magra, masa grasa y contenido mineral óseo) se determinó por absorciometría con rayos X de doble energía (DEXA) al inicio y a los 12 meses.

Resultados: **se estudiaron 29 pacientes (edad 69,5 ± 11,5; 75,9% mujeres; BMI 27,1 ± 5,7 kg/m^2; tirotropina sérica (TSH) 0,20 ± 0,21 μUI/mL; tiroxina libre sérica(T4) 1,01 ± 0,19 ng/dL), 17 pertenecientes al grupo tratamiento y 12 al grupo control.**

Los grupos de estudio fueron comparables, aunque existía una tendencia del grupo tratamiento a presentar más masa grasa. No se detectaron cambios en la composición corporal en ningún grupo, salvo una tendencia general a ganar masa grasa. Sin embargo, cuando se seleccionaron los individuos con edad > 65 años, sólo los pacientes que recibieron tratamiento con radioyodo mostraron un significativo incremento de peso (de 64,1 ± 10,0 a 66,9 ± 9,2 kg), IMC (de 27,3 ± 4,8 a 28,7 ± 4,5 kg/m^2), masa grasa (de 26,1 ± 8,5 a 27,8 ± 7,9 kg), masa magra (de 36,3 ± 0,4 a 37,4 ± 0,4 kg) e índice de masa muscular esquelética (de 6,0 ± 0,6 a 6,3 ± 0,6 kg/m^2).

Conclusions: **treatment of SHT has impact on body composition in subjects older than 65 years. Weight gain reflects increases in fat and, more interestingly, in lean mass.**

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Key words: *Subclinical hyperthyroidism. Body composition. Radioiodine. Goiter. Hyperthyroidism.*

Conclusiones: **el tratamiento del HS tiene impacto sobre la composición corporal en sujetos mayores de 65 años. La ganancia de peso refleja incrementos en la masa grasa y, lo que es más interesante, en la masa magra.**

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Palabras clave: *Hipertiroidismo subclínico. Composición corporal. Radioyodo. Bocio. Hipertiroidismo.*

Abbreviations

SHT: subclinical hyperthyroidism.
OHT: overt hyperthyroidism.
DEXA: dual-energy X-ray absorptiometry.
TSH: serum thyrotropin.
T4: serum free thyroxine.
T3: serum free triiodothyronine.
SMI: skeletal muscle mass index.
BMD: bone mineral density.
FM: fat mass.
MM: lean mass.
BIA: bioelectrical impedance analysis.
RAI: radioiodine.
rs: Spearman's correlation coefficient.

Introduction

Subclinical hyperthyroidism (SHT) is defined by a low serum thyrotropin (TSH) level, under the reference range (0.45 to 4.5 mIU/L), and normal serum free thyroxine (T4) and/or triiodothyronine (T3) levels.

The prevalence depends on age, sex and iodine ingestion. In the NHANES III survey[1], SHT was founded in 0.7% of the U.S. population (excluding those taking thyroid replacement therapy).

In elderly people, toxic nodular goiter is the most prevalent etiology of endogenous SHT[2]. Endogenous SHT might have more clinical impact than exogenous SHT because of its chronic character and higher levels of T3[3].

The main related adverse effects of SHT include cardiovascular disease, with increase risk of atrial fibrillation[4,5] and cardiovascular death[6,7], but also all-cause mortality[7].

The risk of progression to overt hyperthyroidism (OHT) varies between studies 1-15% / year, depending on the concentration of TSH (high probability if the serum TSH is suppressed) and the underlying pathology (most likely if the cause is nodular goiter)[8].

In most studies, postmenopausal women with SHT have bone mineral density (BMD) decreased, especially at the cortical bone[9,10]. There is less data on these effects in men and premenopausal women.

Sarcopenia, whose concept includes loss of lean mass, is a relevant clinical problem in elderly people with risk of adverse outcomes such as physical disability, poor quality of life and mortality[11]. Causes of secondary sarcopenia also include hyperthyroidism.

It is well known that OHT is associated with loss of weight, despite of an increase in the caloric content of the diet and the recovery of the euthyroidism status is associated with weight gain.

However, changes in body composition following treatment of OHT have been hardly studied.

The results presented so far are rather mixed. Some authors have shown that bone mass, fat mass (FM) and lean mass (MM) increase in parallel[12].

Lönn *et al*. described that initially after treatment, patients recovered only MM, but at 12 months it was also found an increase in FM[13].Whilst, other groups have reported that weight gain reflects only increments of the MM[14,15]. Two studies using methodology based on the BIA showed only increases in FM[16,17] (Table I).

In the case of SHT, only one work has addressed this issue[18]. Greenlund *et al*. studied 21 women with SHT who were treated with high doses of radioiodine (RAI) and reevaluated after 6 months of normal thyroid function. Fat free-mass determined by DEXA increased from a mean of 40.3 Kg to 42.2 Kg and FM increased in a similar magnitude. BMD also increased in a significant way.

The indications for treatment of SHT are matter of discussion, but in elderly individuals, despite of the absence of supportive data from intervention trials[19], clinicians might consider treatment due to the possible cardiovascular risk. In this context, RAI therapy is a definitive, safe and effective option of treatment.

Further investigation of the impact of SHT on body composition is required, specially in older people, where the probability of clinical adverse outcomes is higher. The aim of our study was to assess changes in body composition after radioiodine therapy for SHT due to toxic nodular goiter.

Material and methods

Thirty-one patients with endogenous SHT due to nodular goiter were recruited prospectively over a 21-months period in the outpatient endocrinology unit of a tertiary referral hospital.

Inclusion criteria were older than 18 years, both sexes, persistent endogenous subclinical hyperthyroidism, nodular goiter (including toxic multinodular

Table I
Studies assessing body composition of hyperthyroid subjects before and after treatment

	n	*predominant disease*	*method*	*FM (Kg)*	*MM (Kg)*	*BM (Kg)*	*Time evolution*	*Reference*
Zimmermann *et al*. (1998)	10	GD	DEXA	+ 4.0	+ 5.0	n.e.	12 months	(12)
Lönn *et al*. (1998)	9	GD	DEXA	+ 3.5	+ 5.3	no	12 months	(13)
De la Rosa *et al*. (1997)	9	n.e.	DEXA	no	+ 7.2	no	13 months	(14)
Gómez-Acotto *et al*. (2002)	10	GD	DEXA	no	+ 1.9	no	24 months	(15)
Jacobsen *et al*. (2006)	8	n.e.	BIA	+ 3.5	no	-	12 months	(16)
P. Iglesias *et al*. (2006)	29	GD	BIA	+ 4.5	no	-	n.e.	(17)

n, number of patients; n.e., not specified; GD, Graves disease; DEXA, dual-energy X-ray absorptiometry; BIA, bioelectrical impedance analysis; FM, fat mass; MM, lean mass; BM, bone mass; no, no changes.

goiter and autonomous nodule) as underlying thyroid disease, not have received prior treatment for thyroid disease and candidates for treatment with ^{131}I .

Patients were excluded if they refused to participate, had a history of previous thyroid surgery, low TSH of another etiology , suspicion of malignancy, compressive symptoms, RAI therapy contraindication , serious medical illness or weight of loss> 10% in the 6 previous months.

Criteria for withdrawal were patient desire, non-compliance with the study protocol, development of clinical hyperthyroidism, appearance of serious illness or suspicion of malignancy.

The protocol was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki. Written informed consent was obtained from all participants after the nature of the study procedures were explained and prior to conducting any study-related procedures.

The diagnosis of SHT due to nodular goiter was based on biochemical findings (TSH level under the reference range < 0.34 μUI/mL and normal free T4 and T3 levels), technetium thyroid scintigraphy (to identify autonomous hyperfunctioning nodules) and thyroid ultrasound (to define nodules).

This prospective cohort study was designed following standard medical practice. Patients were offered the option of treatment with RAI (intervention group) or post-treatment follow-up at the end of the study, i.e., the option to defer RAI treatment (control group).

All patients received a single standard dose of ^{131}I of 15 mCi (555 MBq).

Body Composition

Assessment of lean mass, fat mass and bone mineral density was made at baseline and at the end of the study (12 months) using dual-energy x-ray absorptiometry scanning on a Hologic QDR 1000W scanner.

The body mass index (BMI) was calculated from the formula BMI = weight (Kg) / height^2 (m^2).

Body weight (Kg) was determined on a scale Soehnle Professional 2755 model, which has a maximum weight of 200 Kg and a precision of 100 g, with the patient without shoes and in light clothing. Height (cm) was measured with the metal stadiometer Asimed, whose measurement range is from 95 to 200 cm and has a precision of 1 mm, with the patient standing, fully stretched, placing feet in parallel.

The skeletal muscle mass index (SMI) was calculated as the sum of the muscle mass of the four limbs determined by DEXA divided by height (m^2).

Serum TSH and Thyroid Hormone Assays

Serum TSH was measured using a third generation automated sandwich 2-site chemiluminometric immunoassay (Bayer Advia, East Walpole, Massachusetts).

Serum T4 was measured by the direct dialysis method (Bayer Advia, East Walpole, Massachusetts).

Serum T3 was measured using an automated chemiluminometric immunoassay (Bayer Advia, East Walpole, Massachusetts).

Statistical methods

The Mann-Whitney U-test was used to test if groups were initially comparable. Within each group, before and after treatment measurements were compared using Wilcoxon Signed Rank Test.

Fisher's exact test was used to compare thyroid status between groups at the end of study.

The correlation between age and changes in body composition was determined by the Spearman's correlation coefficient (rs).

A p value <0.05 was considered to be statistically significant.

Data are presented as mean ± standard deviation.

The statistical analyses of our study was performed using SPSS statistical software version 17.0.

Results

Twenty-nine patients were finally included. Two patients in the treatment group were withdrawn because of non-compliance with the study protocol.

Population baseline characteristics (Table II) were age 69.5±11.5; 75.9% women (menopausal status did not change during the study in any patient); BMI 27.1±5.7 Kg/m^2; TSH 0.20±0.21 μUI/mL; T4 1.01±0.19 ng/dL. Most patients had multinodular goiter (just one case in the control group had a solitary autonomous nodule in scintigraphy and ultrasound). Time from first blood test showing hyperthyroidism was very variable.

There were no difference in body composition between groups, although there was a trend for the treatment group to have more fat mass (+ 5.0 Kg, p=0.051).

One year after RAI therapy, SCH was resolved in most (94.1%) patients, and "hypothyroidism" (low T4 with normal TSH) was mild and temporary in two patients at 4 and 8 months, respectively (5.9%). One (5.9%) of the treated patients progressed to overt mild hyperthyroidism at the end of the study and received again another dose of 15 mCi of ^{131}I.

In the control group, two (16.7%) patients finished the study with normal thyroid function, while two (16.7%) patients progressed to T3 thyrotoxicosis and eight (66.7%) maintained SHT .

Within each group, the statistical analysis for the comparisons before and after did not show significant differences (Table III). A trend to gain FM was observed in both groups (+1.3 Kg in the control group and +0.5 Kg in the treatment group).

In the treatment group, age correlated significantly with changes in body composition: weight gain (rs=0.692, p=0.002), BMI gain (rs=0.705, p=0.002), MM gain (rs=0.615, p=0.009) and with skeletal muscle mass index (SMI) change (rs=0.644, p=0.005) (Fig. 1). In contrast, in the control group age did not correlate with any change in body composition.

A subgroup analysis selecting individuals with age >65 was performed.

Only patients who had received RAI therapy showed a significant increase in body weight (from 64.1±10.0 to 66.9±9.2 Kg), BMI (from 27.3±4.8 to 28.7±4.5 Kg/m^2), FM (from 26.1±8.5 to 27.8±7.9 Kg), MM (from 36.3±0.4 to 37.4±0.4 Kg) and SMI (from 6.0±0.6 to 6.3±0.6 Kg/m^2) (Table IV).

Discussion

No changes were found in body composition after treatment of SHT in the whole population study. This result contrasts with the studies mentioned in the introduction[12-16]. They did find differences with a smaller

Table II
Baseline characteristics of the study population

	control group (n=12)	*treatment group (n=17)*	*p value*
age (years)	67.0 ± 12.0	71.2 ± 11.2	
sex (male/female)	3/9	4/13	
TSH (μUI/mL)	0.26 ± 0.27	0.15 ± 0.16	0.325
T4 (ng/dL)	1.0 ± 0.2	1.0 ± 0.2	0.711
T3 (pg/mL)	3.4 ± 0.6	3.4 ± 0.5	0.478
premorbid weight (Kg)	67.7 ± 21.1	71.8 ± 12.5	0.327
weight (Kg)	63.9 ± 21.3	69.5 ± 13.1	0.156
height (cm)	157.9 ± 10.3	157.7 ± 9.4	0.875
BMI (Kg/m^2)	25.9 ± 7.2	27.9 ± 4.4	0.184
FM (Kg)	22.3 ± 13.5	27.3 ± 8.5	0.051
MM (Kg)	39.9 ± 10.0	40.4 ± 9.4	0.626
BM (Kg)	1.8 ± 0.5	1.9 ± 0.6	0.690
BMD (g/cm^2)	1.01 ± 0.1	1.2 ± 0.5	0.658
t score	-1.3 ± 1.2	-0.8 ± 1.6	0.492
% FM	33.2 ± 9.0	39.0 ± 8.6	0.092
SMI (Kg/m^2)	6.6 ± 1.3	6.5 ± 1.2	0.866

TSH, serum thyrotropin; T4,serum free thyroxine; T3,serum free triiodothyronine; BMI, body mass index; FM, fat mass; MM, lean mass; BM, bone mass; BMD, bone mineral density; SMI, skeletal muscle mass index.
Mean ± S.D. and the proportion are shown where appropriate.

sample size. There could be several explanations for this fact.

All studies, except the Greenlund *et al*.[18], included only patients with OHT. The present study has evaluated the effect of treatment of SHT, that represents a milder degree of thyroid dysfunction, so it was expected that the effect size was the same.

Graves disease is the most prevalent pathology in all the studies. This thyroid disease is metabolically more active than toxic nodular goiter, which also may have influenced the magnitude of the differences.

The body composition analysis method used in the other studies has not always been the gold standard, so that the results are not always validated from the methodological point of view.

It is necessary to consider possible confounding variables (besides sex and age) when interpreting changes in body composition such as prevalence of obesity (30% in our study), previous weight loss related to SHT (-2.7 Kg in the control group and -0.1 Kg in the treatment group), duration of hyperthyroidism (330 days in the control group and 422 days in the treatment group) or development of hypothyroidism after RAI (2 cases of transient hypothyroidism in our study). These have not always been reported in all studies.

Only a trend to gain FM over time was observed in both groups (+ 1.3 Kg in the control group, p=0.084, and + 0.5 Kg in the treatment group, p=0.093), which could be a physiological phenomenon in the aging process.

The effect of age was analyzed as one of the typical confusion variable and a key factor for the indication of treatment in specific clinical situations[8].

Table III
Longitudinal changes in body composition

	Control Group			*Treatment Group*		
	before (n=12)	*after (n=12)*	*p value*	*before (n=17)*	*after (n=17)*	*p value*
weight (Kg)	63.9 ± 21.3	65.4 ± 20.8	0.272	69.5 ± 13.1	70.2 ± 10.3	0.227
height (cm)	157.9 ± 10.3	156.5 ± 12.4	0.400	157.7 ± 9.4	157.3 ±9.5	0.229
BMI (Kg/m^2)	25.9 ± 7.2	26.7 ± 6.9	0.084	27.9 ± 4.4	28.4 ± 3.7	0.124
FM (Kg)	22.3 ± 13.5	23.6 ± 13.2	0.084	27.3 ± 8.5	27.8 ± 6.8	0.093
MM (Kg)	39.9 ± 10.0	40.0 ± 10.4	0.875	40.4 ± 9.4	40.5 ± 7.8	0.407
BM (Kg)	1.8 ± 0.5	1.8 ± 0.5	0.136	1.9 ± 0.6	1.9 ± 0.5	0.943
BMD (g/cm^2)	1.0 ± 0.1	0.8 ± 0.7	0.937	1.2 ± 0.5	1.0 ± 0.2	0.679
t score	-1.3 ± 1.2	- 1.3 ± 1.1	0.722	-0.8 ± 1.6	-0.8 ± 1.3	0.682
% FM	33.2 ± 9.0	34.7 ± 8.9	0.136	39.0 ± 8.6	39.5 ± 7.2	0.309
SMI (Kg/m^2)	6.6 ± 1.3	6.5 ± 1.4	0.929	6.5 ± 1.2	6.5 ± 0.9	0.619

BMI, body mass index; FM, fat mass; MM, lean mass; BM, bone mass; BMD, bone mineral density; SMI, skeletal muscle mass index. Mean ± S.D.

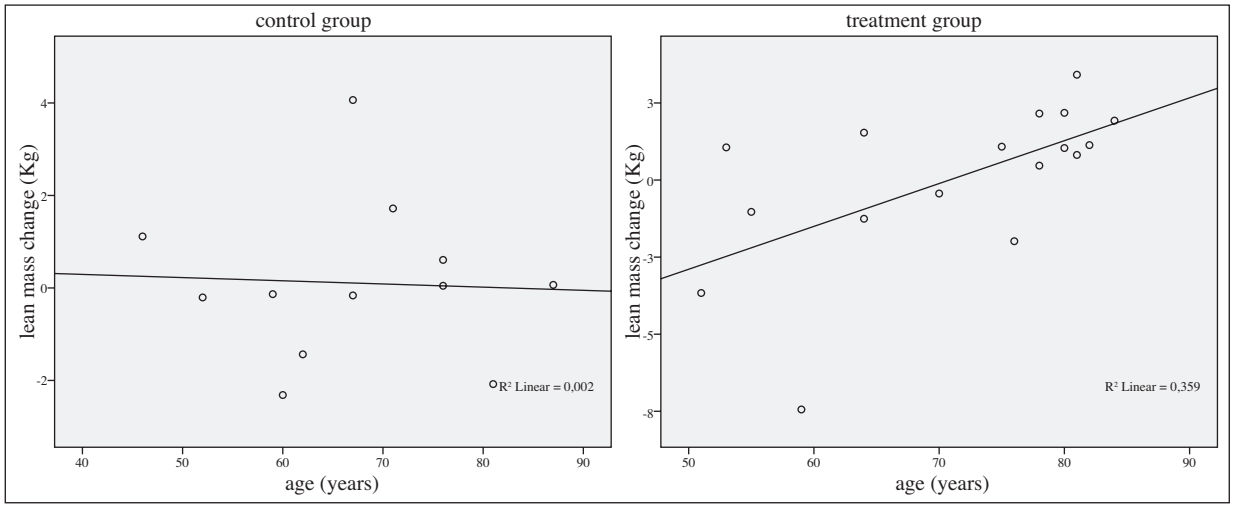

Fig. 1.—Scatter plot of age and changes of lean mass (difference before-after follow up) in each group.

Table IV
Longitudinal changes in body composition in older individuals

	Control Group			*Treatment Group*		
	before (n=7)	*after (n=7)*	*p value*	*before (n=11)*	*after (n=11)*	*p value*
weight (Kg)	60.2 ± 13.8	62.3 ± 14.4	0.310	64.1 ± 10.0	66.9 ± 9.2	0.010*
height (cm)	158.5 ± 12.8	157.8 ± 16.9	0.854	153.8 ± 7.9	153.0 ± 7.1	0.124
BMI (Kg/m^2)	24.7 ± 4.5	25.4 ± 3.2	0.398	27.3 ± 4.8	28.7 ± 4.5	0.004*
FM (Kg)	18.0 ± 0.7	19.5 ± 0.6	0.237	26.1 ± 8.5	27.8 ± 7.9	0.013*
MM (Kg)	40.4 ± 10.1	41.0 ± 11.1	0.398	36.3 ± 0.4	37.4 ± 0.4	0.033*
BM (Kg)	1.7 ± 0.6	1.8 ± 0.6	0.128	1.6 ± 0.5	1.8 ± 0.4	0.328
BMD (g/cm^2)	1.0 ± 0.1	0.7 ± 0.9	0.735	1.2 ± 0.6	1.0 ± 0.1	0.540
t score	-1.5 ± 1.4	-1.4 ± 1.4	0.396	-1.0 ± 1.4	-0.9 ± 1.3	0.672
% FM	29.8 ± 8.0	31.4 ± 7.6	0.499	40.1 ± 8.1	41.0 ± 7.0	0.248
SMI (Kg/m^2)	6.6 ± 1.2	6.8 ± 1.1	0.600	6.0 ± 0.6	6.3 ± 0.6	0.033*

BMI, body mass index; FM, fat mass; MM, lean mass; BM, bone mass; BMD, bone mineral density; SMI, skeletal muscle mass index.
Mean ± S.D.
*statistically significant result.

In the treatment group, age correlated significantly with weight gain (rs=0.692, p=0.002), BMI (rs=0.705, p=0.002), MM gain (rs=0.615, p=0.009) and improvement of SMI (rs=0.644, p=0.005). In the control group these correlations were not observed.

When only individuals age > 65 were selected, patients who have received RAI exhibited a significant gain of weight, BMI, FM and MM. The percentage of FM remained constant because the weight gain was the result of FM and MM gain.

The gain of MM and FM in this study was lower than in the Greenlund *et al.*[18]. Besides, bone mineral density (BMD) was unchanged in our study. It is unknown whether monitoring time beyond 12 months would yield positive data on bone mineralization. The fact that the control group has not changed its BMD down as expected over time makes prudent to extend the monitoring period at least another year.

The international guidelines for the management of SHT[20] consider the positive effect of restoring euthyroidism on bone metabolism in postmenopausal women. This is based on two studies. Mudde *et al.*[21] found that distal forearm BMD, expressed as a percentage of the base-line value, was significantly (P<0.05) higher in patients who had received treatment for SHT at 24 months after therapy. Faber *et al.*[22] found that spine and hip BMD of patients who received RAI (the median dose of ^{131}I administered was the same as in our study) did not go down over time, in contrast with the control group where patients experimented an annual loss of 2%.

The qualitative results obtained in this work in terms of increments of FM and MM are consistent with those reported by Lonn *et al.*[13] in patients with OHT . However, changes in the latter were higher, the sample size was the third part and the predominant pathology was different. In their study, DEXA showed as FM did not increase at 3 months, but it did at 12 months. Computerized Tomography scan was also used and detected an increase in intraperitoneal adipose tissue at 3 months, whereas at 12 months subcutaneous adipose tissue also increased. Similarly, DEXA detected an early increase in MM. The bone mineral content showed no improvement and this was attributed to a small sample size. Authors concluded that during the first months after normalization of thyroid function, the priority is to refill body skeletal muscle and intraperitoneal adipose tissue, whereas subcutaneous adipose tissue increases thereafter.

Several studies support from a physiological perspective the former changes in body composition after treatment of SHT. Martin *et al.*[23] demonstrated that hyperthyroidism accelerates protein catabolism (+12%) and the oxidation of amino acids (+24%), while protein synthesis increases only slightly (9%), resulting in a net loss of protein. Lipid accumulation during recovery of hyperthyroidism appears to be related with the decrease in lipolysis[24] because it has been shown that the activity of lipoprotein lipase in this situation does not increase[25]. Also, during treatment of hyperthyroidism, MM and body mineral content increase judging by potassium[26] and calcium[27] measurements.

Increasing the MM is a clinically relevant fact, especially in elderly patients. Sarcopenia leads to dysfunction of the lower extremities, what predisposes to falls, which, together with the presence of osteopenia can increase the rate of fracture[28,29], morbidity and mortality. Gómez-Acotto *et al.*[15] showed that the recovery of MM occurred mainly in the limbs and trunk. It has not been a purpose of this paper to assess locoregional changes in body composition.

Current international recommendations for the treatment of SHT[20] are based on the degree of TSH suppression, age and patient comorbidities. There is an explicit recommendation for treating patients with TSH <0.1 and age >65 years, and patients with TSH <0.1 and heart disease, osteoporosis and symptoms of hyperthyroidism. There is lack of evidence to recommend for or against treatment when TSH is between 0.1-0.5, but it should be considered in subjects >65 years and <65 years with heart disease, symptoms of hyperthyroidism and menopausal status.

This work opens the door to further prospective studies, preferably controlled studies, with the purpose of setting the indication for treatment of SHT based on changes in body composition. The indication when TSH is between 0.1-0.5 could be limited to those subjects over 65 years, as it has been the case of treatment based on cardiovascular risk assessment and the impact on bone metabolism.

In this study, only treatment of patients over 65 years has been associated with a significant gain in fat mass and, which is more important and interesting, in lean mass at 12 months.

Once again, age over 65 years seems to be a factor *per se* to indicate definitive treatment for SHT.

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Author Disclosure Statement

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