Effects of Acute Hypothyroidism on Body Composition in Differentiated Thyroid Cancer Patients Undergoing I-131 Therapy

Tarık Şengöz

[1]Pamukkale University, Medical Faculty, Department of Nuclear Medicine, Denizli, Turkey
Corresponding Author Email: *tsengoz[at]pau.edu.tr*
ORCID: 0000-0003-2621-7585

Abstract: ***This study investigated the short-term effects of acute hypothyroidism on body composition in patients with differentiated thyroid cancer undergoing I-131 whole-body scintigraphy. A total of 30 patients were evaluated using DEXA scans and biochemical tests both before and after a 3-week discontinuation of L-thyroxine. While thyroid-stimulating hormone levels rose significantly post-discontinuation, no statistically significant changes were observed in fat mass, muscle mass, bone content, or total body composition. However, notable increases were found in LDL, HDL, and total cholesterol levels. These findings suggest that short-term hypothyroidism induced for diagnostic purposes does not adversely affect body composition and may be considered safe in this patient group.***

Keywords: hypothyroidism, body composition, thyroid cancer, I-131 therapy, DEXA scan

1. Introduction

Hypothyroidism causes many changes in the body's metabolism. It causes a decrease in basal metabolic rate and oxygen consumption. Despite reduced appetite, weight gain often results from water-salt retention and fat accumulation. Additionally, hypothyroidism poses a risk for coronary heart disease (1). Body composition refers to the ratio of fat to lean tissues in the body. It is stated in the literature that abnormal body composition may be observed in hypothyroidism due to the relative increase in fat tissue compared to the euthyroid group (2,3). In addition, muscle loss, or sarcopenia, which is said to be related to aging and metabolic syndrome, can also be seen in hypothyroidism due to decreased muscle mass (4).

Although body composition (BC) may be assessed using techniques like bioelectrical impedance analysis, the accuracy of the examination may decrease, especially in those with fluid-electrolyte imbalance. For this reason, some imaging methods are increasingly used in this field today (5). The most commonly used imaging modalities are computed tomography (CT), magnetic resonance imaging (MRI), and dual energy X-ray absorptiometry (DEXA). DEXA can measure BC at the molecular level. Imaging is performed by passing X-rays at two different energy levels through the patient's body. Thanks to the different X-ray attenuation coefficients of human tissues, different body compartments such as fat mass, muscle mass and bone mineral content can be measured and information about body composition can be obtained (5).

The most common treatment option for differentiated thyroid cancer is total thyroidectomy followed by radioactive iodine therapy (RAIT). I-131 whole body scan scintigraphy (I-131 WBS) can be performed to evaluate the effectiveness of treatment and detect possible recurrence/metastases in follow-ups after RAIT. Before I-131 WBS, thyroid stimulating hormone (TSH) levels should be above 30 mIU/L to increase the potential entry of I-131 into thyroid tissues. Therefore, L-thyroxine medication is stopped for 2-3 weeks. This condition creates temporary hypothyroidism in the patient and patients are exposed to the effects of hypothyroidism.

Understanding the physiological implications of short-term hypothyroidism is essential for optimizing diagnostic protocols in thyroid cancer management. This study contributes to the sparse literature on the safety and metabolic neutrality of temporary L-thyroxine withdrawal in this population.

This study aims to evaluate the changes in body composition and selected biochemical markers in differentiated thyroid cancer patients undergoing acute hypothyroidism due to L-thyroxine withdrawal before I-131 imaging.

2. Materials and Methods

Type of study
This study is a prospective study.

Universe and sample of the research
Thirty patients (5 males, 25 females; mean age 49.96±11.29 (28-71)) who were followed up for thyroid cancer at Pamukkale University Faculty of Medicine Nuclear Medicine Polyclinic and for whom we planned to perform I-131 whole body scan (I-131-TVT) which required the discontinuation of L-thyroxine treatment were included in the study. All patients had undergone total/near-total thyroidectomy, were diagnosed with pathologically differentiated thyroid cancer, and were given RAIT for ablation/metastasis treatment.

Data collection tools
Information about the patient and his/her disease was obtained from patient files. In patients scheduled for I-131 WBS scintigraphy, low-density lipoprotein (LDL cholesterol), high-density lipoprotein (HDL cholesterol), total cholesterol, triglyceride, sodium, potassium, calcium, phosphorus, chloride, thyroid stimulating hormone (TSH), thyroglobulin (Tg) and antithyroglobulin (ATg) tests and

DEXA whole body imaging were performed before and 21 days after L-thyroxine discontinuation. Body composition analysis was performed on a DEXA device (Hologic Horizon Wi, QDR 4500, USA). DEXA scans were performed by the same technician who had received adequate training for this procedure. The device was calibrated daily. Patients were laid on the device table in a supine position. Whole body protocol imaging was performed. Each scan required approximately 15 minutes. Bone mineral content (g), fat mass (g), muscle mass (g), muscle+bone mass (g), total mass (g), fat percentage (%), appendicular lean mass (LFM) and appendicular lean mass index (LFMI) ($LFM/height^2$) parameters were obtained using the ICE 60601-1-4 system.

Statistical analysis

All statistical analyses were performed using SPSS 23.0 (IBM, Armonk, NY, USA) software. Continuous variables were given as mean±standard deviation. Since the number of data was <100, the Kolmogorov-Smirnov test was performed for normality analysis. It was determined that the variables were normally distributed. Parametric Student T test was used for statistical analysis. $p<0.05$ values were considered statistically significant.

Ethical aspects of the study

Patients signed an informed consent form for all procedures. Ethics committee approval was obtained from the Pamukkale University Non-invasive Clinical Research Ethics Committee (E-60116787-020-39807). The study was conducted in accordance with the Declaration of Helsinki.

3. Results

The patients' weight was 76.33±13.56 (58-119) kg and their height was 161.7±6.77 (150-179) cm. The mean TSH value before L-thyroxine discontinuation was 0.27±0.38 (0.008-1.88) mIU/L, while the mean TSH value 3 weeks after L-thyroxine discontinuation was 65.04±39.19 (30.2-216) mIU/L. No statistically significant difference was found in bone mineral content, fat mass, muscle mass, muscle+bone mass, total mass, fat percentage and LFMI values obtained from the DEXA examination performed before and 3 weeks after discontinuation of L-thyroxine ($p>0.005$) (Table 1).

While total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol values before L-thyroxine was discontinued were found to be statistically significantly lower than the values measured after the drug was discontinued ($p=0.001$), no significant difference was found in blood mineral values (sodium, potassium, calcium, phosphorus, and chloride) ($p>0.05$) (Table 2).

4. Discussion

In patients diagnosed with differentiated thyroid cancer, I-131 WBS is frequently used to evaluate the response to treatment after RAIT and to detect possible recurrence and distant metastasis during follow-up. To increase the sensitivity of the test, TSH should be>30 mIU/L. Therefore, L-thyroxine medication is stopped for a while and the patient becomes hypothyroid. After the examination is completed, L-thyroxine is restarted and the patient returns to a euthyroid or subclinical hyperthyroid state. During the clinical follow-up process, I-131 WBS is performed several times depending on the patient's risk status, and the patient is exposed to hypothyroidism, even for a short time. The relationship between hypothyroidism and changes in body composition is known (2,3). Potential alterations in body composition and some biochemical parameters in this group of patients who have been hypothyroid for 3-4 weeks are an issue that needs to be investigated.

In our study, we did not detect any statistically significant changes due to hypothyroidism in the bone mineral content, fat mass, muscle mass, muscle+bone mass, total mass, fat percentage and LFMI parameters obtained by DEXA examination. In our study, no differences in body composition were observed due to hypothyroidism. We did not find any study in the literature investigating the changes in body composition in the DTC patient group with total thyroidectomy and iatrogenic hypothyroidism. In the study by Tekin E. et al., 141 patients diagnosed with diabetes mellitus and hypothyroidism were included, and no significant difference was found in parameters such as total fat mass and fat percentage before and after L-thyroxine treatment. This finding is consistent with our findings. However, the researchers used bioelectrical impedance analysis (BEA) instead of DEXA for body composition assessment (6). In the study by Sirigiri S. et al., 27 patients diagnosed with hypothyroidism (TSH>50 mIU/L) and without any other metabolic disease were subjected to DEXA whole body examination before L-thyroxine treatment and 2 months after they became euthyroid. No significant difference was found in regional and whole body fat mass, fat percentage and bone mineral content (7). This finding is also consistent with our findings.

Hypothyroidism is known to be a cause of secondary hyperlipidemia (8). In our study, LDL, HDL and total cholesterol levels were found to be higher in hypothyroidism compared to subclinical hyperthyroidism, while no significant difference was found in triglyceride values. The relationship between hypothyroidism and cholesterol levels has been investigated in many studies and different findings have been found (9). In the study of Asranna et al., total and LDL cholesterol were found to be significantly higher in hypothyroidism, and a significant decrease was found in total cholesterol, LDL, VLDL and triglyceride after 3 months of L-thyroxine treatment (10). In the study by Tekin E et al., no significant difference was found in blood lipid values between the hypothyroid and non-hypothyroid groups (6). No significant change was found in hypothyroidism in terms of mineral values. No study on this subject was found in the literature. These findings support the clinical safety of transient hypothyroid induction protocols without compromising patient metabolic stability.

5. Limitations of the Study

The study has some limitations. First, the number of patients is small. Second, differences in patients' lifestyle and dietary habits may affect the results to some extent. Third, the patients were only stopped taking L-thyroxine for 3 weeks. Therefore, they were exposed to the effects of hypothyroidism for a short time.

6. Conclusion

Our findings show that there is no significant difference in the body composition of patients during short-term hypothyroidism compared to the values before drug discontinuation. Before the I-131 WBS test, TSH must be >30 mIU/L, and L-thyroxine is discontinued for 3 weeks to ensure this. This causes patients to experience hypothyroid effects, albeit for a short time. Our results show that hypothyroidism does not cause a significant change in body composition, and it can be concluded that iatrogenic short-term hypothyroidism before I-131 TVT examination is safe in the DTC patient group.

Ethical Aspects of the Study

Patients signed an informed consent form for all procedures. Ethics committee approval was obtained from the Pamukkale University Non-Interventional Clinical Research Ethics Committee (E-60116787-020-39807). The study was conducted in accordance with the Declaration of Helsinki.

Informed Consent

Informed consent was obtained from all patients participating in the study.

Author Contributions

The idea/concept, design, sources, data collection and processing, analysis and interpretation, literature review, and writing stages were carried out by T.Ş.

Conflict of Interest

The authors declare that they have no conflict of interest.

Research Support

There is no person/organization that financially supports the study.

References

[1] Hulusi Atmaca. Hipotiroidizm. *Journal of Experimental and Clinical Medicine.* 2012;29:301-308.

[2] Seppel T, Kosel A, Schlaghecke R. Bioelectrical impedance assessment of body composition in thyroid disease. *Eur J Endocrinol.* 1997;136:493–498.

[3] Aguilar-Salinas CA, Gardun O-Garcia JJ, Alvirde-Garcia U, et al. TSH and free thyroxine concentrations are associated with differing metabolic markers in euthyroid subjects. *Eur J Endocrinol*. 2010;163:273–278.

[4] Xin Hu, Lina Zhang, Mengjie Zhang, et al. Correlation of subclinical hypothyroidism with sarcopenia and its components in the Chinese older adults. *Endocrine*. 2024;84:1030–1039.

[5] Messina C , Maffi G , Vitale JA , Ulivieri FM , Guglielmi G , Sconfienza LM. Diagnostic imaging of osteoporosis and sarcopenia: a narrative review. *Quantitative Imaging in Medicine and Surgery*. 2018;8(1):86-99.

[6] Tekin E, Tüzün S, Çetin H, Şimşek EE. The Relationship Between Hypothyroidism and Body Fat Mass and Metabolic Parameters by Gender in Patients with Type 2 Diabetes Mellitus. *Ankara Med J.* 2020;1:170-179.

[7] Sirigiri S, Vaikkakara S, Sachan A, et al. Correction of Hypothyroidism Leads to Change in Lean Body Mass without Altering Insulin Resistance. *Eur Thyroid J.* 2016;5:247–252.

[8] Duntas LH, Brenta G. A Renewed Focus on the Association Between Thyroid Hormones and Lipid Metabolism. *Front Endocrinol (Lausanne)*. 2018;9:511.

[9] Delitala AP, Scuteri A, Maioli M, Mangatia P, Vilardi L, Erre GL. Subclinical hypothyroidism and cardiovascular risk factors. *Minerva Med.* 2019;110(6):530-545.

[10] Asranna A, Taneja RS, Kulshreshta B. Dyslipidemia in subclinical hypothyroidism and the effect of thyroxine on lipid profile. *Indian J Endocrinol Metab*. 2012;16(2):347-349.

Table 1: Comparison of whole body DEXA parameters

	Before stopping L-thyroxine (mean±standard deviation)	After stopping L-thyroxine (ortalama±standart sapma)	p
Bone mineral content (g)	2067,26±311,21	2090,02±315,53	0,17
Fat mass (g)	33376,48±9661,69	33539±9188,04	0,71
Muscle mass (g)	40978,46±7384,98	40031,32±10379,53	0,52
Muscle+bone mass (g)	43044,83±7614,62	43527,84±7370,48	0,09
Total mass (g)	76422,23±13883,46	76734,32±13591,82	0,33
Fat percentage (%)	30,58±7,01	31,21±6,73	0,48
LFMI (g/m^2)	6,53±1,11	6,61±1,03	0,17

Table 2: Comparison of biochemical values

	Before stopping L-thyroxine (mean±standard deviation)	After stopping L-thyroxine (ortalama±standart sapma)	p
LDL cholesterol (mg/dL)	111,20±40,30	141,52±55,03	**0,01**
HDL cholesterol (mg/dL)	50,48±9,84	59,28±13,13	**0,01**
Total cholesterol (mg/dL)	192,04±47,12	232,29±64,11	**0,01**
Triglyceride (mg/dL)	171,04±114,93	166,41±63,59	0,79
Sodium (mmol/L)	140,26±2,52	139,78±2,04	0,41
Potassium (mmol/L)	4,51±0,37	4,43±0,43	0,33
Calcium (mg/dL)	9,05±0,51	9,25±0,55	0,07
Phosphorus (mg/dL)	3,51±0,52	3,56±0,43	0,61
Chlorine (mmol/L)	102,73±2,68	102±2,73	0,11