HİTİT MEDICAL JOURNAL
HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ
e-ISSN: 2687-4717 Cilt|Volume: 7 • Sayı|Issue: 3 - Ekim|October 2025

Influence of Lean Body Mass and Disease Etiology on Levothyroxine Requirements in Patients with Hypothyroidism

Hipotiroidili Hastalarda Yağsız Vücut Kütlesi ve Hastalık Etiyolojisinin Levotiroksin Gereksinimlerine Etkisi

Ülkem Şen Uzeli | Duygu Tutan

Hitit University Faculty of Medicine, Department of Internal Medicine, Çorum, Türkiye

Sorumlu Yazar | Correspondence Author
Ülkem Şen Uzeli
ulkem_sen@hotmail.com
Address for Correspondence: Hitit University Faculty of Medicine, Department of Internal Medicine, 19040, Çorum, Türkiye.

Makale Bilgisi | Article Information
Makale Türü | Article Type: Araştırma Makalesi | Research Article
Doi: https://doi.org/10.52827/hititmedj.1705311
Geliş Tarihi | Received: 23.05.2025
Kabul Tarihi | Accepted: 18.08.2025
Yayım Tarihi | Published: 13.10.2025

Atıf | Cite As
Şen Uzeli Ü, Tutan D. Influence of Lean Body Mass and Disease Etiology on Levothyroxine Requirements in Patients with Hypothyroidism. Hitit Medical Journal 2025;7(3):386-393. https://doi.org/10.52827/hititmedj.1705311

Hakem Değerlendirmesi: Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
Etik Beyanı: Çalışma için 10/07/2024 tarihinde Hitit Üniversitesi Tıp Fakültesi Araştırmalar Etik Kurulu'ndan onay alınmıştır. Karar no: 2024-32.
İntihal Kontrolleri: Evet (iThenticate)
Çıkar Çatışması: Yazarlar çalışma ile ilgili çıkar çatışması beyan etmemiştir.
Şikayetler: hmj@hitit.edu.tr
Katkı Beyanı: Fikir/Hipotez: ÜŞU, DT; Tasarım: ÜŞU, DT; Data Collection/Data Processing: ÜŞU, DT; Veri Analizi: ÜŞU, DT; Makalenin Hazırlanması: ÜŞU, DT.
Hasta Onamı: Tüm hastalardan yazılı bilgilendirilmiş onam ve yayın için izin alınmıştır.
Finansal Destek: Bu çalışma ile ilgili herhangi bir finansal kaynaktan yararlanılmamıştır.

Peer Review: Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
Ethical Statement: Approval for the study was obtained from the Hitit University Faculty of Medicine Research Ethics Committee on 10/07/2024. Decision no: 2024-32.
Plagiarism Check: Yes (iThenticate)
Conflict of Interest: The authors declared that, there are no conflicts of interest.
Complaints: hmj@hitit.edu.tr
Authorship Contribution: Idea/Hypothesis: ÜŞU, DT; Design: ÜŞU, DT; Data Collection/Data Processing: ÜŞU, DT; Data Analysis: ÜŞU, DT; Manuscript Preparation: ÜŞU, DT.
Informed Consent: Written informed consent and consent for publication was obtained from the patients.
Financial Disclosure: There are no financial funds for this article.

Influence of Lean Body Mass and Disease Etiology on Levothyroxine Requirements in Patients with Hypothyroidism

ABSTRACT

Objective: It was aimed to evaluate the dose requirement depending on the etiology and to compare lean body mass and total body weight in the calculation of drug dose in patients receiving levothyroxine sodium replacement.

Material and Method: A total of 124 patients who were receiving levothyroxine sodium treatment for total thyroidectomy, hypothyroidism due to radioactive iodine therapy treatment, and autoimmune hypothyroidism were included in this cross-sectional study. Patients' drug doses, height, weight, thyroid-stimulating hormone, T4, and T3 values were recorded on the hospital documentation system. Lean Body Mass was calculated, and the doses of drugs were calculated based on total body weight and Lean Body Mass. Patients were separated into three groups as normal weight, overweight, and obese according to body mass index.

Results: Patients with Hashimoto's thyroiditis required lower daily levothyroxine doses compared to those who had undergone total thyroidectomy. Similarly, the daily levothyroxine dosage per kilogram of lean body mass and total body weight was significantly lower in the Hashimoto's group than in the total thyroidectomy group. While the RAI group showed intermediate values that did not differ significantly from either group

Conclusion: This study shows that the use of lean body mass is more significant than body mass index in determining the dose of levothyroxine in hypothyroid patients. The findings show that the dose of levothyroxine varies according to the etiology of hypothyroidism and that treatment doses should be determined accordingly.

Keywords: Hypothyroidism, Lean Body Mass, Levothyroxine Sodium.

ÖZET

Amaç: Levotiroksin sodyum replasmanı alan hastalarda etyolojiye bağlı doz gereksinimini değerlendirmek ve ilaç dozunun hesaplanmasında yağsız vücut kütlesi ile toplam vücut ağırlığını karşılaştırmak amaçlandı.

Gereç ve Yöntem: Total tiroidektomi, radyoaktif iyot tedavisine bağlı hipotiroidi ve otoimmün hipotiroidi nedeniyle levotiroksin sodyum tedavisi alan toplam 124 hasta kesitsel çalışmaya dahil edildi. Hastaların ilaç dozları, boy, kilo, tiroid uyarıcı hormon, T4 ve T3 değerleri hastane dokümantasyon sistemine kaydedildi. Yağsız Vücut Kütlesi hesaplandı ve ilaç dozları toplam vücut ağırlığı ve Yağsız Vücut Kütlesi değerlerine göre hesaplandı. Hastalar vücut kitle indeksine göre normal kilolu, kilolu ve obez olmak üzere 3 gruba ayrıldı.

Bulgular: Hashimoto tiroiditi olan hastaların, total tiroidektomi geçiren hastalara kıyasla daha düşük günlük levotiroksin dozlarına ihtiyaçları vardı. Benzer şekilde, yağsız vücut kütlesi ve toplam vücut ağırlığının kilogramı başına günlük levotiroksin dozu, Hashimoto grubunda total tiroidektomi grubuna göre anlamlı derecede düşüktü. RAI grubu ise her iki gruptan da anlamlı farklılık göstermeyen orta düzeyde değerler gösterdi.

Sonuç: Bu çalışma, hipotiroid hastalarında levotiroksin dozunun belirlenmesinde yağsız vücut kütlesi kullanımının vücut kitle indeksinden daha önemli olduğunu göstermektedir. Bulgular, levotiroksin dozunun hipotiroidizmin etyolojisine göre değiştiğini ve tedavi dozlarının buna göre belirlenmesi gerektiğini göstermektedir.

Anahtar Sözcükler: Hipotiroidizm, Levotiroksin Sodyum, Yağsız Vücut Kütlesi.

Introduction

Hypothyroidism is a common endocrine disorder worldwide characterized by inadequate regulation of thyroid hormones. In nearly all cases (99%), hypothyroidism is primary hypothyroidism and develops due to thyroid gland dysfunction. The most common etiologies of hypothyroidism are Hashimoto's thyroiditis, thyroid surgery, radioactive iodine therapy (RAI), and radiation therapy-induced hypothyroidism (1).

Thyroid hormone replacement therapy with levothyroxine (LT4) is recommended for all causes of hypothyroidism, whether primary hypothyroidism, central hypothyroidism, or, rarely, peripheral hypothyroidism. With its long elimination half-life (approximately one week), once-daily use of LT4 provides appropriate T4 and T3 blood levels and is sufficient as a standalone replacement (2). The dose of LT4 depends on the age, gender, and weight of the patient. Patients with hypothyroidism usually need an oral LT4 replacement dose of 1.6–1.8 mcg/kg actual body weight to achieve euthyroid status (3).

However, the literature shows that the necessity of using alternative methods to total body weight was discussed upon the detection of unexplained dose requirement differences in patients of similar age and body weight, and the observation that the dose required decreased in obese and elderly patients. Studies have suggested that actual body mass, ideal body mass, and lean body mass (LBM) may influence LT4 dose requirements (4). In these studies, LBM was considered the best predictor of daily requirements for LT4. It is known that the deiodination process, which converts T4 to T3, occurs mainly in muscle tissue rather than adipose tissue (5). Furthermore, most metabolic processes of T4 occur within the LBM, which include type 1 deiodinase, glucuronidation, and sulfation in the liver, and deiodinase type 3 in the skin (6). Although hypothyroid obese patients require higher absolute doses of LT4 than normal-weight individuals, obese patients require a lower dose of LT4 relative to body weight to maintain euthyroid status. It is suggested that a higher LT4 dose requirement in morbidly obese individuals may be associated with increased LBM and a higher volume of distribution (7,8). This study aimed to investigate whether lean body mass (LBM) provides a more accurate basis for levothyroxine dose adjustment compared to total body weight or body mass index, and to evaluate whether this relationship varies according to the underlying etiology of hypothyroidism.

Material and Method

This investigation received authorization from the Hitit University Clinical Research Ethics Committee (July 10, 2024, approval 2024-32), and all protocols undertaken in investigations involving human subjects were conducted in strict compliance with the ethical guidelines outlined by the institutional and/or national research governing body, the 1964 Declaration of Helsinki, and its subsequent revisions or analogous ethical criteria.

Patients with normal thyroid-stimulating hormone (TSH) values, who had undergone total thyroidectomy, hypothyroidism due to RAI treatment, or LT4 sodium treatment due to autoimmune hypothyroidism, and who applied to the Department of Internal Medicine of Hitit University Erol Olçok Training and Research Hospital between July 2024 and September 2024, were included in this cross-sectional study. Demographic characteristics of the patients, drug doses (LT4 dose [mcg]), height (cm), weight (kg), body mass index (BMI), TSH, T4, and T3 values were recorded. Patients included in the study were those whose LT4 sodium dose had not been changed for the last year. Patients with more than one cause of hypothyroidism, patients under the age of 18, patients who did not comply with treatment, patients with gastrointestinal absorption problems, patients using drugs that interact with LT4 sodium, patients whose TSH values were not within the expected range, and patients who were pregnant or breastfeeding were excluded from the study (Figure I). The patients were first divided into three separate groups according to their etiological causes: autoimmune hypothyroidism, hypothyroidism due to RAI treatment, and hypothyroidism due to total thyroidectomy. These three groups of patients were compared in terms of age, gender, height, weight, mean TSH value, daily LT4 sodium medication dose used per kg, daily medication dose used per LBM, and body mass index. The patients were divided into three groups (18.5–24.9 kg/m^2, 25–29.9 kg/m^2, and 30 kg/m^2 and above) according to the World Health Organization classification of BMI (kg/m^2) values. The differences in LT4 medication doses were evaluated among groups categorized by etiology as well as groups classified by BMI. The Boer formula, an equation used for measuring lean body mass, was used for the LBM. It was calculated as (0.407 × weight) + (0.267 × height) − 19.2 for men and (0.252 × weight) + (0.473 × height) − 48.3 for women.

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized using descriptive statistics, presented as counts and percentages, while continuous variables were expressed as mean ± standard deviation or median (minimum–maximum), depending on the distribution pattern. The Shapiro–Wilks test was employed to assess the normality of the data distribution. Pearson or Spearman correlation coefficients were used to analyze the relationships between variables, depending on the distribution characteristics.

The ANOVA test was utilized to compare numeric variables, such as age and height, between groups, while other continuous variables were compared using the Kruskal–Wallis test due to their non-Gaussian distribution. For variables analyzed with ANOVA, Bonferroni-adjusted pairwise comparisons were performed. For variables analyzed with the Kruskal–Wallis test, where significant differences were found, pairwise group comparisons were performed using Mann–Whitney U tests with the Bonferroni correction for post-hoc comparisons. Categorical data comparisons between groups were conducted using the chi-square test. The patients were categorized into three groups based on the etiology of their hypothyroidism, and statistical analyses were performed to identify significant differences between these groups. The patients were also categorized into three additional groups based on BMI: normal, overweight, and obese, and the differences between these categories were similarly analyzed. A multivariate linear regression analysis was conducted to evaluate the effects of etiology, LBM, age, BMI, weight, and height on LT4 requirements. Statistical significance was defined as *p<0.05*.

Results

A total of 124 eligible patients were included in the study, with a mean age of 50.05 ± 13.35 years. The median BMI was 29.16 (range 16.53–51.89), and the median TSH level was 2.19 (range 0.21–4.3). The median LBM was 46.72 kg (range 35.5–66.25), while the median daily LT4 dosage requirement was 88.25 mcg (range 10–200 mcg). Among the participants, 36 patients (29%) had undergone total thyroidectomy as the etiology for hypothyroidism, 4 patients (3.3%) had received RAI therapy, and 84 patients (67.7%) were diagnosed with Hashimoto's thyroiditis

Table I. Characteristics of Patients and Comparison Between Etiology Groups

Variables	All Patients (n=124)	Total Thyroidectomy (n=36; 29%)	After RAI (n=4; 3.3%)	Hashimoto Thyroiditis (n=84; 67.7%)	*p Value*
Age	50.05±13.35	56.86±9.55	37±12.38	47.75±13.66	*<0.001*
Weight (kg)	75 (45-143)	78.5 (50-130)	63 (58-86)	73.5 (45-143)	*0.150*
Height (cm)	1.61±0.06	1.61±0.07	1.64±0.06	1.6±0.06	*0.473*
BMI (kg/m^2)	29.16 (16.53-51.89)	30.59 (20.81-46.61)	24.1 (20.55-31.59)	28.83 (16.53-51.89)	*0.117*
TSH (uU/ml)	2.19 (0.21-4.3)	1.73 (0.21-4.3)	2.95 (1.7-4.02)	2.41 (0.41-4.2)	*0.129*
fT3 (ng/dL)	2.55 (1.22-3.34)	2.36 (1.22-3.1)	2.58 (2.01-2.83)	2.61 (1.22-3.34)	*0.055*
fT4 (ng/dL)	1.32 (0.44-2.81)	1.4 (0.97-2.12)	1.27 (1.2-1.34)	1.3 (0.44-2.81)	*0.049*
LBM (kg)	46.72 (35.5-66.25)	46.83 (37.61-63.45)	46.41 (41.36-51.42)	46.72 (35.5-66.25)	*0.616*
Daily LT4 (mcg/day)	88.25 (10-200)	100 (10-100)	100 (57-132)	75 (25-200)	*<0.001*
Daily LT4 per LBM	1.90 (0.19-3.83)	2.32 (0.19-3.83)	2.06 (1.38-2.81)	1.57 (0.38-3.33)	*<0.001*
Daily LT4 per kg	1.10 (0.10-2.69)	1.47 (0.10-2.69)	1.44 (0.90-2.10)	0.98 (0.17-2.38)	*<0.001*

RAI: radioactive iodine therapy, BMI: Body Mass Index, TSH: thyroid-stimulating hormone, LBM: Lean body Mass, fT3: free T3 hormone, fT4: free T4 hormone, Daily LT4: daily levothyroxine T4

Patients in the total thyroidectomy group were significantly older than those in the other two groups (*p<0.001*). No significant differences were observed between the etiology groups concerning weight, height, BMI, TSH, fT3, or LBM (*p=0.150, p=0.473,* *p=0.117, p=0.129, p=0.055, and p=0.616*, respectively). The fT4 levels were marginally higher in the total thyroidectomy group; this difference was statistically significant (*p=0.049*) but not considered clinically relevant.

Table II. Levothyroxine Dosage Comparison between BMI Groups

Variables	Normal Weight (n=32)	Overweight (n=37)	Obese (n=55)	*p value*
Daily LT4(mcg/day)	72.5 (25-175)	82 (25-167)	100 (10-200)	*0.119*
Daily LT4 per LBM	1.51 (0.52-3.83)	2.05 (0.52-3.33)	1.87 (0.19-3.47)	*0.300*
Daily LT4 per kg	1.06 (0.37-2.69)	1.28 (0.33-2.11)	1.07 (0.10-2.00)	*0.157*

BMI: Body Mass Index, Daily LT4: daily levothyroxine T4

Patients with Hashimoto's thyroiditis required lower daily LT4 doses compared to those who had undergone total thyroidectomy (median 75 mcg vs. 100 mcg, *p<0.001*). Similarly, the daily LT4 dosage per kilogram of LBM and total body weight was significantly lower in the Hashimoto's group than in the total thyroidectomy group (*p<0.001* for both; Table I).

Table III. Multivariate Regression Analysis for Estimation of Required LT4 Dosage

Coefficients	Unstandardized Coefficients		Standardized Coefficients			%95 Confidence Intervals
	B	Std. Error	Beta	t	Sig.	
(Constant)	7.230	28.102		0.257	0.797	-48.405 - -62,866
Hypothyroidism Etiology	-17.096	3.612	-0.374	-4.733	<0.001	-24.248 - -9.945
LBM (kg)	2.169	0.572	0.300	3.790	<0.001	1.036 – 3.302
Age	-0.020	0.082	-0.018	-0.219	0.827	-0.180 – 0.144
BMI (kg/m^2)	-0.031	0.104	-0.035	-0.335	0.738	-0.240 – 0.170
Weight (kg)	-0.027	0.160	-0.047	-0.293	0.770	-0.363 – 0.269
Height (cm)	0.027	0.099	0.029	0.293	0.770	-0.167 – 0.225

LT4: levothyroxine T4, LBM: Lean body Mass, BMI: Body Mass Index

The comparison of daily dosage requirements across BMI categories showed that normal-weight patients required a median of 72.5 mcg (range 25–175 mcg), overweight patients required 82 mcg (range 25-167mcg), and obese patients required 100 mcg (range 10-200 mcg) of LT4 daily. Although there was an observed increase in LT4 dose requirements with a higher BMI, this trend did not reach a statistically significant level (*p=0.300*). In addition, no significant differences were found in the median daily LT4 dosage per LBM or per kilogram across the BMI groups (*p=0.300 and p=0.157*, respectively; Table II).

Table IV. Univariate Linear Regression Results of LBM and LT4 in Subgroups (every row reports an analysis in a subgroup)

Model Summary and Parameter Estimates	Model Summary					Parameter Estimates	
Subgroups	R Square	F	df1	df2	Sig.	Constant	b1
Hashimoto	0.079	7.027	1	82	0.010	-13.950	1.888
RAI	0.385	1.252	1	2	0.379	-117.035	4.618
Thyroidectomy	0.160	6.471	1	34	0.016	-14.217	2.608
All Patients	0.111	15.301	1	122	<0.001	-28.188	2.417

RAI: radioactive iodine therapy, LBM: Lean Body Mass, LT4: levothyroxine T4

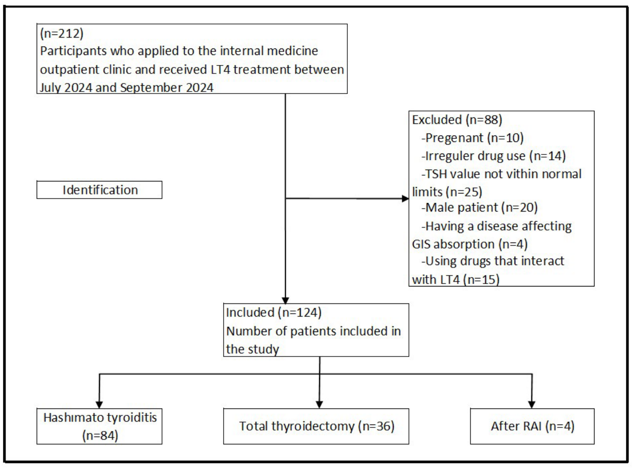

Figure I. STROBE Flow Chart

A multivariate linear regression analysis was conducted, incorporating hypothyroidism etiology, LBM, age, BMI, weight, and height as covariates to assess their predictive value for LT4 dosage requirements. The analysis revealed no significant effects of age, BMI, weight, or height between the groups (*p=0.827, p=0.738, p=0.770, and p=0.770*, respectively; Table III). The regression model was significant (*R^2=0.250, p<0.001*), with hypothyroidism etiology and LBM emerging as independent predictors of LT4 dosage even after adjusting for potential confounders (*β=−0.374, t=−4.733, p<0.001* for etiology and *β=0.300, t=3.790, p<0.001* for LBM). Univariate linear regression analysis and curve estimation between LBM and LT4 dosage yielded the following predictive formula: [required LT4 dosage] = (2.42 * LBM) – 28.2 (*p<0.001*; Figure II).

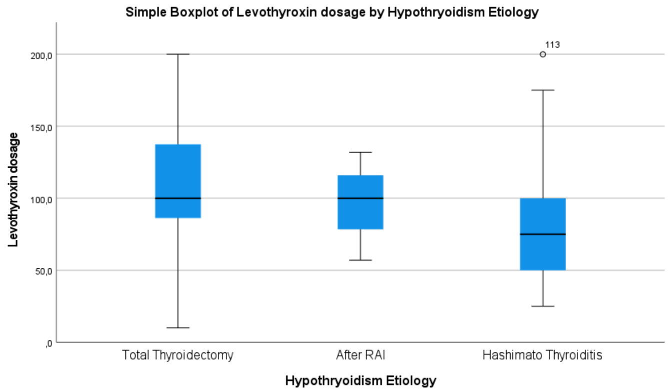

Figure II. Boxplot diagram of levothyroxine dosage requirements (µg/day) according to hypothyroidism etiology. The horizontal line within each box represents the median; the box edges represent the interquartile range (IQR); whiskers extend to the minimum and maximum values within 1.5 × IQR; circles indicate mild outliers. Numerical labels next to outliers (e.g., "113") correspond to case identifiers in the dataset.

Further linear regression analyses were performed to evaluate the predictive accuracy of LBM for LT4 requirements across different etiologies. In both the Hashimoto's thyroiditis and total thyroidectomy groups, LBM was a significant predictor of LT4 dosage (*p=0.010 and p=0.016,* respectively). However, in the RAI group, LBM demonstrated limited predictive capability (*p=0.379*; Table IV).

Discussion

This is the first study in Türkiye to show that LBM is more meaningful in determining the dose of L-thyroxine used in hypothyroidism treatment. The findings of this study may aid clinicians in optimizing LT4 dosing by prioritizing LBM over BMI.

The basis of hypothyroidism treatment is LT4, which is formed by the conversion of the biologically active hormone T3 from T4. A stable dose of LT4 is maintained when the amount of hormone entering the bloodstream equals the amount metabolized. As much as 80% of LT4 is absorbed, and serum T4 level reaches peak level in 2–4 hours and decreases to basal level in approximately 6 hours. The plasma half-life of T4 in euthyroid states is approximately 7 days, and clearance is mainly dependent on deiodination (9,10). The average daily LT4 replacement dose is 1.6 µg/kg to normalize serum TSH. The daily dose requirement for LT4 varies according to age, sex, and body weight. Since the therapeutic range of LT4 is not extensive, a minimal increase or decrease in the dose of LT4 may cause a significant change in the TSH value (11). With these changes, altered TSH levels may cause unexpected signs of hypothyroidism or hyperthyroidism. For this reason, it is crucial that the necessary dosage of LT4 therapy be regulated in patients with hypothyroidism, regardless of the etiology. There is a consensus in the literature that ideal body weight should be considered to calculate the amount of LT4 for each patient (12). Although total daily LT4 requirements are related to body mass, unexplained differences can occur between individuals of the same age and body size, even in the absence of functional thyroid tissue. Our study aimed to investigate whether normal body weight or lean body mass should be used to determine the LT4 dose in female hypothyroid patients.

In a previous study, the daily dose requirement between BMI groups was compared, and it was found that obese patients had a lower LT4 dose requirement per kilogram than normal-weight patients. Moreover, this study found that actual body weight and daily dose of LT4 were negatively correlated (13). Devdhar et al. found that age had no significant role in determining the dose of LT4 and was negatively correlated with body weight (14). It was found that body weight is not a variable parameter alone in determining the required dose of LT4 in patients with total thyroidectomy associated with thyroid cancer, but it decreases with increasing age and BMI (15). In our study, we observed an increase in LT4 dose requirements as BMI increased, but this was not statistically significant (*p=0.300*). We consider that this finding may be due to the fact that our study was conducted only on female patients and included patients who were already receiving treatment.

We think that although there was an increase in LT4 dose with increasing BMI in our study, it was not statistically significant and that BMI and LT4 dose were negatively correlated in studies in the literature, this may be related to the increase in muscle mass of the patients. However, we believe that retrospective studies with many participants are needed, including patients who will start new treatment, to reveal these more clearly.

Currently, the LT4 dose required to achieve euthyroidism is based on the demand per total body weight. Previous studies have shown that different doses of LT4 are necessary in individuals of the same age, with the same etiologic cause, and with the same body mass index. For this reason, new studies are being performed on the use of lean body mass in determining the dose of LT4. Inspired by this, we evaluated the relationship between lean body mass and LT4 dose, and we compared LBM and total body weight between BMI groups. Most of the increase in total body weight when weight gain occurs is due to fat mass. Fat mass is not metabolically active, so when total weight is used as the basis for determining the dose of LT4, it may result in overdose exposure. The concept of LBM as a predictor of drug dosage has been applied to the sensitive assessment of body composition by dual-energy X-ray absorptiometry. In a retrospective study of 271 hypothyroid patients in Thailand, it was found that a lower dose of LT4 was needed compared to LBM (16). A retrospective study of 75 hypothyroid adults aged 24–88 years on full replacement therapy was conducted in another study. LBM was found to be a stronger predictor of LT4 requirements than age or weight for all gender subgroups over 51 years of age. A retrospective study including 200 patients showed that LBM was a better indicator for the calculation of an appropriate LT4 replacement dose than actual BM (17). In our study, we demonstrated that LMB was a more powerful parameter than BMI in determining LT4 dose (*p=0.010, p=0.016*). A previous study of 264 total thyroidectomy patients showed that patients with malignant pathology had a higher LT4 requirement despite having the same body weight (18). Some studies have reported that not only body weight but also medications and comorbidities are effective in determining the dose of LT4 (19). In a prospective study of 60 patients undergoing total thyroidectomy for benign causes, the daily dose of LT4 was correlated with body mass. However, to explain the correlation, it has been stated that other etiologic causes should also be investigated after the initiation of LT4 treatment (20). When the literature was reviewed, it was observed that parameters such as the etiology of hypothyroidism, age, gender, body mass index, and lean body mass of the patients were important in determining the dose of LT4. However, most of these studies were mainly performed on patients with total or subtotal thyroidectomy for malignant or benign etiologies. It was shown that Hashimoto's thyroiditis or ablative therapy-associated hypothyroidism required a lower dose of LT4 than patients with complete loss of thyroid tissue after total thyroidectomy (21,22). In a study by Gordon et al., it was stated that the dose of LT4 varied depending on the etiology of hypothyroidism (23). In contrast, the study which included patients using 75 mcg or more of LT4 , which included patients using 75 mcg or more of LT4, the required dose of LT4 was found to be 1.45 mcg/kg/day in hypothyroidism associated with Hashimoto's disease (70% of study patients) and 1.48 mcg/kg/day in hypothyroidism associated with total thyroidectomy and radioactive iodine; no statistical difference was observed between the groups (*p=0.56*). In our study, it was found that patients with Hashimoto's thyroiditis required lower daily doses of LT4 than patients with total thyroidectomy (*p<0.001*).

Our findings contribute to the growing body of evidence supporting the use of LBM over BMI in LT4 dose determination. Furthermore, we found that there was a significant difference in the dose of LT4 between patients with Hashimoto's disease and patients with total thyroidectomy, even if they had the same BMI.

The limitations of our study include the fact that it was performed on patients who had previously started LT4 treatment, that it included patients of a single ethnic group, calculating LMB with the formulation, is limited due to the limited number of patients receiving RAI treatment in the patient population and that it was performed in a single center. We recommend that large population, multicenter, randomized controlled trials with strong and robust evidence to determine the dose of LT4 based on LMB and not BMI in hypothyroid patients should be conducted to clarify this issue in the future.

Conclusion

This study demonstrates that lean body mass (LBM) is a stronger and more reliable predictor of levothyroxine (LT4) dose requirements than body mass index (BMI). Furthermore, the underlying etiology significantly influences LT4 needs and should be considered when titrating therapy. These findings highlight the importance of individualized dosing strategies in hypothyroidism management.

References

1. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Publisher Correction: Hypothyroidism. Nat Rev Dis Primers 2022;8(1):39.

2. Almandoz JP, Gharib H. Hypothyroidism: etiology, diagnosis, and management. Med Clin North Am 2012;96(2):203-221.

3. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. Thyroid 2014;24(12):1670-1751.

4. Santini F, Pinchera A, Marsili A, et al. Lean body mass is a major determinant of levothyroxine dosage in the treatment of thyroid diseases. J Clin Endocrinol Metab 2005;90(1):124-127.

5. Salvatore D, Bartha T, Harney JW, Larsen PR. Molecular biological and biochemical characterization of the human type 2 selenodeiodinase. Endocrinology 1996;137(8):3308-3315

6. Van der Spek AH, Fliers E, Boelen A. The classic pathways of thyroid hormone metabolism. Mol Cell Endocrinol 2017; 458:29-38.

7. Elfenbein DM, Schaefer S, Shumway C, Chen H, Sippel RS, Schneider DF. Prospective Intervention of a Novel Levothyroxine Dosing Protocol Based on Body Mass Index after Thyroidectomy. J Am Coll Surg 2016;222(1):83-88.

8. Biondi B, Cooper DS. Thyroid hormone therapy for hypothyroidism. Endocrine 2019;66(1):18-26.

9. Fish LH, Schwartz HL, Cavanaugh J, Steffes MW, Bantle JP, Oppenheimer JH. Replacement dose, metabolism, and bioavailability of levothyroxine in the treatment of hypothyroidism. Role of triiodothyronine in pituitary feedback in humans. N Engl J Med 1987;316(13):764-770.

10. Leonard JL, Koerle J. Intracellular pathways of iodothyronine metabolism. Werner, Ingbar's The thyroid. A fundamental and clinical text. Philadelphia: Lippincott Williams, Wilkins; 136–173

11. Ernst FR, Barr P, Elmor R, et al. The Economic Impact of Levothyroxine Dose Adjustments: the CONTROL HE Study. Clin Drug Investig 2017;37(1):71-83.

12. Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA 2004;291(2):228-238.

13. Cunningham JJ, Barzel US. Lean body mass is a predictor of the daily requirement for thyroid hormone in older men and women. J Am Geriatr Soc 1984; 32(3):204-207.

14. Devdhar M, Drooger R, Pehlivanova M, Singh G, Jonklaas J. Levothyroxine replacement doses are affected by gender and weight, but not age. Thyroid 2011;21(8):821-827.

15. Di Donna V, Santoro MG, De Waure C, et al. A new strategy to estimate levothyroxine requirement after total thyroidectomy for benign thyroid disease. Thyroid 2014 Dec 1;24(12):1759–1764

16. Mathiphanit S, Yenseung N, Chatchomchuan W, et al. Profile of Levothyroxine Replacement Therapy in Graves' Disease Patients with Hypothyroidism Post-Radioactive Iodine Ablation: Focus on Different Weight-Based Regimens. J ASEAN Fed Endocr Soc 2022;37(1):62-68.

17. Ratanapornsompong G, Sriphrapradang C. Appropriate dose of levothyroxine replacement therapy for hypothyroid obese patients. J Clin Transl Endocrinol 2021;25:100264.

18. Baehr KM, Lyden E, Treude K, Erickson J, Goldner W. Levothyroxine dose following thyroidectomy is affected by more than just body weight. Laryngoscope 2012;122(4):834-838.

19. Miccoli P, Materazzi G, Rossi L. Levothyroxine Therapy in Thyrodectomized Patients. Front Endocrinol (Lausanne) 2021;11:626268

20. Mistry D, Atkin S, Atkinson H, et al. Predicting thyroxine requirements following total thyroidectomy. Clin Endocrinol (Oxf) 2011;74(3):384-387.

21. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid 2012;22(12):1200-1235.

22. Jonklaas J. Optimal Thyroid Hormone Replacement. Endocr Rev 2022;43(2):366-404.

23. Gordon MB, Gordon MS. Variations in adequate levothyroxine replacement therapy in patients with different causes of hypothyroidism. Endocr Pract 1999;5(5):233-238.