International Journal of Gerontology 19 (2025) 244–248
https://doi.org/10.6890/IJGE.202510_19(4).0009

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

The Effect of Age-Related Endocrine Changes on Thyroid Hormone Replacement Therapy in Elderly Patients with Hypothyroidism

Hongyan Li [a], Lili Qiao [a], Jinhui Ma [a], Xuying Liu [a], Kaiyue Xu [a], Yanrong Chen [a], Lili Tan [b *]

[a] *Endocrine Department, Affiliated Hospital of Hebei University, Baoding, 071000 China,* [b] *Geriatrics Department, Affiliated Hospital of Hebei University, Baoding, 071000 China*

ARTICLE INFO

Accepted 6 March 2025

Keywords:
aged,
body mass index,
hypothyroidism,
thyroid hormones

SUMMARY

Background: Hypothyroidism commonly affects elderly individuals, involving complex interactions within the endocrine system. This study explores the relationship between various endocrine factors and the effectiveness of thyroid hormone replacement therapy (THRT) in an elderly hypothyroid population.

Methods: A total of 150 elderly patients diagnosed with hypothyroidism and subsequently treated with THRT were enrolled. Clinical evaluations, laboratory data, and symptom assessments were recorded. Multivariate regression models were then employed to investigate the impact of endocrine changes on THRT efficacy.

Results: The overall success rate of THRT was 85.3%, with a significant association between hormone levels and treatment effectiveness. When stratified by body mass index (BMI), patients with a normal BMI (18.5–24.9) demonstrated the highest success rate (93.5%), while those classified as obese (BMI ≥ 30) showed the lowest (75.8%). Furthermore, both insulin and leptin levels were significantly correlated with THRT outcomes; abnormal levels were linked to diminished response rates. Logistic regression confirmed that insulin and leptin were strong predictors of THRT efficacy, highlighting their critical roles in guiding treatment.

Conclusion: Endocrine factors — particularly insulin and leptin — exert a notable influence on the effectiveness of THRT in elderly hypothyroid patients. Early evaluation of these parameters may enable more targeted and successful treatment strategies, ultimately improving therapeutic outcomes in this population.

1. Introduction

Hypothyroidism is a common endocrine disorder characterized by inadequate production of thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3), which are essential for regulating metabolism, protein synthesis, and overall growth and development.[1,2] The condition may manifest as primary hypothyroidism, resulting from intrinsic thyroid gland dysfunction, or as central hypothyroidism, stemming from disturbances in the hypothalamic-pituitary-thyroid (HPT) axis.[2] Globally, iodine deficiency remains a major cause of hypothyroidism, especially in developing regions. In iodine-sufficient areas, autoimmune thyroiditis — most notably Hashimoto's thyroiditis — is more prevalent.[3,4] Risk factors include female sex, age over 60 years, and a family history of thyroid disease.[3] Diagnosis primarily relies on detecting elevated thyroid-stimulating hormone (TSH) levels alongside reduced serum free T4.[2,3] Lifelong hormone replacement therapy with levothyroxine is the cornerstone of treatment, with regular monitoring and dosage adjustments crucial for managing the condition effectively and preventing complications such as cardiovascular issues and infertility.[1,5]

The intricate relationship among endocrinology, metabolism, and hypothyroidism underscores the multifaceted nature of thyroid dysfunction. Hypothyroidism induces a hypoactive metabolic state that can exacerbate insulin resistance and impair glucose metabolism, thereby heightening the risk of both Type 1 and Type 2 diabetes.[6,7] The interplay between thyroid hormones and insulin is especially pivotal: thyroid hormones regulate key metabolic pathways, while insulin in turn modulates thyroid function — creating a bidirectional dynamic that complicates disease management in patients with multiple comorbidities.[6,8] In addition, hypothyroidism is linked to dyslipidemia and heightened cardiovascular risk.[7,9] Notably, the prevalence of subclinical hypothyroidism is higher among individuals with obesity.[10] Thyroid hormones, chiefly T4 and T3, are central to metabolic regulation, influencing processes such as insulin sensitivity and lipid metabolism.[11,12] Levothyroxine (LT4) remains the standard treatment for hypothyroidism, effectively restoring metabolic balance and improving insulin resistance in those with subclinical hypothyroidism.[11,13]

The interplay between hypothyroidism and sex hormones — namely estrogen, testosterone, and cortisol — remains complex. In men, hypothyroidism is associated with reduced testosterone levels, a decline that can often be reversed through thyroid hormone replacement therapy.[14] Moreover, a genetic predisposition to hypo-

* Corresponding author. Geriatrics Department, Affiliated Hospital of Hebei University, No. 212, Yuhua East Road, Baoding, Hebei Province, 071000 China.
E-mail address: tanlili0000@163.com (L.I. Tan)

thyroidism correlates with decreased sex hormone-binding globulin and testosterone levels.[15] In women, hypothyroidism impairs follicular development and estradiol secretion.[16] Cortisol also shows varied correlations with psychological traits and behaviors, implying that broader hormonal balance, including thyroid function, may influence psychological outcomes differently in men and women.[17]

Building on the complex interplay of various endocrine factors and thyroid hormones, this study aims to determine which endocrine parameters may be associated with the efficacy of thyroid hormone replacement therapy (THRT) in elderly patients with hypothyroidism. We hypothesize that these endocrine factor levels could influence therapeutic outcomes, potentially necessitating dosage adjustments to enhance treatment effectiveness in this population. By identifying and examining these factors, our investigation seeks to lay the groundwork for more tailored, effective treatment protocols for managing hypothyroidism in the elderly.

2. Subjects and methods

This study was a retrospective observational analysis involving 150 elderly patients with hypothyroidism. Approval was obtained from the Ethics Committee of the Affiliated Hospital of Hebei University, and informed consent was secured from all participants. The inclusion criteria were: (1) age $\geq$ 65 years; (2) a diagnosis of hypothyroidism confirmed by clinical evaluation and laboratory tests; and (3) no prior THRT. The exclusion criteria were: (1) severe comorbidities such as cardiovascular disease or chronic kidney disease; (2) any condition that affects thyroid hormone metabolism (e.g., pituitary dysfunction or adrenal insufficiency); (3) a history of thyroid cancer or pituitary disease; and (4) use of medications known to significantly interfere with thyroid hormone metabolism (e.g., glucocorticoids or amiodarone).[18]

Blood samples were collected by venipuncture into serum separator tubes (BD Vacutainer® SST™) and left at room temperature for 30 minutes to clot before centrifugation at 3,000 $\times$ g for 15 minutes. The resulting serum was then aliquoted and stored at –80 °C until further analysis. Thyroid function tests (T3, T4, and TSH) were conducted using standardized assays (Tellgen, China). Estrogen, testosterone, cortisol, insulin, leptin, and ghrelin levels were measured with commercially available enzyme-linked immunosorbent assay (ELISA) kits, following the manufacturers' instructions. Each sample and standard were measured in triplicate, and optical density readings were obtained using a microplate reader. The inter- and intra-assay coefficients of variation were maintained below 10%, ensuring accuracy and reliability of the hormone measurements.

Thyroid hormone replacement therapy generally involves administering levothyroxine (LT4) to restore normal thyroid function in hypothyroid patients. An initial daily dose of approximately 1.6 μg/kg is commonly recommended for otherwise healthy adults, with dose calculations based on ideal body weight in patients who are overweight. After therapy is initiated, serum TSH (and occasionally free T4) levels are measured at around 6–8 weeks to evaluate dose adequacy. If TSH remains elevated, indicating under-replacement, the daily dose is typically increased by 12.5–25 μg. Conversely, if TSH is suppressed below the normal range, the dose is lowered by a similar increment. Once TSH levels stabilize within the normal or target range and clinical symptoms are controlled, routine follow-up every 6–12 months is generally sufficient.

Data collection aimed to gather comprehensive clinical, biochemical, and symptomatic information for each participant. Demographic data included age, sex, and body mass index (BMI). Medication history was recorded in detail, covering both prescribed and over-the-counter medications, as well as any prior or current use of THRT.

2.1. Statistical analysis

Baseline characteristics were analyzed using either the t-test or the χ^2 test, as appropriate. Univariable and multivariable logistic regression analyses were then conducted to assess independent factors associated with treatment efficacy. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using STATA version 9 (StataCorp LP, College Station, TX).

3. Result

3.1. Baseline characteristics of the study population

Table 1 summarizes the clinical characteristics of the 150 study participants, including age, gender, and BMI. Most individuals (87.3%, n = 131) had no family history of thyroid disease, while 12.7% (n = 19) reported a positive familial history. Among the cohort, 54.7% (n = 82) presented with unilateral thyroid nodules, and 45.3% (n = 68) had bilateral thyroid nodules. Hormone levels — TSH, T3, T4, parathyroid hormone (PTH), insulin, leptin, ghrelin, estrogen, testosterone, and cortisol — were also measured.

3.2. Complete efficacy of thyroid hormone replacement therapy

As expected, TSH levels decreased significantly from a baseline mean of 4.99 $\pm$ 1.48 mU/L to 2.30 $\pm$ 0.95 mU/L (p < 0.001), and this difference remained significant even after Holm–Bonferroni correction (adjusted p < 0.01) (Supplementary Table S1). Although T3 and T4 also showed improvement in unadjusted analyses, they did not retain significance once corrected for multiple comparisons (Supplementary Table S1). No other hormone (insulin, leptin, ghrelin, estrogen, testosterone, cortisol, PTH) exhibited statistically significant changes between baseline and post-treatment values.

We defined efficacy as the proportion of patients who achieved

Table 1
Clinical characteristics of participants.

Characteristic	Total participants (n = 150)
Age (years)	65.8 $\pm$ 5.6
Gender	
Male, n (%)	69 (46.0%)
Female, n (%)	81 (54.0%)
BMI (kg/m²)	23.3 $\pm$ 3.1
Family history of thyroid disease	
No	131 (87.3%)
Yes	19 (12.7%)
Admission diagnosis	
Unilateral nodule	82 (54.7%)
Bilateral nodule	68 (45.3%)
Hormone levels	
TSH (mU/L)	4.99 $\pm$ 1.48
T3 (ng/dL)	0.99 $\pm$ 0.20
T4 (μg/dL)	5.18 $\pm$ 1.12
PTH (pg/mL)	55.79 $\pm$ 22.88
Insulin (μU/mL)	10.24 $\pm$ 3.05
Leptin (ng/mL)	30.71 $\pm$ 8.07
Ghrelin (pg/mL)	101.86 $\pm$ 30.27
Estrogen (pg/mL)	29.94 $\pm$ 10.21
Testosterone (ng/dL)	213.96 $\pm$ 58.31
Cortisol (nmol/L)	150.00 $\pm$ 37.00

a euthyroid state, as determined by TSH levels falling within the laboratory's normal reference range (0.4–4.5 mU/L), as well as symptomatic improvement. Table 2 displays the efficacy of thyroid hormone replacement therapy across various demographic and clinical subgroups within the study population. Overall efficacy was 85.3%.

Although unadjusted analyses suggested modest efficacy differences by age, sex, BMI, and hormone levels, none remained significant after Holm–Bonferroni correction (all adjusted p > 0.05) (Table 2). Lower efficacy was initially observed for overweight (78.7%) and obese (75.8%) participants compared to those with normal (93.5%) or underweight (91.7%) BMI, but this association was lost after correction (Table 2). Higher insulin (> 20 μU/mL) or leptin (> 20 ng/mL) also showed lower efficacy (~74%), yet these relationships did not persist post-adjustment (Table 2). No significant differences emerged in any hormone subgroups (Table 2).

3.3. Correlation analysis between hormone levels and therapy efficacy

Table 3 displays the correlation analysis results for various hormone levels and the efficacy of thyroid hormone replacement therapy (THRT), as determined by TSH levels. Insulin showed a significant negative correlation with therapy efficacy (r = –0.45, p = 0.0002), indicating that higher insulin levels are linked to reduced treatment effectiveness. A similarly significant negative correlation was observed with leptin (r = –0.38, p = 0.001).

In contrast, ghrelin, estrogen, testosterone, and cortisol did not exhibit statistically significant relationships with treatment efficacy. Their correlation coefficients — ghrelin (–0.12, p = 0.35), testosterone (–0.10, p = 0.28), estrogen (0.13, p = 0.15), and cortisol (0.05, p = 0.52) — reflected only weak associations, none of which reached significance (Table 3).

3.4. Logistic regression analysis on factors influencing the efficacy of thyroid hormone replacement therapy

Table 4 details the outcomes of logistic regression analyses assessing the influences on the efficacy of thyroid hormone replacement therapy in elderly patients with hypothyroidism.

In the univariate analysis, BMI, insulin, and leptin were significantly associated with therapy efficacy (Table 4). After adjusting for potential confounders in the multivariate analysis, insulin and leptin remained significant predictors, whereas BMI's effect was no longer statistically significant (Table 4). Other factors, including age, ghrelin, estrogen, testosterone, and cortisol, did not show any significant influence on treatment efficacy in either the univariate or multivariate models (Table 4).

4. Discussion

This study sought to investigate the influence of various endocrine factors on the efficacy of thyroid hormone replacement therapy in elderly patients with hypothyroidism. Our findings indicate that insulin and leptin levels are key predictors of treatment success. Consequently, closer monitoring of TSH and thyroid hormone levels may be advisable for patients at higher risk. This investigation lays the groundwork for more personalized and effective management strategies for hypothyroidism in the elderly.

Hypothyroidism markedly influences body metabolism by altering thyroid hormone levels and subsequent metabolic processes. Because thyroid hormones regulate energy expenditure, lipid metabolism, and glucose homeostasis, hypothyroidism often leads to insulin resistance and dyslipidemia.[19,20] Thyroid hormone replacement therapy (THRT), especially levothyroxine, has demonstrated improvements in metabolic markers, such as insulin sensitivity and lipid pro-

Table 2
Complete efficacy of thyroid hormone replacement therapy.

	Efficacy (%)	*p* value	Holm–Bonferroni adjusted p-value
Overall	85.3%	-	
Age		0.35	1.26
65–74 (n = 59)	88.1%		
75–84 (n = 65)	84.6%		
85+ (n = 26)	80.8%		
Gender		0.21	1.26
Male (n = 65)	84.6%		
Female (n = 85)	85.9%		
BMI		0.01	0.09
Underweight (< 18.5) (n = 12)	91.7%		
Normal (18.5–24.9) (n = 62)	93.5%		
Overweight (25.0–29.9) (n = 47)	78.7%		
Obese (≥ 30) (n = 29)	75.8%		
Insulin		0.02	0.16
Low (< 5.0 mU/L) (n = 23)	87.0%		
Normal (5.0–20.0 mU/L) (n = 88)	90.0%		
High (> 20.0 mU/L) (n = 39)	74.4%		
Leptin		0.02	0.16
Low (< 2.0 ng/mL) (n = 27)	85.2%		
Normal (2.0–20.0 ng/mL) (n = 89)	90.0%		
High (> 20.0 ng/mL) (n = 34)	73.5%		
Ghrelin		0.51	1.92
Low (< 500 pg/mL) (n = 34)	82.3%		
Normal (≥ 500 pg/mL) (n = 116)	86.2%		
Estrogen		0.48	1.92
Low (< 20 pg/mL) (n = 29)	82.8%		
Normal (≥ 20 pg/mL) (n = 121)	86.0%		
Testosterone		0.59	1.92
Low (< 3 ng/mL) (n = 22)	81.8%		
Normal (≥ 3 ng/mL) (n = 128)	85.9%		
Cortisol		0.73	1.92
Low (< 5 μg/dL) (n = 28)	85.7%		
Normal (≥ 5 μg/dL) (n = 122)	85.2%		

Table 3
Correlation analysis between hormone levels and therapy efficacy.

Hormone	Correlation coefficient	*p* value	Holm–Bonferroni adjusted p-value
Insulin	-0.45	0.0002	0.0012
Leptin	-0.38	0.001	0.005
Ghrelin	-0.12	0.35	0.60
Estrogen	0.13	0.15	0.84
Testosterone	-0.10	0.28	0.84
Cortisol	0.05	0.52	0.84

Table 4
Logistic regression analysis.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.05 (0.98–1.11)	0.12		
Gender	0.93 (0.44–1.98)	0.22		
BMI	0.83 (0.65–1.02)	0.03	0.95 (0.78–1.08)	0.15
Insulin	0.67 (0.47–0.75)	< 0.01	0.72 (0.57–0.87)	< 0.01
Leptin	0.73 (0.55–0.84)	< 0.01	0.78 (0.64–0.91)	0.02
Ghrelin	0.94 (0.80–1.03)	0.27		
Estrogen	1.05 (0.92–1.20)	0.40		
Testosterone	0.98 (0.85–1.12)	0.75		
Cortisol	1.10 (0.92–1.28)	0.28		

files, in individuals with subclinical hypothyroidism.[11,21] This treatment can also normalize metabolic imbalances by enhancing fatty acid oxidation and modifying bile acid production.[21] Insulin, a key modulator of serum leptin levels — particularly under conditions like diabetes and hypothyroidism — further underscores the interwoven nature of these hormones.[22] In subclinical hypothyroidism, levothyroxine therapy improves insulin resistance and metabolic profiles, suggesting a beneficial effect on leptin and overall metabolic health.[11] Additionally, hypothyroidism is linked to weight gain and disrupted leptin levels, potentially impairing reproductive function.[23] Studies have shown that levothyroxine normalizes serum leptin levels in both overt and subclinical hypothyroidism.[24] As indicated by our logistic regression analysis, insulin and leptin emerged as significant predictors of THRT efficacy. Physiologically, both hormones play integral roles in metabolic regulation and energy homeostasis, likely intersecting with thyroid hormone pathways. Elevated insulin may impair thyroid hormone utilization through increased peripheral resistance, as evidenced by research on metabolic syndrome and thyroid function.[25]

We acknowledge the ongoing debate about indications, benefits, and risks of treating subclinical hypothyroidism in elderly patients. Although the TSH (4.99 mU/L) in our cohort falls within the subclinical hypothyroidism range, many participants had repeated TSH measurements above the upper limit of normal and exhibited symptoms suggestive of hypothyroidism (e.g., fatigue, weight gain, and metabolic disturbances). Clinical practice guidelines emphasize an individualized approach for subclinical hypothyroidism, particularly in the elderly who may present with nuanced or atypical symptoms and face higher cardiovascular risks.[26,27] Emerging evidence suggests that even mild thyroid dysfunction can exacerbate insulin resistance, dyslipidemia, and cardiovascular risk in older adults.[28–30] We therefore hypothesized that optimizing thyroid function — even if subclinical — might confer metabolic and symptomatic improvements. Indeed, several participants reported symptomatic benefits following low-dose levothyroxine therapy. Recognizing that there is no universal consensus on treating subclinical hypothyroidism in older adults, we followed an individualized treatment model that considered repeated TSH tests, clinical symptoms, comorbidities, and patient preferences. This approach aligns with recent guidelines recommending shared decision-making and a cautious trial of levothyroxine in symptomatic subclinical hypothyroidism.[26,31]

The relationship among BMI, hypothyroidism, and THRT is intricate and multifaceted. Previous research highlights the difficulties of managing hypothyroidism in patients with obesity.[32] Studies indicate that BMI significantly influences levothyroxine dosing; obese patients often require lower dosages than individuals of normal weight.[33] Additionally, hypothyroidism can trigger metabolic disturbances that promote weight gain, while obesity may disrupt the hypothalamic-pituitary-thyroid axis and elevate TSH levels.[34] Although levothyroxine therapy can lead to modest weight loss, it is largely attributable to water rather than fat loss, and its effect on weight in euthyroid individuals remains inconclusive.[35] As a result, the interplay between thyroid function and obesity calls for careful clinical consideration, especially when initiating THRT in obese patients with hypothyroidism.[34]

In our study, patients with a low or normal BMI demonstrated the highest response rate, while those who were overweight showed a markedly lower efficacy. These findings underscore the importance of considering BMI when individualizing treatment strategies. The influence of BMI on thyroid function is well-documented, with obesity known to alter thyroid hormone metabolism and often necessitate higher medication dosages.[32]

This study offers valuable insights into the efficacy of thyroid hormone replacement therapy in elderly patients. However, several limitations should be acknowledged. First, the small sample size may not have provided sufficient statistical power for subgroup analyses. Second, the single-center nature of the study could introduce selection bias, limiting the generalizability of the results to broader elderly populations. Finally, relying solely on static hormone measurements (e.g., TSH, T3, T4) without accounting for diurnal variations or dynamic testing may reduce the depth of insight into individual hormone responsiveness. Recognizing these limitations underscores the importance of interpreting the findings with caution and highlights the need for additional multicenter and longitudinal research to confirm these results.

This study underscores the essential influence of metabolic and hormonal factors on the efficacy of thyroid hormone replacement therapy in elderly patients. The findings highlight the promise of a precision medicine approach, which integrates metabolic and endocrine profiling into standard care protocols to enhance therapeutic outcomes. Ultimately, the adoption of these personalized strategies offers a promising pathway toward optimizing thyroid hormone therapy and improving quality of life for older adults with hypothyroidism.

Funding

The Baoding Science and Technology Bureau in Hebei Province (2341ZF342).

Ethical approval

The study was approved by the ethical committee of Affiliated Hospital of Hebei University (HDFYLL-KY-2024-013) and informed consent was obtained from all participants.

Conflict of interest

The authors declare no conflict of interest.

Supplementary materials

Supplementary materials for this article can be found at http://www.sgecm.org.tw/ijge/journal/view.asp?id=35.

References

1. Taylor PN, Medici MM, Hubalewska-Dydejczyk A, Boelaert K. Hypothyroidism. *Lancet*. 2024;404(10460):1347–1364. doi:10.1016/S0140-6736(24)01614-3
2. Virippil N, Merck A, Beckett E, Exley S, Kabadi U. Hypothyroidism: Pathophysiology and Management. In: Gensure R, ed. *Hypothyroidism - Causes, Screening and Therapeutic Approaches*. IntechOpen; 2024. doi:10.5772/intechopen.1004851
3. Bhandari P, Manandhar L, Kandel D. Understanding hypothyroidism: Causes, symptoms, diagnosis, and treatment. *Am J Patient Health Info*. 2024;1(2). doi:10.69512/ajphi.v1i2.68
4. Hasan A, Hasan MR, Jafreen R. Thyroid imbalance and hypothyroidism: A review. *Int J Public Health Excellence*. 2024;4:151–162. doi:10.55299/ijphe.v4i1.1046
5. Zamwar UM, Muneshwar KN. Epidemiology, types, causes, clinical presentation, diagnosis, and treatment of hypothyroidism. *Cureus*. 2023;15(9):e46241. doi:10.7759/cureus.46241
6. Singh J, Singh K, Kumar U. Epidemiological and clinical implications of coexisting thyroid dysfunction and diabetes mellitus. *Int J Clin Biochem Res*. 2024;11(2):66–72. doi:10.18231/j.ijcbr.2024.012
7. Vemula SL, Aramadaka S, Mannam R, et al. The impact of hypothyroidism

on diabetes mellitus and its complications: A comprehensive review. *Cureus*. 2023;15(6):e40447. doi:10.7759/cureus.40447
8. Nishi M. Diabetes mellitus and thyroid diseases. *Diabetol Int*. 2018;9(2):108–112. doi:10.1007/s13340-018-0352-4
9. Rowland D. Study about hypothyroidism as an underdiagnosed metabolic disorder. In: Ito S, ed. *Current Overview on Disease and Health Research Vol. 5*. B P International; 2022:39–45. doi:10.9734/bpi/codhr/v5/7941F
10. Biondi B. Subclinical hypothyroidism in patients with obesity and metabolic syndrome: A narrative review. *Nutrients*. 2023;16(1):87. doi:10.3390/nu16010087
11. Roohigilani K, Ebadi SA, Hajighasemi M, Shahrzad MK, Pishgahi M. The effect of thyroid hormone replacement on the metabolic control and insulin resistance in patients with subclinical hypothyroidism. *Arch Men Health*. 2021;5(1):e16. doi:10.22037/mhj.v5i1.34403
12. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. *Physiol Rev*. 2014;94(2):355–382. doi:10.1152/physrev.00030.2013
13. Jonklaas J. Optimal thyroid hormone replacement. *Endocr Rev*. 2022;43(2):366–404. doi:10.1210/endrev/bnab031
14. Meikle AW. The interrelationships between thyroid dysfunction and hypogonadism in men and boys. *Thyroid*. 2004;14 Suppl 1:S17–S25. doi:10.1089/105072504323024552
15. Kjaergaard AD, Marouli E, Papadopoulou A, et al. Thyroid function, sex hormones and sexual function: a Mendelian randomization study. *Eur J Epidemiol*. 2021;36(3):335–344. doi:10.1007/s10654-021-00721-z
16. Tohei A. Studies on the functional relationship between thyroid, adrenal and gonadal hormones. *J Reprod Dev*. 2004;50(1):9–20. doi:10.1262/jrd.50.9
17. Flegr J, Hampl R, Černochová D, et al. The relation of cortisol and sex hormone levels to results of psychological, performance, IQ and memory tests in military men and women. *Neuro Endocrinol Lett*. 2012;33(2):224–235.
18. Cappola AR, Fried LP, Arnold AM, et al. Thyroid status, cardiovascular risk, and mortality in older adults. *JAMA*. 2006;295(9):1033–1041. doi:10.1001/jama.295.9.1033
19. Teixeira PFDS, Dos Santos PB, Pazos-Moura CC. The role of thyroid hormone in metabolism and metabolic syndrome. *Ther Adv Endocrinol Metab*. 2020;11:2042018820917869. doi:10.1177/2042018820917869
20. Moon JH. Hypothyroidism and metabolic syndrome. *J Korean Thyroid Assoc*. 2013;6(2):101–105. doi:10.11106/jkta.2013.6.2.101
21. Benabdelkamel H, Jaber MA, Dahabiyeh LA, et al. Metabolomic profile of patients on levothyroxine treatment for hypothyroidism. *Eur Thyroid J*. 2023;12(4):e230062. doi:10.1530/ETJ-23-0062
22. Kosova F, Sepici-Dincel A, Engin A, Memiş L, Koca C, Altan N. The thyroid hormone mediated effects of insulin on serum leptin levels of diabetic rats. *Endocrine*. 2008;33(3):317–322. doi:10.1007/s12020-008-9093-7
23. Aiceles V, da Fonte Ramos C. A link between hypothyroidism, obesity and male reproduction. *Horm Mol Biol Clin Investig*. 2016;25(1):5–13. doi:10.1515/hmbci-2015-0054
24. Teixeira PF, Cabral MD, Silva NA, et al. Serum leptin in overt and subclinical hypothyroidism: effect of levothyroxine treatment and relationship to menopausal status and body composition. *Thyroid*. 2009;19(5):443–450. doi:10.1089/thy.2007.0393
25. Ghazaryan A, Ovsepian SV, Ntziachristos V. Extended near-infrared optoacoustic spectrometry for sensing physiological concentrations of glucose. *Front Endocrinol (Lausanne)*. 2018;9:112. doi:10.3389/fendo.2018.00112
26. Pearce SH, Brabant G, Duntas LH, et al. 2013 ETA Guideline: Management of subclinical hypothyroidism. *Eur Thyroid J*. 2013;2(4):215–228. doi:10.1159/000356507
27. Biondi B, Cappola AR, Cooper DS. Subclinical hypothyroidism: A review. *JAMA*. 2019;322(2):153–160. doi:10.1001/jama.2019.9052
28. Park SB, Choi HC, Joo NS. The relation of thyroid function to components of the metabolic syndrome in Korean men and women. *J Korean Med Sci*. 2011;26(4):540–545. doi:10.3346/jkms.2011.26.4.540
29. Hussain A, Elmahdawi AM, Elzeraidi NE, Nouh F, Algathafi K. The effects of dyslipidemia in subclinical hypothyroidism. *Cureus*. 2019;11(11):e6173. doi:10.7759/cureus.6173
30. Spira D, Buchmann N, Dörr M, et al. Association of thyroid function with insulin resistance: data from two population-based studies. *Eur Thyroid J*. 2022;11(2):e210063. doi:10.1530/ETJ-21-0063
31. Cooper DS, Biondi B. Subclinical thyroid disease. *Lancet*. 2012;379(9821):1142–1154. doi:10.1016/S0140-6736(11)60276-6
32. Tagliaferri M, Berselli ME, Calò G, et al. Subclinical hypothyroidism in obese patients: relation to resting energy expenditure, serum leptin, body composition, and lipid profile. *Obes Res*. 2001;9(3):196–201. doi:10.1038/oby.2001.21
33. Darquea A, Izquierdo R, Huang D, Greenfield M. ODP490 levothyroxine dosing based on BMI and different causes of hypothyroidism. *J Endocr Soc*. 2022;6(Suppl 1):A770. doi:10.1210/jendso/bvac150.1590
34. Gajdzińska N, Salwa A, Rostkowska W, et al. Thyroid dysfunction and obesity - what comes first? A complex relationship between hypothyroidism and weight gain. *J Educ Health Sport*. 2024;74:51733. doi:10.12775/JEHS.2024.74.51733
35. Pearce EN. Thyroid hormone and obesity. *Curr Opin Endocrinol Diabetes Obes*. 2012;19(5):408–413. doi:10.1097/MED.0b013e328355cd6c