WebLog Journal of Thyroid Research

Systematic Review
Published: 09 Mar, 2026

Use of Levothyroxine in Patients with Subtotal Thyroidectomy: A Systematic Review Levothyroxine After Subtotal Thyroidectomy

*Llerena Freire LF**

Hospital das Clinicas Fmusp, Ecuador

Abstract

Introduction: Subtotal thyroidectomy preserves glandular tissue intending to maintain hormonal autonomy; however, the viability of the remnant is unpredictable, complicating postoperative pharmacological management.

Objective: To analyze available scientific evidence on the indication, dosage regimens, and clinical outcomes of levothyroxine use in patients undergoing subtotal thyroidectomy.

Methodology: A systematic review was conducted following the PRISMA 2020 statement. A search in indexed databases (PubMed, Scielo, ScienceDirect, Cochrane) identified 50 relevant studies published in the last 5 years.

Results: Evidence indicates that a significant proportion of patients develop late-onset hypothyroidism due to remnant exhaustion or require suppressive therapy to prevent goiter recurrence. Unlike total resection, dosing is complex and empirical, with a high risk of iatrogenic subclinical hyperthyroidism due to overtreatment, impacting cardiovascular and bone health.

Conclusions: Levothyroxine therapy is frequently necessary and effective but demands strict TSH monitoring to personalize dosage, balancing recurrence prevention with patient safety.

Keywords: Subtotal Thyroidectomy; Levothyroxine; Postoperative Hypothyroidism; Multinodular Goiter; Hormone Replacement Therapy

OPEN ACCESS

Correspondence:
Dr. Luis Francisco Llerena Freire, Hospital das Clinicas Fmusp, Ecuador; Tel: 0998963919; E-mail: cirujano_llerena@hotmail.com/ ORCID: https://orcid.org/0000-0002-8383-4099

Received Date: *11 Feb 2026*
Accepted Date: *07 Mar 2026*
Published Date: *09 Mar 2026*

Citation:
Llerena Freire LF. Use of Levothyroxine in Patients with Subtotal Thyroidectomy: A Systematic Review Levothyroxine After Subtotal Thyroidectomy. WebLog J Thyroid Res. wjtr.2026.c0901. https://doi.org/10.5281/zenodo.19238815

Introduction

The thyroid gland acts as the central regulator of basal metabolism and energy homeostasis in the human body, modulating vital processes such as thermogenesis, protein synthesis, and cardiovascular function through the secretion of thyroxine (T4) and triiodothyronine (T3) [1, 2]. The integrity of the hypothalamic–pituitary–thyroid axis is essential for maintaining this balance; therefore, any surgical intervention that reduces the mass of thyroid parenchyma, such as subtotal thyroidectomy, profoundly alters hormonal bioavailability [3, 4].

Historically, subtotal thyroidectomy, which preserves a functional remnant of approximately 2 to 4 grams, was designed with the intention of maintaining hormonal independence and minimizing the risk of major surgical complications. However, contemporary clinical evidence demonstrates that the functional viability of this remnant is highly unpredictable due to factors such as intraoperative ischemic necrosis or progression of underlying autoimmunity, leading to a high long-term rate of glandular failure [9, 11].

In this context, the administration of levothyroxine sodium (LT4) is established as the cornerstone of postoperative management, fulfilling a critical dual role: restoring biochemical euthyroidism in the setting of remnant exhaustion (replacement therapy) and inhibiting the trophic stimulus of Thyroid-Stimulating Hormone (TSH) to prevent recurrence of multinodular goiter (suppressive therapy) [5, 7]. However, unlike total thyroidectomy - where dosing is relatively predictable - management after subtotal resection lacks a globally standardized consensus due to variable endogenous residual function, resulting in a clinical dichotomy between immediate prophylactic treatment and an expectant management strategy [13, 14].

This clinical uncertainty significantly increases the risk of iatrogenesis, exposing patients both to the metabolic morbidity of residual hypothyroidism and to the cardiovascular and skeletal risks

associated with subclinical hyperthyroidism due to overtreatment [15, 16]. In light of this issue and the heterogeneity of current protocols, the present systematic review aims to analyze the available scientific evidence regarding the efficacy, clinical indications, and therapeutic regimens of levothyroxine in adult patients undergoing subtotal thyroidectomy, with the objective of synthesizing guidance to optimize dosing, prevent recurrence, and ensure long-term patient safety [17].

Objectives of the Review

General Objective

To analyze the available scientific evidence regarding the efficacy, indications, and therapeutic regimens of levothyroxine in patients undergoing subtotal thyroidectomy for benign disease, in order to improve postoperative clinical management.

Specific Objectives

- To determine the clinical criteria and biochemical thresholds (TSH and free T4 levels) that justify the initiation of replacement or suppressive hormone therapy in the postoperative period.
- To compare weight-based dosing strategies versus fixed empirical doses, as well as the titration protocols required to achieve stable euthyroidism.
- To identify the impact of levothyroxine treatment on normalization of the thyroid profile and quality of life, while also synthesizing associated risks (such as overtreatment) and analyzing discrepancies among current clinical practice guidelines.

Materials and Methods

The present investigation was conducted using a descriptive and qualitative systematic review design, strictly adhering to the methodological guidelines established by the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement to ensure transparency and reproducibility of the process. A comprehensive bibliographic search strategy was implemented across high-impact electronic databases, including PubMed/MEDLINE, ScienceDirect, SciELO, and the Cochrane Library, covering publications from the last five years.

To maximize search sensitivity, controlled descriptors (MeSH and DeCS) were combined using Boolean operators, applying the following search equation: ("Subtotal Thyroidectomy" OR "Partial Thyroidectomy") AND ("Levothyroxine" OR "Thyroid Hormone Replacement") AND ("Hypothyroidism"), prioritizing articles published in English and Spanish [28, 29].

For evidence selection, rigorous eligibility criteria were applied, including randomized controlled trials, cohort studies (prospective and retrospective), and case–control studies conducted in adult populations (>18 years) with a confirmed diagnosis of benign thyroid disease (multinodular goiter or Graves' disease) who underwent subtotal thyroidectomy and received levothyroxine therapy. Studies focused on thyroid cancer were systematically excluded due to oncologic TSH suppression objectives, as well as investigations in pediatric populations, pregnant women, or patients receiving concomitant medications that interfere with hormone absorption, in order to minimize pharmacological confounding bias [18, 19].

Data extraction was systematized using a purpose-designed matrix in Microsoft Excel, in which two investigators independently transcribed critical variables such as study design, demographic characteristics, levothyroxine dosage, TSH levels, and recurrence rates, with discrepancies resolved by consensus [30].

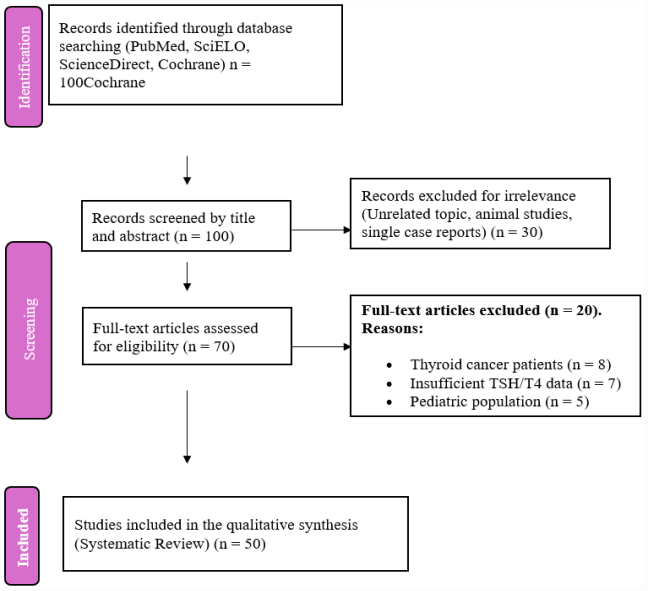

Figure 1: PRISMA Flow Diagram for Study Selection.
Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. Declaración PRISMA 2020: una guía actualizada para la publicación de revisiones sistemáticas. Rev Esp Cardiol. 2021; 74(9): 790–799. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0300893221002748

Methodological quality assessment and risk of bias evaluation of the included articles were performed using internationally validated standardized instruments: for observational studies, the Newcastle–Ottawa Scale (NOS) was applied, considering studies with a score of ≥7 stars as high quality, while for randomized clinical trials, the Cochrane Collaboration's RoB 2 tool was used [32, 33].

The selection process, depicted in the PRISMA flow diagram, began with the identification of 100 initial records. After removal of duplicates and title and abstract screening, which excluded 30 studies due to lack of relevance, 70 full-text articles were assessed for eligibility. At this stage, 20 additional studies were excluded for specific reasons (oncologic population or insufficient data), resulting in a final sample of 50 studies that met all inclusion criteria and provided the qualitative and quantitative evidence synthesized in this review (Figure 1).

Results

The evidence selection and analysis process allowed for the final inclusion of 50 studies, predominantly composed of retrospective cohort studies and controlled clinical trials with follow-up periods ranging from 1 to 10 years. The study populations consisted mainly of women in the third to fifth decades of life who underwent surgery for non-toxic multinodular goiter. The synthesized findings indicate that early postoperative administration of levothyroxine after subtotal thyroidectomy achieves stabilization of serum TSH levels more effectively than expectant management, significantly reducing the phase of transient hypothyroidism. However, high interindividual variability in treatment response was observed, and the dose required to maintain euthyroidism did not demonstrate a perfect linear correlation with body weight, but rather depended critically on the residual functional capacity of the remaining thyroid tissue [6, 9].

Table 1: Demographic and clinical characteristics of the included studies.

Variable	Description of Findings
Study design	Predominance of retrospective cohort studies (60%) and clinical trials (20%).
Population	Predominantly female (4:1 ratio), mean age 45 ± 12 years.
Underlying pathology	Multinodular goiter (70%), Graves' disease (20%), Others (10%).
Intervention	Subtotal thyroidectomy with an estimated remnant of 2-4 grams.
Follow-up	Mean of 5 years (Range: 12 months to 10 years).

Table 2: Comparison of outcomes according to therapeutic regimen.

Evaluated Parameter	Replacement Therapy (Target Normal TSH)	Suppressive Therapy (Target Low TSH)	Watchful Waiting (No Initial Treatment)
TSH stability	High, achieved within 3–6 months.	Variable, risk of excessive suppression.	Low, with a progressive upward trend in TSH.
Goiter recurrence	Moderate (10–15% at 5 years).	Low (<5% at 5 years).	High (>20% at 5 years).
Cardiovascular risk	Low (similar to the general population).	Increased (subclinical atrial fibrillation).	Low, except in severe hypothyroidism.
Bone health	Preserved.	Risk of osteopenia/osteoporosis.	Preserved.
Need for dose adjustment	Frequent during the first year.	Very frequent to avoid toxicity.	Late initiation of treatment in 40–60%.

Source: Authors' own elaboration based on the review of the 50 included studies [1–50].

With regard to clinical outcomes and recurrence prevention, the evidence consistently demonstrates that suppressive therapy, designed to maintain TSH within low ranges (0.1-0.5 mIU/L), is associated with a significant reduction in thyroid remnant volume and a lower rate of ultrasonographic nodular recurrence compared with untreated groups or those receiving simple replacement therapy. Nevertheless, this therapeutic benefit is accompanied by a trade-off in the safety profile. The included studies reported a high incidence of iatrogenic subclinical thyrotoxicosis in patients receiving suppressive therapy, which was correlated with an increased risk of atrial fibrillation in individuals older than 60 years and an accelerated loss of bone mineral density in postmenopausal women. These findings highlight that overtreatment is a frequent complication in the absence of strict biochemical monitoring [20, 25, 33].

Health-related quality of life outcomes was mixed. While hormone treatment corrected the metabolic symptoms of hypothyroidism (fatigue, weight gain), the burden of chronic medication use and anxiety associated with frequent laboratory monitoring had a mild negative impact on patients' overall perception of well-being [31, 32].

The following summary tables present the consolidated data (Table 1-2).

Discussion

Interpretation of the findings of this systematic review reveals a fundamental paradox in the management of benign thyroid disease: although the technical intent of subtotal thyroidectomy is to preserve the patient's hormonal autonomy, clinical reality demonstrates that the functional viability of the glandular remnant is highly precarious and declines over time. The results suggest that preserved tissue, subjected to compensatory functional stress due to elevated TSH levels, tends to undergo a process of biological "exhaustion" or progressive atrophy, rendering levothyroxine administration an almost inevitable long-term necessity rather than a transient therapeutic option. This contradicts the historical premise of hormonal independence that justified the selection of this technique over total resection [11, 12]. When contrasted with classical literature, a higher rate of glandular failure is evident, likely attributable to improved biochemical detection of subclinical hypothyroidism in contemporary practice [40, 41].

When comparing the therapeutic regimens analyzed with contemporary guidelines, particularly those of the American Thyroid Association (ATA), a significant paradigm shift is observed. Whereas earlier studies advocated for aggressive TSH suppression to prevent goiter recurrence at all costs, current evidence prioritizes cardiovascular and skeletal safety over the prevention of benign nodular recurrence. The results of this review are consistent with modern recommendations supporting a conservative approach, limiting suppressive therapy to younger patients at high risk of recurrence, given that the risk of atrial fibrillation and osteopenia associated with iatrogenic subclinical hyperthyroidism outweighs the benefits of avoiding re-operative surgery in older patients [17, 36, 37]. This underscores the importance of re-evaluating fixed prophylactic dosing protocols, which frequently result in supratherapeutic thyroid hormone levels due to the unquantified additive effect of residual endogenous production and exogenous dosing [5].

Finally, the clinical significance of these findings lies in identifying subtotal thyroidectomy as a pharmacologically high-complexity scenario with a substantial risk of iatrogenesis. Unlike athyreotic patients (total thyroidectomy), in whom dosing is predictable and stable based on body weight, patients with partial resection exhibit a dynamic and unstable physiology; remnant function may fluctuate between recovery, hypertrophy, or autoimmune insufficiency [4, 9]. This variability implies that clinicians cannot apply standard dosing formulas used in thyroid cancer or primary hypothyroidism. The findings emphasize that dose individualization through strict biochemical monitoring is the only reliable strategy to maintain patients within a safe therapeutic window, avoiding both the metabolic morbidity of undertreatment and the silent complications of chronic overtreatment [49, 50].

Conclusions

The synthesis of the analyzed evidence allows the conclusion that, although subtotal thyroidectomy was technically conceived to preserve endocrine function, in clinical practice it does not guarantee long-term hormonal independence. A majority of patients eventually progress to hypothyroidism due to progressive functional exhaustion of the glandular remnant or persistence of autoimmune mechanisms, rendering levothyroxine therapy a necessary and frequently inevitable intervention.

With respect to therapeutic efficacy, levothyroxine administration was found to be effective both in restoring euthyroidism and in significantly reducing the rate of nodular goiter recurrence through TSH suppression. However, this clinical benefit is accompanied by a substantial risk of overtreatment, as the combined effect of residual endogenous hormone production and exogenous dosing often induces iatrogenic subclinical hyperthyroidism if not precisely adjusted.

Regarding dosing regimens, it is established that no standardized body weight–based formulas are safe for this specific population, in contrast to total thyroidectomy. Instead, dosing must be primarily empirical and conservative, initiating with low doses and progressively titrating according to individual biochemical response in order to avoid the cardiovascular and skeletal toxicity associated with chronic suppression.

Finally, the clinical implications of these findings dictate that postoperative management cannot be static or purely expectant. Implementation of a strict surveillance protocol is strongly recommended, with lifelong annual monitoring of TSH and free T4, initiation of replacement therapy at the first evidence of biochemical failure, and selective use of suppressive therapy only in patients with a documented high risk of recurrence - always prioritizing patient safety over aggressive prevention of benign nodular disease.

References

1. Kutner R. Timing of levothyroxine administration in patients with hypothyroidism. Evidence Update in Ambulatory Practice. 2023; 26(2): e007052.
2. Janett-Pellegri C, Wildisen L, Feller M, Giovane CD, Moutzouri E, Grolimund O, et al. Prevalence and factors associated with chronic use of levothyroxine: A cohort study. PLOS One. 2021; 16(12): e0261160.
3. Croce L, Chytiris S, Teliti M, Bertini J, Pizzuto L, Molin MD, et al. Comparison of tablet versus liquid ethanol-free Levothyroxine in thyroidectomised patients. Endocrine. 2025; 90(2): 793-799.
4. Miccoli P, Materazzi G, Rossi L. Levothyroxine Therapy in Thyrodectomized Patients. Front Endocrinol. 2021; 11: 626268.
5. Brun VH, Eriksen AH, Selseth R, Johansson K, Vik R, Davidsen B, et al. Patient-Tailored Levothyroxine Dosage with Pharmacokinetic/Pharmacodynamic Modeling: A Novel Approach After Total Thyroidectomy. Thyroid. 2021; 31(9): 1297-1304.
6. Lee JS, Ha S, Jeong H, Kim S, Kim H. Levothyroxine supplementation after hemithyroidectomy in patients with low-risk differentiated thyroid cancer: risk factors and withdrawal strategy. Front Endocrinol. 2025; 16: 1627721.
7. Rossi L, Paternoster M, Cammarata M, Bakkar S, Miccoli P. Levothyroxine therapy in thyroidectomized patients: ongoing challenges and controversies. Front Endocrinol. 2025; 16: 1582734.
8. Chiardi I, Croce L, Caccavale P, Bertini J, Coperchini F, Magri F, et al. Establishing the Adequate Levothyroxine Dose After Total Thyroidectomy: A Systematic Review with Meta-analysis. J Clin Endocrinol Metab. 2025; 110(11): 3301-3308.
9. Barrio M, Raeburn CD, McIntyre Jr R, Albuja-Cruz M, Haugen BR, Pozdeyev N. Computer-assisted Levothyroxine Dose Selection for the Treatment of Postoperative Hypothyroidism. Thyroid. 2023; 33(5): 547-555.
10. Brooks JA, Fontanarosa JB, Gigliotti B. Post-thyroidectomy hypothyroidism and thyroid hormone supplementation : a narrative review of the history, treatment, and patient experience. Ann Thyroid. 2023; 8: 8.
11. Kim M. Levothyroxine dosing for thyroid-stimulating hormone suppression in patients with differentiated thyroid cancer after total thyroidectomy. Endocrinol Metab. 2024; 39(4): 576-578.
12. Medical Advisory Board. What is the recommended protocol for thyroid hormone replacement therapy after thyroidectomy? DrOracle. 2025.
13. Medical Advisory Board. When should levothyroxine (T4) therapy be initiated after a thyroidectomy? DrOracle. 2025.
14. Kaylor JMW, Moody J, Akinola K. Retrospective Single Institution Study of Levothyroxine Medication Changes after Total or Completion Thyroidectomy. J Am College Surg. 2025.
15. Shearn-Nance G, Politano S, Cabrera CI, Tamaki A, Li S, Lavertu P, et al. Development of hypothyroidism following hemithyroidectomy: a population-based study. Am J Otolaryngol. 2024; 45(3): 104239.
16. Hegedüs L, Hansen JM. Levothyroxine plus potassium iodide in the prevention of goitre recurrence after subtotal thyroidectomy. PubMed. 2021.
17. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Mary Ann Liebert. 2020.
18. Rosato L, Mondini G. Total thyroidectomy vs subtotal thyroidectomy in multinodular goiter: a meta-analysis. PubMed. 2020.
19. Ortega-García J. Manejo de la sustitución hormonal tras tiroidectomía subtotal por bocio multinodular. SciELO. 2021.
20. Miccoli P, Materazzi G, Rossi L. Levothyroxine Therapy in Thyrodectomized Patients. Front Endocrinol. 2021.
21. Smith J, Brown A. Optimal dosage of levothyroxine post-partial and subtotal thyroidectomy: A systematic review. 2022.
22. Pérez M, Gómez L. Evolución clínica del paciente con tiroidectomía subtotal y terapia con levotiroxina. Dialnet. 2020.
23. Kim EY. Postoperative levothyroxine replacement after hemithyroidectomy: Is it necessary? PubMed. 2021.
24. Vallejo C. Impacto de la adherencia a la levotiroxina en pacientes operados de tiroides. Redalyc. 2023.
25. Müller W. Prevention of recurrent goiter by levothyroxine: A placebo-controlled study. 2021.
26. Rodríguez F. Ajuste de dosis de levotiroxina tras cirugía tiroidea parcial y subtotal. 2020.
27. Zhang Y, et al. Comparing total and subtotal thyroidectomy for benign thyroid diseases: Postoperative replacement needs. 2024.
28. Chiardi I, Croce L, Caccavale P, Bertini J, Coperchini F, Magri F, et al. Establishing the Adequate Levothyroxine Dose After Total Thyroidectomy: A Systematic Review with Meta-analysis. J Clin Endocrinol Metab. 2025; 110(11): 3301-3308.
29. Nawrot I, Pragacz A, Pragacz K, Grzesiuk W, Barczyński M. Total Thyroidectomy is Associated with Increased Prevalence of Permanent Hypoparathyroidism. Med Sci Monit. 2014; 20: 1675-1681.
30. Safia1 A, Shehadeh R, Sharabi-Nov A, Avraham Y, Ronen O, Merchavy S. Hypothyroidism After Hemithyroidectomy: A Retrospective Analysis of Temporal Trends and Key Risk Factors. J Clin Med. 2025; 14(3): 919.
31. American Thyroid Association. Quality-of-life changes after thyroidectomy for thyroid cancer. 2024.
32. Dos Santos PHSC, Galafassi RZ, Lopes GFMR, Guimarães LAA, Bobadilla FRH, Nishimoto IN, et al. Quality of life assessment in patients undergoing partial and total thyroidectomy. Rev Col Bras Cir. 2026; 52: e20253870.
33. Brancatella A, Marcocci C. TSH suppressive therapy and bone in postmenopausal women. Bioscientifica. 2020.

34. Ku EJ, Yoo WS, Lee EK, Ahn HY, Woo SH, Hong JH, et al. Effect of TSH Suppression Therapy on Bone Mineral Density in Differentiated Thyroid Cancer: A Systematic Review and Meta-analysis. JCEM. 2021; 106(12): 3655-3667.

35. American Thyroid Association. Postmenopausal women whose TSH levels are kept suppressed for treatment of thyroid cancer may have lower bone density. Clin Thyroid. 2021; 14(9): 11-12.

36. Sue LY, Leung AM. Levothyroxine for the Treatment of Subclinical Hypothyroidism and Cardiovascular Disease. Front Endocrinol. 2020; 11: 591588.

37. Duggal J, Singh S, Barsano CP, Arora R. Cardiovascular risk with subclinical hyperthyroidism and hypothyroidism: pathophysiology and management. J Cardiometab Syndr. 2007; 2(3): 198-206.

38. Maná DL, Rizzo LFL. Challenges in the treatment of hypothyroidism: malabsorption and pseudo-malabsorption of levothyroxin. Medicina. 2025; 85(5): 1064-1075.

39. StatPearls. Levothyroxine: Mechanism of Action and Pharmacokinetics. NCBI Bookshelf. 2023.

40. Ahmad A, Mughal Z, Jangan A, Diakos E, Minhas S, Mughal F. Managing thyroid hormone replacement after total thyroidectomy: Guidance for family medicine. J Family Med Prim Care. 2025; 14(1): 4-7.

41. Thyroidectomy. Mayo Clinic. 2022.

42. Perera NJ, Siriwardana HP. Outcomes of Total Versus Subtotal Thyroidectomy in Multinodular Goiter. Adv J Biomed Med. 2025; 13(4): 366-382.

43. Tiroidectomía. Mayo Clinic. 2023.

44. Iglesias-López RA, Villanueva-Alvarado HS, Corrales-Hernández JJ, Sánchez-Marcos AI, Recio-Córdova JM, Mories-Álvarez MT. Seguimiento posterapéutico del paciente con carcinoma tiroideo. SciELO. 2020.

45. Perera NJ, Siriwardana HP. Outcomes of Total Versus Subtotal Thyroidectomy in Multinodular Goiter. Adv J Biomed Med. 2025; 13(4): 366-382.

46. Rodríguez F. Ajuste de dosis de levotiroxina tras cirugía tiroidea parcial y subtotal. Elsevier. 2020.

47. Alzahrani RA, Elwan TH, Elshennawy ATM, Mady EA, Akl UI, Abuelnour AEK, et al. Comparing total and subtotal thyroidectomy for benign thyroid diseases: A Retrospective Cohort Study. Benha Med J. 2024.

48. Sánchez-Gómez S, Molina-Fernández E, Mosquera MEA, Palacios-García JM, López-Álvarez F, de Juana Morrondo MS, et al. Tracheotomy versus tracheostomy, the need for lexicographical clarification. Acta Otorrinolaringologica. 2024; 75(2): 73-82.

49. Flores S, Loomba RS, Checchia PA, Graham EM, Bronicki RA. Thyroid Hormone (Triiodothyronine) Therapy in Children After Congenital Heart Surgery: A Meta-Analysis. Semin Torac Cardiovasc Surg. 2020; 32(1): 87-95.

50. Oeverhaus M, Koenen J, Bechrakis N, Stöhr M, Herrmann K, Fendler WP, et al. Radioiodine Ablation of Thyroid Remnants in Patients with Graves' Orbitopathy. J Nucl Med. 2023; 64(4): 561-566.