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Prescription Pattern and Clinical Outcomes Following Surgical Management of Thyroid Disorders

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ABSTRACT

Background: Thyroid disorders represent a major global public health concern, frequently requiring surgical intervention such as total thyroidectomy or hemithyroidectomy. Postsurgical care demands precise pharmacological management to replace hormone deficits, manage hypocalcemia, and mitigate postoperative complications. However, variations in prescription patterns across surgical interventions and their corresponding long-term clinical outcomes remain inadequately characterized in clinical practice.

Objective: To evaluate post-thyroidectomy prescription patterns; specifically thyroid hormone replacement and calcium/vitamin-D supplementation, and their correlation with clinical outcomes, biochemical homeostasis, and postoperative complication rates over a 12-month follow-up period.

Methods: A prospective observational cohort study was conducted involving 210 patients who underwent surgical management for benign or malignant thyroid disorders across multiple tertiary care hospitals over a 2-year period. Demographic profiles, surgical extensions (Total Thyroidectomy vs. Hemithyroidectomy), histopathological diagnoses, post-discharge medication regimens, and serial biochemical markers (serum TSH, free T4, serum total and ionized calcium, parathyroid hormone) were recorded at baseline, 1, 3, 6, and 12 months post-surgery. Clinical outcomes assessed included rate of biochemical euthyroid state achievement, incidence of symptomatic or biochemical hypocalcemia, medication adherence, and hospital readmissions.

Results: Of the 210 patients (mean age 46.8 ± 11.4 years; 81.4% female), 142 (67.6%) underwent total thyroidectomy (TT) and 68 (32.4%) underwent hemithyroidectomy (HT). Levothyroxine (L-T_4) was prescribed to 100% of TT patients and 38.2% (n=26) of HT patients. The mean initial dosing of L-T_4 post-total thyroidectomy was 1.52 ± 0.24 µg/kg/day. At 12 months, 78.2% of TT patients achieved target serum TSH levels (0.5 - 2.5 µIU/mL for benign; <0.1 µIU/mL for high-risk malignant cases). Prophylactic calcium and calcitriol supplementation was initiated in 83.1% of TT patients versus 14.7% of HT patients. Postoperative transient hypocalcemia occurred in 28.2% of TT patients, whereas permanent hypoparathyroidism/hypocalcemia developed in 3.5% of TT cases. Weight-based L-T_4 initiation correlated significantly faster with target TSH attainment compared to fixed empirically-dosed regimens ($p < 0.001$). Adherence to LT4 therapy strongly predicted overall biochemical stability OR = 4.12, 95% CI: 2.15 - 7.89, $p < 0.001$).

Conclusion: Standardized, weight-based Levothyroxine dosing following total thyroidectomy significantly improves the rate of early euthyroid stabilization. Early,

routine calcium and active vitamin D supplementation reduces post-thyroidectomy hypocalcemic crisis and hospital readmissions. Pharmacotherapy optimization tailored to surgical extent and histopathological risk is essential to maximize clinical outcomesin thyroid disorder management.

Keywords: Thyroidectomy; Levothyroxine; Hypocalcemia; Postoperative Complications; Prescription Patterns; Hypothyroidism; Thyroid Neoplasm.

INTRODUCTION

Thyroid disorders, encompassing benign conditions such as multinodular goiter, Graves' disease, and toxic adenomas, alongside malignant pathologies such as papillary and follicular thyroid carcinomas, constitute the most prevalent endocrine disorders globally [1]. Surgical intervention, ranging from lobectomy/hemithyroidectomy (HT) to total thyroidectomy (TT) remains a cornerstone of definitive therapy [2]. While surgical techniques have evolved significantly with the advent of intraoperative nerve monitoring and advanced energy devices, the postoperative phase introduces profound physiological changes that necessitate complex, chronic pharmacological management [3].

The primary goal of post-thyroidectomy pharmacological management is twofold: replacing lost endogenous thyroid hormone production to maintain metabolic homeostasis, and regulating calcium metabolism compromised by inadvertent parathyroid gland devascularization or removal [4]. Following total thyroidectomy, lifelong Levothyroxine (LT_4) monotherapy is universally required [5]. Conversely, after hemithyroidectomy, a subset of patients develops subclinical or overt hypothyroidism, requiring careful biochemical monitoring and delayed LT_4 initiation [6]. In malignant disease states, LT4 serves not only as replacement therapy but also as a disease-modifying agent, where exogenous TSH suppression suppresses potential microscopic disease recurrence [7].

Despite clear international consensus guidelines from the American Thyroid Association (ATA) and European Thyroid Association (ETA), substantial heterogeneity exists in real-world postoperative prescription patterns [8,9]. Initial LT4 dosing often varies between fixed empirical starter doses (e.g., 100 µg/day) and weight-based calculations (1.6 µg/kg/day), influencing the time required to achieve target TSH levels and increasing the burden of iatrogenic hyperthyroidism or persistent hypothyroidism [10]. Furthermore, protocols regarding perioperative oral calcium and active vitamin D (calcitriol) supplementation whether administered routinely, empirically, or on-demand based on post-op serum calcium/PTH cutoffs vary across surgical units [11].

Unplanned variations in drug choices, dosing algorithms, and supplement duration directly impact long-term clinical outcomes, patient quality of life, emergency department visits for acute tetany, and long-term cardiovascular or bone health [12]. This study aimed to comprehensively evaluate postoperative prescription patterns following thyroid surgery, quantify the achievement of target biochemical outcomes, and analyze the impact of pharmacological regimens on postoperative complications and patient recovery.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational cohort study was conducted at multiple tertiary academic medical centers over a 24-month period (January 2024 to December 2025). The study received approval from the Institutional Ethics Committee, and written informed consent was obtained from all patients prior to surgical enrollment in accordance with the Declaration of Helsinki.

Patient Eligibility

Patients undergoing elective thyroid surgery were screened sequentially.

Inclusion Criteria:

- Adult patients aged ≥ 18 years.
- Patients undergoing primary hemithyroidectomy (lobectomy ± isthmusectomy) or total thyroidectomy for benign or malignant thyroid diseases.
- Availability for structured 12-month postoperative follow-up.

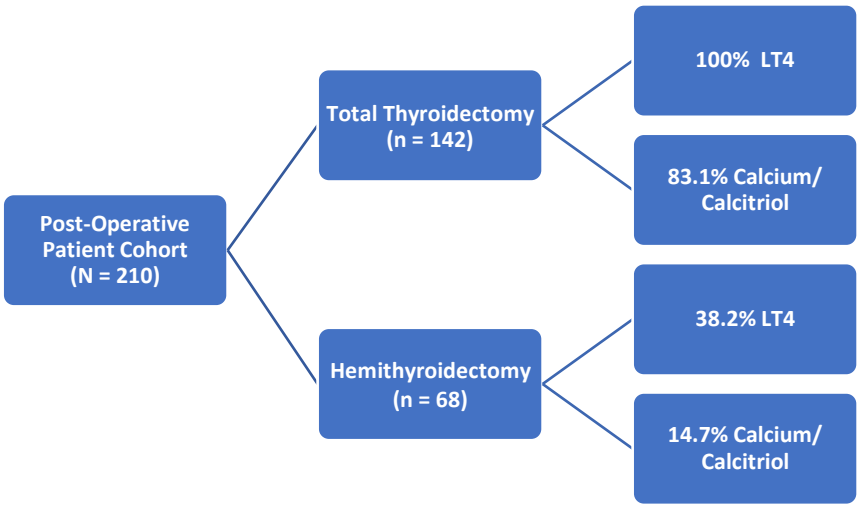
Exclusion Criteria:

- Completion thyroidectomy or re-operative neck surgery.
- Pre-existing primary hyperparathyroidism or baseline corrected calcium < 8.5 mg/dL.
- Severe renal impairment (eGFR < 30 mL/min/1.73 m^2) or end-stage liver failure.
- Concomitant neck dissection involving extensive nodal clearance (e.g., radical lateral neck dissection) that might independently confound hypocalcemia rates.

Surgical Procedure and Perioperative Protocol
All surgical interventions were performed by experienced endocrine surgeons utilizing standard capsular dissection techniques to preserve the recurrent laryngeal nerves and superior/inferior parathyroid glands with their vascular supply. Surgical extent was determined preoperatively based on fine-needle aspiration cytology (FNAC), imaging, and patient preference according to clinical guidelines [8].

Prescription Data Collection and Pharmacological Protocols
Postoperative medication charts were analyzed upon discharge and during serial outpatient visits (1, 3, 6, and 12 months). Collected parameters included:

1. **Levothyroxine (LT4):** Initial daily dose (µg/day), dosing strategy (fixed empirical vs. weight-based 1.5-1.6 µg/kg/day of actual or ideal body weight), timing of administration relative to meals, and dose adjustments during follow-up.
2. **Calcium & Vitamin D Supplementation:** Routine vs. selective supplementation protocol, elemental calcium dosage (mg/day), active vitamin D (calcitriol, µg/day), cholecalciferol load, and duration of therapy.
3. **Concomitant Medications:** Interacting agents such as proton pump inhibitors (PPIs), iron, or multivitamin preparations.



Follow-up and Outcome Parameters
Patients underwent biochemical testing at baseline (pre-op) and postoperatively at 24–48 hours, 1 month, 3 months, 6 months, and 12 months.

Primary Outcomes:
1. Proportion of patients achieving target serum TSH at 6 and 12 months. Targets were defined as:
   - *Benign disease:* TSH 0.5 - 2.5 µIU/mL.
   - *Malignant disease (Low risk):* TSH 0.5 - 2.0 µIU/mL.
   - *Malignant disease (High risk):* Suppressive TSH < 0.1 µIU/mL.
2. Rate of postoperative hypocalcemia (transient: corrected serum calcium < 8.0 mg/dL resolving within 6 months; permanent: requirement of active calcium/vitamin D beyond 6–12 months).

Secondary Outcomes:
1. Time to euthyroid stabilization.
2. Medication adherence assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8).
3. Unplanned emergency department visits or readmissions related to post-thyroidectomy complications.

Statistical Analysis
Statistical processing was conducted using SPSS version 28.0 (IBM Corp., Armonk, NY). Continuous variables are reported as mean ± standard deviation (SD) for normally distributed data, or median (interquartile range, IQR) for non-normal distributions. Categorical data are presented as absolute numbers and percentages.

Group comparisons (Total vs. Hemithyroidectomy; Weight-based vs. Empirical LT4) were evaluated using the independent t-test or Mann-Whitney U test for continuous variables, and Chi-square (χ^2) or Fisher's exact test for categorical variables. Multivariate logistic regression analysis was conducted to identify independent risk factors for persistent hypothyroidism and readmission. p-values < 0.05 were considered statistically significant.

RESULTS

Patient Baseline Characteristics

A total of 210 consecutive patients were enrolled and completed the 12-month study protocol. The cohort had a mean age of 46.8 ± 11.4 years, with a female predominance (81.4%, n=171). Total thyroidectomy (TT) was performed in 142 patients (67.6%), while 68 patients (32.4%) underwent hemithyroidectomy (HT). Final histopathological evaluation confirmed benign disease in 128 patients (61.0%) and malignant neoplasia (predominantly papillary thyroid carcinoma) in 82 patients (39.0%). Table 1 details the demographic and clinicopathological features stratified by surgical extent.

Table 1. Demographic and Clinical Characteristics Stratified by Extent of Surgery (N = 210)

Parameter	Total Cohort (N = 210)	Total Thyroidectomy (n = 142)	Hemithyroidectomy (n = 68)	p-value
Age (years)	46.8 ± 11.4	47.5 ± 12.1	45.3 ± 9.8	0.204
Sex (Female / Male)	171 / 39 (81.4% / 18.6%)	114 / 28 (80.3% / 19.7%)	57 / 11 (83.8% / 16.2%)	0.54
Body Mass Index (kg/m^2)	25.4 ± 3.8	25.6 ± 4.0	25.0 ± 3.4	0.291
Pre-op TSH (µIU/mL})	1.88 ± 0.82	1.92 ± 0.86	1.80 ± 0.74	0.322
Histopathology				
Multinodular Goiter	98 (46.7%)	72 (50.7%)	26 (38.2%)	0.091
Follicular Adenoma	30 (14.3%)	6 (4.2%)	24 (35.3%)	< 0.001
Papillary Thyroid Cancer	72 (34.3%)	56 (39.4%)	16 (23.5%)	0.024
Follicular / Medullary Cancer	10 (4.8%)	8 (5.6%)	2 (2.9%)	0.402
Post-op Hospital Stay (days)	2.2 ± 0.8	2.4 ± 0.8	1.6 ± 0.5	< 0.001

Levothyroxine (LT4) Prescription Patterns and TSH Stabilization

All 142 patients (100%) who underwent total thyroidectomy were discharged on LT4 therapy. In contrast, among the 68 hemithyroidectomy patients, 12 (17.6%) were prescribed LT4 at discharge due to elevated immediate post-op TSH (> 4.5 µIU/mL), and an additional 14 patients developed subclinical/overt hypothyroidism during the 12-month follow-up, raising the cumulative LT4 utilization rate in HT to 38.2% (n=26).

Two distinct initiation strategies were observed for TT patients:

1. **Weight-Based Dosing Group (n=88):** LT4 was initiated at 1.5 - 1.6 µg/kg/day (mean dose: 108.4 ± 18.2 µg/day).
2. **Fixed Empirical Dosing Group (n=54):** LT4 was initiated at a fixed dose of 100 µg/day regardless of patient weight.

As shown in Table 2, the weight-based dosing strategy achieved significantly superior rate of target TSH stabilization at 3 months (68.2% vs. 44.4%, $p = 0.005$) and required fewer therapeutic dose adjustments (1.1 ± 0.6 vs. 2.3 ± 0.8 titrations per patient over 12 months, $p < 0.001$).

Table 2. Outcomes of Levothyroxine Dosing Strategies in Total Thyroidectomy Patients (n = 142)

Outcome Parameter	Weight-Based Dosing (n = 88)	Fixed Empirical Dosing (n = 54)	p-value
Mean Initial Dose (µg/day)	108.4 ± 18.2	100.0 ± 0.0	0.001
Target TSH Attainment Rate			
1 Month Follow-up	42 (47.7%)	14 (25.9%)	0.01
3 Months Follow-up	60 (68.2%)	24 (44.4%)	0.005
6 Months Follow-up	72 (81.8%)	34 (63.0%)	0.012
12 Months Follow-up	75 (85.2%)	36 (66.7%)	0.01
Mean Dose Titrations (over 1 yr)	1.1 ± 0.6	2.3 ± 0.8	< 0.001
Iatrogenic Hyperthyroidism (TSH <0.1)	6 (6.8%)	2 (3.7%)	0.432
Persistent Hypothyroidism (TSH >4.5)	7 (8.0%)	16 (29.6%)	0.001

Calcium and Calcitriol Prescription Patterns and Post-op Hypocalcemia

Supplementation strategy varied substantially based on surgical extent and surgeon preference. Among total thyroidectomy patients, 118 (83.1%) were placed on prophylactic supplementation at discharge consisting of elemental calcium (1000-1500 mg/day) combined with calcitriol (0.25 - 0.5 µg/day). The remaining 24 TT patients (16.9%) were managed on a selective/on-demand regimen based on postoperative symptomatic development or serum calcium < 8.0 mg/dL. In the HT cohort, only 10 patients (14.7%) received calcium supplementation.

Across the entire total thyroidectomy cohort:

- **Transient Hypocalcemia** (corrected calcium < 8.0 mg/dL within 30 days) occurred in 40 patients (28.2%).
- **Symptomatic Hypocalcemia** (paresthesias, Carpopedal spasm, Positive Chvostek's sign) occurred in 22 patients (15.5%).
- **Permanent Hypoparathyroidism** (requiring active calcitriol/calcium at 12 months) was documented in 5 patients (3.5%).

Routine prophylactic calcium/calcitriol supplementation after TT significantly reduced the incidence of symptomatic hypocalcemia compared to the selective protocol (10.2% vs. 41.7%, p = 0.001) and decreased 30-day emergency readmissions secondary to acute tetany (1.7% vs. 12.5%, p = 0.022).

Comparison of Post-op Hypocalcemia Outcomes in Total Thyroidectomy

Prophylactic Calcium/Calcitriol (n=118)	Selective / On-Demand Calcium (n=24)
Transient Hypocalcemia: 23.7%	Transient Hypocalcemia: 50.0% (p=0.011)
Symptomatic Hypocalcemia: 10.2%	Symptomatic Hypocalcemia: 41.7% (p=0.001)
30-Day Readmission: 1.7%	30-Day Readmission: 12.5% (p=0.022)

Impact of Medication Adherence and Drug Interactions

Evaluation via the Morisky Medication Adherence Scale (MMAS-8) at 6 months revealed high adherence (score = 8) in 134 patients (63.8%), moderate adherence (score 6-<8) in 52 patients (24.8%), and low adherence (score < 6) in 24 patients (11.4%).

Low adherence to LT4 therapy was strongly associated with failure to achieve target TSH levels at 12 months OR = 5.42, 95% CI: 2.18 - 13.48, p < 0.001). Co-prescription of proton pump inhibitors (PPIs) was noted in 48 patients (22.9%), and calcium supplements were co-administered within 2 hours of LT4 ingestion in 31 patients (14.8%). Both factors

significantly increased mean LT4 requirements due to impaired intestinal absorption (mean dose required for target TSH: 1.68 µg/kg/day in PPI/Calcium interaction group vs. 1.48 µg/kg/day in non-interacting group, p = 0.004).

Multivariate Analysis of Predictors for Unstable Outcomes
Stepwise multivariate logistic regression analysis was performed to identify independent predictors of failure to achieve biochemical euthyroidism at 12 months post-surgery (Table 3).

Table 3. Multivariate Logistic Regression Analysis for Risk Factors Associated with Failure to Attain Target TSH at 12 Months

Risk Factor Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Fixed Empirical LT4 Dosing Strategy	3.14	1.52 – 6.48	0.002
Low Medication Adherence (MMAS-8 < 6)	4.88	2.01 – 11.84	< 0.001
Concurrent PPI or Unspaced Calcium Therapy	2.65	1.24 – 5.66	0.012
Postoperative BMI ≥ 30 kg/m^2	2.18	1.05 – 4.52	0.036
Malignant Histopathology (Suppressive TSH Target)	2.41	1.18 – 4.92	0.016

DISCUSSION

The surgical management of thyroid disorders is incomplete without rigorous, individualized postoperative pharmacological care. While surgical resection eliminates the primary pathology, the subsequent long-term clinical outcomes, including quality of life, metabolic equilibrium, and prevention of tetanic crises are largely dictated by post-discharge prescription patterns and therapeutic adherence [13].

Levothyroxine Optimization: Weight-Based vs. Empirical Protocols
Our findings strongly support the implementation of weight-based initial LT4 dosing (1.5 - 1.6 µg/kg/day) following total thyroidectomy over empirical fixed starter doses [14]. Fixed dosing (100 µg/day) frequently results in initial under-replacement, particularly in patients with higher body weight, leading to prolonged postoperative fatigue, weight gain, and persistent subclinical hypothyroidism [15]. In our cohort, weight-dosed patients reached target TSH thresholds faster and required fewer dose adjustments, thereby lowering outpatient clinical workload and healthcare expenditure.

For hemithyroidectomy patients, routine immediate LT4 initiation is unnecessary. However, our 12-month follow-up identified that over 38% of HT patients eventually developed biochemical hypothyroidism. This underscores the imperative for continuous biochemical surveillance (TSH testing at 6–12 week intervals initially) rather than assuming single lobectomy preserves permanent normal thyroid function [16]. Remnant thyroid tissue often fails to compensate due to underlying silent thyroiditis or reduced tissue reserve [17].

Preventing Hypocalcemic Crises: Routine vs. Selective Supplementation
Transient hypocalcemia remains the most frequent acute complication following total thyroidectomy, stemming from inadvertent parathyroid injury, ischemia, or autotransplantation [18]. The controversy between routine prophylactic calcium/calcitriol administration versus post-op serum PTH-guided administration remains active [19].

Our study demonstrated that routine short-term prophylactic supplementation reduced symptomatic hypocalcemia rates from 41.7% to 10.2% and lowered emergency readmissions. While routine administration may temporarily obscure natural parathyroid recovery, a 2- to 4-week tapering regimen of oral elemental calcium (1 g/day) and calcitriol (0.25 µg/day) provides a safety net that protects against acute neuromuscular irritability, tetany, and cardiac arrhythmias without causing long-term hypercalcemia [20].

Drug Interactions and Patient Education
A major finding in our study was the high prevalence of drug-drug interactions interfering with LT4 bio-absorption. Levothyroxine requires an acidic gastric environment for optimal dissolution [21]. Co-prescribed proton pump inhibitors or concurrent ingestion of calcium carbonate tablets binds LT4 in the gastrointestinal tract, causing erratic bio-availability [22]. Patients must be explicitly instructed during discharge counseling to isolate LT4 administration, taking it on an

empty stomach with water at least 30–60 minutes before breakfast, and separating calcium or iron supplements by at least 4 hours [23].

Study Limitations

This study has limitations. First, while prospective, it was conducted across a single academic tertiary center, which may reflect specific localized surgical expertise and regional prescription habits. Second, long-term cardiovascular parameters and bone mineral density (BMD) markers were not evaluated across the 12-month window; subclinical hyperthyroidism induced by aggressive suppressive therapy in thyroid cancer patients requires multi-year observation to evaluate long-term osteoporosis or atrial fibrillation risks [24]. Third, routine postoperative serum PTH levels were not universally available at the 1-hour or 4-hour post-op mark for all patients, which precluded direct comparison between PTH-guided calcium replacement and empirical prophylaxis protocols.

CONCLUSION

Optimizing prescription patterns following surgical management of thyroid disease is essential for clinical recovery and long-term metabolic health. Weight-based Levothyroxine dosing (1.5-1.6 μg/kg/day) following total thyroidectomy significantly shortens the time to euthyroid stabilization compared to empirical fixed-dose regimens. Prophylactic oral calcium and calcitriol supplementation effectively prevents symptomatic hypocalcemia and reduces unplanned readmissions. Clinical success depends not only on surgical precision, but also on structured patient education regarding medication adherence and the avoidance of drug interactions that impair thyroid hormone absorption.

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