

## REVIEW ARTICLE

# Diagnostic evaluation, risk stratification, and peri-surgical management strategies in thyroid disorders

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## ABSTRACT

**Aim:** To discuss the indications for elective thyroid surgery and peri-surgical clinical strategy in patients with thyroid diseases.

**Materials and Methods:** A comprehensive literature review was conducted from October 2024 to April 2025, analyzing relevant publications published between June 2005 and January 2024, sourced from PubMed, Scopus, Web of Science, and the Cochrane Library.

Thyroid disorders encompass various conditions, including Graves' disease, hyperthyroidism, and thyrotoxicosis. Hypothyroidism manifests as subclinical or overt. Surgical indications for thyroidectomy include symptomatic nodules, indeterminate/Bethesda III-V cytology, malignancy (Bethesda VI), or compressive symptoms. Ultrasound-guided Fine-Needle Aspiration (FNA), based on nodule size and EU-TIRADS risk stratification, is pivotal for evaluation. Advanced aids in risk assessment. Surgical complications (hemorrhage, hypoparathyroidism, recurrence laryngeal nerve injury) require prompt management. Molecular testing refines indeterminate cytology diagnoses. Thyroidectomy is contraindicated in anaplastic cancer and/or high surgical risk cases. Postoperative monitoring for hypocalcemia, voice changes, and bleeding is essential.

**Conclusions:** Resource constraints hinder widespread adoption of advanced thyroid diagnostics, creating challenges in optimal nodule management.

**KEY WORDS:** risk stratification, EU-TIRADS, thyroid disorders, elective thyroid surgery

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## INTRODUCTION

Thyroid nodules are among the most frequently encountered abnormalities of the thyroid gland, documented clinically in roughly 1% of men and 5% of women worldwide. Despite their high occurrence, the majority of nodules do not harbor malignant potential, and only a small fraction - close to 5% - are confirmed to represent cancer. High-resolution ultrasonography has dramatically increased recognition of such lesion, with studies demonstrating their presence in as many as 68% of individuals undergoing imaging, particularly women and older patients.

Surgical management of thyroid disease is considered in spectrum of settings, ranging from benign to malignant conditions. Indications include nodular thyroid disease, hyperthyroidism, large obstructive goiters with or without substernal extension, and the various histologic types of thyroid cancer - most notably papillary and follicular carcinoma, but also medullary and anaplastic subtypes. In addition, thyroidectomy may be undertaken for diagnostic purposes in rare cases

such as primary thyroid lymphoma or in situations where the gland is affected by secondary deposits, most commonly metastases originating from renal cell or lung carcinoma.

Why do we need elective thyroid surgery:

Patients may be considered for thyroidectomy in several clinical contexts, encompassing both malignant and benign thyroid disease. Indications include differentiated thyroid carcinoma, toxic multinodular goiter, autonomously functioning adenomas, and goiters that lead to compressive manifestations such as dysphagia or airway compromise. Thyroidectomy may also be warranted in patients with Graves' disease who do not achieve adequate control with antithyroid medication or in whom medical therapy is contraindicated - for instance, women planning pregnancy [1].

## AIM

In this review, we aim to discuss the clinical indications for elective thyroidectomy and to outline perioperative

strategies in the management of patients with thyroid disease.

## MATERIALS AND METHODS

The review was performed in the period from 10.2024 to 04.2025. The materials for the literature review were publications on research from June 2005 to January 2024. Relevant articles were identified by two authors (OG, JK) searching PubMed's, Scopus, Web of Science databases, and Cochrane Library.

## REVIEW AND DISCUSSION

### DEFINITIONS IN THYROID DISEASE

Graves' disease represents an autoimmune condition in which antibodies aberrantly activate the thyrotropin (TSH) receptor on thyroid cells, driving hormone overproduction [2].

Hyperthyroidism denotes hormone excess due to intrinsic overactivity of thyroid gland, whereas thyrotoxicosis refers to the broader clinical state resulting from elevated circulating thyroid hormones regardless of source. Thus, while all hyperthyroidism results in thyrotoxicosis, the syndrome may also occur through other mechanisms, such as exogenous thyroid hormone administration (factitious thyrotoxicosis) or release of hormone from glandular destruction, as in subacute thyroiditis - neither of which represent true hyperthyroidism. The ability to reliably differentiate between these entities underpins both diagnostic accuracy and therapeutic decisions [2].

Hypothyroidism is defined as a deficiency of circulating thyroid hormones. It may present as subclinical hypothyroidism, where TSH is elevated but free thyroxine (FT4) and triiodothyronine (T3) remain within the reference range, or as overt hypothyroidism, characterized by reduced FT4 or total thyroxine (TT4) levels in conjunction with elevated TSH. This review focuses primarily on overt hypothyroidism [3].

Hypoparathyroidism is an uncommon endocrine disorder marked by hypocalcemia in the setting of inappropriately low or undetectable parathyroid hormone (PTH) concentrations [4].

Primary hyperparathyroidism, characterized by hypercalcemia accompanied by elevated or inappropriately normal PTH levels [5].

Secondary hyperparathyroidism most often arises in the context of chronic kidney disease, where disturbances in calcium-phosphate balance drive compensatory PTH secretion. In advanced stages, surgical intervention may become necessary as the only defin-

itive therapy, but it is reserved for clearly established indications [6].

Tertiary hyperparathyroidism represents the progression of long-standing secondary disease, in which the parathyroid glands acquire autonomy and continue to oversecrete PTH even after successful renal transplantation [7].

Voice assessment is central in thyroid disease. Patients with hoarseness frequently describe their voice as weak, rough, unstable, or report difficulties with pitch control. In otolaryngology, the term "dysphonia" broadly refers to any abnormality in vocal quality. Persistent hoarseness lasting more than two weeks should be regarded as an alarm symptom and investigated further, as it may indicate significant underlying disease.

Voice changes following thyroid surgery, including hoarseness, are frequently the result of recurrent laryngeal nerve (RLN) injury. Such deficits may be transient, but if they persist for more than six months, they are regarded as permanent [9].

Intraoperative bleeding remains another critical risk during thyroid surgery. Blood loss can vary considerably, but volumes exceeding 200 mL are considered clinically significant. The accumulation of a cervical hematoma may lead to tracheal compression and potentially life-threatening airway obstruction, requiring urgent surgical intervention [10].

Tetany, most commonly resulting from postoperative hypocalcemia, represents a further complication. It is characterized by neuromuscular irritability, with patients often reporting tingling, "pins and needles," or current-like sensations in the fingers, toes, or perioral region. In more severe cases, intermittent muscle spasms may occur [11].

Radiologically, thyroid nodules appear as discrete lesions separated from the surrounding parenchyma. Regular evaluation of nodular thyroid disease is necessary due to possibility of malignancy, toxicity or compressive symptoms [12].

Goiter refers to an abnormal enlargement of the thyroid gland, typically defined as a volume exceeding >18-20 ml in female and >25 ml in male. It can be classified as diffuse or nodular, and further divided into toxic (associated with thyrotoxic symptoms) or non-toxic forms. Globally, the leading cause of goiter remains iodine deficiency and in endemic areas prevalence may approach 25%, particularly among older populations. In these regions, many goiters remain clinically silent and do not require operative management. By contrast, in iodine-sufficient settings, multinodular goiter is more commonly associated with autoimmune thyroid conditions, including Hashimoto's thyroiditis and Graves' disease [1].

Surgical removal also provides a definitive histopathological diagnosis, particularly in nodules with uncertain malignant potential. Where available, molecular testing can further refine risk assessment. The extent of resection depends on disease distribution: lobectomy is usually sufficient for unilateral nodules, whereas near-total thyroidectomy may be warranted in multinodular cases. Even cytologically benign lesions may require surgery when large (>4 cm), symptomatic, or substernal in location, while toxic nodules - whether solitary or multinodular - also represent clear indications for operative management [2].

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) established levels of histopathological findings in Fine-Needle Aspiration biopsy (FNA) and supported making a decision with treatment (surgical or non-surgical). I grade of the TBSRTC inform that FNA is nondiagnostic or unsatisfactory, II grade - the lesion is benign, III grade - atypia of undetermined significance (AUS), IV - follicular neoplasm or suspicious for a follicular neoplasm, V grade - suspicious of malignancy and VI grade - malignant [13,14].

## EVALUATION AND MANAGEMENT OF THYROID NODULES

Most thyroid nodules do not require surgical intervention. However, non-functioning nodules exceeding 1 cm or those exhibiting suspicious sonographic features should be further evaluated, most often by fine-needle aspiration (FNA).

The American Thyroid Association highlights that the decision to perform FNA should be based on two major criteria: the nodule's size and the level of sonographic suspicion [1].

As part of the initial assessment, TSH measurement is recommended; if suppression is observed, thyroid scintigraphy should follow. In this setting, nodules larger than 1 cm with increased radionuclide uptake may warrant aspiration. Subsequent ultrasound-based risk stratification then refines the evaluation by linking morphological features with the likelihood of malignancy, thereby informing FNA indications [15].

## ULTRASOUND AND ADVANCED IMAGING IN THYROID EVALUATION

Ultrasound serve as the primary imaging tool in the assessment of thyroid nodules. Its clinical utility includes:

Characterizing nodules with respect to their number, anatomical location, dimensions, and internal echotexture [16, 17].

Evaluating substernal extension and cervical anatomy [16, 17].

Assigning risk categories using standardized systems such as the European Thyroid Imaging and Reporting Data System [16, 17].

Detecting lymph nodes with suspicious features and guiding the choice of nodules most appropriate for FNA [16, 17].

Doppler ultrasonography provides valuable information on nodule vascularity and is particularly helpful in distinguishing solid components from cystic or necrotic areas. In addition, it guides the selection of appropriate sites for FNA and contributes to overall risk characterization [17].

Elastography has been introduced as a complementary technique to evaluate tissue stiffness, given that malignant nodules - most notably classical papillary thyroid carcinoma (PTC) - tend to be firmer than benign lesions. Despite this association, elastographic findings are not universally reliable across all thyroid malignancies and are therefore not formally included in the current risk stratification frameworks [17].

Contrast-enhanced ultrasound (CEUS) has demonstrated encouraging diagnostic accuracy, with some meta-analyses reporting high positive predictive values for malignancy. Nevertheless, the literature is inconsistent and susceptible to publication bias, and regulatory approval remains restricted to a limited number of countries. Where available, CEUS plays a particularly useful role in post-treatment monitoring, especially after thermal ablation, by enabling precise visualization of ablation margins and perfusion deficits [17].

Strain elastography assesses the relationship between applied compression and tissue deformation. By alternating probe pressure, elastographic maps can be generated and superimposed onto B-mode images, with stiffness represented through a color-coded scale [18].

Shear wave elastography (SWE), in contrast, provides quantitative data by creating elasticity maps and measuring stiffness in kilopascals. Nodules with stiffness values exceeding 65 kPa, or demonstrating a stiffness ratio above 3.7 when compared with adjacent normal thyroid tissue, should raise suspicion for malignancy [19].

Thyroidectomy, once regarded as the standard approach for goiter, has become a more selective intervention with the advent of advanced imaging techniques and effective non-surgical alternatives. In the setting of differentiated thyroid cancer, lobectomy is typically sufficient for microcarcinomas, whereas total thyroidectomy is considered in larger tumors (>1 cm), tall-cell histology, cases with extrathyroidal extension, bilateral disease, or lymphovascular invasion. Evaluation of suspicious cervical lymph nodes should include FNA [15].

Molecular analysis has emerged as an increasingly important adjunct in the evaluation of thyroid nodules

with indeterminate cytology, particularly those within Bethesda categories III to V. The most commonly investigated alterations involve mutations in BRAF and RAS, as well as rearrangements such as RET/PTC and PAX8/PPAR $\gamma$ . The 2023 Bethesda update introduced a separate AUS category with nuclear features due to their higher malignancy risk. Given the false-negative rate of FNA (~4.36%), combining cytology with molecular testing and repeat aspiration enhances diagnostic accuracy.

Absolute contraindications to thyroidectomy are rare in clinical practice. Surgical eligibility should instead be weighed against factors such as patient age, comorbid conditions, and the generally indolent behavior of most thyroid cancers. In the setting of anaplastic carcinoma, surgery is usually discouraged unless a complete resection can be achieved with acceptable morbidity and in the absence of distant metastases. For outpatient thyroidectomy, certain scenarios are better regarded as relative limitations rather than strict contraindications - these include very large goiters, substernal extension, pronounced thyroiditis, or challenging surgical anatomy [15].

## COMPLICATIONS OF THYROID SURGERY

Common complications following elective thyroidectomy include:

**Hemorrhage:** Although rare, it can be life-threatening due to airway compromise from hematoma. Immediate decompression is essential.

**Hypoparathyroidism:** Occurs in up to 33% of total thyroidectomies. Leads to hypocalcemia and may cause paresthesia, tetany, or seizures. Prophylactic calcium administration is often part of postoperative protocols.

**Recurrent laryngeal nerve (RLN) injury:** Leads to hoarseness, voice fatigue, or aspiration. Most cases are transient, but permanent paralysis occurs in less than 1%.

**Superior laryngeal nerve injury:** Affects voice pitch and quality. Incidence ranges widely (0–58%).

**Infection:** Reported in approximately 6% of cases.

**Other complications:** Esophageal or tracheal injury, Horner's syndrome, dysphagia, chyle leak [15].

Among the early complications of thyroidectomy, transient hypocalcemia is the most frequent, affecting roughly 20–30% of patients and recurrent laryngeal nerve (RLN) injury, which occurs in 5–11% of cases. Although bilateral RLN damage is exceedingly rare (<0.1%), its occurrence represents a critical event requiring immediate airway intervention.

Postoperative bleeding, reported in 0–6.5% of procedures, most often results from slipped ligatures or venous tears. Intraoperative hemostasis, maintenance of stable thyroid function, and the use of the Valsalva maneuver to identify occult bleeding are important preventive measures. Compressive hematomas need immediate surgical evacuation, in contrast to minor, non-compressive hematomas, which may be observed and treated conservatively.

Other postoperative issues include:

**Dysphagia:** Generally resolves with neck massage and conservative management.

**Seroma or lymphatic leakage:** Often resolve with aspiration.

**Horner's syndrome:** A rare complication due to sympathetic chain injury, usually self-limited.

**Wound healing issues:** More frequent in obese patients. Proper drainage and care improve outcomes.

**Tracheal or esophageal injury:** Rare, however may require stenting or conservative management.


**Thyrotoxic storm:** Rare today due to routine use of preoperative beta-blockers [20].

## CONCLUSIONS

Regarding diagnostic approaches, advances in imaging techniques have greatly expanded diagnostic accuracy, yet their prohibitive cost can limit availability in developing countries and in healthcare systems with restricted resources. Likewise, while molecular testing may in the future refine management of Bethesda category III nodules and support decisions regarding elective thyroid surgery, the expense of such methods currently prevents their broad adoption in many settings. Diagnostic lobectomy offers the advantage of preserving thyroid function; however, it may still necessitate a second operation if malignancy is later identified, which increases patient risk - particularly in those with comorbidities that make repeated exposure to general anesthesia hazardous.

As for alternative management, watchful waiting combined with appropriate outpatient care can represent a reasonable strategy. Yet, systemic barriers, including procedural costs, shortages of trained personnel, and limited access to equipment, may hinder feasibility not only in low-income countries but also in some developed nations where healthcare systems are underfunded or inefficiently managed.

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## CONFLICT OF INTEREST

The Authors declare no conflict of interest

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