

Executive Summary of the American Association of Endocrine Surgeons Guidelines for the Definitive Surgical Management of Thyroid Disease in Adults

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Objective: The aim of this study was to develop evidence-based recommendations for safe, effective and appropriate thyroidectomy.

Background: Surgical management of thyroid disease has evolved considerably over several decades leading to variability in rendered care. Over 100,000 thyroid operations are performed annually in the United States.

Methods: The medical literature from January 1, 1985 to November 9, 2018 was reviewed by a panel of 19 experts in thyroid disorders representing multiple disciplines. The authors used the best available evidence to construct

surgical management recommendations. Levels of evidence were determined using the American College of Physicians grading system, and management recommendations were discussed to consensus. Members of the American Association of Endocrine Surgeons reviewed and commented on preliminary drafts of the content.

Results: These clinical guidelines analyze the indications for thyroidectomy as well as its definitions, technique, morbidity, and outcomes. Specific topics include Pathogenesis and Epidemiology, Initial Evaluation, Imaging, Fine Needle Aspiration Biopsy Diagnosis, Molecular Testing, Indications, Extent and Outcomes of Surgery, Preoperative Care, Initial Thyroidectomy, Perioperative Tissue Diagnosis, Nodal Dissection, Concurrent Parathyroidectomy, Hyperthyroid Conditions, Goiter, Adjuncts and Approaches, Laryngology, Familial Thyroid Cancer, Postoperative Care and Complications, Cancer Management, and Reoperation.

Conclusion: Evidence-based guidelines were created to assist clinicians in the optimal surgical management of thyroid disease.

Keywords: biopsy, cancer, carcinoma, concurrent parathyroidectomy, diagnosis, endocrine, extent of resection, goiter, hyperthyroidism, imaging, lymph nodes, management and complications, molecular markers, nodules, pathogenesis, postoperative care, preoperative care, staging, surgery, thyroid, thyroidectomy indications, ultrasound

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Surgical management of thyroid disease has evolved considerably over several decades leading to variability in rendered care. To help provide safe, effective, and appropriate care of patients, these AAES-sponsored multidisciplinary clinical guidelines analyze the conduct, indications, and outcomes of adult thyroid surgery guided by a comprehensive evidence-based review of the medical literature. Several specific cautions to implementation exist. These guidelines were endorsed by the American Thyroid Association, the International Association of Endocrine Surgeons, the Society of Surgical Oncology, and the Graves' Disease and Thyroid Foundation.

PATHOGENESIS AND EPIDEMIOLOGY

Thyroidectomy, a term used herein to include any type of thyroid surgery, is commonly performed for symptomatic benign disease, concern for malignancy, and hyperthyroid conditions. Non-functioning thyroid nodules occur in over half of the population and most are benign.

Thyroid cancer (TC) incidence is rising, mostly from increased detection of small papillary thyroid carcinomas (PTCs). Tumors derived from follicular cells are the well-differentiated thyroid carcinomas [DTC, broadly characterized as PTC, follicular TC (FTC), and Hurthle cell carcinoma (HCC)], poorly differentiated carcinoma (PDTC), and anaplastic (undifferentiated) thyroid carcinoma (ATC). The diagnosis of classical PTC requires papillary

cytoarchitectural and nuclear features of PTC. FTC, comprising approximately 8% of DTC, is divided into minimally invasive (capsular invasion only), grossly encapsulated angioinvasive FTC, and widely invasive FTC. PDTCs have mortality of ~50% and exhibit high-grade features. ATC is found in <1% of cases but accounts for 40% of TC deaths.

Medullary TC (MTC) originates in the calcitonin-producing parafollicular C-cells that predominate in the upper thyroid poles. Sporadic MTC is 3 times as common as hereditary MTC. Regardless of the setting, parafollicular cells are not iodine-avid, making extirpative surgical treatment of MTC critical. Primary thyroid lymphoma (PTL) is rare and the principal treatment is chemotherapy and/or external beam radiation therapy (EBRT); however, given that 90% of patients present with rapidly enlarging goiter and/or acute airway compromise, surgeons are frequently involved in the management.

INITIAL EVALUATION

The initial evaluation of a patient with thyroid disease provides pivotal information about malignancy risk including radiation exposure, symptomatology, and possible thyroid hormonal dysfunction. Findings also can guide laboratory, laryngeal, and imaging evaluation and may influence the conduct and extent of thyroidectomy.

Recommendation 1: Evaluation of thyroid disease should include specific inquiry about personal history, family history, clinical characteristics, and symptoms. (Strong recommendation, low quality of evidence)

Recommendation 2: The preoperative physical examination should include voice assessment. (Strong recommendation, moderate-quality evidence)

Recommendation 3: Thyroid-stimulating hormone (TSH) should be measured in patients with nodular thyroid disease. Additional laboratory studies may help in specific circumstances. (Strong recommendation, low-quality evidence)

IMAGING

Successful thyroid surgery is contingent on thorough and accurate imaging, which also impacts preoperative planning, extent of surgery, and postoperative management. Inadequate preoperative imaging may be a root cause of incomplete initial surgery.

The initial and most valuable thyroid imaging study is cervical ultrasound (US) which is widely utilized to characterize thyroid nodules and guide practitioners in recommending fine-needle aspiration biopsy (FNAB). US is useful in localizing concurrent parathyroid disease (which is diagnosed biochemically) and is critical in the preoperative evaluation of cervical lymph node (LN) disease and surgical planning.

Recommendation 4: A diagnostic US should be performed in all patients with a suspected thyroid nodule. (Strong recommendation, high-quality evidence)

Recommendation 5:

- a. **US assessment of bilateral central and lateral LN compartments should be performed in the preoperative evaluation of patients with cytologic evidence of thyroid carcinoma. (Strong recommendation, low quality of evidence).**
- b. **US assessment of bilateral central and lateral LN compartments may be performed in the preoperative evaluation of patients with indeterminate cytologic evidence of thyroid carcinoma. (Strong recommendation, insufficient evidence).**

Cross-sectional imaging, namely, computerized tomography (CT) or magnetic resonance imaging (MRI), has a supplemental role

in the preoperative evaluation of thyroid disease, and is recommended with intravenous contrast for patients with clinical suspicion of advanced disease, including invasive primary tumor, or clinically apparent multiple or bulky LN. Thyroid scintigraphy is not indicated in a euthyroid patient.

Recommendation 6: CT or MRI with intravenous contrast should be used preoperatively as an adjunct to US in selected patients with clinical suspicion for advanced locoregional TC (Strong recommendation, low quality of evidence)

In the postoperative setting, US is an important tool for TC surveillance, and also aids in the detection, localization, and planning of revision surgery for recurrent/persistent disease. Radioiodine (RAI) whole body scanning has traditionally been the primary functional imaging modality, and 18FDG-PET has also been widely accepted as a method for detecting TC recurrence, particularly in patients who are thyroglobulin (Tg)-positive and RAI-negative.

FNAB DIAGNOSIS

FNAB is used for evaluation of suspicious thyroid nodules and LNs, and the results guide management. Evidence-based guidelines for deciding which thyroid nodules need FNAB have been described by both the American Thyroid Association (ATA) and American College of Radiology (Figure 1). Independent of size or US features, other indications for FNAB include nodules in patients with risk factors for malignancy or associated with clinically concerning findings such as fixation, immobility, hoarseness, or recurrent laryngeal nerve (RLN) dysfunction.

Suspicious US features of cervical LN include loss of fatty hilum, location, size, shape, microcalcifications, hyperechoic or cystic character, and peripheral hypervascularity. Preoperative LN FNAB should be considered if the results will change the planned operative approach.

Recommendation 7:

- a. **FNAB is a standard component of thyroid nodule evaluation, and its indications should follow established guidelines based on US characteristics, size, and clinical findings. (Strong recommendation, moderate-quality evidence)**
- b. **FNAB of a sonographically suspicious cervical LN should be performed when the results will alter the treatment plan. (Strong recommendation, low-quality evidence)**

US guidance is recommended for nonpalpable nodules, those with >25% cystic component, and when an initial FNAB result is inadequate. In general, US guidance is preferred for all thyroid FNABs, but nodules that meet imaging criteria and are readily palpable may be biopsied with palpation guidance, particularly if US guidance is logistically difficult to access.

Recommendation 8: In most circumstances, FNAB yield and adequacy may be optimized using US-guidance, with or without onsite cytologic assessment. (Strong recommendation, moderate-quality evidence)

Thyroid FNAB results are classified into 1 of the 6 conventional Bethesda System categories, and the associated risk of malignancy or premalignancy (ie, noninvasive follicular thyroid neoplasm with papillary-like features, NIFTP) is used to guide clinical management.

Recommendation 9: The Bethesda System for Reporting Thyroid Cytopathology should be used to report and stratify the risk of malignancy in a thyroid nodule. (Strong recommendation, high-quality evidence)

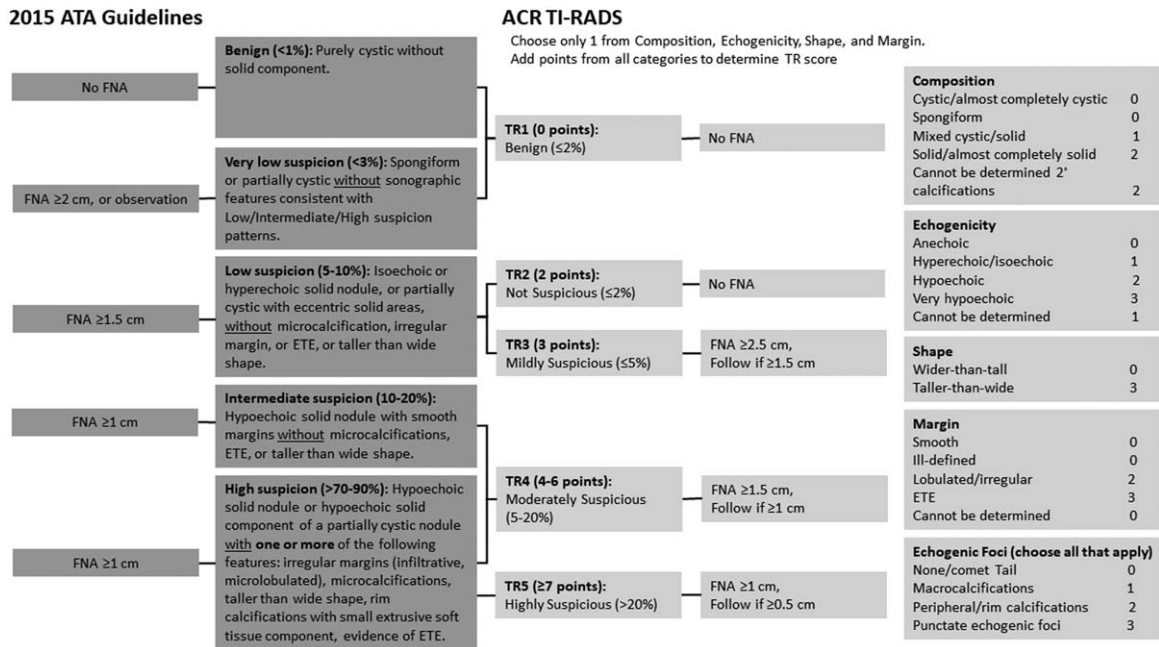


FIGURE 1. Comparison of the ATA 2015 Guidelines and ACR TI-RADS classification systems for recommending FNAB.

MOLECULAR TESTING

Molecular testing (MT) to examine somatic changes is primarily utilized in thyroid disease as a preoperative adjunct to refine the cancer risk in cytologically indeterminate thyroid nodules.

Avoiding surgery for a cytologically indeterminate nodule can be considered in an appropriate setting and preoperative MT results can refine the assessment of TC risk. Negative or benign results have a TC risk that is approximately equivalent to that for a benign FNAB result (≤5%). The type, indication for, and interpretation of MT should consider nodule and clinical variables and whether the results will change planned recommendations. In clinical scenarios leading to nodule observation, patient willingness or ability to continue surveillance should be carefully considered before obtaining MT. If thyroidectomy is indicated regardless of cancer risk, then ordering MT for the purpose of avoiding surgery is not indicated.

Recommendation 10: *If thyroidectomy is preferred for clinical reasons, then MT is unnecessary. (Strong recommendation, moderate-quality evidence)*

MT use should be evaluated in a systematic framework to ensure that each test has analytical validity, clinical validity, and clinical utility. A summary of the commercially available molecular tests and corresponding results from the index clinical validation

study appears in Table 1. The use of MT results to make clinical decisions relies on the positive (PPV) and negative (NPV) predictive values which are contingent on regional cancer prevalence for each cytologic category.

Recommendation 11: *When the need for thyroidectomy is unclear after consideration of clinical, imaging, and cytologic features, MT may be considered as a diagnostic adjunct for cytologically indeterminate nodules. (Strong recommendation, moderate-quality evidence)*

Recommendation 12: *Accuracy of MT relies on institutional malignancy rates and should be locally examined for optimal extrapolation of results to TC risk. (Strong recommendation, moderate-quality evidence)*

To date, no MT has been studied for correct surgical guidance under the 2015 ATA guidelines which substantially modified recommendations on the extent of thyroidectomy so that lobectomy or total thyroidectomy are potential options for 1 to 4 cm TCs. To be useful for directing the initial extent of surgery, a given MT needs to first provide reliable prognostic information. Another variable that will likely impact MT performance is the recent terminology shift to NIFTP which will likely decrease the risk of true malignancy for the indeterminate Bethesda categories. Validation, utility, and cost efficacy studies are needed for all MTs.

TABLE 1. Commercially Available Molecular Tests for Bethesda III and IV Nodules

| Test Name | Type of Test | False Negatives* | Sensitivity (95% CI)* | Specificity (95% CI)* |
|-----------------------------------|----------------------------------|------------------|-----------------------|-----------------------|
| Afirma Gene Sequencing Classifier | Multigene expression (RNA-based) | 4/103 (4%) | 91% (79%–98%) | 68% (60%–76%) |
| Interpace ThyGenX+ThyraMir | 7 gene panel + 10 miRNA | 4/67 (6%) | 89% (73%–97%) | 85% (75%–92%) |
| CBLPath ThyroSeq version 3 | Multigene NGS | 4/150 (3%) | 94% (86%–98%) | 82% (75%–87%) |

*Includes only results with histologic correlation and before post hoc exclusions. CI indicates confidence intervals; miRNA, micro-RNA; NGS, next-generation sequencing; RNA, ribonucleic acid.

INDICATIONS, EXTENT, AND OUTCOMES OF SURGERY

The indications for thyroidectomy are grouped into the general categories of local compressive symptoms, malignancy risk, and hyperthyroidism.

Although most cytologically benign nodules can be safely observed, thyroidectomy should be considered for patients with significant local compressive symptoms, progressive enlargement, or significant cosmetic concerns; rarely, the same criteria apply for thyroiditis. No absolute threshold for nodule size mandates thyroidectomy, but some experts cite FNAB sampling error to routinely consider resection for nodules measuring ≥ 3 or 4 cm.

Although most asymptomatic goiters in euthyroid patients can be observed, many surgeons routinely consider surgery for goiter associated with dyspnea, dysphagia, tracheal or esophageal compression, or thoracic outlet syndrome, as well as for nodular goiter with substernal extension.

Recommendation 13: *Patients with a thyroid nodule, goiter, or thyroiditis who exhibit local compressive symptoms or progressive enlargement should be considered for thyroidectomy. (Strong recommendation, low-quality evidence)*

Many patients with hyperthyroidism can be managed with antithyroid medications, but some will be refractory, develop adverse reactions, have large glands or nodules not amenable to RAI ablation, have contraindications to RAI, or have coexisting conditions that may prompt thyroidectomy.

Recommendation 14: *Thyroidectomy is one of several options for treatment of hyperthyroidism and should be preferentially considered when RAI or medical therapy is contraindicated or undesirable. (Strong recommendation, moderate-quality evidence)*

Patients with cytologically indeterminate nodules may be considered for repeat biopsy, MT, or diagnostic surgery depending on clinical factors, radiographic features, and patient preference. Patients with cytologically suspicious nodules >1 cm should undergo thyroidectomy.

With malignant cytology, initial risk stratification is very often performed by the surgeon, who determines (based on imaging, clinical, cytologic, molecular findings, and so on) whether and when to operate, the initial extent of resection, and what technique(s) to use. For patients with malignant cytology, the extent of resection is determined by multiple factors including tumor size, local invasion, presence of other nodules, LN involvement, and/or evidence of MTC. Overall, lobectomy for DTC 1 to 4 cm yields disease-specific mortality and recurrence outcomes that are similar to those of total thyroidectomy, but there is also continuing controversy.

Active surveillance of malignant cytology (AS) may be appropriate with significant comorbidity or limited life expectancy and is also a new option for selected patients with small (<1.0 cm) and stable PTC. AS requires specific patient counseling, selection, and a commitment to long-term follow-up.

Recommendation 15: *For nodules that are cytologically categorized as Bethesda III, clinical factors, radiologic features, and patient preference should inform decision-making regarding whether to proceed with repeat biopsy, MT, diagnostic thyroidectomy, or observation. (Strong recommendation, moderate-quality evidence)*

Recommendation 16: *Diagnostic thyroidectomy and/or MT are accepted options for patients with nodules cytologically categorized as Bethesda IV. (Strong recommendation, moderate-quality evidence)*

Recommendation 17: *Thyroidectomy is indicated for thyroid nodules >1 cm cytologically categorized as Bethesda V or VI. (Strong recommendation, moderate-quality evidence)*

Strict age or comorbidity thresholds do not exist beyond which thyroidectomy is invariably unsafe; surgeon judgment and rational patient selection remain the standards for assuring optimal outcomes. Numerous studies have demonstrated improved outcomes of thyroid surgery when performed by a high-volume thyroid surgeon.

Recommendation 18: *When possible, thyroidectomy should be performed by a high-volume thyroid surgeon. (Strong recommendation, moderate-quality evidence)*

PREOPERATIVE CARE

Surgical site infection is a very uncommon complication after routine transcervical thyroidectomy, with an incidence of 0.09% to 2%. Because infection is associated with both preoperative (obesity, alcohol use) and intraoperative factors (operative time, airway injury), high-risk patients may benefit from selective use of antimicrobial prophylaxis, in which case Gram-positive coverage should be administered before or on induction. With rare exceptions, postoperative antimicrobial prophylaxis is not indicated.

Recommendation 19: *Antimicrobial prophylaxis is not necessary in most cases of standard transcervical thyroid surgery. (Strong recommendation, high-quality evidence)*

Several studies have demonstrated that intravenous dexamethasone is associated with a reduction in postoperative nausea and vomiting as well as pain after thyroidectomy. Data are inconsistent about the impact of perioperative steroids on voice outcomes after thyroidectomy and such use is not yet widely advocated.

Recommendation 20: *Before thyroidectomy, in the absence of contraindications, a single preoperative dose of dexamethasone should be considered to reduce nausea, vomiting, and pain. (Strong recommendation, high-quality evidence)*

Thyroid storm may be precipitated by anesthetic agents, the stress of surgery, or thyroid manipulation and may be prevented by pretreatment with antithyroid drugs (ATDs). Whenever possible, thyrotoxic patients should be rendered clinically and medically euthyroid before surgery. In exceptional circumstances, for example, with ATD allergy or if the need for thyroidectomy is urgent, the patient should be treated with beta-adrenergic blockade, potassium iodide, glucocorticoids, and other modalities in the immediate preoperative period. Use of preoperative potassium iodide (given as SSKI or as Lugol solution) in Graves disease (GD) is controversial but recent evidence suggests that it can beneficially decrease thyroid blood flow, vascularity, and intraoperative blood loss while blocking conversion of T4 to T3.

Recommendation 21: *If surgery is chosen as treatment for GD: a. Ideally patients should be rendered clinically euthyroid preoperatively. (Strong recommendation, low-quality evidence) b. A potassium iodide-containing preparation can be considered before surgery. (Weak recommendation, low-quality evidence)*

Before total or reoperative thyroidectomy, patients who have had previous gastric bypass surgery should be counseled about a higher risk of severe postoperative hypocalcemia and if deficient, their vitamin D and calcium stores should be aggressively repleted.

Recommendation 22: *Gastric bypass patients should be counseled about a higher risk of severe postoperative hypocalcemia after total or completion thyroidectomy. (Strong recommendation, low-quality evidence)*

Vitamin D deficiency is a probable risk factor for hypocalcemia after total thyroidectomy. GD itself seems to be itself a risk factor for postoperative hypocalcemia and recent data suggest that preoperative supplementation of oral calcium and/or vitamin D may reduce the post-thyroidectomy risk of hypocalcemia in GD patients.

Recommendation 23: *Before thyroid surgery for GD, calcium and 25-hydroxy vitamin D levels may be assessed and repleted or supplemented prophylactically. (Strong recommendation, moderate-quality evidence)*

Although VTE prophylaxis is relatively routine in other surgical procedures, it remains controversial for routine thyroid operations, as not only is the overall risk for VTE after thyroidectomy quite low (0.02%–0.2%) but also any postoperative hemorrhage may cause acute airway compromise requiring emergency decompression; thus, many thyroid surgeons believe that the risk of bleeding outweighs the benefits of VTE prophylaxis. Immediate postoperative ambulation is routinely utilized after thyroidectomy.

Recommendation 24: *Chemical VTE prophylaxis should be reserved for selected patients determined to be at high risk for VTE after thyroidectomy. (Strong recommendation, low-quality evidence)*

Mutual multidisciplinary communication is an important component of optimal patient care and should be systematically encouraged perioperatively.

INITIAL THYROIDECTOMY

When an indication for thyroidectomy is present and the patient is medically optimized, the decision regarding initial operative extent depends on multiple factors including the etiology, presence of contralateral nodular disease, thyroid function, comorbidities, family history, surgical risk, comparative outcomes, and patient preferences (Table 2). Descriptions of commonly used nomenclature for thyroidectomy are shown in Table 3. Nodulectomy and subtotal thyroidectomy are rarely indicated. Lobectomy with isthmusectomy is the minimum extent of surgical resection in most cases of TC.

On the day of surgery, interdisciplinary communication is essential and a plan for managing a potentially difficult airway should be discussed with anesthesiology so that appropriate expertise and equipment are available. Following intubation, the patient is generally placed in a semi-Fowler position with shoulder-bump to extend the neck. After skin prep and drape, a transverse-centered incision is made, preferably in a natural skin crease for optimal cosmetic results.

The order of the critical steps of thyroid dissection will vary based on surgeon preference, disease process, and patient anatomy. In general, thyroidectomy proceeds from a ventral to dorsal direction. The middle thyroid vein is ligated and divided, allowing for the lobe to be rotated medially and exposing the tracheal esophageal groove. The inferior parathyroid is seen and preserved near the inferior thyroid capsule (typically anterior and medial to the RLN). Many experts routinely clear off the trachea inferior and superior to the isthmus, dissecting the pyramidal lobe with care taken to preserve the cricothyroid muscle fibers, and assessing the prelaryngeal “Delphian” LN(s) if present. Exposure of the superior pole is facilitated with inferolateral retraction followed by dissection and ligation of the vascular pedicle close to the thyroid capsule to avoid potential external branch of the superior laryngeal nerve (EBSLN) injury.

Recommendation 25: *The superior pole vessels should be ligated close to the thyroid capsule to avoid potential EBSLN injury. (Strong recommendation, insufficient evidence)*

TABLE 2. Clinical Factors That Favor Initial Total Thyroidectomy Versus Lobectomy

| | |
|-----------------------------------|--|
| Favor total thyroidectomy | <ol style="list-style-type: none"> 1) Planned RAI for known or suspected DTC, including: <ol style="list-style-type: none"> a. Malignant FNAB for >4 cm lesion b. Gross ETE on US or intraoperatively c. Clinical, IOPE or US evidence for CLNM d. Known distant metastasis e. Adverse MT result (ie, BRAF V600E + TERT) 2) MTC 3) Bilateral thyroid disease, including: <ol style="list-style-type: none"> a. Euthyroid or toxic nodular goiter b. Graves' Disease c. Contralateral dominant/index nodule d. History of XRT e. Familial predisposition syndrome f. Need for concurrent contralateral parathyroidectomy 4) Struma ovarii |
| Controversial/no consensus | <ol style="list-style-type: none"> 1) Uni-lobar known or suspected DTC 1–4 cm that appears low-risk on US 2) Index lesion plus existing thyroid hormone dependence 3) Uni-lobar DTC with need to facilitate Tg/US surveillance 4) Uni-lobar lesion with complex medical situation 5) Uni-lobar lesion and patient preference for TT |
| Favor lobectomy and isthmusectomy | <ol style="list-style-type: none"> 1) Uni-lobar PTMC that appears low-risk on US 2) Uni-lobar lesion with indolent MT result 3) Unilateral goiter |

When thyroidectomy is already indicated, the listed factors can help inform decision-making about the initial surgical extent, that is, the choice of initial bilateral versus unilateral thyroidectomy. The content is based on the expert opinion of the authors and is not intended to be prescriptive or solely applicable to individual clinical circumstances (see “Cautions to Implementation,” “Abbreviations Table”).

Identification and protection of the RLN throughout its course is critical and improves outcomes. The most common site of RLN injury is at the ligament of Berry.

Recommendation 26: *The RLN should be identified to help preserve it. (Strong recommendation, low-quality evidence)*

The superior parathyroid should be carefully preserved in situ; it typically lies anatomically posterior to the RLN and superior-lateral to

TABLE 3. Thyroidectomy Nomenclature

| Name of Procedure | Extent of Resection |
|-----------------------------|---|
| Lobectomy | One entire thyroid lobe without isthmus |
| Lobectomy and isthmusectomy | One entire thyroid lobe with isthmus and pyramidal lobe |
| Isthmusectomy | Isolated isthmus resection |
| Subtotal thyroidectomy | Preservation of small posterior remnant(s) of the contralateral or bilateral lobe(s) (Rarely recommended today) |
| Near-total thyroidectomy | Resection of all but a very small posterior remnant, ie, at the ligament of Berry |
| Total thyroidectomy | All visible thyroid tissue |
| Completion Thyroidectomy | Reoperative resection of any remaining thyroid tissue |

the intersection of the inferior thyroid artery and RLN. If the blood supply to a normal parathyroid is compromised, parathyroid auto-transplantation should be strongly considered.

Recommendation 27:

- a. *Dissection should be performed along the thyroid capsule to help preserve the parathyroid glands. (Strong recommendation, low-quality evidence)*
- b. *If a parathyroid gland cannot be preserved, parathyroid auto-transplantation should be performed. (Strong recommendation, low-quality evidence)*

The pyramidal lobe should be identified and resected during thyroid surgery. If it is indicated to proceed to total thyroidectomy, the same steps are performed to mobilize and resect the contralateral thyroid lobe.

Obtaining a dry field is important before closure. Drain use after thyroidectomy is rare and in meta-analysis is not associated with differences in reoperation rate, hematoma, or seroma formation, whereas use is associated with increased pain and a trend for increased wound infection. The operative report should include standard recommended detail and features.

There are important additional considerations in thyroidectomy for TC. Inspection and dissection of abnormal prelaryngeal, pretracheal, and paratracheal LNs are recommended, along with en bloc resection, if possible, of all gross tumor. Gross TC should not be left behind (ie, with the intent of preserving parathyroids or nerves) with the expectation that RAI ablation will kill residual disease (especially not in MTC). The risks and benefits of leaving residual TC to preserve an involved RLN are considered on a case by case basis.

PERIOPERATIVE TISSUE DIAGNOSIS

FNAB is the first line of investigation for suspicious thyroid nodules and cervical LN, but has nondiagnostic results in 5% to 15% of cases. Core needle biopsy (CNB) is an alternative that examines a tissue sample, rather than dissociated cells and colloid. CNB is associated with few complications when performed by experienced operators but has a sensitivity of only 68% for detecting TC. CNB may serve as a primary method for diagnosis of suspected PTL and ATC.

Recommendation 28: *Core needle biopsy should be rarely utilized in the initial evaluation of a thyroid nodule. (Strong recommendation, low-quality evidence)*

Intraoperative pathologic evaluation (IOPE), which is typically performed by frozen section analysis and/or cytologic touch or scrape analysis. With overall low utility, IOPE may be utilized in thyroidectomy to assure tissue identity and/or adequacy of collection in the setting of an unknown diagnosis. Given that only the assessment of nuclear features is required to diagnose PTC, IOPE may be useful in cases where PTC is suspected and its intraoperative diagnosis would change the extent of operation. When PTC is diagnosed preoperatively by FNAB, IOPE is not recommended or useful.

Recommendation 29: *Thyroid IOPE should only be utilized in settings in which the information it provides has a high likelihood of altering the operative procedure. (Strong recommendation, low-quality evidence)*

IOPE of a cervical LN can confirm its identity as opposed to parathyroid or extrathyroidal thyroid tissue, and can also help determine whether an LN harbors malignancy. In both situations, IOPE data may change the extent of operation, that is, by preventing autograft of misidentified parathyroid tissue, or by potentially

altering the extent of LN dissection. The overall accuracy rate of IOPE in distinguishing parathyroid from nonparathyroid tissue is 99.2%.

Recommendation 30: *IOPE is of value in confirming identification of parathyroid tissue. (Strong recommendation, moderate-quality evidence)*

Recommendation 31: *IOPE is of value in identification of CLN metastases when the information may alter extent of surgery. (Strong recommendation, moderate-quality evidence)*

The use of synoptic pathology reporting minimizes variability between institutions and ensures inclusion of appropriate information required for patient care. The College of American Pathologists provides a widely utilized checklist-format synoptic for TC.

Recommendation 32: *A standardized synoptic pathology report is recommended when reporting thyroid neoplasms. (Strong recommendation, low-quality evidence)*

NODAL DISSECTION

Lymph node metastasis (LNM) occurs subclinically in a majority of MTC and PTC patients; thus, a preoperative diagnosis of TC by cytology or MT should prompt imaging to assess for LNM. Neck US that includes evaluation of central and lateral LN basins is recommended in patients with cytologic evidence of TC. Preoperative FNAB of an abnormal LN, with Tg washout testing, is recommended if a diagnosis of locally metastatic TC would change the operative plan.

Nodal basins (see Table 4) are defined by anatomic boundaries and include the central (level VI and VII) and lateral (levels I-V) compartments. The extent of any lymphadenectomy needs to consider whether the nodal basins ipsilateral and/or contralateral to the primary cancer are affected. To limit recurrence, initial nodal dissection (either central or lateral) for TC should be a compartment-oriented clearance of the fibrofatty and lymphoid tissue within the defined anatomic boundaries of the compartment while avoiding berry-picking of only grossly positive LN.

The central compartment is often the first site of LNM in both PTC and MTC and should be pre- and intraoperatively assessed for suspicious lymphadenopathy. Bilateral prophylactic central compartment LN dissection (CND) for known MTC is recommended at initial surgery. Prophylactic CND for low-risk PTC is controversial; it is suggested for advanced primary DTC tumors and/or if lateral LNMs are present. There are no conclusive data showing that aggressive prophylactic extirpation of microscopic PTC LNM improves disease-specific outcomes. Whether to do prophylactic CND for PTC during initial thyroidectomy should depend on tumor and patient characteristics and surgeon expertise. Prophylactic CND for DTC in the reoperative setting is not indicated.

Therapeutic CND is indicated for PTC or MTC patients who have clinical or imaging-apparent nodal disease with the goal of complete resection at initial surgery to achieve local and regional control. Because preoperative imaging has low sensitivity for detecting central LNM when the thyroid is in situ, the central compartment should also be inspected during initial thyroidectomy so that therapeutic CND may be performed concurrently, if appropriate.

Recommendation 33: *During initial thyroidectomy for PTC, the central compartment should be assessed for suspicious lymphadenopathy. If clinical or imaged LNM is present (ie macroscopic disease), a therapeutic CND is recommended. (Strong recommendation, high-quality evidence)*

TABLE 4. Anatomic Boundaries of the Neck and Involvement in PTC

| Level | Anatomic Boundaries | Likelihood of LNM [95% CI] |
|-------|--|---|
| I | S: body of the mandible P: stylohyoid muscle A: anterior belly of the contralateral digastric muscle I: hyoid Triangular boundaries comprising anterior bellies of digastric muscles and hyoid separates Ia and Ib | 5%–9% [na] |
| II | S: skull base P: posterior SCM A: stylohyoid muscle I: hyoid CN XI separates IIa and IIb IIa nodes lie anterior to IJV | IIa: 53% [47%–60%] IIb: 16% [8%–27%] |
| III | S: hyoid P: posterior SCM A: sternohyoid muscle I: horizontal plane defined by the cricoid cartilage | 71% [67%–74%] |
| IV | S: inferior border of the cricoid cartilage P: posterior SCM A: sternohyoid muscle I: clavicle | 66% [61%–71%] |
| V | S: convergence of SCM and trapezius P: anterior border of trapezius A: posterior SCM I: clavicle Inferior border of cricoid separates Va and Vb | Va: 8% [3%–20%] Vb: 22% [8%–48%] |
| VI | S: hyoid superiorly P: deep layer of the cervical fascia A: anterior layer of the cervical fascia I: sternal notch | 40%–60% [na] |
| VII | S: sternal notch P: deep layer cervical fascia A: sternum I: innominate on right and equivalent plane on the left | |

A indicates anterior; I, inferior; na, not available; P, posterior; S, superior; SCM, sternocleidomastoid muscle.

In extensive study, prophylactic lateral neck dissection (ND) has not been shown to improve PTC survival or recurrence rates thus selective/lateral ND is typically performed only for clinically evident disease. In MTC, the suspicion for lateral nodal disease is based on US findings and/or serum calcitonin levels. Ipsilateral and contralateral lateral LNM are signaled by basal calcitonin levels >20 and >200 pg/mL, respectively. Some therefore advocate for prophylactic selective neck dissection of the ipsilateral neck for MTC although this is controversial.

Recommendation 34:

- A compartment-oriented therapeutic lateral ND is recommended for lateral LNM. (Strong recommendation, high-quality evidence)*
- Prophylactic lateral ND is not indicated for PTC. (Strong recommendation, high-quality evidence)*

Nodal dissections in either the central or lateral compartment are associated with increased operative morbidity, including but not limited to hypoparathyroidism, RLN injury, bleeding, cranial nerve XI palsy, and chyle leak.

Prognostic implications of PTC with LNM depend on age of patient, number of metastatic nodes and extranodal disease. In MTC, the number of positive LNM is associated with decreased overall survival.

CONCURRENT PARATHYROIDECTOMY

Concomitant hyperparathyroidism (pHPT) occurs in 0.2–5% of patients with thyroid disease, thus various groups have recommended routine assessment of calcium and/or PTH levels prior to planned thyroidectomy. When pHPT is present, the cost-effectiveness of surgical treatment is well-established, and the potential benefits of proceeding with parathyroidectomy at the same time as thyroidectomy are numerous. Although published data support routine preoperative assessment, no data exist regarding the cost-effectiveness of routine screening for pHPT.

Recommendation 35: Hypercalcemia should be evaluated preoperatively in a patient being evaluated for thyroid surgery. (Strong recommendation, low-quality evidence)

Multiple studies have advised that patients with a diagnosis of pHPT should undergo concurrent parathyroidectomy at the time of planned initial thyroidectomy. In a patient diagnosed with concurrent thyroid and parathyroid disease, US is the preferred initial imaging modality for both disease types. Further parathyroid-specific imaging can guide parathyroidectomy, especially if results allow a unilateral approach when thyroid lobectomy is planned, indicate a contralateral exploration, or diagnose an ectopic abnormal parathyroid. However, when total thyroidectomy is already planned, further parathyroid imaging may be unnecessary given the expectation that

all parathyroid glands will be examined in dissection. In the setting of concomitant thyroid disease, parathyroid imaging studies are less sensitive and less specific. Incidental removal of normal parathyroid tissue occurs during 4% to 22% of thyroid resections.

Recommendation 36: *Patients undergoing initial thyroidectomy who are diagnosed with primary hyperparathyroidism should undergo concurrent parathyroidectomy. (Strong recommendation, moderate-quality evidence)*

In patients on dialysis, at the time of thyroidectomy the opportunity should be taken to treat secondary HPT if present. Specific guidelines for the screening and management of co-existing thyroid and parathyroid disorders exist for patients with multiple endocrine neoplasia (MEN) 1 and MEN2A.

Recommendation 37: *Evaluation for HPT is recommended in patients scheduled to undergo thyroid surgery who have a history of familial pHPT. (Strong recommendation, moderate-quality evidence)*

HYPERTHYROID CONDITIONS

The prevalence of hyperthyroidism in the United States is about 1.2%. Decisions about the type and urgency of treatment are determined by factors including the time-course of disease, urgency of cure, costs, regional practices, compliance, access to care, and disease severity which can range from subclinical to life-threatening. Overall, although long-term treatment with anti-thyroid medications can be used even for a patient in the thyrotoxic state, it is not recommended as a first- or second-line choice. RAI ablation or surgery may be selected as definitive treatment (Table 5).

RAI ablation is well tolerated in most patients, but can fail to completely treat hyperthyroidism, cause keratoconjunctivitis sicca and xerostomia, and/or exhibit differential uptake in nodules or various areas of the gland which may require continued surveillance and additional long-term treatment. Compared to thyroidectomy, hyperthyroidism treated with RAI takes slightly longer to resolve and is less likely (92% vs 100%) to achieve full remission.

Surgery for GD is performed commonly in the United States, for which total thyroidectomy is the surgical procedure of choice. Appropriate preoperative preparation is important and may necessitate use of various medications (above); additional factors affecting treatment selection arise in patients with Graves ophthalmopathy (GO) or pregnancy. In patients with moderate to severe GO, surgery is preferred over RAI because it has less potential for acute worsening of GO.

Recommendation 38: *In patients with moderate to severe Graves' ophthalmopathy, total thyroidectomy should be considered as first line definitive treatment. (Strong recommendation, moderate-quality evidence)*

Complications such as RLN and EBSLN paralysis, hypoparathyroidism, and hematoma are more likely to occur with thyroidectomy for GD; however, when performed by a high volume thyroid surgeon, permanent complications rates are no higher than for thyroidectomy done for other reasons.

Recommendation 39: *Due to the higher risk and greater technical difficulty, thyroidectomy in Graves disease is best performed by high volume thyroid surgeons. (Strong recommendation, low-quality evidence)*

GOITER

Surgical treatment of nontoxic goiter is indicated for symptoms related to compression of the trachea, esophagus, RLN, or superior vena cava. The most common symptoms are nonspecific and include shortness of breath (50%), dysphagia (30%), and voice change (13%). Whereas medical or RAI therapy may result in partial size reduction, resection of goiter offers the best opportunity for definitive treatment.

Recommendation 40:

- When surgery is indicated, total thyroidectomy is preferred for treatment of bilateral goiter. (Strong recommendation, low-quality evidence)*
- When the contralateral lobe is normal, lobectomy and isthmusectomy are recommended for treatment of unilateral goiter. (Strong recommendation, low-quality evidence)*

When findings suggest substernal extension, CT or MRI should be performed to evaluate for tracheal compression and may aid in surgical planning.

Recommendation 41: *Cross-sectional imaging of goiter is recommended if there is concern for a substernal component. (Strong recommendation, moderate-quality evidence)*

Surgery for a large cervical and/or substernal goiter is multifaceted and best handled by experienced thyroid surgeons. An anesthesia team experienced in managing complex airway issues is also vital if there is significant tracheal compression, and video-laryngoscopy with awake fiberoptic intubation and/or rigid bronchoscopy may be useful when difficult laryngeal exposure is

TABLE 5. Recommended Treatment for Causes of Hyperthyroidism

| Cause of Thyrotoxicosis | Typical Treatment* | Additional Treatment Options | Other (ETOH Ablation, RFA) | Extent of Surgery |
|---|------------------------------------|---|--|-----------------------------|
| Single toxic nodule | Surgery | RAI | ETOH ablation or RFA | Lobectomy and isthmusectomy |
| TMNG | Surgery | RAI | | Total thyroidectomy |
| Graves' disease 1) No or mild GO 2) + GO | 1) RAI or Surgery 2) Surgery | Methimazole | | Total thyroidectomy |
| Acute, subacute, chronic thyroiditis | Supportive (Beta-blockers, NSAIDs) | Steroids Surgery† | | Total thyroidectomy† |
| Functional thyroid cancer metastases or benign thyroid deposits | RAI or surgery | Image/catheter guided therapy Chemotherapy | ETOH ablation RFA | Complete resection |
| Hypothalamic pituitary axis | Surgery | XRT | Medication (octreotide, bromocriptine) | Complete resection |
| Extrathyroidal neoplasms | Surgery | Image/catheter guided therapy | | Complete resection |

*Selection of therapy depends on the clinical situation and patient factors.

†Surgery for thyroiditis is rarely needed is performed in highly selected situations.

ETOH indicates ethanol; GO, Graves ophthalmopathy; NSAID, nonsteroidal anti-inflammatory drug; RFA, radiofrequency ablation.

anticipated. In the hands of experienced anesthesiologists, intubation complications are uncommon.

Recommendation 42: *When performing surgery for substernal goiter, good communication, preparation, and cooperation of experienced surgical and anesthesia teams are recommended. (Strong recommendation, low-quality evidence)*

ADJUNCTS AND APPROACHES

Although the basic principles of safe thyroidectomy have remained constant since the early 20th century, numerous technical adjuncts have been introduced. Control of bleeding during thyroidectomy may be achieved using fine ties, titanium clips, and/or electrocautery. Two additional devices that have achieved widespread use are the electrothermal bipolar cautery and the ultrasonic coagulator; both have safety and efficacy profiles similar to conventional knot-tying, and can reduce operative times.

In an attempt to reduce rates of RLN injury in thyroidectomy, numerous studies have evaluated intraoperative recurrent laryngeal nerve monitoring (RLNM), with no clear demonstration of benefit in preventing RLN injury. Selective use of RLNM is nevertheless common today, with some surgeons advocating for utility in more challenging settings such as reoperations or operations for TC or large goiter. RLNM may also be useful during planned total thyroidectomy: after completion of initial thyroid lobectomy, if the RLN is intact but RLNM suggests loss of function, the surgeon may consider stopping the operation for possible staged completion surgery later.

Recommendation 43: *Although it does not prevent RLN injury, RLNM is safe and may assist the surgeon during initial or reoperative thyroidectomy. (Strong recommendation, moderate-quality evidence)*

Recommendation 44: *During planned total thyroidectomy, after completion of the initial lobectomy, if RLNM results suggest loss of function, the surgeon may consider stopping the operation for possible completion at a later date. (Strong recommendation, low-quality evidence)*

Methods for rapid or intraoperative parathyroid monitoring may assist in identification and management of patients who are at higher risk for postoperative hypocalcemia after total or reoperative thyroidectomy.

Recommendation 45: *Rapid PTH measurement during or after total or completion thyroidectomy may help to manage patients at risk for hypocalcemia. (Weak recommendation, moderate-quality evidence)*

Numerous remote-access approaches for thyroidectomy using endoscopic and robotic techniques have gained popularity. The primary advantage of remote-access thyroidectomy is improved cervical cosmesis; however, such techniques also demonstrate longer operative times, longer length of stay, and somewhat higher risk. An ATA consensus statement advised that remote-access thyroidectomy should only be performed in carefully selected patients by surgeons experienced in the approach.

Recommendation 46: *Remote-access thyroidectomy should only be performed in carefully selected patients, by surgeons experienced in the approach. (Strong recommendation, low-quality evidence)*

A wide variety of topical hemostatic agents are currently available with the intention of facilitating surgical hemostasis, but data do not demonstrate efficacy in preventing bleeding.

LARYNGOLOGY

The impact of vocal fold dysfunction (VFD) is significant. Preoperative knowledge of vocal fold abnormalities may alter the conduct or extent of operation or delay thyroidectomy. When evaluating patients for thyroidectomy, the surgeon should assess voice function and quality. Visualization of the vocal folds is recommended routinely by some medical societies and selectively by others for patients determined to be at risk, that is, those with notable voice change, known VFD, previous neck, mediastinal, or upper thoracic surgery, apparent invasive TC, large substernal goiter, or extensive LNM. The utilized methods vary widely and include auditory assessment, mirror examination, transcutaneous laryngeal ultrasound, flexible laryngoscopy, and videolaryngostroboscopy.

Recommendation 47: *In preoperative discussion of thyroidectomy, the surgeon should disclose to the patient the possibility, likelihood, and implications of permanent laryngeal dysfunction. (Strong recommendation, moderate-quality evidence)*

Recommendation 48: *Before thyroidectomy, laryngeal examination should be performed in patients determined to have vocal abnormalities as assessed by the surgeon, preexisting laryngeal disorders, previous at-risk surgery, or locally advanced TC. (Strong recommendation, low-quality evidence)*

If VFD is known or suspected to have occurred intraoperatively, immediate careful observation after extubation is warranted, assessing in particular for altered respiratory status, stridor, and aspiration. Immediate management of suspected unilateral VFD varies depending on the setting and severity of the condition. Early intervention in those with RLN paresis or paralysis is associated with superior functional outcomes. EBSLN dysfunction can be difficult to assess and confirm. When assessed during thyroid surgery by RLNM, reported EBSLN injury rates range from 0% to 58%, with permanent paralysis in 0% to 5%.

Functional voice assessment should be performed for all patients post thyroid surgery. However, an area of continued debate is the routine postoperative anatomic assessment of the vocal folds. Two recent decision-analyses found that routine laryngoscopy for all patients was not cost-effective.

Recommendation 49: *Voice assessment should be performed at the postoperative visit. (Strong recommendation, low-quality evidence)*

Recommendation 50: *After thyroidectomy, laryngeal examination should be performed in patients with known or suspected new RLN dysfunction or aspiration. (Strong recommendation, moderate-quality evidence)*

Patients with known or suspected VFD, or those with particular concern about their voice after thyroidectomy, should be referred to a laryngologist for further evaluation and treatment.

Recommendation 51: *If vocal fold motion impairment is suspected or identified, early referral of the patient to a laryngologist is recommended. (Strong recommendation, moderate-quality evidence)*

FAMILIAL TC

More than 90% of all TC is sporadic in nature, secondary to somatic genetic alterations. Approximately 3% to 9% of TC is familial nonmedullary TC (FNMTTC) with PTC the most common histologic subtype (85%–91%), followed by FTC (6%–10%), ATC (1.6%), and HCC. FNMTTC is nonsyndromic in 95% of cases. MTC accounts for 3% to 5% of all TCs with approximately 25% of cases being hereditary.

The decision to perform germline genetic testing for TC, as well as the associated counseling and interpretation of results, should involve an experienced professional team.

Recommendation 52: Germline genetic testing should include pre- and post-test counseling by a knowledgeable health care provider. (Strong recommendation, low-quality evidence)

Nonsyndromic familial nonmedullary TC (NFMNMT) is defined by the presence of follicular cell-based TC with 3 affected first-degree relatives in the absence of predisposing environmental risk factors or a known familial syndrome. Currently, there are no clinically available germline tests and no data to support prophylactic thyroidectomy. With a clinical diagnosis of this condition, the surgical decision about extent of thyroidectomy should take into consideration the potentially higher rates of observed multifocality and bilaterality.

Recommendation 53: DTC screening should be performed in at-risk individuals from families with ≥ 3 affected first-degree relatives. (Strong recommendation, low-quality evidence)

Syndromic familial nonmedullary TC is rare and the decision for germline testing and TC screening is based on the individual syndrome (Table 6).

Mutations of the *RET* proto-oncogene are responsible for almost all cases of hereditary MTC. Penetrance of MTC nears 100% in patients who harbor a *RET* germline mutation. The 2015 ATA guidelines on MTC recommend that all hereditary MTCs be classified into either MEN2A or 2B.

Recommendation 54: All patients diagnosed with MTC should undergo genetic testing for a germline *RET* mutation. (Strong recommendation, high-quality evidence)

Familial MTC age of onset and course cannot be determined by the kindred's specific history, which should be used cautiously in counseling. Discussion between the parents and the experienced health care team is essential.

Recommendation 55: An experienced multidisciplinary care team should manage patients diagnosed with MEN2A and MEN2B. (Strong recommendation, low-quality evidence)

POSTOPERATIVE CARE AND COMPLICATIONS

After total thyroidectomy, testing of thyroid function should be coordinated with the patient's endocrinologist and/or primary care physician. TSH level should be checked at 6 to 8 weeks postoperatively and T4 dose adjusted accordingly. Patients undergoing lobectomy should be aware that they are at risk for developing subclinical hypothyroidism even with the contralateral lobe intact and should have their TSH level checked as well.

The decision between inpatient and outpatient recovery depends on local resources, access for readmission should an emergency arise, surgeon experience, and in some cases patient preference.

Prompt communication with referring physician(s) is courteous, helps ensure a cohesive postoperative plan, and provides a reminder of any issues to be handled in a safe and timely manner. After surgery for hyperthyroidism, anti-thyroid medications should be stopped, and beta-blockade weaned in communication with the prescribing physician. T4 replacement dosing is initially started based on the patient's weight (0.8 $\mu\text{g}/\text{lb}$ or 1.6 $\mu\text{g}/\text{kg}$), with adjustments made for age (round up for younger patients, down for older patients), body mass index, and pregnancy. T4 suppressive dosing should be performed per 2015 ATA guidelines based on risks and benefits. If RAI ablation is a possibility, communication with the referring endocrinologist is prudent before starting T4.

Postoperative pain after thyroidectomy is general reported as minimal, and studies show low opioid use in patients who receive preoperative education about the issue. The use of nonsteroidal anti-inflammatory drugs or nonpharmacological options is preferred and effective. If opioids are prescribed, the lowest-effective, immediate-release options are preferred.

TABLE 6. Inherited Predisposition Syndromes for Thyroid Cancer

| | Familial Adenomatous Polyposis | <i>PTEN</i> -Hamartoma Tumor (Cowden) | Carney Complex Type 1 | <i>RET</i> -Associated | <i>DICER1</i> |
|-----------------------------|---|--|--|---|---|
| Gene | <i>APC</i> | <i>PTEN</i> | <i>PRKARIA</i> | <i>RET</i> | <i>DICER1</i> |
| Pathognomonic criteria | >100 colorectal adenomatous polyps | Mucocutaneous lesions, cerebellar tumors (Lhermitte-Duclos disease) | Multiple pigmented skin lesions (eg, nevi, blue nevi, lentiginos) | Medullary thyroid cancer | Pleuropulmonary blastoma |
| Other major manifestations | – | Breast, endometrial, thyroid cancer, macrocephaly | Blue nevi, pigmented nodular adrenals, cardiac myxomas | Primary hyperparathyroidism, pheochromocytoma, mucosal neuromas | Ovarian sex cord-stromal tumors, cystic nephroma, and multinodular goiter |
| Minor manifestations | Extracolonic polyps, congenital hypertrophy of retinal pigment epithelium, thyroid nodules/cancer, soft tissue tumors, desmoids, osteomas | Fibrocystic breast disease, gastrointestinal hamartomas, lipomas, fibromas, renal cell carcinomas uterine fibromas | Thyroid nodules, melanotic schwannomas, adrenal or pituitary adenomas, hepatocellular carcinoma, pancreatic cancer | Hirschsprung's disease, cutaneous lichen amyloidosis | Wilms tumor, rhabdomyosarcoma, ciliary body medulloepithelioma, pineoblastoma, pituitary blastoma, nasal chondromesenchymal hamartoma |
| Thyroid disease prevalence: | | | | | |
| Benign | | | | | |
| Cancer | 40% | 75% | Up to 75% | – | Up to 30% |
| | 0.4-12% | 35% | <5% | 100% | – |
| Cancer | | PTC 50% | PTC | | |
| Subtypes | CMV-PTC 63% | FV-PTC 28% | FTC | MTC | FTC |
| | FV-PTC 25% | FTC 14% | | | FV-PTC |
| | PTC 12% | | | | |

CMV indicates cribriform-morular variant. FV, follicular variant.

Recommendation 56:

- a. *Use of nonopioid and nonpharmacologic therapies and patient education should be the first-line pain management after thyroidectomy. (Strong recommendation, moderate-quality evidence)*
- b. *If opioids are prescribed for postoperative pain management, the lowest effective dose of immediate release opioids (<10 oral morphine equivalents) should be prescribed. (Strong recommendation, moderate-quality evidence)*

A postoperative visit should be scheduled to evaluate the patient's recovery, incision, voice, and symptoms to provide potential adjustment of medications, to review surgical pathology, and to schedule further treatment or follow-up. Published evidence does not support the use of over-the-counter scar treatments.

Postoperative bleeding is a well-known complication of thyroidectomy. The reported incidence varies by institution and patient population and is 0.7% to 1.5%. Approximately 50% of cervical hematomas requiring reoperation occur within 6 hours and 80% within 24 hours of the surgery. Multiple risk factors for post-thyroidectomy hematoma have been reported. No device or topical agent has been demonstrated to reduce the incidence compared to conventional vessel ligation. Safe treatment of hematoma relies on early detection and expeditious evacuation to prevent or alleviate airway compromise.

Recommendation 57: *Patients at higher risk for cervical hematoma should be considered for overnight observation following thyroid surgery. (Weak recommendation, moderate-quality evidence)*

The timing of intervention for post-thyroidectomy hematoma depends on the severity of airway compromise as well as surgeon judgment and setting. If the patient is in extremis, bedside evacuation by opening the cervical incision is required. If the patient is more stable, they may be transported to the operating room for urgent management. Nonoperative management of an acute post-thyroidectomy hematoma is not recommended.

Recommendation 58: *Patients with suspected hematoma after thyroidectomy should be evaluated immediately with appropriate intervention as indicated. (Strong recommendation, low-quality evidence)*

Injury to the RLN is a recognized risk of thyroidectomy. Most series report temporary VFD rates of 0.5% to 10%, and permanent rates of 0% to 5%. Several risk factors for RLN dysfunction have been described, including reoperation, TC, large goiter, and GD. If transection of the RLN is recognized intraoperatively, reanastomosis should be performed. This does not restore vocal fold mobility but can improve voice outcomes. In cases of RLN traction or stretch, administration of calcium channel blockers, such as nimodipine, can improve recovery.

Recommendation 59: *If unilateral RLN transection occurs during thyroidectomy, an attempt should be made at repair. (Strong recommendation, moderate-quality evidence)*

Hypoparathyroidism leading to hypocalcemia is a recognized complication of total or completion thyroidectomy. Reported rates vary considerably depending on definitions and frequency of monitoring, but range from 27% to 50% for temporary and 1% to 5% for permanent. Risk factors include GD and concurrent CND. Often, serum calcium levels (with or without PTH) are measured postoperatively and oral calcium with or without calcitriol supplementation is administered based on the results. Other experts provide prophylactic calcium with or without calcitriol to all patients undergoing total or

completion thyroidectomy with low observed rates of symptomatic hypocalcemia. As a third alternative, rapid PTH levels are checked intraoperatively or in the recovery room (above) to guide postoperative supplementation.

Recommendation 60: *To prevent and/or manage postoperative symptoms of hypocalcemia following total or completion thyroidectomy, a strategy for calcium and/or vitamin D supplementation should be considered. (Strong recommendation, moderate-quality evidence)*

The preferred method of treatment of postoperative hypocalcemia is oral calcium; if significant hypocalcemia persists, oral calcitriol may be administered. IV calcium and calcitriol should be reserved for patients with life-threatening sequelae of hypocalcemia who are refractory to oral therapy.

Recommendation 61: *Patients with significant post-thyroidectomy hypocalcemia should receive oral calcium as first-line therapy, calcitriol as necessary, and intravenous calcium in severe or refractory situations. (Strong recommendation, low-quality evidence)*

CANCER MANAGEMENT

Active surveillance (AS) is a possible management strategy for small PTC; however, it is not yet a widely adopted option and requires informed surgical discussion, patient motivation, potentially more cost, an experienced multidisciplinary team, and high-quality neck US.

Recommendation 62: *An active surveillance protocol for PTMC may be appropriate for carefully selected, informed, and compliant patients. (Strong recommendation, moderate-quality evidence)*

The AJCC TNM classification is often used for DTC staging, but, to assess recurrence risk, additional prognostic variables are frequently considered such as TC type, histologic features including angiolymphatic invasion, and adequacy of initial treatment.

Recommendation 63: *A validated postoperative staging system such as the AJCC TNM classification should be used in TC care. (Strong recommendation, moderate-quality evidence)*

Total thyroidectomy (either as a 1- or 2-stage procedure) is typically recommended for high-risk cancers, when RAI therapy is indicated, and for patients undergoing prophylactic thyroidectomy for MTC. In the absence of imaged structural disease, there is no indication for reoperative CND for any TC histology. If MTC is diagnosed preoperatively, total thyroidectomy with central compartment neck dissection is the minimum initial recommended procedure.

Recommendation 64: *Consider completion thyroidectomy for high-risk disease and/or when postoperative RAI therapy is indicated. (Strong recommendation, moderate-quality evidence)*

Recommendation 65: *Total thyroidectomy should be performed for patients undergoing prophylactic thyroidectomy for medullary TC. (Strong recommendation, moderate-quality evidence)*

RAI is given for remnant ablation to facilitate surveillance (~30 mCi), as adjuvant therapy to treat microscopic disease (<150 mCi), and to treat distant metastasis if not surgically resectable. Indications for adjuvant RAI ablation include: DTC considered high risk or intermediate risk especially with aggressive histologies, and lateral LNM at presentation (Table 7). RAI can be given either after T4 withdrawal or recombinant TSH administration; both management protocols function to raise TSH and increase absorption of iodine.

TABLE 7. ATA Risk Stratification Definitions and Treatment

| Risk Category | Characteristics | Likelihood of NED After TT and RAI Ablation, % | Minimal Extent of Thyroidectomy | RAI? | Goal TSH, mU/L |
|---------------|--|--|---------------------------------|--|----------------|
| Low | Intrathyroidal, completely resected PTC or encapsulated FV-PTC No local or distant metastasis No aggressive histology (tall cell, hobnail, or columnar cell) Intrathyroidal FTC with capsular and/or <4 foci vascular invasion Clinical N0 or ≤5 pathologic N1 micrometastasis (<2 mm) | 78–91 | Lobectomy | Usually no | 0.5–2 |
| Intermediate | PTC with microscopic extrathyroidal extension, vascular invasion Incomplete response to treatment Clinical N1 or >5 pathologic N1 <3 cm | 52–64 | Total | Strongly considered esp with aggressive histologies, older age, and/or lateral LNM | 0.1–0.5 |
| High | Gross extrathyroidal extension Incomplete tumor resection Distant metastases Nodal metastasis ≥3 cm FTC with extensive vascular invasion | 31–32 | Total | Yes | <0.1 |

NED indicates no evidence of disease, for example, Tg undetectable and no radiographic evidence of disease.

Although the use of T4 to suppress TSH is a strategy that is routinely used to reduce the risk of DTC recurrence, long-term TSH suppression even to subclinical levels can increase the risks of atrial fibrillation, angina, and osteoporosis. As a result, the need for and degree of TSH suppression should follow established guidelines and be adjusted both for recurrence risk and patient comorbidities. There is no indication for TSH suppression in MTC or ATC.

If complete surgical resection for DTC was performed, there is no indication for external beam radiation therapy (EBRT). Tyrosine kinase inhibitors and small molecule inhibitors are reserved for patients with RAI non-avid and progressive metastatic disease.

MTC patients should have postoperative CEA and calcitonin levels checked at least 2 to 3 months after surgery, although levels may take up to 6 months to reach nadir. Calcitonin doubling time is independently and directly correlated to survival. Rapidly increasing CEA levels may indicate MTC de-differentiation.

Surveillance for DTC patients typically includes Tg and TgAb levels and US every 6 to 12 months. Patients with negative imaging and a suppressed Tg <0.2 ng/mL are considered to have an excellent response with a 1% to 4% risk of recurrence. In patients with Tg levels >10 ng/mL, CT of the chest and/or 18FDG-PET imaging can be considered. Serum Tg doubling time can be an important prognostic variable and in a single-institution study, Tg doubling time <1 year was associated with 50% cause-specific survival at 10 years.

REOPERATION

Thyroid reoperation is defined as occurring in a previously dissected cervical compartment (ie, previous thyroid resection, tracheostomy, parathyroidectomy, anterior cervical discectomy, or carotid endarterectomy) and may be grouped into 3 categories: central or lateral resection for persistent/recurrent TC or LNM, remnant ipsilateral thyroid tissue resection after prior partial thyroidectomy, and completion total thyroidectomy after previous contralateral lobectomy. In patients with persistent or recurrent TC or

LNM, decision-making regarding observation versus reoperation or other therapy is based upon tumor/LN size and appearance, interval growth, presence of progressive systemic disease, and trends in serial Tg levels.

DTC patients with radiographically detected recurrent LNM may be candidates for observation for a central compartment LN ≤8 mm or lateral compartment LN ≤10 mm with minimal (<3–5 mm/year) or no growth on serial imaging. In addition, patients with a strong preference to avoid further operation, significant comorbidities, or progressive systemic disease also may be selected for observation.

Recommendation 66: Selected patients with stable, low-volume persistent or recurrent LNM can undergo active surveillance. (Weak recommendation, low-quality evidence)

For patients with persistent or recurrent MTC, calcitonin and CEA doubling times as well as size and radiographic features are the key determinants of the decision for reoperation.

In TC patients who have undergone thyroid lobectomy, completion thyroidectomy (removal of the contralateral lobe) may be recommended if intermediate to high-risk pathologic features are identified, especially if RAI therapy is planned, as well as when there is concern for contralateral disease or familial MTC.

Thyroid reoperation requires careful preoperative planning, including review of all documentation from previous operation(s), current comprehensive preoperative imaging, and laryngeal evaluation. Due to scarring and altered anatomy, the risks of injury to the parathyroid glands and RLN are significantly higher than for initial surgery.

Perioperative diagnostic evaluation of the reoperative patient often requires specialized radiologic and endocrine pathology expertise. Moreover, decision-making about optimal management of persistent or recurrent disease often requires the input not only of the thyroid surgeon and endocrinologist, but also of nuclear medicine, radiation oncology, and medical oncology team members in a multidisciplinary setting.