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Optimal Thyroid Health for All

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Willems JIA, et al. Fasting vs non-fasting, dose-adjusted levothyroxine ingestion in hypothyroidism: a randomized clinical trial. J Clin Endocrinol Metab. Epub 2025 Dec 23; doi: 10.1210/clinem/dgaf686. PMID: 41431302.

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Swaminathan N, et al. Malignancy risk and diagnostic accuracy of fine-needle aspiration in thyroid nodules ≥4 cm: a retrospective analysis of incidental cancer. Am Surg. Epub 2025 Dec 9; doi: 10.1177/00031348251407348. PMID: 41363024.

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Jensen CB, et al. Factors associated with receiving thyroid cancer care from high-volume surgeons. J Am Coll Surg. Epub 2025 Dec 8.

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2025 ATA Differentiated Thyroid Cancer Guidelines: Completion Thyroidectomy
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Ringel MD et al. 2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer. Thyroid 2025;35(8):841-985.

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2025 ATA Differentiated Thyroid Cancer Guidelines: TSH suppression
In the 2015 thyroid cancer guidelines, assigning risk of thyroid cancer recurrence (risk stratification) based on the assessment after the initial surgery drove initial TSH suppressive therapy decisions, as very specific TSH targets were recommended. However, treatment changes the risk of recurrence, with an excellent response to therapy having a different prognosis even in a patient with a high-risk cancer. In the 2025 guidelines, a focus on re-evaluating risk stratification allows for initial treatment response to play a role in the selection of TSH suppression therapy.
Ringel MD et al. 2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer. Thyroid 2025;35(8):841-985.

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While the majority of patients with thyroid cancer do very well with an excellent prognosis, 5 to 15% of patients have more advanced cancer which can develop resistance to radioactive iodine therapy, which is linked to markedly worse clinical outcomes. Systemic therapy (ie chemotherapy) is reserved for patients with progressive, symptomatic cancer that fails to respond to radioactive iodine therapy and cannot be surgically removed. The 2025 ATA thyroid cancer guidelines provide the first comprehensive framework directly linking molecular gene mutations in the cancer to available options for treatment.
Ringel MD et al. 2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer. Thyroid 2025;35(8):841-985.

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Editor's Comments

Welcome to another issue of *Clinical Thyroidology for the Public*! In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through X (previously known as Twitter) at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association®, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association,* and *Thyroid Federation International.*

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association® (ATA®) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA® mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA® is a 501(c)3 nonprofit organization and your gift is tax deductible.

March is Medullary Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Can levothyroxine be taken with breakfast?
- Can you believe benign biopsy results in large thyroid nodules?
- How easy is it to have your thyroid surgery performed by a high-volume thyroid surgeon?
- When should you have a completion thyroidectomy after a lobectomy for thyroid cancer?
- How low should your TSH be if you have thyroid cancer?
- When should your thyroid cancer be treated with chemotherapy drugs?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD

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HYPOTHYROIDISM

Can levothyroxine be taken with breakfast?

BACKGROUND

Hypothyroidism occurs when the thyroid stops working and thyroid hormone levels fall into the low range. Treatment of hypothyroidism is usually levothyroxine to replace the thyroid hormones in the blood. The absorption of levothyroxine is affected by acid levels in the stomach. Taking levothyroxine with food, iron, calcium, or certain medications used for gastritis or reflux disease can decrease levothyroxine absorption and its efficacy. Therefore, patients are advised to take levothyroxine in an empty stomach and wait at least 30-60 minutes before eating breakfast. However, some patients may find this recommendation difficult to follow due to various circumstances, leading to missed or decreased effectiveness of levothyroxine and inadequate treatment of hypothyroidism.

The researchers of the study aimed to assess if taking a higher dose of levothyroxine with breakfast would still result in stable thyroid function compared to taking a lower dose of levothyroxine before breakfast.

THE FULL ARTICLE TITLE

Willems JIA, et al. Fasting vs non-fasting, dose-adjusted levothyroxine ingestion in hypothyroidism: a randomized clinical trial. J Clin Endocrinol Metab. Epub 2025 Dec 23; doi: 10.1210/clinem/dgaf686. PMID: 41431302.

SUMMARY OF THE STUDY

A total of 88 patients with hypothyroidism taking levothyroxine were enrolled in this clinical trial done in the Netherlands. Patients were taking at least 1mcg/kg of levothyroxine every day and had stable serum TSH levels prior to the study. Patients were not included if they had history of thyroid or other cancers, malabsorption disorders, other severe chronic disease such as advanced heart failure or end-stage kidney disease, or if pregnant.

Patients were divided to either the fasting group (43 patients taking levothyroxine 30-60 minutes before breakfast) or the breakfast group (45 patients taking levothyroxine with breakfast). Levothyroxine dose was increased by 15% for patients in the breakfast group to make up for lower absorption. TSH level was measured every 6 weeks with appropriate adjustment of levothyroxine dose, until it was stable over 2 consecutive checks or until 24 weeks after study started (the end of the study). Patients also answered questionnaires regarding their overall well-being and preferred regimen. At the end of the study, all 43 patients in the initial fasting group were invited to change to the breakfast regimen. Those who participated further by switching to the breakfast regimen were referred to as the crossover group.

Similar number of patients achieved stable TSH levels in both groups, including 74.4% in the fasting group and 73.3% in the breakfast group. The average time for reaching stable TSH level was 12 weeks, similar in both groups. More patients in the breakfast group (33.3%) reported improvement in well-being compared to those in the fasting group (16.3%). Reasons for improvement in well-being in the breakfast group included feeling more fit, less stress and easier adherence with regimen, decrease in stomach discomfort after switching to taking levothyroxine with breakfast, and more consistent breakfast routine. At the end of the study, 89% of the patients in the breakfast group opted to continue taking levothyroxine with breakfast.

Among the 32 patients in the fasting group whose TSH levels were stable, 18 patients opted to crossover to the breakfast regimen with levothyroxine dose increase, with 66.7% achieving stable TSH level. No significant change was seen in their overall well-being after crossover, but 78% of these patients preferred taking levothyroxine with breakfast over fasting.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The researchers of this study concluded that stable TSH levels can be achieved with 15% increase in levothyroxine

HYPOTHYROIDISM, continued

dose if patients take levothyroxine with breakfast consistently. Patients in this study also preferred taking levothyroxine with breakfast over fasting. Previous studies by the researchers of this study reported that 50% of patients found taking levothyroxine before breakfast burdensome and 33% of patients were not taking it consistently. This study shows that taking a slightly higher dose of levothyroxine with breakfast may be a practical option to improve consistency and to achieve treatment target in patients with well-controlled hypothyroidism.

— Sun Y. Lee, MD

ATA RESOURCES

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/

Thyroid Hormone Treatment: https://www.thyroid.org/thyroid-hormone-treatment/

ABBREVIATIONS & DEFINITIONS

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

Levothyroxine (T4): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tirosint™ and generic preparations.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

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THYROID NODULES

Large thyroid nodules: how reassuring is a benign biopsy result?

BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of individuals that get any imaging test that includes the neck. The concern with a thyroid nodule is whether it is a cancer. Fortunately, only ~5% of thyroid nodules are cancerous, so the vasy majority of nodules are benign. However, there is some data that shows that large nodules (≥4 cm) have a higher cancer risk. Thyroid biopsy is the main test to determine whether a nodule is cancer or benign. However, some studies suggest that a thyroid biopsy is less reliable in evaluating large nodules. Larger nodules may have a higher rate of missed cancer, especially those nodules with different areas within the nodule as compared to nodules that appear to be the same throughout. As a result, clinicians remain divided on whether benign biopsy findings in large thyroid nodules can safely be followed as benign nodules or whether the need to consider surgery instead.

The goal of this study was to determine the cancer rate of large thyroid nodules and evaluate the diagnostic accuracy of biopsy results of large nodules by comparing the biopsy findings with the final surgical pathology results.

THE FULL ARTICLE TITLE

Swaminathan N , et al. Malignancy risk and diagnostic accuracy of fine-needle aspiration in thyroid nodules ≥4 cm: a retrospective analysis of incidental cancer. Am Surg. Epub 2025 Dec 9; doi: 10.1177/00031348251407348. PMID: 41363024.

SUMMARY OF THE STUDY

This study evaluated 95 adult patients with thyroid nodules ≥4 cm who underwent thyroid biopsy and then surgical removal of their nodules (partial or total thyroidectomy) at a large care center between January 2015 and December 2024. Of note, at this institution, patients with large thyroid nodules typically undergo thyroidectomy even when the biopsy results are benign.

The biopsy results were categorized according to the Bethesda System for Reporting Thyroid Cytopathology, an international standardized reporting system that includes six cytologic categories, each category having a different cancer risk. In this study, the cytology results were grouped as low-risk (Bethesda I-III) and high risk for malignancy (Bethesda IV-VI). The cytology results from thyroid biopsies were compared with the final surgical results.

Among patients with thyroid nodules ≥4 cm who underwent thyroid biopsy, 15% were cancer at surgery, while 85% had benign results. Thyroid biopsy results and surgery results were in agreement in 64 of 81 patients (79%) with benign nodules and in 12 of 14 patients (86%) with cancerous nodules. Notably, over one-third (36%) of cancers were not detected by thyroid biopsy prior to surgery, highlighting the potential for missed cancers in large thyroid nodules despite benign results. A total of 86% of the patients with biopsy results showing high-risk cytology (Bethesda IV-VI) had cancer on final pathology, while 79% of those with low-risk cytology (Bethesda I-III) had truly benign thyroid nodules.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study highlights that a benign biopsy result does not always guarantee the absence of cancer in large thyroid nodules. A larger study with better characterization of the nodule features on ultrasound may be helpful in determining the risk of a false benign biopsy result. Understanding this risk enables informed shared decision-making regarding following a large nodule with a benign biopsy with ultrasound versus referring for surgery.

— Elie Naous, MD
— Alina Gavrila, MD, MMSC

THYROID NODULES, continued

ATA RESOURCES

Fine Needle Aspiration Biopsy of Thyroid Nodules: https://www.thyroid.org/fna-thyroid-nodules/

Thyroid Nodules: https://www.thyroid.org/thyroid-nodules/

ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (benign), ~5-10% are cancerous (malignant).

Thyroid biopsy: a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Cytology: microscopic examination of individual cells (not the whole tissue) collected from body fluids, fine needle aspirations or surface scrapings, commonly used to screen for disease.

Thyroidectomy: surgery to remove the entire thyroid gland (total thyroidectomy) or only part of the thyroid gland, usually one lobe with or without the isthmus (partial thyroidectomy).

Surgical Pathology: gross and microscopic examination of tissue specimens removed during surgery used to diagnose disease.

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THYROID SURGERY

Reaching a high-volume thyroid surgeon depends on more than where you live

BACKGROUND

Thyroidectomy, the surgical removal of the thyroid, is one of the most common operations in the US. It is performed for thyroid cancer as well as non-cancer reasons such as benign nodules and hyperthyroidism due to Graves' disease. Thyroidectomy is generally very safe, but because the thyroid is located in a sensitive area, damage to the structures around it can lead to complications such as voice changes, low calcium levels, or the need for additional treatments. Past research has shown that surgeons who perform a higher number of thyroid surgeries each year tend to have lower complication rates and better overall outcomes. High-volume thyroid surgeons are those that perform >25-100+ operations annually and have better outcomes, lower complication rates and shorter hospital stays as compared to low-volume surgeons. In addition, people with thyroid cancer who have their surgery done by high-volume thyroid surgeons have a lower chance of needing a second operation and may have improved cancer-related outcomes.

However, many thyroid surgeries in the US are performed by surgeons who do very few of these procedures each year. Where a patient lives, their insurance, and other personal factors may affect whether they are treated by a high-volume thyroid surgeon. This study aimed to better understand how these factors influence access to more experienced surgical care.

THE FULL ARTICLE TITLE

Jensen CB, et al. Factors associated with receiving thyroid cancer care from high-volume surgeons. J Am Coll Surg. Epub 2025 Dec 8.

SUMMARY OF THE STUDY

Researchers reviewed data from 2015 to 2022 from a statewide database that includes information from multiple insurers. The database, called Michigan Value Collaborative registry, covers 84% of Michigan's insured population. They studied adult patients with thyroid cancer who had thyroidectomies. Surgeons were classified as high-volume thyroid surgeons if they did 25 or more thyroid surgeries per year, and as low-volume thyroid surgeons if they did 25 or fewer surgeries per year. The researchers checked patient and neighborhood details, like age, sex, insurance type, estimated income, and education level based on zip code, as well as surgical outcomes and complications after thyroidectomy. They determined how far patients lived from an endocrinologist, how far they traveled to the treating facility, and to their surgeon. Then, they compared these factors between patients who were treated by high-volume thyroid surgeons and those treated by low-volume thyroid surgeons.

The study included 3,839 patients with thyroid cancer who had thyroidectomy, traveled less than 550 miles for care, and had complete data available. Overall, 46% (1,771) were treated by high-volume thyroid surgeons and 54% by low-volume thyroid surgeons. Patients treated by high-volume thyroid surgeons were slightly younger (53.2 vs 55.6 years), more often female (76.4% vs 70.5%), and more likely to live in areas with higher average income and education levels. They traveled slightly farther for surgery (33.7 vs 28.9 miles) but lived closer to an endocrinologist (10.3 vs 18.3 miles). Patients with Medicare Advantage plans were more likely to be treated by high-volume thyroid surgeons, while those with traditional Medicare, those living in areas with lower education levels, and those living farther from an endocrinologist were less likely to receive care from a high-volume thyroid surgeon. High-volume thyroid surgeons were more likely to do complete thyroid removal and lymph node removal when needed, and complication rates were lower, voice problems (6.3% vs 10.7%), the need for breathing tube (0.2% vs 1.2%), and bleeding after surgery (0.6% vs 2.1%)

THYROID SURGERY, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study found that less than half of the patients with thyroid cancer who had thyroid surgery were treated by a high-volume thyroid surgeon. Insurance type, where a person lives, and how close they live to an endocrinologist affected whether they saw a more experienced surgeon. Patients traveled slightly farther to see an high-volume thyroid surgeon. These results are based only on data from Michigan, so more studies in other states are needed. More research is also needed to better understand how patients are referred and decide which surgeon to see. Patients should also keep in mind that, along with their questions about surgery, it is appropriate to ask their referring doctor and surgeon about experience and how their care will be organized.

— Ebru Sulanc, MD

ATA RESOURCES

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS & DEFINITIONS

Thyroidectomy: surgery to remove the thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

High-volume thyroid surgeons: surgeons that perform >25-100+ operations annually High-volume thyroid surgeons have better outcomes, lower complication rates and shorter hospital stays as compared to low-volume surgeons.

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THYROID CANCER

2025 ATA Differentiated Thyroid Cancer Guidelines: Completion Thyroidectomy

BACKGROUND

A significant change from prior guidelines was recommendations of lobectomy for patients with cancer limited to one lobe ≤2 cm without extension outside of the thyroid or spread to lymph nodes in the neck. The guidelines also state that a lobectomy could be considered in patients with cancer limited to one lobe >2 and ≤4 cm without extension outside of the thyroid or spread to lymph nodes in the neck. This means more patients will continue to have 1 lobe intact after their initial surgery.

If the diagnosis is confirmed as cancer after a lobectomy, there is always the question of whether the patient needs a 2nd surgery to remove the remaining lobe. This is called completion thyroidectomy. In general, completion thyroidectomy is considered in up to 20% of patients with a lobectomy and cancer >2 and ≤4 cm. This paper summarizes the changes recommendations for a completion thyrodectomy in the 2025 ATA thyroid cancer guidelines.

THE FULL ARTICLE TITLE

Ringel MD et al. 2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer. Thyroid 2025;35(8):841-985.

SUMMARY OF THE STUDY

The 2025 ATA thyroid cancer guidelines refer to patients with differentiated thyroid cancer, almost all of which are papillary thyroid carcinoma. The 2015 guidelines stated that "completion thyroidectomy *should be offered* to patients for whom a bilateral thyroidectomy would have been recommended had the diagnosis of cancer been available before the initial surgery." The 2025 guidelines now suggest that completion thyroidectomy is no longer routine. These guidelines state this: "Completion thyroidectomy *may be considered* to address persistent cancer, to consider radioactive iodine therapy, or to assist follow-up based upon monitoring thyroglobulin levels. The shift that completion thyroidectomy "should be offered" to "may be considered," reflects less convincing evidence and increasing acceptance of lobectomy as definitive treatment in most low-risk cancers.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The shift to recommend that completion thyroidectomy is no longer routine likely reflects broader cultural movements among both clinicians and patients toward less aggressive treatment of low-risk thyroid cancer. The decision for recommending lobectomy should include a discussion of "Who needs completion?" as well as "Who underwent lobectomy, and why?" As always, the choice of surgery should be a result of a shared decision-making discussion between patients and their doctors.

— Alan P. Farwell, MD

ATA RESOURCES

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer: the most common type of thyroid cancer, includes papillary, follicular and oncocytic thyroid cancer

Papillary thyroid cancer: the most common type of differentiated thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Follicular thyroid cancer: the second most common type of differentiated thyroid cancer.

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

Lobectomy: surgery to remove one lobe of the thyroid.

Completion thyroidectomy: surgery to remove the remaining thyroid lobe in thyroid cancer patients who initially had a lobectomy.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

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MARCH
Medullary Thyroid Cancer
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Clinical Thyroidology® for the Public

THYROID CANCER

2025 ATA Differentiated Thyroid Cancer Guidelines: TSH suppression

BACKGROUND

Thyroid hormone suppressive therapy means adjusting the levothyroxine dose after thyroidectomy to very low/undetectable levels. This is designed to prevent the growth of any remaining thyroid cancer cells after surgery, with or without radioactive iodine therapy. Early studies in advanced thyroid cancer showed clear benefits from this strategy if persistent cancer was present. However, there is no reason to pursue it in patients who do not have any evidence of persistent cancer. Therefore, the use of suppressive therapy should be guided by the risk of recurrence.

In the 2015 thyroid cancer guidelines, assigning risk of thyroid cancer recurrence (risk stratification) based on the assessment after the initial surgery drove initial TSH suppressive therapy decisions, as very specific TSH targets were recommended. This included complete suppression (TSH, <0.2 mU/L) in patients with an initial high-risk of recurrence, moderate suppression (TSH, 0.1–0.5 mU/L) in patients with an initial intermediate risk of recurrence, and a TSH in the lower half of the reference range for patients with a low initial risk of recurrence. How to evaluate the ongoing benefit versus risk of TSH suppressive therapy was not directly addressed previously, and at least five years of suppression was recommended.

However, treatment changes the risk of recurrence, with an excellent response to therapy having a different prognosis even in a patient with a high-risk cancer. In the 2025 guidelines, a focus on re-evaluating risk stratification allows for initial treatment response to play a role in the selection of TSH suppression therapy.

THE FULL ARTICLE TITLE

Ringel MD et al. 2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer. Thyroid 2025;35(8):841-985.

SUMMARY OF THE STUDY

The 2025 ATA thyroid cancer guidelines refer to patients with differentiated thyroid cancer, almost all of which are papillary thyroid carcinoma. A major difference from the 2015 guidelines for the use of TSH suppression after surgery is that the 2025 recommendations base TSH goals on the continual re-evaluation of the patient's response to therapy rather than on the risk evaluation based after initial therapy.

TSH suppressive therapy is now suggested only in those with evidence of possible persistent cancer, based on continued detectable thyroglobulin levels or possible abnormal thyroid tissue in the thyroid bed or abnormal lymph nodes. Ongoing reassessment of the patient's response to therapy is recommended so that if no longer indicated (thyroglobulin levels become barely detectable/undetectable and concerning lymph nodes are no longer present), TSH suppression may be stopped. It is no longer recommended to continue TSH suppression for 5 years based on the initial surgical findings, because of the lower risk of recurrence if the postoperative assessment is consistent with an excellent response to therapy, regardless of the characteristics of the initial pathology.

The second major difference is that complete suppression (undetectable TSH) is no longer recommended. In fact, the current guidelines do not provide target TSH ranges for any patients, but simply state that TSH should be maintained "below" or "within" the reference range.

The support for these new guidelines are studies that show no benefit for levothyroxine treatment to a TSH less than 2 mU/L and 1 study that shows an increased risk of death from heart problems in thyroid cancer patients that is attributable to complete TSH suppression.

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The new guidelines provide more flexibility than the prior guidelines by shifting the "one size fits all" approach based on the initial treatment results. This allows clinicians to continually reassess the risk of thyroid cancer recurrence at every visit and to adjust levothyroxine therapy and TSH levels based on the response to therapy. As always, these decisions should result from a shared-decision making discussion with the patient and their doctor.

— Alan P. Farwell, MD

ATA RESOURCES

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer: the most common type of thyroid cancer, includes papillary, follicular and oncocytic thyroid cancer

Papillary thyroid cancer: the most common type of differentiated thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

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Lobectomy: surgery to remove one lobe of the thyroid.

Completion thyroidectomy: surgery to remove the remaining thyroid lobe in thyroid cancer patients who initially had a lobectomy.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

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THYROID CANCER

2025 ATA Differentiated Thyroid Cancer Guidelines: Systemic Therapy

BACKGROUND

The majority of patients with thyroid cancer do very well with an excellent prognosis. This is because we have very effective treatments, including surgery to remove the cancer and radioactive iodine therapy to destroy any remaining thyroid cancer after surgery. However, 5 to 15% of patients have more advanced cancer which can develop resistance to radioactive iodine therapy, which is linked to markedly worse clinical outcomes. Systemic therapy (ie chemotherapy) is reserved for patients with progressive, symptomatic cancer that fails to respond to radioactive iodine therapy and cannot be surgically removed. Systemic therapy is typically started when cancer growth exceeds 20% over 12 to 14 months.

The 2025 ATA thyroid cancer guidelines provide the first comprehensive framework directly linking molecular gene mutations in the cancer to available options for treatment.

THE FULL ARTICLE TITLE

Ringel MD et al. 2025 American Thyroid Association management guidelines for adult patients with differentiated thyroid cancer. Thyroid 2025;35(8):841-985.

SUMMARY OF THE STUDY

The 2025 ATA thyroid cancer guidelines refer to patients with differentiated thyroid cancer, almost all of which are papillary thyroid carcinoma. A major change is that comprehensive molecular testing of the cancer is now mandated prior to selecting first-line systemic therapy in patients with persistent thyroid cancer that no longer responds to radioactive iodine therapy.

If the patient's cancer does not have any cancer mutation that can be targeted with specific systemic therapy, the majority of patients will receive multi-kinase inhibitor drugs as first-line treatment. Lenvatinib is generally preferred over sorafenib. However, for the subset of patients whose cancers that have mutations that can be targeted by specific chemotherapy drugs, selective inhibitors are now preferred for first-line therapy—a significant shift in recommendations. In addition, combination therapy can be selected based on specific cancer gene mutations.

The guidelines also emphasize the importance of dose decreases and early management of common toxic side effects, including high blood pressure, kidney disease and fatigue, are critical to continuing treatment and maximizing clinical benefits.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Molecular testing of thyroid cancer now defines first-line systemic therapy in progressive thyroid cancer that no longer responds to radioactive iodine therapy and cannot be removed by surgery. The 2025 ATA thyroid cancer management guidelines redefine the management of advanced DTC, shifting the question from "Which drug?" to "What gene mutation is driving the cancer?" As always, these decisions should result from a shared-decision making discussion with the patient and their doctor.

— Alan P. Farwell, MD

ATA RESOURCES

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of differentiated thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Follicular thyroid cancer: the second most common type of differentiated thyroid cancer.

Thyroidectomy: surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

Mutation: A permanent change in one of the genes.

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC, TERT and RAS.

microRNA: a short RNA molecule that has specific actions within a cell to affect the expression of certain genes.

Tyrosine kinases: proteins that are overactive in many of the pathways that cause cells to be cancerous.

Tyrosine kinase inhibitors: Chemotherapy drugs that are used to treat thyroid cancer that no longer responds to radioactive iodine and cannot be removed by surgery. These drugs can target a single tyrosine kinase or multiple tyrosine kinases. Examples of these drugs are Levatinib and Sorafinib.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 19 | Issue 3 | March 2026

Clinical Thyroidology® for the Public

ATA® Alliance for Thyroid Patient Education

GOAL The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases. We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.

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Light of Life Foundation
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info@checkyourneck.com

MCT8 – AHDS Foundation
mct8.info
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Thyca: Thyroid Cancer Survivors' Association, Inc.
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