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AMERICAN THYROID ASSOCIATION
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A major aspect of the treatment of thyroid cancer is the extent of initial surgery once a diagnosis of thyroid cancer is made. Since 2015, several studies evaluating lobectomy versus total thyroidectomy have been performed and form the basis for the new recommendations in the 2025 guidelines. This paper summarizes the changes in the initial extent of surgery in the 2025 ATA differentiated thyroid cancer guidelines.

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: Risk stratification

Cancer risk stratification plays a pivotal role in guiding treatment decisions, which must be tailored to individual patient characteristics. The 2025 guidelines expand the risk stratification groups to help identify which patients will benefit from additional treatment, such as radioactive iodine therapy. This paper summarizes the changes in risk stratification in the 2025 ATA differentiated thyroid cancer guidelines.

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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Is my thyroid cancer marker increasing too quickly after my surgery?

Thyroglobulin is a protein only produced by thyroid cells, both normal and cancerous. After a total thyroidectomy, and especially after radioactive iodine therapy, the thyroglobulin level can be used as a cancer marker. This study combines the thyroglobulin levels obtained after total thyroidectomy and the thyroglobulin doubling rate to see if they accurately predict a thyroid cancer recurrence.

Ito Y, et al. Dynamic risk assessment using unstimulated serum thyroglobulin level and thyroglobulin doubling rate after total thyroidectomy for papillary thyroid carcinoma. *Thyroid*. Epub 2025 Aug 11; doi: 10.1177/10507256251367242. PMID: 40794485.

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Iatrogenic Hyperthyroidism in Older Adults

In hypothyroidism, the dose of levothyroxine is often calculated based on body weight. If the treatment of hypothyroidism over-shoots and causes the TSH level to be low with high normal or increased T4, then the patient can be made hyperthyroid ("iatrogenic hyperthyroidism"). Since it has been reported that over-replacement with thyroid hormone occurs more frequently in women, this study sought to identify the potential factors that contribute to the increased risk of iatrogenic hyperthyroidism in women.

Adams, R and Mammen JS. Sex Differences in Risk for Iatrogenic Thyrotoxicosis Among Older Adults: An Analysis from Real-World Clinical Data. *Thyroid*. 2025;35(5):485-493; doi: 10.1089/thy.2024.0604. PMID: 40117123.

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Response to treatment with steroids in patients with thyroid eye disease

Thyroid eye disease (TED) is a condition that occurs in up to 40% of patients with Graves' disease. Treatment of TED often includes steroid therapy to try to suppress the immune system, which is believed to be the cause of TED. This study aimed to investigate the factors associated with outcomes after intravenous glucocorticoid treatment in a group of patients with moderate-to-severe TED.

Baczewska N, et al. factors associated with response to intravenous glucocorticoids in active moderate-to-severe thyroid eye disease. *Thyroid*. 2025;35(4):424-432; doi: 10.1089/thy.2024.0629. PMID 40053436.

GRAVES' DISEASE.....15

Functional TSI tests: a new step in personal care for Graves' Disease?

Graves' disease is caused by the body producing an antibody (TSI) that attacks and turns on the thyroid and makes it overactive. This study compared a functional TSI assay with a traditional thyroid receptor antibody assay (TRAb) to determine if the new assay could better determine remission or relapse of Graves' disease.

Peng R et al. Significance of thyroid-stimulating immunoglobulin and thyrotropin receptor antibody in Graves disease. *J Clin Endocrinol Metab* 2025;110(9):e3002-e3010. doi: 10.1210/clinem/dgae892. PMID: 39715350.

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PATIENT EDUCATION17

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www.thyroid.org

Editor

Alan P. Farwell, MD
Boston Medical Center
Boston University Chobanian & Avedisian
School of Medicine
720 Harrison Ave., Boston, MA 02115
American Thyroid Association®
Email: thyroid@thyroid.org
www.thyroid.org/patients/ct/index.html

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Pam Mechler, CAE
American Thyroid Association®
2000 Duke Street, Suite 300
Alexandria, VA 22314
Telephone: 703-998-8890
Fax: 703-998-8893
Email: thyroid@thyroid.org

Designed by

Karen Durland, kdurland@gmail.com

Clinical Thyroidology® for the Public

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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](https://twitter.com/thyroidfriends) and on [Facebook](https://www.facebook.com/thyroidfriends). 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](https://www.allianceforthyroidpatienteducation.org). The [Alliance](https://www.allianceforthyroidpatienteducation.org) 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](https://www.thyroid.org/donate) 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.

December is [Thyroid and Development Awareness Month](https://www.thyroid.org/development-awareness-month).

In this issue, the studies ask the following questions:

- What surgery should I have for my thyroid cancer?
- Should I have radioactive iodine therapy to treat my thyroid cancer?
- Is my thyroid cancer marker increasing too quickly after my surgery?
- Can levothyroxine make you hyperthyroid?
- Can steroids help moderate-to-severe thyroid eye disease?
- Are functional TSI tests a new step in personal care for Graves' Disease?

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



ATA THYROID CANCER GUIDELINES

2025 American Thyroid Association Differentiated Thyroid Cancer Guidelines

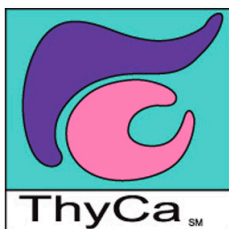
Thyroid cancer is common. Fortunately, most forms of thyroid cancer are slow-growing, and most patients do very well, with an excellent prognosis. Even when thyroid cancer can't be cured, patients may live long lives and not die of the cancer. Very rarely, thyroid cancer can be advanced and cause patients to die. There are 2 general types of thyroid cancer: differentiated thyroid cancer — the most common type and includes papillary, follicular and oncocytic thyroid cancer — and medullary thyroid cancer — a relative rare form that may run in families. These guidelines refer to the management of differentiated thyroid cancer.

Treatment of thyroid cancer usually begins with removal of a thyroid lobe (lobectomy) or the whole thyroid (total thyroidectomy). However, with some small thyroid cancers, following by ultrasound and deferring surgery (active surveillance) is an option. In some more advanced

thyroid cancer, radioactive iodine therapy may be used to destroy any remaining thyroid cancer cells, even if they have spread outside of the thyroid and outside of the neck. Finally, some patients with advanced thyroid cancer may be treated with radiation therapy or chemotherapy.

Periodically, experts in thyroid cancer diagnosis and treatment come together and develop guidelines to treat all aspects of thyroid cancer. In 2009 and 2015, the American Thyroid Association (ATA) published guidelines for the management of thyroid cancer. In 2025, these guidelines were updated.

The following 2 papers discuss 2 important updates that the 2025 ATA thyroid cancer guidelines for the management of thyroid cancer: Extent of initial surgery and Risk stratification.



ThyCa: Thyroid Cancer
Survivors' Association, Inc.™
www.thyca.org





THYROID CANCER

2025 ATA Differentiated Thyroid Cancer Guidelines: Extent of surgery

BACKGROUND

A major aspect of the treatment of thyroid cancer is the extent of initial surgery once a diagnosis of thyroid cancer is made. The 2009 ATA thyroid cancer guidelines recommended total thyroidectomy for nearly all thyroid cancers >1 cm in size and lobectomy for cancers <1 cm in size. The recommendations changed in 2015 to suggest lobectomy as an option for cancer that is located only in 1 lobe and is <4 cm in size with low-risk features and no spread outside of the thyroid. Since 2015, several studies evaluating lobectomy versus total thyroidectomy have been performed and form the basis for the new recommendations in the 2025 ATA guidelines.

This paper summarizes the changes in the initial extent of surgery in the 2025 ATA differentiated 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 guidelines refer to patients with differentiated thyroid cancer diagnosed prior to surgery, almost all of which are papillary thyroid carcinoma. The recommended surgical approach planned should be determined after a discussion with shared decision making with the patient. Additional factors, including patient sex, family history of thyroid cancer, and history of radiation exposure may also impact decision-making.

1. Patients with cancer limited to one lobe ≤ 2 cm without extension outside of the thyroid or spread to lymph nodes in the neck should undergo a lobectomy.
2. 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 may undergo lobectomy or total thyroidectomy depending on the cancer features, presence of nodules in the other lobe, and patient preference. If lobectomy is performed, the patient should be advised on the 20% risk of conversion to a total thyroidectomy during the operation or potential for completion thyroidectomy after the pathology returns.
3. Patients with cancer >4 cm in size extension outside of the thyroid or spread to lymph nodes in the neck or elsewhere in the body should receive a total thyroidectomy and resection of all concerning lymph nodes in the neck.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While prior guidelines recommended a lobectomy as an option for low-risk thyroid cancer limited to 1 lobe, the 2025 ATA cancer guidelines recommend that lobectomy is now the recommended surgical option based on a large body of evidence supporting lobectomy for low-risk thyroid cancers. These recommendations should help patients and surgeons feel more comfortable offering a lobectomy in these situations. The final plan for a lobectomy or total thyroidectomy still should rest with a shared decision making discussion between the surgeon and the patient.

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).

Papillary microcarcinoma: a papillary thyroid cancer smaller than 1 cm in diameter.

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

Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): a new term has been used to describe a type of papillary thyroid cancer which is non-invasive. These cancers behave less aggressively than typical papillary thyroid cancer and have been shown to have low risk for recurrence and low risk for spread outside of the thyroid.

Follicular variant of papillary thyroid cancer: one of the subtypes of papillary thyroid carcinoma, which has been classified to three different forms: non-invasive follicular thyroid neoplasm with papillary-like nuclear features, invasive encapsulated and infiltrative FVPTC.

Oncocytic thyroid cancer: least common type of differentiated thyroid cancer, which has a higher rate of recurrence outside of the neck. Further, oncocytic thyroid cancer is more resistant to radioactive iodine therapy than other forms 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*).

Active Surveillance: following a small, low-risk thyroid cancer with ultrasound and deferring surgery until the cancer grows significantly



THYROID CANCER

2025 ATA Differentiated Thyroid Cancer Guidelines: Risk stratification

BACKGROUND

Cancer risk stratification plays a pivotal role in guiding treatment decisions, which must be tailored to individual patient characteristics. This depends on the stage of the cancer, which depends on the type of cancer and the spread of the cancer to elsewhere in the body. The main pathology staging system of cancers (AJCC/UICC) is designed to predict the risk of death from cancer. However, the excellent prognosis of differentiated thyroid cancer led to the development of additional risk stratification systems focused on cancer recurrence rather than death. The 2009 ATA cancer guidelines introduced 3 groups (low, intermediate, and high risk) to estimate the likelihood of recurrence of the cancer after the initial treatment. In 2015, the ATA guidelines, after incorporating new evidence, substantially refined and expanded this model. The 2025 guidelines expand the risk stratification groups to help identify which patients will benefit from additional treatment, such as radioactive iodine therapy.

This paper summarizes the changes in risk stratification in the 2025 ATA differentiated 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 risk classification introduces several important updates compared with the 2015 system. A major role in this classification is to help identify which patients will benefit from additional treatment, such as radioactive iodine therapy.

1. The traditional three-tier model has been replaced by a four-tier classification based on the risk of thyroid cancer recurrence. This mainly divided the intermediate group into intermediate vs high risk. The current groups are:
 - a. Low risk: risk of recurrence: <10%
 - b. Low–intermediate risk: 10–15%
 - c. Intermediate–high risk: 16–30%
 - d. High risk: >30%
2. The model now clearly distinguishes recurrence behavior of thyroid cancer based on the pathology results.
 - a. Papillary thyroid cancer and its subtypes most commonly present with spread to the lymph nodes in the neck, but recurrence is rare when the cancer is limited to the thyroid and completely removed.
 - b. Follicular thyroid cancer and invasive encapsulated follicular variant of papillary thyroid cancer typically spread through the blood, with the extent of vascular invasion serving as one of the main risk determinants.
 - c. Oncocytic thyroid cancer has a higher rate of recurrence outside of the neck and extensive vascular invasion markedly increases recurrence risk. Further, oncocytic thyroid cancer is more resistant to radioactive iodine therapy than other forms of differentiated thyroid cancer.
3. New features, such as margin involvement, multiple areas of cancer within the thyroid, cancer size, and spread outside of the thyroid have been incorporated into the 2025 classification.
4. The 2025 model emphasizes that the combination of features can have an additive effect on the overall recurrence risk. For instance, the coexistence of two low–intermediate-risk factors reclassify the cancer as being intermediate–high risk of recurrence. This underscores that the increase in the number of adverse features significantly magnifies overall risk.
5. Follicular and oncocytic thyroid cancer are now evaluated separately and extensively characterized in the 2025 guidelines



THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The 2025 ATA thyroid cancer guidelines have clarified cancer recurrence risk assessment by the division of intermediate risk of recurrence cancer into either low–intermediate or intermediate–high risk and the subclassification of thyroid cancer subtypes (papillary, follicular and oncocytic). In doing so, the guidelines provide the most

comprehensive set of recommendations to date to help clinicians associate a cancer's pathologic features with a percentage range for risk of cancer recurrence after initial treatment. This risk assessment, in turn, helps patient–doctor discussions and decision-making by identifying which patients would benefit from additional therapy, such as radioactive iodine therapy.

— 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

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THYROID CANCER, continued

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Active Surveillance: following a small, low-risk thyroid cancer with ultrasound and deferring surgery until the cancer grows significantly

DECEMBER Thyroid & Development Awareness Month



AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All



THYROID CANCER

Is my thyroid cancer marker increasing too quickly after my surgery?

BACKGROUND

Papillary thyroid cancer is the most common type of thyroid cancer. Fortunately, papillary thyroid cancer is generally a slow-growing cancer. The initial treatment of thyroid cancer is surgery to remove the thyroid. When the entire thyroid gland is removed in the treatment of thyroid cancer it is called a total thyroidectomy. If the cancer removed is moderate to high risk, a total thyroidectomy may be followed by radioactive iodine therapy to destroy both the remaining normal thyroid cells as well as the cancer cells.

Thyroglobulin is a protein only produced by thyroid cells, both normal and cancerous. After a total thyroidectomy, and especially after radioactive iodine therapy, the thyroglobulin level can be used as a cancer marker. If the thyroglobulin level is barely detectable or undetectable, it is likely that there is no significant thyroid cancer present in the body. If the thyroglobulin level is detectable but stable, that likely means that there may be thyroid tissue present that may include cancer but the cancer is not growing or spreading. If the thyroglobulin level increases over time, then it is likely that thyroid cancer is present and is growing.

The time needed for a patient's thyroglobulin level to double can also be studied. The measurement of the thyroglobulin doubling time and the thyroglobulin doubling rate are more recently being studied to see if they might predict a thyroid cancer recurrence. This study combines the thyroglobulin levels obtained after total thyroidectomy and the thyroglobulin doubling rate to see if they accurately predict a thyroid cancer recurrence.

THE FULL ARTICLE TITLE

Ito Y, et al. Dynamic risk assessment using unstimulated serum thyroglobulin level and thyroglobulin doubling rate after total thyroidectomy for papillary thyroid carcinoma. *Thyroid*. Epub 2025 Aug 11; doi: 10.1177/10507256251367242. PMID: 40794485.

SUMMARY OF THE STUDY

This study included 1,818 patients from the Kuma hospital in Japan from 2012 to 2022 who had total thyroidectomies were studied to see if papillary thyroid cancer was found in the surgical specimen. The doubling time of the thyroglobulin was calculated from three measurements obtained after the surgery. Patients were studied to see if they had a cancer recurrence in the neck or other areas of the body.

From the 131 patients (7%) who had thyroglobulin levels above 3 mg/dL, 88 patients had recurrences in the neck and 32 patients had recurrences in other parts of the body. As the thyroglobulin level went up, the chance of having a recurrence in the neck or other part of the body increased. Out of 1,245 patients, 119 (9.6%) had thyroglobulin doubling rates of more than 0.33/ year and had an increased risk of a neck cancer recurrence or a cancer recurrence in another area of the body.

A total of 1,212 patients who did not receive radioactive iodine therapy and 290 patients who received low dose radioactive iodine therapy were studied. The patients with the most recurrence of thyroid cancer in the neck (97.7% in 10 years) and recurrences other places in the body (99.5% in 10 years) had a thyroglobulin level of >3 ng/mL and a thyroglobulin doubling rate of >0.33/year. These outcomes were worse than those patients who had EITHER a thyroglobulin level <3 ng/mL OR a thyroglobulin doubling rate of <0.33/year. There was not an important difference in outcomes among the patients who had either <3 ng/mL of thyroglobulin level OR a thyroglobulin doubling rate of <0.33/year

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These data suggest that a thyroglobulin level of >3 mg/dL corresponded to cancers sized >4 cm and detection age of >55. If the thyroglobulin is >3 mg/dL and the thyroglobulin doubling rate is >0.33 mg/dL per year, the risk of having a cancer recurrence around the neck or other area



THYROID CANCER, continued

of the body is higher. Only 1% of patients fall into this category meeting BOTH thresholds and should be more closely monitored. Most patients (80%) did not meet the threshold of EITHER these numbers and have a low risk of recurrence.

During a time when patients are treated with less radioactive iodine, patients might have higher baseline thyroglobulin levels after surgery. Incorporating a

doubling rate of thyroglobulin might help separate normal thyroid tissue from more aggressive thyroid cancers producing the thyroglobulin. In addition, now physicians are using lower doses of levothyroxine to protect patients' heart and bone health, which can also result in higher thyroglobulin levels. Combining the thyroglobulin level and the doubling rate of the thyroglobulin might more accurately predict thyroid cancer recurrences.

— Pinar Smith, MD

ATA RESOURCES

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of 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).

Cancer metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

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.

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies.

Thyroglobulin antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

Radioactive iodine therapy: 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).



HYPOTHYROIDISM

Iatrogenic Hyperthyroidism in Older Adults

BACKGROUND

Hypothyroidism is a common condition in which the thyroid gland does not make enough thyroid hormone to meet the body's needs. This is diagnosed by high levels of thyroid-stimulating hormone (TSH) and low levels of thyroxine (T4). Hypothyroidism can be due to numerous causes including destruction by antibodies (autoimmune thyroid disease), surgical removal, destruction after radioactive iodine therapy, inflammation (thyroiditis), pituitary disease, and medications. It is more common in women than men. Hypothyroidism is usually treated by starting thyroid hormone replacement therapy in the form of levothyroxine. Starting doses of levothyroxine are often calculated based on body weight. In patients with the most common types of hypothyroidism, therapy is guided by TSH levels with a typical goal to return the TSH level to the normal range.

If the treatment of hypothyroidism over-shoots and causes the TSH level to be low with high normal or increased T4, then the patient can be made hyperthyroid. This is called "iatrogenic hyperthyroidism," meaning that it is caused but taking too much levothyroxine. Hyperthyroidism is associated with symptoms of thyroid overactivity (weight loss, heat intolerance, elevated heart rate, anxiety, tremor, insomnia) as well as bone loss and abnormal heart rhythms, especially atrial fibrillation. For these reasons, over-replacement of hypothyroidism with thyroid hormone should be avoided in most cases.

It has been reported that over-replacement with thyroid hormone occurs more frequently in women. This study sought to identify the potential factors that contribute to the increased risk of iatrogenic hyperthyroidism in women.

THE FULL ARTICLE TITLE:

Adams, R and Mammen JS. Sex Differences in Risk for Iatrogenic Thyrotoxicosis Among Older Adults: An Analysis from Real-World Clinical Data. *Thyroid*. 2025;35(5):485-493; doi: 10.1089/thy.2024.0604. PMID: 40117123.

SUMMARY OF THE STUDY:

The study looks at data from a review of the electronic medical record. The study included 20,734 patients with hypothyroidism over the age of 50 that received healthcare in the John Hopkins Health System between January 2014 and February 2024. Patients had to have at least two visits and data available for a variety of different measures including gender, height, weight, levothyroxine dose, medications, and other medical conditions. Severity of hypothyroidism over-treatment was classified as moderate (TSH low - ≥ 0.1 and $<$ lower normal limit or < 0.45 mIU/L) or severe (TSH suppressed - < 0.1 mU/L) based on the degree of TSH suppression. Thyroid cancer patients were excluded from the analysis as sometimes TSH suppression is recommended to reduce risk of cancer recurrence.

Overall, 34% of patients had a low TSH with 14% having a suppressed TSH (severe). As expected, higher rates of TSH suppression were seen with higher doses of levothyroxine treatment. Women (36.7%) were more likely than men (23.9%) to have a suppressed TSH and these differences remained when controlling for several variables such as levothyroxine dose per actual body mass, demographics, use of the health care system and comorbidities. However, the gender differences in risk of iatrogenic hyperthyroidism went away when the levothyroxine dose was adjusted by lean body mass instead of body weight. When men and women were receiving comparable levothyroxine doses per lean body mass, there were no differences in risk of iatrogenic hyperthyroidism. This suggests that using body weight to calculate the required thyroid hormone dose in women may overestimate thyroid hormone needs. Using lean body mass to calculate thyroid hormone dose in women may lead to prescribing lower doses and result in fewer cases of iatrogenic hyperthyroidism.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

Over-replacement of hypothyroidism with levothyroxine results in iatrogenic hyperthyroidism and should usually



HYPOTHYROIDISM, continued

be avoided due to its association with multiple negative health consequences. Iatrogenic hyperthyroidism is more common in women compared to men. Using lean body mass, instead of actual body mass, to estimate thyroid

hormone dose requirements may reduce the risk of iatrogenic hyperthyroidism in women.

— Whitney W. Woodmansee MD

ATA RESOURCES

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

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

Older Patients and Thyroid Disease: <https://www.thyroid.org/thyroid-disease-older-patient/>

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

ABBREVIATIONS & DEFINITIONS: FROM ACTIVE LIST

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™, Tyrosint™ and generic preparations.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine to return their thyroid hormone levels to normal. *Replacement therapy* means the goal is a TSH in the normal range and is the usual therapy. *Suppressive therapy* means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.

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.

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).



THYROID EYE DISEASE

Response to treatment with steroids in patients with thyroid eye disease

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism (overactive thyroid). Thyroid eye disease (TED) is a condition that occurs in up to 40% of patients with Graves' disease. TED can include inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision, and can have a significant impact on the quality of life. The severity of the eye disease is often measured in terms of a score called the clinical activity score (CAS). This takes into account the patient's symptoms and an examination by the physician.

Treatment of TED often includes steroid therapy given by vein into the body (intravenous glucocorticoids) to try to suppress the immune system, which is believed to be the cause of TED. The response to this form of therapy is variable with clinical trials reporting up to 80% response rates, but 20 to 41% of patients do not either respond or experience relapses of TED despite treatment. Newer therapies are now available, therefore identifying factors which can predict a poor response to steroid therapy is increasingly important.

This study aimed to investigate the factors associated with outcomes after intravenous glucocorticoids treatment in a group of patients with moderate-to-severe TED.

THE FULL ARTICLE TITLE

Baczewska N, et al. factors associated with response to intravenous glucocorticoids in active moderate-to-severe

thyroid eye disease. *Thyroid*. 2025;35(4):424-432; doi: 10.1089/thy.2024.0629. PMID 40053436.

SUMMARY OF THE STUDY

This study included patients who have active moderate to severe thyroid eye disease and had a follow-up of at least 6 months. The medical records of 64 patients were analyzed and the data collected included the CAS, smoking status, thyroid function, antibody levels, and other medical problems. Treatment response was evaluated 6 months after intravenous glucocorticoid therapy.

The results showed that TED was diagnosed an average of 1 month after diagnosis of Graves' disease and intravenous glucocorticoids were started after an average of 4 months after the diagnosis of TED. Study results showed that ~3/4 of patients responded to intravenous glucocorticoid therapy. The patients that responded were significantly younger (50.1 vs 56.6 years) and had a lower CAS. Active smoking and TSH receptor antibody levels were not independently associated with treatment response.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that older age and elevated levels of the CAS before the start of treatment were associated with worse response to intravenous glucocorticoids. This knowledge may help identify patients who may, in this case, use alternative therapies such as immunotherapies for management of their thyroid eye disease.

—Vibhavasu Sharma, MD, FACE

ATA RESOURCES

Graves' Disease: <https://www.thyroid.org/graves-disease/>

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

Thyroid Eye Disease: <https://www.thyroid.org/thyroid-eye-disease/>



THYROID EYE DISEASE, continued

ABBREVIATIONS & DEFINITIONS

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Thyroid eye disease (TED): also known as Graves ophthalmopathy. TED is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

Steroids/Glucocorticoids: general anti-inflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation

CAS: Clinical Activity Score, a scoring system used to evaluate patients with Graves' ophthalmopathy, and is based on classical signs of inflammation (pain, redness, swelling and function) and that helps predict which patients will benefit from immunosuppressive treatment.



GRAVES' DISEASE

Functional TSI tests: a new step in personal care for Graves' Disease?

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States. It is caused by the body producing an antibody that attacks and turns on the thyroid and makes it overactive. When the antibody is active, Graves' disease is active and requires treatment with antithyroid medications. When the antibody level drops or becomes inactive, Graves' disease can go into remission. While in remission, if the antibody returns or becomes active, Graves' disease relapses. This antibody is called thyroid stimulating immunoglobulin (TSI). TSI can be active (stimulating the thyroid), inactive (no effect on the thyroid) or blocking (actually block thyroid function). A new functional TSI test can determine if the TSI is actually stimulating the thyroid to make thyroid cells work harder.

This study compared a functional TSI assay with a traditional thyroid receptor antibody assay (TRAb) to determine if the new assay could better determine remission or relapse of Graves' disease.

THE FULL ARTICLE TITLE

Peng R et al. Significance of thyroid-stimulating immunoglobulin and thyrotropin receptor antibody in Graves disease. *J Clin Endocrinol Metab* 2025;110(9):e3002-e3010. doi: 10.1210/clinem/dgae892. PMID: 39715350.

SUMMARY OF THE STUDY

This study in China looked at 957 people with newly diagnosed Graves' disease. They measured TRAb and

functional TSI levels when patients started antithyroid medication (ATD), during treatment and after the antithyroid medication was stopped. The main outcome was remission (sustained normal thyroid levels ≥ 12 months after ATD withdrawal) or relapse (recurrent hyperthyroidism after stopping ATDs).

Both baseline TRAb and functional TSI levels were positive in patients with newly diagnosed Graves' disease. Patients with relapsed or persistent hyperthyroidism showed less decline in antibody levels during treatment compared to patients in remission. In a subset of 206 patients with at least 12 months of follow-up after ATD withdrawal, the overall relapse rate was 41.26%. Relapses were more common in patients with positive functional TSI levels at the time of ATD withdrawal compared to those who were TSI-negative (54.84% vs. 35.42%). TRAb levels at the time of ATD withdrawal did not significantly differ between the relapse group and the remission group. Positive functional TSI at withdrawal, younger age, prior episode of hyperthyroidism due to Graves' disease, and mild thyroid eye disease were independently associated with relapse.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that a functional TSI test may help doctors personalize treatment for Graves' disease and better predict who might relapse. More studies are needed before this test becomes part of everyday thyroid care.

— Joanna Miragaya, MD

ATA RESOURCES

Graves' Disease: <https://www.thyroid.org/graves-disease/>

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>



GRAVES' DISEASE, continued

ABBREVIATIONS & DEFINITIONS

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

TRAb: antibodies often present in the serum of patients with Graves disease that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism.

Thyroid stimulating immunoglobulin (TSI): antibodies often present in the serum of patients with Graves' disease that are directed against the TSH receptor, that cause stimulation of this receptor resulting in increased levels of thyroid hormones in the blood and hyperthyroidism



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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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www.thyroid.org

ATA® Patient Resources:

www.thyroid.org/thyroid-information/

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(Toll-free): 1-800-THYROID

thyroid@thyroid.org

Bite Me Cancer

www.bitemecancer.org

info@bitemecancer.org

Graves' Disease and Thyroid Foundation

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

Light of Life Foundation

www.checkyourneck.com

info@checkyourneck.com

MCT8 – AHDS Foundation

mct8.info

Contact@mct8.info

Thyca: Thyroid Cancer Survivors' Association, Inc.

www.thyca.org

(Toll-free): 877-588-7904

thyca@thyca.org

Thyroid Federation International

www.thyroid-federation.org

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