Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

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 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, Thyroid Cancer Canada, Thyroid Cancer Alliance* 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.

The COVID-19 pandemic has caused an unprecedented upheaval in our daily lives and presented extremely difficult challenges to our healthcare system. We at the American Thyroid Association would like to make sure that you all have access to most accurate, reliable, fact-based and updated information. (https://www.thyroid.org/covid-19/)

June is Differentiated Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- How common is thyroid cancer in the United States and is the risk of dying from this disease changing?
- What is new in the treatment of thyroid cancer?
- Is radioactive iodine therapy indicated in patients with low-risk thyroid cancer?
- How common is hypothyroidism in children who have survived cancer?
- Is the treatment of hypothyroidism caused by ICI cancer drugs different from the treatment of other types of hypothyroidism?
- What do the experts say about RFA ablation of thyroid nodules?

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

THYROID CANCER

How common is thyroid cancer in the United States and is the risk of dying from this disease changing?

BACKGROUND

The number of people diagnosed with thyroid cancer every year in the United States started rising in 1974, with more cases found each year thereafter until 2014. However, the number of people in the United States dying each year from thyroid cancer did not change during this time period, suggesting that at least some of the new cases of thyroid cancer found each year were not actually dangerous. In addition, many experts believe that the reason for increasing number of thyroid cancers over this time period was mostly related to improvements in thyroid cancer detection rather than an actual increase in the number of new thyroid cancers every year. Starting in 2014, the number of U.S. thyroid cancer cases per year stabilized and then, for each of the next three years (through 2017), this number actually went down.

Understanding these trends is important because this helps doctors better understand how big a problem thyroid cancer is to the United States population, why thyroid cancer might develop, and which people might have the highest risk of developing this disease. Monitoring changes in how many people die of thyroid cancer each year also helps doctors understand how effective treatments are for this disease. The research described here aims to update our knowledge of the number of thyroid cancer cases diagnosed and the number of people who die of this disease in the United States each year.

FULL ARTICLE TITLE

Megwalu UC, Moon PK 2022 Thyroid cancer incidence and mortality trends in the United States: 2000–2018. Thyroid. Epub 2022 Mar 15. PMID: 35132899.

SUMMARY OF THE STUDY

The authors of this study used two large databases that collect and store medical information for people living in the United States to update our knowledge of thyroid cancer incidence and mortality. Together, these two databases include medical information for 28% of the United States population. A total of 197,070 thyroid cancer cases were identified for the study timeframe using these databases. The investigators specifically collected data starting with the year 2000 and then for every subsequent year through 2018. The study confirmed previous findings that the number of thyroid cancers diagnosed increased until 2014, after which the number decreased through 2018. Death from thyroid cancer, on the other hand, increased somewhat for the most common type of thyroid cancer (papillary thyroid cancer) and for the rarest form of thyroid cancer (anaplastic thyroid cancer), but not for the less common follicular and medullary thyroid cancer subtypes.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study authors' findings confirm that the number thyroid cancers in the United States went up until 2014, and then began decreasing. Similarly, the authors conclude that the reason the number of thyroid cancers started going down after 2014 was because doctors stopped trying to identify small thyroid cancers that are not dangerous, leaving these thyroid cancers undiagnosed. In contrast, the authors conclude that the increase in death from papillary thyroid cancer seen in their study is the result of a true increase in advanced (more dangerous and difficult to treat) disease. The reasons for this increase in advanced thyroid cancer is not clear but certainly is an area for additional future studies.

— Jason D. Prescott, MD PhD

THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/
Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/
Anaplastic Thyroid Cancer: https://www.thyroid.org/anaplastic-thyroid-cancer/
Medullary Thyroid Cancer: https://www.thyroid.org/medullary-thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

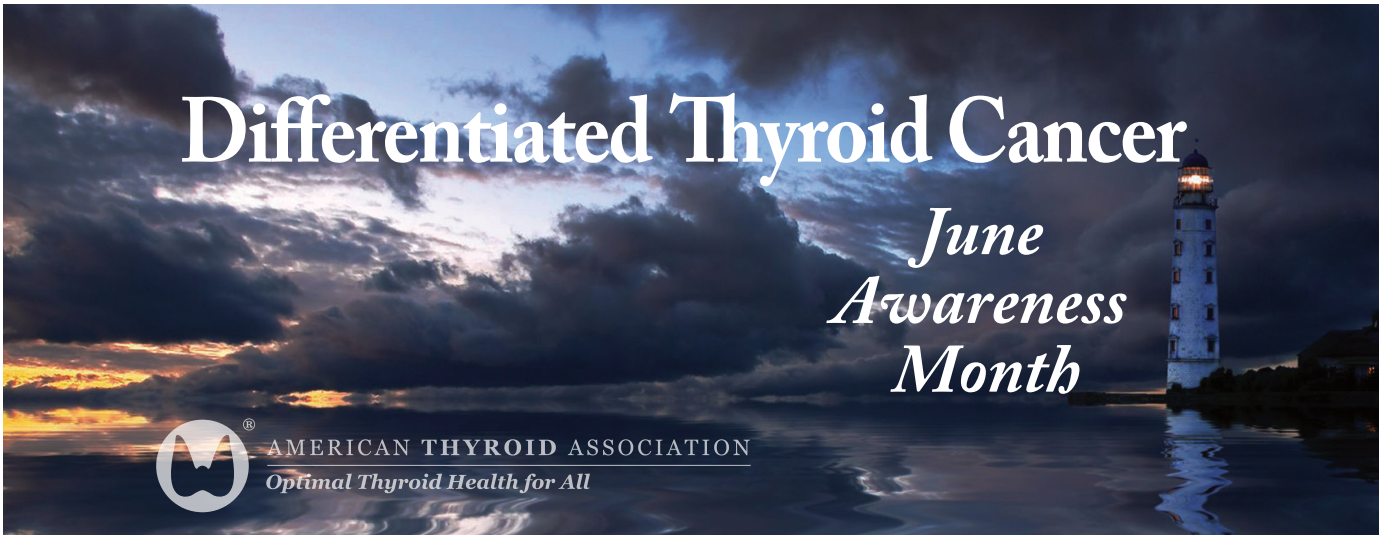
SEER: Surveillance, Epidemiology and End Results program, a nation-wide anonymous cancer registry generated by the National Cancer Institute that contains information on 26% of the United States population. Website: http://seer.cancer.gov/

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).

Anaplastic thyroid cancer: a very rare but very aggressive type of thyroid cancer. In contrast to all other types of thyroid cancer, most patients with anaplastic thyroid cancer die of their cancer and do so within a few years.

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

Medullary thyroid cancer: a relatively rare type of thyroid cancer that often runs in families. Medullary cancer arises from the C-cells in the thyroid.



AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

THYROID CANCER

A thyroid cancer consensus statement from the American Thyroid Association, the European Association of Nuclear Medicine, the European Thyroid Association, and the Society of Nuclear Medicine and Molecular Imaging

BACKGROUND

Thyroid cancer is common, especially in women. The major thyroid medical societies across the world have guidelines regarding treatment of thyroid cancer. The American Thyroid Association (ATA), the European Association of Nuclear Medicine (EANM), the European Thyroid Association (ETA), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) created a working group to annually assess current changes in the diagnosis and treatment of thyroid cancer. This task force has reviewed the latest evidence to develop a Consensus Statement for improving the diagnosis and treatment of thyroid cancer.

THE FULL ARTICLE TITLE

Gulec SA et al A Joint Statement from the American Thyroid Association, the European Association of Nuclear Medicine, the European Thyroid Association, the Society of Nuclear Medicine and Molecular Imaging on Current Diagnostic and theranostic approaches in the management of thyroid cancer. Thyroid. Epub 2021 Apr 1. PMID: 33789450.

SUMMARY OF THE STUDY

The working group consisted of experts in basic, diagnostic, and clinical aspects of thyroid cancer from all of the involved societies. These multidisciplinary teams accurately assessed three important topics that were identified in 2019.

i. Risk stratification prior to surgery is needed to guide the extent of thyroid surgery and to determine the need to treat with radioactive iodine therapy after surgery

Primary risk factors to determine the severity of thyroid cancer were determined as: the primary type of cancer; the age at diagnosis (< 55 vs. ≥55 years); primary cancer size (<4 cm vs. ≥ 4 cm); presence or absence of spread to the lymph nodes; presence or absence of extension of the cancer outside the thyroid; specific structures invaded by cancer; incomplete cancer resection with a known cancer left behind; presence or absence of spread of the cancer outside the neck; the level of thyroglobulin after surgery and radioactive iodine uptake outside thyroid bed, if performed. These data should be routinely obtained to accurately assign patients to a specific prognostic stage for risk of death and ATA risk category (low, intermediate, or high) for risk of cancer recurrence risk. Additional information from molecular studies could help to individualize initial management decisions in patients with thyroid cancer.

ii. There is a restricted role of diagnostic radioactive iodine imaging in initial staging.

Diagnostic radioactive iodine imaging is important for clinical decision-making only in intermediate-risk patients. The multidisciplinary task force suggested selective use of diagnostic radioactive iodine imaging in ATA intermediate-risk patients, rather than routine use for all patients belonging to this category. The task force supported that posttreatment scans should always be obtained for staging thyroid cancer.

iii. Identifying indicators of response to radioactive iodine therapy in the setting of residual thyroid cancer.

The task force acknowledged that the current reporting system supported by the ATA guidelines (excellent response, indeterminate response, biochemically incomplete response, and structurally incomplete response) after initial radioactive iodine therapy is very

THYROID CANCER, continued

helpful. However, they suggested that the evaluation of the response after radioactive iodine therapy should also include the use of a high-sensitivity serum thyroglobulin assay as a specific biomarker.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The existing risk-stratification models provide highly accurate predictive and prognostic information.

Traditional risk-stratification systems should be improved by incorporating patient- and cancer-specific molecular markers to individualize treatment decisions. radioactive iodine imaging is an important component of risk stratification; post-treatment scans should always be obtained for cancer staging. There is the need for a uniform classification system that includes imaging criteria.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

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

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

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).

Follicular thyroid cancer: the most 2nd most common type of 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*.

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.

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*).

Post-Radioactive iodine Whole Body Scan (post-RAI WBS): the scan done after radioactive iodine treatment that identifies what was treated and if there is any evidence of metastatic thyroid cancer.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

THYROID CANCER

Radioactive iodine therapy does not appear to be helpful in patients with in low-risk thyroid cancer

BACKGROUND

Thyroid cancer is the 9th most common cancer in the world. Overall, thyroid cancer has an excellent prognosis. Thyroidectomy followed by radioactive iodine therapy used to be recommended as standard treatment in all patients with thyroid cancer. However, radioactive iodine therapy has its own risks and significantly increases health care costs. Further, recent studies have shown that many patients are at very low risk for complications and recurrence and they may not benefit from radioactive iodine therapy. Therefore, the more recent American Thyroid Association (ATA) guidelines have recommended a less aggressive approach with less extensive surgery and a more selective use of radioactive iodine therapy. Currently, radioactive iodine therapy is not routinely recommended after thyroidectomy for low-risk thyroid cancer patients. There is little evidence to suggest that radioactive iodine therapy may improve death related to thyroid cancer, which is very low, and there is conflicting evidence regarding improving the risk of thyroid cancer recurrence in these patients. This is the first study aimed to directly compare radioactive iodine therapy to no radioactive iodine therapy in patients with low-risk thyroid cancer after total thyroidectomy.

THE FULL ARTICLE TITLE:

Leboulleux S et al 2022 Thyroidectomy without radioiodine in patients with low-risk thyroid cancer. N Engl J Med **386:**923–932. PMID: 35263518.

SUMMARY OF THE STUDY:

This study included low risk adult thyroid cancer patients. The low risk criteria are: cancers smaller than 2 cm within the thyroid, no cancer extension outside the thyroid, no spread of the cancer to lymph nodes in the neck and no aggressive-type cancer. The cancers were either single measuring between 1 cm and 2 cm or several small cancers (smaller than 1 cm and the sum of largest diameters of all cancers being smaller than 2 cm). All patients underwent total thyroidectomy with or without lymph node removal and had a neck ultrasound after surgery showing no abnormalities. Patients were randomly assigned to receive radioactive iodine therapy or not to receive this treatment. The radioactive iodine therapy group received 30 mCI of I-131 with recombinant human TSH stimulation and had a post-treatment whole body iodine scan. All patients were followed with serum thyroglobulin (Tg) and Tg antibody tests and neck ultrasound over the next 3 years. The study evaluated the number of patients in the two groups who had abnormal test results worrisome for thyroid cancer recurrence during the first 3 years of follow-up, including abnormal findings on neck ultrasound or whole-body iodine scanning after the radioactive iodine therapy and elevated levels of Tg or Tg antibodies. This trial was designed to answer the question of whether the percentage of patients with normal follow-up tests in the no therapy group is similar to the radioactive iodine therapy group.

A total of 776 patients were randomly assigned to the two treatment groups at 35 centers in France between May 2013 and March 2017. Of these, 730 patients were evaluated at 3 years (367 in the no therapy group and 363 in the radioactive iodine therapy group). Most study patients had normal follow-up tests without evidence of recurrence (95.6% in the no therapy group and 95.9% in the radioactive iodine therapy group). A similar number of patients had abnormal follow-up tests with only a 0.3% difference between groups (4.4% in the no therapy group and 4.1% in the radioactive iodine therapy group). A total of 14 patients required additional therapy with surgery, radioactive iodine therapy, or both (4 in the therapy group and 10 in the radioactive iodine therapy group). Analysis of the quality of life, anxiety, fear of recurrence and salivary dysfunction reported by the patients showed similar results in the two groups, while the radioactive iodine therapy group reported more dry eyes. The *BRAF* V600 mutation was present in more than 50% of patients, however, it was not associated with thyroid cancer recurrence.

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In adults with low-risk thyroid cancer, radioactive iodine therapy has similar outcomes to the group that did not receive radioactive iodine therapy. The presence of the *BRAF* V600 mutation does not appear to increase the recurrence risk and should not influence the decision for radioactive iodine therapy in this group. This study supports treating patients with low risk thyroid cancers without the use of radioactive iodine therapy.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

Thyroid cancer: The most common types are papillary and follicular thyroid cancer.

Thyroidectomy: surgery to remove the thyroid gland.

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 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).

Cancer recurrence: this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

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

Thyroglobulin (Tg) antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease. When serum Tg antibodies are high, they can be used as a thyroid cancer marker instead of Tg, which cannot be measured accurately in this condition.

BRAF gene: this is a gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations (permanent changes) in the BRAF gene in adults appear to cause cancer.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

HYPOTHYROIDISM

Hypothyroidism is common among childhood cancer survivors

BACKGROUND

Hypothyroidism (low thyroid hormone levels) is one of the most common endocrine diseases, affecting about 5% of general population. A previous study suggested that 15-20% of people who survived cancer in childhood may develop hypothyroidism later in life, which is much more common than in the general population. St. Jude Children's Research Hospital has a large group of patients who are followed after their diagnosis and treatment of cancer in childhood. The researchers of this study assessed how often hypothyroidism occurred in these patients, what the risk factors of developing hypothyroidism were, and how the diagnosis of hypothyroidism affected these patients.

THE FULL ARTICLE TITLE

Chemaitilly W et al 2022 Primary hypothyroidism in childhood cancer survivors: Prevalence, risk factors, and long-term consequences. Cancer **128:**606–614. PMID: 34643950.

SUMMARY OF THE STUDY

Patients who were at least 18 years old and had cancer in the last 10 years were included in the study. Patient who had serum thyrotropin (TSH) level above the upper limit of the normal range, indicating low thyroid hormone levels, or those who were taking thyroid hormone replacement, such as levothyroxine, were identified as having diagnosis of hypothyroidism. Whether a patient received radiation therapy to neck where thyroid gland is located was recorded. Later development of high blood pressure, diabetes, and high cholesterol levels, as well as physical and mental health, cognitive problems, and quality of life of these patients were assessed.

A total of 2965 patients, whose average age was 31 years old and had the initial cancer diagnosis 22.3 years ago on average, were included in the study. Primary hypothyroidism was diagnosed in 14.7% (436 patients). Of those 436 patients with hypothyroidism, 31.9% (139 patients) had hypothyroidism after thyroidectomy to remove thyroid nodules, thyroid cancer, or enlarged thyroid gland (goiter). Radiation therapy to the area of thyroid gland as a part of the cancer treatment increased risk of developing hypothyroidism later. Patients with hypothyroidism were more likely to have high cholesterol levels and problems with physical health, such as having muscle weakness, low muscle mass, low energy level, or slow walking speed, or feeling less physically fit. Patients with free thyroxine (free T4) level on the lower end of normal range were more likely to have fat around abdomen and less likely to have problem with physical health and those with free T4 level on the higher end of normal range. Patients with low free T4 levels were more likely to have lower quality of life.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Hypothyroidism was diagnosed in almost 15% of patients who survived childhood cancer in this study. Hypothyroidism was about three times more common in these patients than in general population. Those with a diagnosis of hypothyroidism were also more likely to have high cholesterol levels and reported more problems with physical health.

Given the high prevalence and its potential association with other health problems, it would be important for treating clinicians of childhood cancer survivors, including primary care providers and oncologists, to watch out for development of thyroid dysfunction in these patients. It would be also important to educate childhood cancer survivors to be aware of potential symptoms of hypothyroidism to prompt screening if they develop symptoms consistent with hypothyroidism.

— Sun Y. Lee, MD MSc

HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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

Primary hypothyroidism: the most common cause of hypothyroidism cause by failure of the thyroid grand.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order 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.

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*.

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

Goiter: a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a *nodular goiter*; if there is more than one nodule it is called a *multinodular goiter*.

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.

Thyroxine (T4): the major hormone produced by the thyroid gland. T4 gets converted to the active hormone T3 in various tissues in the body.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

HYPOTHYROIDISM

Thyroid hormone requirement in ICI-associated hypothyroidism is higher than in Hashimoto's hypothyroidism

BACKGROUND

Immune checkpoint inhibitor (ICI) drugs are an extremely valuable new class of drugs for the treatment of many types of cancers. As such, they are being used a lot currently with excellent results. The ICI drugs work by turning on the immune system to attack and destroy the cancer cells. Occasionally, this results in turning on the immune system to attack normal cells and this often includes the thyroid. This is known as ICI–associated thyroiditis, which causes a destructive inflammation in the thyroid. The most common result of this is ICI-associated hypothyroidism. When it occurs, most patients end up requiring thyroid hormone replacement.

Older patients who develop ICI-associated hypothyroidism are prone to worsening of osteoporosis and developing heart issues because of thyroid hormone overtreatment or to lower quality of life because of thyroid hormone undertreatment. Hence, finding the best levothyroxine dose would be beneficial in improving this population's medical care, especially given their advanced cancer and the potential other adverse effects of ICI drugs. This study evaluates the dose of thyroid hormone replacement required to achieve stable normal thyroid function in patients with ICI-associated hypothyroidism, as compared with those with Hashimoto's thyroiditis and those without a thyroid.

THE FULL ARTICLE TITLE

Mosaferi T et al 2022 Optimal thyroid hormone replacement dose in immune checkpoint inhibitor-associated hypothyroidism is distinct from Hashimoto's thyroiditis. Thyroid. Epub 2022 Feb 24. PMID: 35199588.

SUMMARY OF THE STUDY

This study of adults was conducted at an academic medical center from January 1, 2015, through August 24, 2020. Cases included adults with ICI-associated thyroiditis who presented with high thyroid levels followed by either: (i) hypothyroidism (TSH >4.7 mIU/L) requiring thyroid hormone replacement or (ii) resolution to normal thyroid status (consecutive normal TSH levels not requiring thyroid hormone replacement). Controls included adults with Hashimoto's thyroiditis or absent thyroid gland requiring levothyroxine replacement. A stable normal thyroid state was defined as two consecutive normal TSH levels (0.3–4.7 mIU/L) at least 6 weeks apart.

Of 103 adults with ICI-associated thyroiditis (average age ~65 years; 57.6% female), 66 (64.1%) achieved a stable normal thyroid state while 37 (36%) developed ICI-associated hypothyroidism. The most common cancers in this group were lung and skin cancers, and the most common ICI was PD-1 (programmed cell death-1) monotherapy (71.2%). The average time to thyrotoxicosis was 6 weeks (longer for monotherapy and shorter for combination therapy). Patients with ICI-associated hypothyroidism were more frequently likely to have coronary artery disease or osteoporosis and to use medications that interfere with thyroid hormone requirements (magnesium, PPIs, TKIs, and glucocorticoids) than in the controls with Hashimoto's thyroiditis and no thyroid gland.

The average levothyroxine dose needed to achieve a stable normal thyroid state in patients with ICI-associated hypothyroidism (~1.45 mcg/kg/day) was higher than that of the average dose in the Hashimoto's thyroiditis controls (1.25 mcg/kg/day). The dose was not different from that for patients without a thyroid (1.54 mcg/kg/day). Age and use of interfering medications were not predictive of the differences in dosing and there was no difference according to sex.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Thyroid hormone dose requirements for patients with ICI-associated hypothyroidism were similar to those in

HYPOTHYROIDISM, continued

patients without a thyroid gland but higher than for those with Hashimoto's thyroiditis. The authors recommend that in patients with ICI-associated hypothyroidism, levothyroxine therapy should be started at an initial weight-based dose of 1.45 µg/kg/day once serum free thyroxine levels fall below the reference range.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/
Hashimoto's Thyroiditis: https://www.thyroid.org/hashimotos-thyroiditis/
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.

Hashimotos thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

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

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order 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.

Immune checkpoint inhibitors (ICI drugs): cancer drugs that help the body recognize cancer and use the body's immune system to attack and destroy cancer cells. These drugs are now standard-of-care treatments for several types of cancer, including melanoma and kidney cancer.

Thyroiditis: inflammation of the thyroid, most commonly cause by antibodies that attack the thyroid as seen in Hashimoto's thyroiditis and post-partum thyroiditis. It can also result from an infection in the thyroid or due to certain drugs/medications.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

Clinical Thyroidology® for the Public

THYROID NODULES

Ultrasound-guided thermal ablation of thyroid nodules—what do the experts say about who, what, and when?

BACKGROUND

Thyroid nodules are the most common endocrine disorder, as up to 50% of the US population will have a thyroid nodule after imaging that includes the thyroid. Evaluation of thyroid nodules currently include thyroid ultrasound and thyroid biopsy. Nodules that are cancerous are usually removed by surgery, as are large benign nodules.

Alternative treatments to surgery for thyroid nodules are continually being developed. These techniques involve inserting needles into the nodule through the skin to deliver either substances, sound waves or current to destroy and/or shrink nodule (ablation). The newest one to generate a lot of interest is radiofrequency (RFA) ablation that uses current to generate heat to destroy cells. Other techniques to shrink thyroid nodules outside of surgery include injecting ethanol into the nodule (ETOH ablation), microwave ablation, laser ablation and high-intensity focused ultrasound (HIFU) ablation.

An international collaborative panel comprising surgeons, endocrinologists, and radiologists with expertise in ultrasound-guided ablation got together to discuss the indications, techniques, complications, expectations of successful treatments, and recommended follow-up of thyroid nodules treated with non-surgical ablation. The goal was to develop a best practice manual of thyroid ablation techniques, including the indications for the different thyroid nodule ablation techniques, their best use, and reported outcomes.

THE FULL ARTICLE TITLE

Orloff LA et al 2021 Radiofrequency ablation and related ultrasound-guided ablation technologies for treatment of benign and malignant thyroid disease: An international multidisciplinary consensus statement of the American Head and Neck Society Endocrine Surgery Section with the Asia Pacific Society of Thyroid Surgery, Associazione Medici Endocrinologi, British Association of Endocrine and Thyroid Surgeons, European Thyroid Association, Italian Society of Endocrine Surgery Units, Korean Society of Thyroid Radiology, Latin American Thyroid Society, and Thyroid Nodules Therapies Association. Head Neck 44:633–660. PMID: 34939714.

SUMMARY OF THE STUDY

This consensus statement was based on the review of 690 sentinel articles by a group of clinicians with expertise in thyroid ablation techniques. Five techniques (ETOH, microwave, laser, RFA, and HIFU ablation) were reviewed to assess their common indications, ideal candidates, and specific advantages and disadvantages. Complications and issues related to starting these technologies in a clinical thyroid practice were discussed.

In general, the indications for the use of these treatments included overactive thyroid nodules, non-cancerous large compressive goiters and certain small thyroid cancers. Overall, 18 recommendations were proposed, representing panel-supported, evidence-based statements to guide providers considering starting to use this technology. These recommendations include clear indications, pretreatment considerations, and technical suggestions for performing these ultrasound-guided ablative therapies for thyroid nodules. The recommendations also contain expectations from treatments, complications and ways to measure successful treatment. Longer-term follow-up recommendations and indications for retreatments are stated, as well.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Ultrasound-guided ablation for thyroid nodules are rapidly growing as a possible treatment option, including in patients who may have otherwise undergone thyroid surgery. This consensus statement by an international group of experts provides 18 recommendations for their use. Experience in ultrasound and procedural assessment and follow-up are important components for their successful incorporation into a clinical thyroid practice.

— Alan P. Farwell, MD

THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

Goiter: a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a *nodular goiter*; if there is more than one nodule it is called a *multinodular goiter.*

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

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Radiofrequency ablation (RFA): a nonsurgical, minimally invasive technique that uses alternating electromagnetic current to generate heat to destroy cancer cells.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 15 | Issue 6 | June 2022

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.

ATA® *Optimal Thyroid Health for All*

GRAVES' DISEASE & THYROID FOUNDATION®

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

Light of Life Foundation checkyourneck.com

BITE ME CANCER!

MCT8 - AHDS Foundation

THYROID CANCER ALLIANCE

Thyroid Cancer Canada / Cancer de la thyroïde Canada

Thyroid Federation International

American Thyroid Association
www.thyroid.org
ATA Patient Resources:
www.thyroid.org/thyroid-information/
Find a Thyroid Specialist: www.thyroid.org
(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 Cancer Alliance
www.thyroidcanceralliance.org
www.thyroidcancerpatientinfo.org
Rotterdam, The Netherlands

Thyroid Cancer Canada
www.thyroidcancercanada.org
416-487-8267
info@thyroidcancercanada.org

Thyroid Federation International
www.thyroid-fed.org
tfi@thyroid-fed.org

AMERICAN THYROID ASSOCIATION
ATA | *Founded 1923*

Friends of the ATA

FOUNDED 2005

Get the latest thyroid health information. You'll be among the first to know the latest cutting-edge thyroid research that is important to you and your family.

Become a Friend of the ATA!
Subscribe to *Friends of the ATA e-news*

By subscribing to *Friends of the ATA Newsletter*, you will receive:

- ✔ *Friends of the ATA e-news*, providing up-to-date information on thyroid issues, summaries of recently published articles from the medical literature that covers the broad spectrum of thyroid disorders., and invitations to upcoming patient events
- ✔ Updates on the latest patient resources through the ATA website and elsewhere on the world wide web
- ✔ Special e-mail alerts about thyroid topics of special interest to you and your family

We will use your email address to send you *Friends of the ATA e-news* and occasional email updates. We won't share your email address with anyone, and you can unsubscribe at any time.

www.thyroid.org