

# Clinical Thyroidology® for the Public



AMERICAN THYROID ASSOCIATION  
Optimal Thyroid Health for All



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Thyroid cancer is one of the fastest rising cancers in the world. It is unclear if this increase is because of increased use of imaging studies or represents a true increase in cancer. This study examined the mode of detection for thyroid nodules that subsequently led to thyroid surgery in varying parts of the world to determine whether there was a true increase in papillary thyroid cancer or if this trend is secondary to an increase in nodule detection.

Sajisevi M et al 2022 Evaluating the rising incidence of thyroid cancer and thyroid nodule detection modes: A multinational, multi-institutional analysis. JAMA Otolaryngol Head Neck Surg 148:811–818. PMID: 35834240.

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Hypothyroidism is a common medical condition and occurs in about 11% of the US population. Unfortunately, many patients on thyroid hormone are not adequately treated and TSH levels may remain abnormal despite being on treatment. This study examines whether inadequately treated hypothyroidism may cause any complications for patients admitted to the hospital.

Ettleson MD et al. 2022 Suboptimal thyroid hormone replacement is associated with worse hospital outcomes. J Clin Endocrinol Metab. Epub 2022 Apr 26. PMID: 35472082.

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#### Thyroid hormones enhance the growth of estrogen receptor–positive breast cancers

Some studies have suggested an association between thyroid disorders and breast cancer where thyroid hormone appears to play an important role. Further, up to 30% of patients with breast cancer are on thyroid hormone for treatment of hypothyroidism. This study aimed at investigating the effects of thyroid hormone treatment for hypothyroidism on the outcome of patients with stage I breast cancer.

Wahdan-Alaswad RS et al 2021 Exogenous thyroid hormone is associated with shortened survival and upregulation of high-risk gene expression profiles in steroid receptor-positive breast cancers. Clin Cancer Res 27:585–597. PMID: 33097494.

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Overt hyperthyroidism and hypothyroidism have impact on fertility. It is currently not clear whether mildly abnormal thyroid hormone levels cause infertility. This study aimed to assess whether blood TSH levels in the upper half of the normal range are associated with infertility.

Li N et al. 2022 The impact of moderately high preconception thyrotropin levels on ovarian reserve among euthyroid infertile women undergoing assisted reproductive technology. Thyroid 32:841–848. PMID: 35317605.

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T3 levels are low in patients admitted with heart attack and after heart surgery. This is known as the low T3 syndrome and has led to studies using T3 therapy in patients acutely sick with heart problems to increase T3 levels back to normal to try to improve outcomes. This study was aimed to evaluate the effect of high-dose liothyronine (LT3) shortly after a heart attack.

Pantos CI et al 2022 Effects of acute triiodothyronine treatment in patients with anterior myocardial infarction undergoing primary angioplasty: Evidence from a pilot randomized clinical trial (ThyRepair Study). Thyroid. Epub 2022 May 5. PMID: 35297659.

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One of the more effective cancer immunotherapy drugs belong to a class known as immune checkpoint inhibitors (ICI). Since these ICI drugs activate the patient's immune system, it is not surprising that other autoimmune diseases may develop or flare during the treatment with ICI. The goal of this study was to characterize the association of antithyroid antibodies with the development of ICI-related thyroid disease.

Muir CA et al 2022 Association of antithyroid antibodies in checkpoint inhibitor-associated thyroid immune-related adverse events. J Clin Endocrinol Metab 107(5):e1843–e1849. PMID: 35104870.

## ATA ALLIANCE FOR THYROID PATIENT EDUCATION .....15



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## Editor

Alan P. Farwell, MD  
Boston Medical Center  
Boston University School of Medicine  
720 Harrison Ave., Boston, MA 02115  
American Thyroid Association  
Email: [thyroid@thyroid.org](mailto:thyroid@thyroid.org)  
[www.thyroid.org/patients/ct/index.html](http://www.thyroid.org/patients/ct/index.html)

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### Executive Director

Amanda K. Perl  
American Thyroid Association  
2000 Duke Street, Suite 300  
Alexandria, VA 22314  
Telephone: 703-998-8890  
Fax: 703-998-8893  
Email: [thyroid@thyroid.org](mailto:thyroid@thyroid.org)

### Designed by

Karen Durland, [kdurland@gmail.com](mailto: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 [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](http://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.

While the Covid-19 pandemic is winding down, it 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/>)

October is [Thyroid Nodule Awareness Month](#).

In this issue, the studies ask the following questions:

- How often does thyroid cancer occur in asymptomatic individuals?
- Does inadequate treatment of hypothyroidism during hospitalization lead to worse hospital outcomes?
- Does thyroid hormone cause increased growth of breast cancer?
- Do high normal TSH values increase the risk of infertility?
- Is there any role for the use of T3 therapy in the setting of an acute heart attack?
- Do thyroid antibodies predict the development of thyroid disease in patients getting cancer immunotherapy 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



## THYROID NODULES

### The asymptomatic patient and thyroid nodule surgery

#### BACKGROUND

Thyroid cancer is one of the fastest rising cancers in the world. Part of this increase is due to the detection of thyroid nodules on imaging studies done for another reason. Many of the cancers identified are small and may never cause significant problems. However, other lines of evidence support a true increase in papillary thyroid cancer (the most common type of thyroid cancer) that have more advanced-stage disease at diagnosis, and higher associated death rate. It is projected that by 2040, thyroid cancer will be one of the top four cancer diagnoses, along with breast, colorectal, and kidney and pelvis cancers. Overall, the prognosis of thyroid cancer is excellent, with surgery often the only treatment needed. However, it is unclear for the need for surgery in some patients with small thyroid cancers that are at very low risk of spreading outside of the thyroid. Indeed, some patients with small thyroid cancers are watched without surgery (active surveillance).

The objective of this study was to determine the mode of detection for thyroid nodules that subsequently led to thyroid surgery in varying parts of the world. The goal is to determine whether there was a true increase in papillary thyroid cancer or if this trend is secondary to an increase in nodule detection.

#### THE FULL ARTICLE TITLE

Sajisevi M et al 2022 Evaluating the rising incidence of thyroid cancer and thyroid nodule detection modes: A multinational, multi-institutional analysis. JAMA Otolaryngol Head Neck Surg 148:811–818. PMID: 35834240.

#### SUMMARY OF THE STUDY

This is a study of patients who underwent thyroid surgery in 2019 at 16 centers in four different countries. From survey responses provided by investigators at each of the centers, patients were classified into groups by the mode of thyroid detection that led to surgery. The authors

found that of the 1328 patients (average age 52 years, 75% women) included in this study, 41% of patients were asymptomatic at the time of detection, 34% had symptoms related to the thyroid nodule, 14% had other endocrine conditions, and 12% were under surveillance (nodules with original mode of detection unknown). Mode of detection within the asymptomatic category included 20% noted on imaging studies done of other reasons, 1% by patient-requested screening, and 13% by clinician screening examination. CT scan of the chest was the most common imaging test that led to the discovery of thyroid nodules, comprising 31% of the imaging studies done for other reasons.

Thyroid surgery was more often performed in the US and Canada for asymptomatic nodules. Denmark and South Africa had the highest rates of nodules discovered secondary to patient symptoms. The surgical thyroid pathology revealed cancer in 613 cases (46%). Of these patients, only 30% had been symptomatic, thus would not have necessarily come to attention otherwise. The average size of the cancer was larger in symptomatic patients compared to those who were asymptomatic (3.2cm vs 2.1cm).

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Overall, this study shows that there are differences in the mode of detection of thyroid nodules, and associated surgical practices, from the four countries (Denmark, South Africa, United States, and Canada) whose clinicians were surveyed in this study. Most patients in this study had no thyroid-related symptoms and 60% of those with thyroid cancer fell into this group. The asymptomatic patients had smaller-sized cancers than patients with symptoms, but the average size was still >2 cm. This suggests that there has been an actual increase in thyroid cancer across the world.

— Alan P. Farwell, MD



## THYROID NODULES, continued

### ATA THYROID BROCHURE LINKS

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

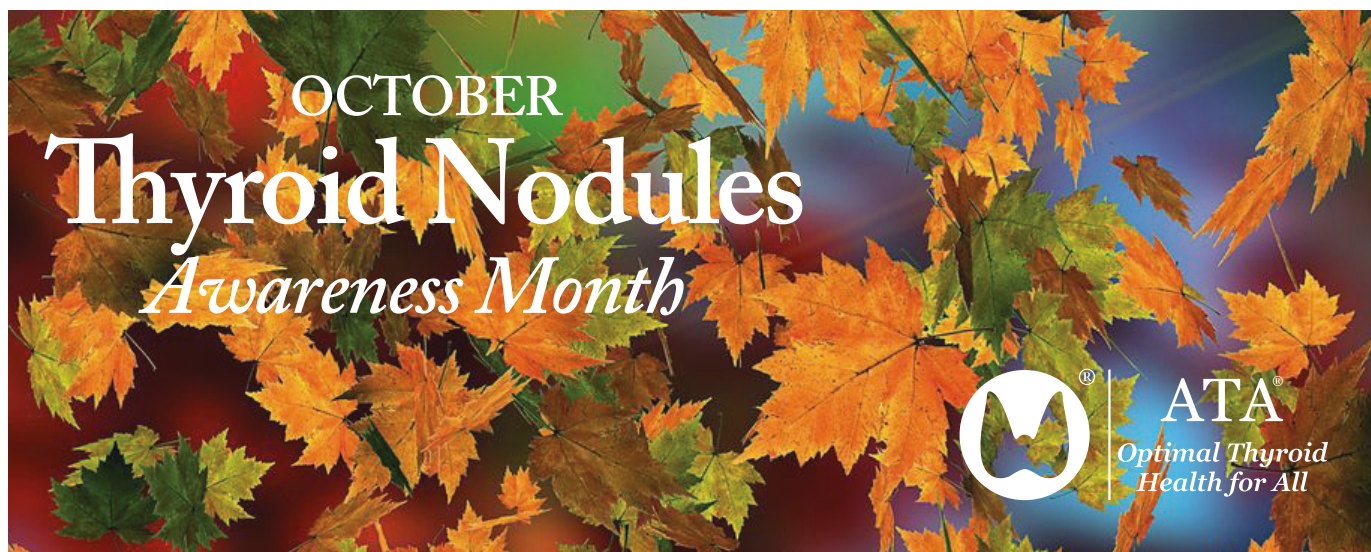
Thyroid Nodules: <https://www.thyroid.org/thyroid-nodules/>

### 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% are cancerous.

**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).

**Active surveillance:** This refers to following low risk thyroid cancers with ultrasound imaging once or twice a year as opposed to proceeding with immediate surgery.







## HYPOTHYROIDISM

### Does inadequate treatment of hypothyroidism during hospitalization lead to worse hospital outcomes?

#### BACKGROUND

Hypothyroidism is a common medical condition and occurs in about 11% of the US population. Symptoms of hypothyroidism include fatigue, lack of concentration and muscle weakness. Hypothyroidism is diagnosed with an increased TSH and low FT4 levels. Subclinical, or mild, hypothyroidism occurs when only the TSH is abnormal. Treatment may not be necessary for subclinical hypothyroidism. American Thyroid Association guidelines suggests starting treatment for patients who have TSH higher than 10 uIU/mL or selected patients with TSH higher than 5 uIU/mL. Hypothyroidism is treated by replacing the thyroid hormone with levothyroxine taken on a daily basis. The goal of treating hypothyroidism is resolution of symptoms related to the hypothyroidism along with returning the TSH and FT4 level into the normal range.

Unfortunately, many patients on thyroid hormone are not adequately treated and TSH levels may remain abnormal despite being on treatment. It is not clear whether inadequately treated hypothyroidism may cause any complications for patients admitted to the hospital. The current study tries to answer this question. Because TSH and T4 levels may change during hospitalization from reasons other than hypothyroidism (like administered medications or the patient's sickness), in this study, the TSH and Free T4 levels before admission (when patient was not sick) were used.

#### THE FULL ARTICLE TITLE

Ettleson MD et al. 2022 Suboptimal thyroid hormone replacement is associated with worse hospital outcomes. J Clin Endocrinol Metab. Epub 2022 Apr 26. PMID: 35472082.

#### SUMMARY OF THE STUDY

The authors reviewed the medical records of patients who were admitted to their hospital and compared the

outcomes between patients with hypothyroidism and without hypothyroidism. To identify the patient who had hypothyroidism they used the medication list in medical record and diagnostic codes used for ordering laboratory tests. Individuals who were 18 to 64 without a history of thyroid cancer, hyperthyroidism or pituitary problems were included. Patients were divided to groups based on the level of their TSH (low, normal, mildly elevated, and elevated). About 10,000 patients were included in the study. A control group of about 21,000 patients was added.

The low TSH group (over-treated) had no differences in hospital outcomes, as compared with the control group. In the normal TSH group, there was a lower risk of both death during the hospitalization and readmission after discharge. The intermediate TSH group demonstrated no differences in hospital outcomes. However, the high TSH (> 10 uIU/ml, under-treated) group had a higher hospital stay (about 1.2 days) and also had a higher rate of readmission in 30 and 90 days.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that under-treatment of hypothyroidism resulting in a continued increase in TSH levels may result in a longer hospital stay or even possibly higher rate of readmission. Interestingly, over-treatment or mild under-treatment did not appear to have any differences compared to those patients with normal thyroid function. These results should lead to additional studies to confirm the findings. However, this study provides a preliminary information regarding the importance of adequately treating hypothyroidism.

— Shirin Haddady, MD



## HYPOTHYROIDISM, continued

### ATA THYROID BROCHURE LINKS

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

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

### ABBREVIATIONS & DEFINITIONS

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

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

**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.

**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.



## HYPOTHYROIDISM

### Thyroid hormones enhance the growth of estrogen receptor–positive breast cancers

#### BACKGROUND:

Some studies have suggested an association between thyroid disorders and breast cancer where thyroid hormone appears to play an important role. This goes both ways, as patients diagnosed with breast cancer have a higher risk than the general population of developing thyroid cancer later in life, while patients with thyroid cancer have a higher risk of also developing breast cancer. Moreover, high thyroid hormone levels into the hyperthyroidism range, either due to hyperthyroidism or to over-replacement of thyroid hormone in hypothyroidism, have been associated with an increased incidence and more aggressive types of breast cancer. Some laboratory studies have suggested that thyroid hormone stimulates breast cancer cell growth. Further, up to 30% of patients with breast cancer are on thyroid hormone for treatment of hypothyroidism. This study aimed at investigating the effects of thyroid hormone treatment for hypothyroidism on the outcome of patients with stage I breast cancer.

#### THE FULL ARTICLE TITLE:

Wahdan-Alaswad RS et al 2021 Exogenous thyroid hormone is associated with shortened survival and upregulation of high-risk gene expression profiles in steroid receptor-positive breast cancers. Clin Cancer Res 27:585–597. PMID: 33097494.

#### SUMMARY OF THE STUDY:

This study examined the association between thyroid hormone therapy, disease-free survival (DFS), and disease-specific survival (DSS) in two groups of patients with stage I lymph node negative breast cancer. The first group included 820 patients treated for breast cancer between 1962 and 1993 and followed for an average of 10 years. Of this group, 69 patients (8.4%) were taking thyroid hormone for hypothyroidism. The second group included 160 patients treated more recently between

2006 and 2009 and followed for a average of 9 years. Of this group, 50 patient (31.3%) were taking thyroid hormone for hypothyroidism. Data regarding the patient age, cancer size, presence or absence of estrogen receptors (ER + or -) in the cancer, and cancer treatment regimen were included in the analysis. The authors also performed experiments in the laboratory using human breast cancer cell lines to investigate the mechanisms underlying the effects of thyroid hormone and estrogen on breast cancer cells.

In patients with ER+ breast cancer, thyroid hormone therapy was associated with a significantly increased risk of recurrence and death, independently of age, cancer size and grade, while thyroid hormone therapy in patients with ER– breast cancer was not associated with worse outcomes. At 10 years of follow-up, the cancer recurrence rate was 39.5% and the DFS was 72.5 months in ER+ breast cancer patients on thyroid hormone therapy compared to 16% and 106 months, respectively in those not taking thyroid hormone therapy. The death rate was 24% and the DSS was 84 months in ER+ breast cancer patients on thyroid hormone therapy versus 8% and 114 months, respectively in those not taking thyroid hormone therapy. Patients with ER+ breast cancer taking both tamoxifen therapy for breast cancer and thyroid hormone therapy experienced the shortest DFS survival of all groups studied at 10 years, with an average DFS of 52 months vs. 65 months in patients taking tamoxifen without thyroid hormone therapy.

Laboratory studies revealed that therapy with thyroid hormone or estrogen stimulates cell growth, the effect being stronger with combination therapy (thyroid hormone and estrogen). Thyroid hormone and estrogen appeared to stimulate cell growth significantly at all dose levels, including levels in the normal range for both hormones.



## HYPOTHYROIDISM, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study shows that stage 1 ER+ breast cancer patients treated with thyroid hormone for management of hypothyroidism have worse outcomes, even in patients taking other

cancer drugs. These results suggest that treatment with thyroid hormone in patients with hypothyroidism and breast cancer should be closely monitored to ensure that the thyroid hormone levels remain in the normal range.

— Alina Gavrilă, MD, MMSC

### ATA THYROID BROCHURE LINKS

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

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

### 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.

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

**Disease-free survival (DFS):** defined as the period after the cancer treatment when the patient survives without any cancer signs or symptoms.

**Disease-specific survival (DSS):** defined as the period that begins at the time of diagnosis or at the start of treatment and ends at the time of death specifically from the cancer.

**Hormone receptor:** a molecule located on a cell membrane or inside the cell that is activated by binding a specific hormone and induces specific changes in the cell function. Estrogen (ER) and thyroid hormone receptors (THR) are members of the nuclear receptor family that bind estrogen and thyroid hormone, respectively and affect gene expression in the cell.

**Tamoxifen:** medication that blocks the effects of estrogen on breast tissue. It is used to prevent and treat breast cancer.

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





## THYROID AND PREGNANCY

### Lower egg quality and quantity were seen in women with infertility and TSH levels in the high-normal ranges.

#### BACKGROUND

Thyroid disorders are common endocrine disease in young women. Abnormal thyroid hormone levels and autoimmune thyroid disease, such as Hashimoto's thyroiditis or Graves' disease, may have impact on fertility. These disorders may interfere with ovarian function and make it more difficult to get pregnant. This is especially true with overt hyperthyroidism and hypothyroidism. It is currently not clear whether mildly abnormal thyroid hormone levels cause infertility.

One of the measures evaluated in the workup for infertility is called diminished ovarian reserve (DOR). DOR indicates that there is either a lower amount or a decrease in the quality of eggs produced by women with infertility and may lead to difficulty getting pregnant. This study aimed to assess whether blood TSH levels in the upper half of the normal range are associated with DOR and infertility.

#### THE FULL ARTICLE TITLE

Li N et al. 2022 The impact of moderately high pre-conception thyrotropin levels on ovarian reserve among euthyroid infertile women undergoing assisted reproductive technology. *Thyroid* 32:841–848. PMID: 35317605.

#### SUMMARY OF THE STUDY

The researchers reviewed medical records of 3501 women who were between 20 and 40 years of age and seen at the Shandong University Hospital infertility clinic in China between 2015 and 2020. All women had TSH levels in normal ranges and no history of thyroid disease or taking thyroid medications. About two-thirds (62.5%) of women had a TSH level in the lower half of the normal range (low-normal group) and about one-third (37.5%) of women had a TSH level in the higher half of the normal range (high-normal group).

Women in the low-normal TSH group had ovarian problems more frequently than women in the

high-normal group. However, women in the high-normal group had lower levels of anti-müllerian hormone (AMH), an ovarian hormone that is important in egg development, and lower numbers of ovarian follicles, both measures of viable eggs, compared to women in the low-normal group. Women in the high-normal group more frequently had positive thyroid peroxidase (TPO) or thyroglobulin (Tg) antibodies, suggesting underlying autoimmune thyroid disease. Overall, women in the high-normal group more frequently had DOR compared to women in the low-normal group (5.1% vs. 3.5%), after taking account of age, BMI, and presence of autoimmune thyroid disease.

Women in the high-normal group also had a slightly lower number of live-births and slightly higher number of very early pregnancy loss compared to women in the low-normal group (54.3% vs. 57.4%, and 9.7% vs. 7.6%, respectively). Overall rates of pregnancy were not different between the two groups. Higher TSH levels were correlated with lower AMH levels or lower follicle counts. Women with thyroid autoimmunity (positive TPO or Tg antibody levels) were also noted to have lower AMH levels or lower follicle counts, regardless of TSH levels.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this study of women with infertility, women with blood TSH levels in the higher half of the normal ranges had lower AMH levels and less ovarian follicle counts, indicating lower egg quality and quantity, compared with women with blood TSH levels in the lower half of normal ranges.

Even though there have been many studies, potential impact of mild thyroid hormone abnormalities and thyroid autoimmunity on fertility has not been clear due to limitations in these studies performed using medical records and different definitions used for thyroid problems and measures of fertility. This study was also limited to Chinese patients, and same effects may not be seen in



## THYROID AND PREGNANCY, continued

other races/ethnicity. The results of this study add to the findings of some previously published studies. However, it does not definitely answer the question of the impact of mild thyroid abnormalities on infertility because lower AMH levels or lower numbers of ovarian follicles do not

always cause infertility. So far, trials have not shown clear benefit of using levothyroxine to treat mild thyroid abnormalities in improving fertility. Thus, it remains unclear who needs to be treated and at what TSH levels.

— Sun Y. Lee, MD, MSc

### ATA THYROID BROCHURE LINKS

Thyroid Disease in Pregnancy: <https://www.thyroid.org/thyroid-disease-pregnancy/>

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

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

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

### ABBREVIATIONS & DEFINITIONS

**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).

**Hashimoto's thyroiditis:** the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy the gland.

**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.

**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.

**TPO 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.

**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.

**Anti-müllerian hormone (AMH):** a blood test that are used to assess the number of remaining eggs that a woman has.

**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

### Preliminary experience of early T<sub>3</sub> therapy in patients with an acute heart attack

#### BACKGROUND

T<sub>4</sub> is the main thyroid hormone secreted from the thyroid gland. T<sub>4</sub> is converted to T<sub>3</sub>, the active hormone, in many tissues outside the thyroid. There is a strong association between thyroid hormones and the heart in both health and in disease. In particular, in patients with congestive heart failure, T<sub>3</sub> levels are often low and are associated with worse outcomes. T<sub>3</sub> levels are also low in patients admitted with heart attack and after heart surgery. This is known as the low T<sub>3</sub> syndrome and has led to studies using T<sub>3</sub> therapy in patients acutely sick with heart problems and with the low T<sub>3</sub> syndrome. The goal in these studies has been to increase T<sub>3</sub> levels back to normal to try to improve outcomes. To date, studies have been unclear of any benefit; importantly no bad effects of T<sub>3</sub> therapy has been shown in these studies.

The degree to which the low T<sub>3</sub> syndrome represents a protective or harmful response to acute heart injury and whether treatment with thyroid hormones will improve patient outcomes remain uncertain. This study was aimed to evaluate the effect of high-dose liothyronine (LT<sub>3</sub>) shortly after a heart attack.

#### THE FULL ARTICLE TITLE

Pantos CI et al 2022 Effects of acute triiodothyronine treatment in patients with anterior myocardial infarction undergoing primary angioplasty: Evidence from a pilot randomized clinical trial (ThyRepair Study). *Thyroid*. Epub 2022 May 5. PMID: 35297659.

#### SUMMARY OF THE STUDY

This trial was conducted in two clinical centers in Greece and included adult patients diagnosed with anterior or anterolateral ST-elevation myocardial infarction (STEMI) presenting within 12 hours of the onset of chest pain.

Patients were randomly assigned to receive intravenous (IV) LT<sub>3</sub> treatment or no hormone. The IV infusion of LT<sub>3</sub> or no hormone was given by continuous infusion for 48 hours.

A total of 52 patients were enrolled. There were no significant differences in baseline characteristics between the two groups. After accounting for participants who did not complete follow-up, a total of 16 patients in the no hormone group and 21 patients in the LT<sub>3</sub> group were analyzed. As expected, total T<sub>3</sub> levels were higher in the LT<sub>3</sub> group than in the no hormone group during the initial 72 hours. There was no significant difference in overall heart function at discharge, although a trend favoring LT<sub>3</sub> therapy was noted. A trend toward a decrease in the size of the damaged heart muscle was noted in the LT<sub>3</sub> group at 6 months. No serious life-threatening adverse effects related to LT<sub>3</sub> treatment were reported. Patients in the LT<sub>3</sub> group had higher heart rates during the initial 72 hours than the no hormone group, but no significant difference was found at discharge or during follow-up. There was a trend of increased incidence of atrial fibrillation (AF) in the LT<sub>3</sub> group during the 48 hours of drug infusion and responded to medical management.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows treatment with IV T<sub>3</sub> in the setting of an acute heart attack resulted in a trend toward improved heart function. Importantly, no serious life-threatening adverse events were noted; however, there was a trend toward a higher incidence of AF in the LT<sub>3</sub> group. This study sets the parameters for future larger studies.

— Alan P. Farwell, MD



## THYROID HORMONE THERAPY, continued

### ATA THYROID BROCHURE LINKS

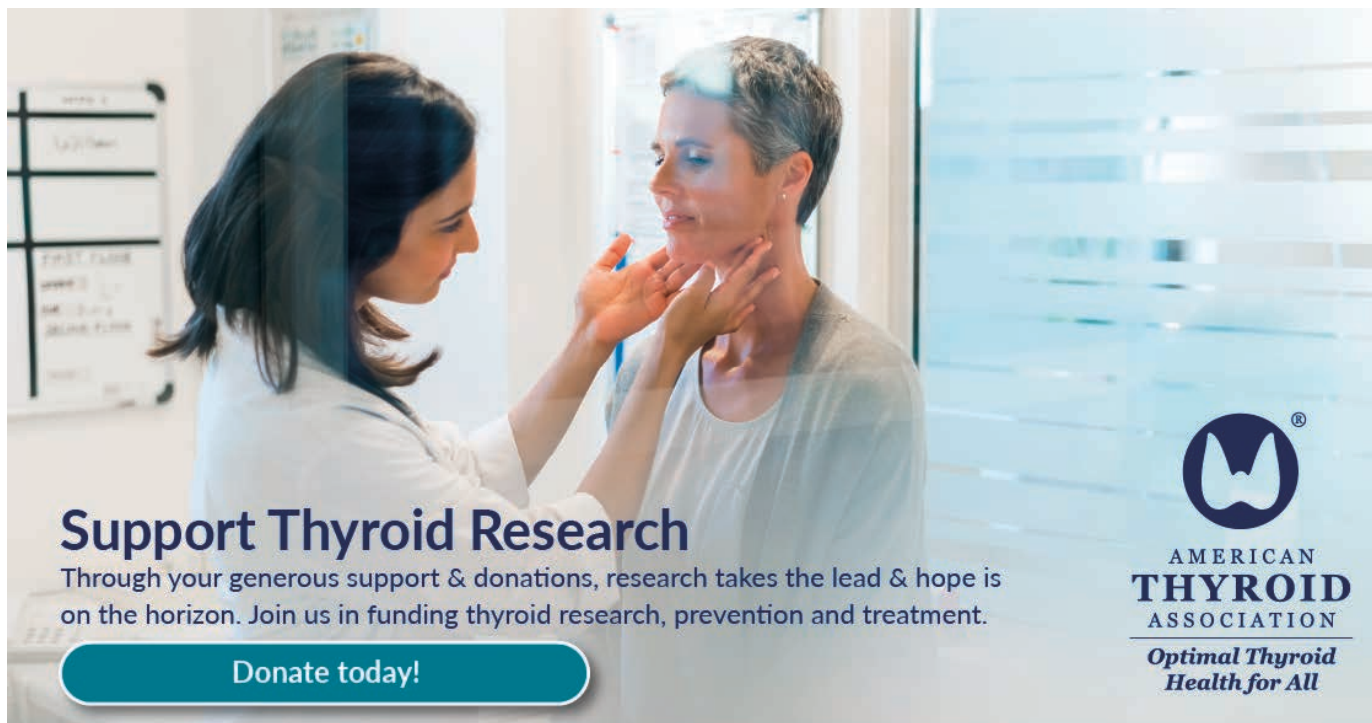
Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>

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

### ABBREVIATIONS & DEFINITIONS

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


**Triiodothyronine (T3):** the active thyroid hormone, usually produced from thyroxine, available in pill form as liothyronine or Cytomel™.



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## AUTOIMMUNE THYROID DISEASE

### Role of serum thyroid antibody status in predicting cancer therapy–associated thyroid disease

#### BACKGROUND

A major breakthrough in treating non-thyroid cancer has been the development of a class of cancer drugs known as immunotherapy. These drugs activate a patient's own immune system to attack and destroy cancer cells. One of the more effective cancer immunotherapy drugs belong to a class known as immune checkpoint inhibitors (ICI). Since these ICI drugs activate the patient's immune system, it is not surprising that other autoimmune diseases may develop or flare during the treatment with ICI. The thyroid is one of the most common glands affected and ICI drugs can cause both hyperthyroidism and hypothyroidism.

Autoimmune thyroid disease, where antibodies get confused and attack the thyroid, is the most common cause of hyperthyroidism and hypothyroidism. Serum thyroid peroxidase antibodies (TPOAbs) and thyroglobulin antibodies (TgAbs) are positive in up to 90% of patients with autoimmune thyroid disease. The role of these antibodies in the pathogenesis of ICI-related thyroid disease remains poorly understood. The goal of this study was to characterize the association of TPOAb and TgAb with the development of ICI-related thyroid disease and to examine the role antibodies may play as to predict the development of ICI-related thyroid disease.

#### THE FULL ARTICLE TITLE

Muir CA et al 2022 Association of antithyroid antibodies in checkpoint inhibitor-associated thyroid immune-related adverse events. *J Clin Endocrinol Metab* 107(5):e1843–e1849. PMID: 35104870.

#### SUMMARY OF THE STUDY

The authors performed a study of adults with melanoma undergoing ICI treatment to characterize the association of antithyroid antibodies with the development of thyroid ICI-related thyroid disease. Serum samples, collected prior to the first dose of ICI and at the onset of any ICI-related thyroid disease (or 30–60 days after first dose of ICI in

patients who remained with normal thyroid function), were retrieved to measure TPOAbs and TgAbs. Additional demographic, treatment, and cancer outcome information was obtained from a central database. The study measured the change in serum TPOAb and TgAb levels from baseline and during ICI treatment and whether increases in antibodies were associated with the development of ICI-related thyroid disease. Change from baseline was defined as new antibody positivity or a >50% increase in level for patients with baseline antibody-positive status. The average age was 65 years; 60% were male, reflecting the male predominance in melanoma diagnoses. The average follow-up time was 13.8 months.

Of 122 patients with paired samples, only 31 (25%) remained with normal thyroid function. For the other 75% of patients, the first thyroid function abnormality was mild hyperthyroidism in 47 (39%), overt hyperthyroidism in 37 (30%), and overt hypothyroidism in 7 (6%). A positive baseline TPOAb level was present in 19 patients (16%), with TgAbs present in 28 patients (23%); 16 patients (13%) were positive for both antibodies. Positive TPOAb/TgAb levels at baseline were 97% and 100%, respectively, specific for the eventual development of a ICI-related thyroid disease. In patients with positive baseline TPOAb and TgAb levels, the average antibody titer was statistically significantly higher in patients who developed overt ICI-related thyroid disease (thyrotoxicosis or hypothyroidism). Although those who were negative for thyroid antibodies at baseline were at lower individual risk of thyroid dysfunction, this group comprised most of the people who developed overt thyroid dysfunction in the study.

Only overt thyrotoxicosis was associated with a statistically significant rise in thyroid autoantibody titer as compared with baseline. In patients with overt hyperthyroidism, TgAb positivity (but not TPOAb positivity) was associated with progression to permanent hypothyroidism.





## AUTOIMMUNE THYROID DISEASE, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that almost all patients with positive TPOAb or TgAb titers at baseline developed a thyroid ICI-related thyroid disease, although the majority of patients who developed overt hyperthyroidism or hypothyroidism were antibody-negative at baseline. A higher level of antithyroid antibody at baseline may predict the

development of overt versus mild disease. Overt hyperthyroidism was associated with a significant increase in TPOAb and TgAb titers and the development of new thyroid antibodies. Both Oncologists as well as Endocrinologists need to be aware of these findings since the use of ICI drugs are increasing all the time.

— Alan P. Farwell, MD

### ATA THYROID BROCHURE LINKS

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

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

### ABBREVIATIONS & DEFINITIONS

**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).

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

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

**Overt Hypothyroidism:** clear hypothyroidism an increased TSH and a decreased T4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

**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.

**Subclinical Hyperthyroidism:** a mild form of hyperthyroidism where the only abnormal hormone level is a decreased TSH.

**Overt Hyperthyroidism:** clear hyperthyroidism a decreased TSH and an increased T4 level. All patients with overt hyperthyroidism are usually treated with antithyroid meds.

**TPO 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.

**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.



# 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.



ThyCa: Thyroid Cancer  
Survivors' Association, Inc.<sup>TM</sup>  
[www.thyca.org](http://www.thyca.org)



MCT8 - AHDS  
Foundation

THYROID CANCER  
ALLIANCE



Thyroid Cancer Canada  
Cancer de la thyroïde Canada



Thyroid  
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### American Thyroid Association

[www.thyroid.org](http://www.thyroid.org)

ATA Patient Resources:

[www.thyroid.org/thyroid-information/](http://www.thyroid.org/thyroid-information/)

Find a Thyroid Specialist: [www.thyroid.org](http://www.thyroid.org)

(Toll-free): 1-800-THYROID

[thyroid@thyroid.org](mailto:thyroid@thyroid.org)

### Bite Me Cancer

[www.bitemecancer.org](http://www.bitemecancer.org)

[info@bitemecancer.org](mailto:info@bitemecancer.org)

### Graves' Disease and Thyroid Foundation

[www.gdatf.org](http://www.gdatf.org)

(Toll-free): 877-643-3123

[info@ngdf.org](mailto:info@ngdf.org)

### Light of Life Foundation

[www.checkyourneck.com](http://www.checkyourneck.com)

[info@checkyourneck.com](mailto:info@checkyourneck.com)

### MCT8 – AHDS Foundation

[mct8.info](http://mct8.info)

[Contact@mct8.info](mailto:Contact@mct8.info)

### Thyca: Thyroid Cancer Survivors' Association, Inc.

[www.thyca.org](http://www.thyca.org)

(Toll-free): 877-588-7904

[thyca@thyca.org](mailto:thyca@thyca.org)

### Thyroid Cancer Alliance

[www.thyroidcanceralliance.org](http://www.thyroidcanceralliance.org)

[www.thyroidcancerpatientinfo.org](http://www.thyroidcancerpatientinfo.org)

Rotterdam, The Netherlands

### Thyroid Cancer Canada

[www.thyroidcancer canada.org](http://www.thyroidcancer canada.org)

416-487-8267

[info@thyroidcancer canada.org](mailto:info@thyroidcancer canada.org)

### Thyroid Federation International

[www.thyroid-fed.org](http://www.thyroid-fed.org)

[tfi@thyroid-fed.org](mailto:tfi@thyroid-fed.org)

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