Volume 14 | Issue 11 | November 2021

Clinical Thyroidology[®] for the Public

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AMERICAN **THYROID** ASSOCIATION **Optimal Thyroid Health for All**

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EDITOR'S COMMENTS2

Long-term benefits of thyroid surgery for Graves' disease

There are 3 options for treatment of Graves' disease: 1) antithyroid medications, 2) radioactive iodine therapy and 3) surgery. The current study compared the outcomes head to head of these 3 possible treatments. They looked at death, related health problems, health care cost, and the risk of relapse of the Graves' disease.

Liu X et al. Outcomes of Graves' disease patients following antithyroid drugs, radioactive iodine, or thyroidectomy as the first-line treatment. Ann Surg 273:1197–1206. PMID: 33914484.

Changes in thyroid function predict brain decline in the very old

Changes in thyroid function are common in older adults have been associated with brain impairment and dementia. Most of the prior studies included very small numbers of the oldest old, i.e., adults aged 85 years and older. This study aimed to examine the relationship between changes in thyroid function and brain function in adults aged 85 years and older.

Gan EH et al. Changes in serum thyroid function predict cognitive decline in the very old: Longitudinal findings from the Newcastle 85+ study. Thyroid. Epub 2021 Jun 2. PMID: 34074153.

HYPOTHYROIDISM

Is thyroid hormone treatment in hypothyroidism a risk factor for stroke?

High thyroid hormone levels, as seen in hyperthyroidism, increases the risk of atrial fibrillation and stroke. However, it is not clear if high thyroid hormones produced by thyroid hormone prescribed for treatment of hypothyroidism is associated with either atrial fibrillation or stroke. The aim of the study was to determine if abnormal thyroid hormone levels in patients taking thyroid hormone is associated with increased risks for atrial fibrillation and stroke over time.

Papaleontiou M et al 2021 Thyroid hormone therapy and incident stroke. J Clin Endocrinol Metab. Epub 2021 Jun 17. PMID: 34137866.

HYPOTHYROIDISM9 You may not need to stay on thyroid hormone replacement indefinitely

Thyroid hormone is one of the most commonly prescribed medications in the US, with most of these prescriptions for levothyroxine. In this study, the authors were interested in understanding the use of levothyroxine in the United States over time.

Brito JP et al 2021 Levothyroxine Use in the United States, 2008-2018. JAMA Intern Med. Epub 2021 Jun 21. PMID: 34152370.

THYROID CANCER.....II Is thyroid cancer really more common in women than men?

Thyroid cancer has always been diagnosed more commonly in women than in men, this difference became more pronounced in recent years. However, a clear biologic reason was not found to explain the difference. This study was designed to understand how thyroid cancer risk varied by sex.

LeClair K et al 2021 Evaluation of gender inequity in thyroid cancer diagnosis: Differences by sex in US thyroid cancer incidence compared with a meta-analysis of subclinical thyroid cancer rates at autopsy. JAMA Intern Med. Epub 2021 Aug 30. PMID: 34459841.

Barriers and motivations for doctors to use active surveillance in patients with thyroid cancer

Active surveillance was introduced into the American Thyroid Association guidelines for the treatment of thyroid cancer in 2015, but many doctors who treat patients with thyroid cancer have not yet started to use it. The purpose of this study was to find out what motivates or prevents thyroid cancer doctors to use active surveillance.

Jensen CB et al 2021 Active surveillance for thyroid cancer: A qualitative study of barriers and facilitators to implementation. BMC Cancer 21:471. PMID: 33910527.

ATA ALLIANCE FOR THYROID

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Clinical Thyroidology for the Public

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Editor's Comments

Welcome to another issue 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 <u>Twitter</u> at <u>@thyroidfriends</u> and on <u>Facebook</u>. 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. <u>thyroid.org/donate</u> 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/)

November is Hyperthyroidism Awareness Month.

In this issue, the studies ask the following questions:

- What are the long-term benefits of thyroidectomy for Graves' disease?
- Is a lower TSH later in life associated with dementia?
- Is thyroid hormone therapy associated with stroke?
- Is thyroid hormone over-prescribed in the United States?
- Is there gender inequity in the diagnosis of thyroid cancer?
- What are the barriers for active surveillance in thyroid cancer?

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

— Alan P. Farwell, MD,

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Clinical Thyroidology[®] for the Public

GRAVES' DISEASE

Long-term benefits of thyroid surgery for Graves' disease

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States. There are 3 options for treatment of Graves' disease: 1) antithyroid medications, 2) radioactive iodine therapy and 3) surgery. Radioactive iodine therapy and surgery are considered "definitive" therapy as they usually result in destroying the thyroid and causing hypothyroidism. In general, radioactive iodine therapy has been the most common treatment in the United States, followed by antithyroid medications. Surgery is often reserved for patients with bad eye disease or the need to control their hyperthyroidism immediately. However, surgery is utilized more frequently in other parts of the world with good outcomes.

The current study compared the outcomes head to head of the 3 possible treatments: antithyroid medications, radioactive iodine therapy and surgery. They looked at death, related health problems, health care cost, and the risk of relapse of the Graves' disease.

THE FULL ARTICLE TITLE

Liu X et al. Outcomes of Graves' disease patients following antithyroid drugs, radioactive iodine, or thyroidectomy as the first-line treatment. Ann Surg 273:1197–1206. PMID: 33914484.

SUMMARY OF THE STUDY

The authors enrolled more than 6000 patients with Graves' disease at a large medical center. Overall, 75%

initially were treated with antithyroid medications, 20% with radioactive iodine therapy and 5% with surgery. Patients that had surgery had a significant and remarkably lower all-cause risk of dying as well as lower rates of cardiovascular disease, neuropsychiatric symptoms, diabetes, and high blood pressure. They also had the lowest rate of disease relapse (return of Graves' disease) at 2.4% and the lowest direct health care costs at 10 years. Radioactive iodine therapy also had better outcomes that medication, but to a much lesser extent. Patients treated with radioactive iodine therapy also had a 20% relapse rate compared to 75% of those treated initially with medication.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Surgery is an excellent, and seemingly superior treatment for Graves' disease, resulting in lower all-cause death rate, less medical and psychological complications, minimal relapse risk, and lower overall health care costs long-term. The only downside is the expected permanent hypothyroidism. This is important information to be relayed to patients who are deciding on the best course of treatment for their Graves disease. Another important factor to consider is the experience of the surgeon, as the best outcomes come from high volume thyroid surgeons.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

Graves' Disease: <u>https://www.thyroid.org/graves-disease/</u> Graves' Eye Disease: <u>https://www.thyroid.org/graves-eye-disease/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u> Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u>

Clinical Thyroidology® for the Public (from recent articles in Clinical Thyroidology)

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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.

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.

Methimazole: an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease. **Propylthiouracil (PTU):** an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

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

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-I23 is the nondestructive 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*).

THYROID FUNCTION

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Changes in thyroid function predict brain decline in the very old

BACKGROUND

Changes in thyroid function are common in older adults, and both overactive thyroid (hyperthyroidism) and underactive thyroid (hypothyroidism) have been associated with brain impairment and dementia. However, the relationship between subclinical thyroid disease (i.e., a mild form of thyroid disease where the only abnormal hormone level is a thyroid stimulating hormone or TSH) and brain function remains unclear. Some prior studies have suggested that the risk of dementia in adults aged 65 years and older increased with low TSH, while mildly high TSH has been shown to be associated with preserved brain function and longevity. Most of these prior studies included very small numbers of the oldest old, i.e., adults aged 85 years and older. This study aimed to examine the relationship between changes in thyroid function and brain function in adults aged 85 years and older.

THE FULL ARTICLE TITLE

Gan EH et al. Changes in serum thyroid function predict cognitive decline in the very old: Longitudinal findings from the Newcastle 85+ study. Thyroid. Epub 2021 Jun 2. PMID: 34074153.

SUMMARY OF THE STUDY

This study included 642 participants from the Newcastle 85+ Study. Participants were 85 years and older from Newcastle and North Tyneside in the United Kingdom, had TSH levels between 0.1 and 10 mIU/L and normal free T_4 and free T_3 levels at baseline. Data collected included questionnaires, measurements such as height and weight, physical and brain testing, and fasting blood samples at baseline, 3 and 5 years. A change of 0.1 mIU/L in the TSH was defined as a change in thyroid function status. Patients taking medications that interfere with thyroid function tests, such as levothyroxine and amiodarone, and patients with overt hypothyroidism

or hyperthyroidism were excluded. Brain function was evaluated using the Mini-Mental State Examination (MMSE), with higher score denoting higher brain performance, and the Cognitive Drug Research (CDR) computerized assessment system which assesses memory and attention.

Overall, 58.1% of participants were women and 54.2% of them were alive for their 3-year follow-up. A total of 63.5% of participants had decreasing TSH over time. Patients with the lowest TSH at baseline had the highest rates of brain impairment and decreasing TSH over time was associated with decreasing scores on MMSE following 3 and 5 years. Lower free T_3 levels at baseline were also associated with development of brain impairment by 5 years. Changes in free T_4 and free T_3 over time were not associated with changes in brain function.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is an important study demonstrating that oldest old adults with decreasing TSH levels are more likely than those with steady levels to experience deterioration in memory and brain function. This may be related to either changes in the hypothalamus and pituitary due to increasing age or high burden of non-thyroidal illness in older adults. However, it is important to take other considerations into account, such as the fact that individuals with brain impairment and dementia have more chronic diseases and associated medication use which can lead to thyroid function changes. In addition, other factors that are associated with brain function issues in the oldest old, such as alcohol abuse, visual and hearing impairment, should be incorporated in future studies aiming to understand the complex relationship between thyroid function and brain function.

— Maria Papaleontiou, MD

THYROID FUNCTION, continued



ATA THYROID BROCHURE LINKS

Older Patients and Thyroid Disease: <u>https://www.thyroid.org/thyroid-disease-older-patient/</u> Thyroid Function Tests: <u>https://www.thyroid.org/thyroid-function-tests/</u>

ABBREVIATIONS & DEFINITIONS

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.

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 T_4 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.

Cognition: the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses.

Thyroxine (T₄): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

Triiodothyronine (T₃): the active thyroid hormone, usually produced from thyroxine.

Mini-Mental State Examination (MMSE): is a widely used test of cognitive function among older adults; it includes tests of orientation, attention, memory, language and visual-spatial skills. It is scored from 0 to 30 possible points, with higher score indicating higher cognitive performance. A normal cognitive status is defined as an MMSE score of 26 points or higher.

Cognitive Drug Research (CDR): computerized assessment system: Assesses episodic memory and attention.

Hypothalamus: this is an area of the brain that produces hormones that control body temperature, hunger, mood, and release of hormones from many glands, especially the pituitary gland.

Pituitary gland: this endocrine gland sits at the base of the brain and secretes hormones that control thyroid and adrenal function, growth and reproduction. The pituitary gland secretes TSH to control thyroid function.

HYPOTHYROIDISM

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Is thyroid hormone treatment in hypothyroidism a risk factor for stroke?

BACKGROUND

Hypothyroidism is a common condition and is treated with thyroid hormone. Levothyroxine was the third most commonly prescribed medication in the United States during 2017 and 2018. Typically, thyroid hormone therapy is lifelong once initiated. There are studies that have shown that despite the widespread use, thyroid hormone overtreatment and undertreatment are common but the long term adverse effects of both are unclear. Some studies have shown that high thyroid hormone levels, as seen in hyperthyroidism, increases the risk of heart disease, specific atrial fibrillation, and stroke. However, it is not clear if high thyroid hormones produced by thyroid hormone prescribed for treatment of hypothyroidism is associated with either atrial fibrillation or stroke.

Stroke is a leading cause of death and serious disability in the United States. Although there is a large amount of knowledge about risk factors for stroke, many of these factors cannot be changed (such as age and sex). Therefore, the attention has moved to identify risk factors that can be changed to reduce the risk of stroke.

The aim of the study was to determine if abnormal thyroid hormone levels in patients taking thyroid hormone is associated with increased risks for atrial fibrillation and stroke over time.

THE FULL ARTICLE TITLE

Papaleontiou M et al 2021 Thyroid hormone therapy and incident stroke. J Clin Endocrinol Metab. Epub 2021 Jun 17. PMID: 34137866.

SUMMARY OF THE STUDY

This study was done using data from 733,208 adult patients who received thyroid hormone therapy in the United States. These patients were followed between January 2004 and December 2017 at the Veterans Health Administration. Medical records of patients who were found to have at least two serum TSH measurements and at least two free thyroxine levels since the start of treatment until either the development of a stroke or atrial fibrillation or the conclusion of the study were selected for review.

Patients who had thyroid cancer (these patients are intentionally slightly over treated with thyroid hormone), or who were on lithium or amiodarone (these medicines may alter the results of thyroid function tests) were excluded from the analysis. Participants were grouped into categories according to TSH level : Serum TSH <0.1mIU/L; 0.1-0.5 mIU/L; >0.5-5.5 mIU/L and >5.5 mIU/L and free T₄ level <0.7 ng/dl;0.7 to 1.9 ng/dl and >1.9ng/dl. A normal thyroid level was considered as having a serum TSH between 0.5-5.5 mIU/L with a free T₄ between 0.7-1.9 ng/dl. The main outcomes measured were the onset of atrial fibrillation and acute stroke after having initiated thyroid hormone therapy.

Overall, 11.08% of patients developed atrial fibrillation, and 6.32% of patients had an acute stroke during time of study. Patients taking thyroid hormone and with a very low TSH (<0.1) or high free T₄ levels had a higher risk for stroke and atrial fibrillation when compared to patients with normal TSH and free T₄, after controlling for other risk factors such as smoking status, age, race, hypertension, diabetes mellitus among others. An unexpected finding was that the patients who had a high TSH or low free T₄ levels (undertreatment), also were found to have a higher risk of atrial fibrillation when compared to patients who had normal thyroid hormone levels. Another important observation is that the risks for atrial fibrillation and stroke continued to increase over time in patients who were overtreated and undertreated with thyroid hormone.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The conclusion of this study is that among patients treated with thyroid hormone, those who have higher or lower than normal thyroid hormone levels have a higher risk to develop a stroke or atrial fibrillation over time. Those



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HYPOTHYROIDISM, continued

patients with normal thyroid hormone levels did not have an increased risk, emphasizing the need to maintain normal thyroid levels in patients that are being treated with thyroid hormone. Although the findings related to low thyroid hormone levels while on treatment are not consistent with other studies, it highlights the need to design other clinical studies to help clarify this association. — Jessie Block-Galarza, MD

ATA THYROID BROCHURE LINKS

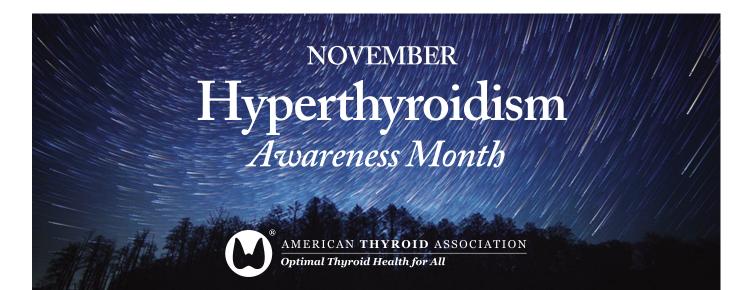
Thyroid Hormone Treatment: https://www.thyroid.org/thyroid-hormone-treatment/

ABBREVIATIONS & DEFINITIONS

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

Levothyroxine (T_4) : the major hormone produced by the thyroid gland and available in pill form as SynthroidTM, LevoxylTM, TirosintTM and generic preparations. TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

Atrial Fibrillation: An irregular heart rhythm which can lead to strokes.



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HYPOTHYROIDISM

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You may not need to stay on thyroid hormone replacement indefinitely

BACKGROUND

Thyroid hormone is one of the most commonly prescribed medications in the US, with most of these prescriptions for levothyroxine. Pharmacy filling of prescriptions of thyroid hormone have increased from 8.9 million in 2007 to 11.6 million in 2016, with 97% being for levothyroxine. The main clinical indication for the use of levothyroxine is overt hypothyroidism, a condition where the TSH level is increased and the FT₄ levels is low. On the other hand, subclinical hypothyroidism, where the FT₄ is normal with an increased TSH, is more common and treatment with levothyroxine is more controversial. Indeed, the treatment of subclinical hypothyroidism contributes significantly to the number of prescriptions.

In this study, the authors were interested in understanding the use of levothyroxine in the United States over time.

THE FULL ARTICLE TITLE

Brito JP et al 2021 Levothyroxine Use in the United States, 2008-2018. JAMA Intern Med. Epub 2021 Jun 21. PMID: 34152370.

SUMMARY OF THE STUDY

The authors were able to access a large data base called OptumLabs Data Warehouse which includes both commercially insured and Medicare Advantage enrollees in the US. Information on prescriptions and labs are available without specific patient identification. They identified adult patients who were newly started on levothyroxine and had a TSH measured within 3 months prior to starting the medication. They excluded patients with a history of thyroid surgery, thyroid cancer, central hypothyroidism and current pregnancy. A total of 110,842 patients were identified between 2008 and 2018. The average age was 46.1 and ~75% of patients were women. The average TSH was 5.3-5.8 mIU/L depending on the year.

There were 58,706 patients who also had thyroxine levels and were further classified according to their hormone status into overt hypothyroidism (elevated TSH with low thyroxine), mild subclinical hypothyroidism (TSH 4.5 to <10 mIU/L, normal thyroxine), moderate subclinical hypothyroidism (TSH 10–19.9 mIU/L, normal thyroxine), severe subclinical hypothyroidism (TSH >19.9 mIU/L, normal thyroxine) and normal thyroid function (normal TSH, normal thyroxine). Only 8.4% of the patients had overt hypothyroidism and 30.5% of patients had normal thyroid function. The remaining 61% were classified as subclinical hypothyroidism. There was a small increase over time in the proportion of patients with overt hypothyroidism (7.6% in 2008 to 8/4% in 2018) and a small decrease in those with severe subclinical hypothyroidism (2.5% in 2008 to 1.3% in 2018). The other classifications did not change significantly.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Only 10% of patients in this study had overt hypothyroidism prior to beginning thyroid hormone treatment. Of more concern, ~30% of prescriptions seemed to be for patients with normal thyroid function. There is no evidence that patients with normal thyroid function will benefit from thyroid hormone therapy. With regards to patients with subclinical hypothyroidism (as defined by an elevated TSH, normal thyroxine level), treatment is debatable.

The study is limited since it is retrospective and we cannot know how many patients were diagnosed with hypothyroidism and were on levothyroxine prior to entry into this database. In addition, we do not know how many patients with biochemical subclinical hypothyroidism had symptoms and do not know whether any of these patients had underlying autoimmune thyroiditis. However, it suggests that there are many patients on thyroid hormone who may not benefit from the medication. In particular, we know that TSH increases with age and the treatment of subclinical hypothyroidism has questionable benefit in patients 65 and older. In addition, in non-pregnant adults,

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HYPOTHYROIDISM, continued

treatment does not uniformly improve quality of life or thyroid related symptoms.

Thus, it is important for patients to discuss their expectations of treatment in detail with their physicians and particularly to repeat thyroid function tests prior to starting medication. It is also important to recognize that thyroid related symptoms can have other causes that need to be addressed to avoid the potential risks of thyroid hormone replacement and unnecessary costs.

– Marjorie Safran, MD

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ATA THYROID BROCHURE LINKS

Thyroid Function Tests: <u>https://www.thyroid.org/thyroid-function-tests/</u> Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u> Thyroid Hormone Treatment: <u>https://www.thyroid.org/thyroid-hormone-treatment/</u>

ABBREVIATIONS & DEFINITIONS

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 T_3 in various tissues in the body.

Levothyroxine (T_4) : the major hormone produced by the thyroid gland and available in pill form as SynthroidTM, LevoxylTM, TirosintTM and generic preparations.

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 T_4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

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Clinical Thyroidology[®] for the Public

THYROID CANCER

Is thyroid cancer really more common in women than men?

BACKGROUND

Thyroid ultrasound and biopsy have been used for evaluation of thyroid nodules since the 1970s. These methods improved detection and accurate diagnosis of thyroid cancer. At the same time pathology became more detailed and new technologies improved safety for thyroid surgeries. New cases of thyroid cancer more than tripled since 1990's in many countries. There had been a question whether this was due to a true increase in cancer or whether we were detecting the cancer more often with better tools or both. Thyroid cancer has always been diagnosed more commonly in women than in men, this difference became more pronounced in recent years. However, a clear biologic reason was not found to explain the difference. This study was designed to understand how thyroid cancer risk varied by sex.

THE FULL ARTICLE TITLE

LeClair K et al 2021 Evaluation of gender inequity in thyroid cancer diagnosis: Differences by sex in US thyroid cancer incidence compared with a meta-analysis of subclinical thyroid cancer rates at autopsy. JAMA Intern Med. Epub 2021 Aug 30. PMID: 34459841.

SUMMARY OF THE STUDY

The researchers used 2 large databases to collect information. Thyroid cancer incidence data from 1975 to 2017 were obtained from SEER (U.S. National Cancer Institute's Surveillance, Epidemiology, and End Results Program-9 Registries). Data for yearly thyroid cancer mortality from 1975 to 2017 were obtained from NVSS (Center for Disease Control and Prevention's National Vital Statistics System). They examined incidence trends (new cases per year) for thyroid cancer for women and men and performed a more detailed analyses by cancer type, stage and cancer size. The authors also identified autopsy studies that examined the entire thyroid gland and that reported the presence of small thyroid cancers that were unrelated to the cause of death and were only found at autopsy. Thyroid cancer diagnoses started to increase in the 1990's and peaked in 2013, mostly due to new diagnosis of papillary thyroid cancer. In the period of 1983 – 2017, the female-to-male ratio of all thyroid cancers was 2.75:1, while the female-to-male ratio of small (<2 cm), localized papillary thyroid cancer was 4.28:1. The ratios remained stable or decreased over time for all other papillary thyroid cancer sizes and for other types of thyroid cancer. As for the more lethal thyroid cancers (medullary and anaplastic), these were found equally in women and men. However, when all thyroid cancer types combined, women and men had an almost equal risk of death and this risk remained stable over time.

When they analyzed the data from autopsy studies that had reported small, incidentally found papillary thyroid cancer in patients who had died of other causes, they did not find any significant difference between women and men. (14% of women and 11% of men had papillary thyroid cancer only discovered at autopsy)

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The findings of this study do not support that women get thyroid cancer more often than men. Papillary thyroid cancer found at autopsy was similar between genders in autopsy studies. The difference between genders was due to detection of small papillary thyroid cancers more often in women. However, the increased detection in women was not associated with an improvement in survival, which is similar in both sexes.

These findings are very important for patients and their physicians. The ideal use of the advanced tools we have to evaluate thyroid abnormalities should be tailored to lead to early detection and treatment of clinically important cancers while avoiding overdetection and unnecessary treatment of clinically insignificant ones. The physicians should have a clear discussion with their patients about the risks, benefits, and extent of evaluation using the current guidelines.

— Ebru Sulanc, MD

THYROID CANCER, continued



ATA THYROID BROCHURE LINKS

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

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/

National Cancer Institute (NCI): a part of the National Institutes of Health in Bethesda, MD, the NCI is the federal government's primary agency for cancer research and training.

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.

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.

THYROID CANCER

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Barriers and motivations for doctors to use active surveillance in patients with thyroid cancer

BACKGROUND

Surgery is the usual recommendation for treatment of thyroid cancer. However, there is evidence that patients with small, low-risk thyroid cancers may not need surgery if they can be followed with ultrasound monitoring. This option is called active surveillance. Doctors in Japan first studied how these low-risk thyroid cancers tend to stay the same size and not to spread after being followed for many years. Then, doctors in many other countries, including the United States, were able to show similar results when following their patients over several years without surgery. Active surveillance was introduced into the American Thyroid Association guidelines for the treatment of thyroid cancer in 2015, but many doctors who treat patients with thyroid cancer have not yet started to use it. The purpose of this study was to find out what motivates or prevents thyroid cancer doctors to use active surveillance.

THE FULL ARTICLE TITLE

Jensen CB et al 2021 Active surveillance for thyroid cancer: A qualitative study of barriers and facilitators to implementation. BMC Cancer 21:471. PMID: 33910527.

SUMMARY OF THE STUDY

Doctors who treat thyroid cancer were selected for interview at a meeting of the American Thyroid Association. The study coordinators picked 12 endocrinologists and 12 surgeons for the study. The doctors were asked their opinions about several possible patient scenarios and asked questions about the guidelines for active surveillance, any thoughts or concerns they have about active surveillance, and how they use active surveillance with their own patients. After the interviews, the researchers then analyzed and grouped together factors that might have been motivations to using active surveillance and factors that might have been barriers. They found that many doctors were worried that they would feel guilty if a bad outcome occurred, that a patient might get lost to follow-up, or that other doctors might not refer patients to them if they learned that this thyroid cancer specialist uses active surveillance with their patients. Other doctors were concerned that the evidence behind the guidelines did not have enough data from the United States or that the guidelines were not clear enough on how active surveillance should be done safely. In addition to these barriers to active surveillance, the doctors also identified some motivations to use active surveillance with their patients. They would be able to make a shared decision with their patients about active surveillance, the process could be done in a multidisciplinary approachmeaning that doctors from different specialties would work together, and that this would be good for patients who have a fear of the risks of surgery.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that there were many factors that either motivated or were barriers to thyroid cancer doctors in adding active surveillance to their practice. This study is important for patients because it shows that discussing the options for treatment of small, low-risk thyroid cancer with their doctors is crucial to making a decision that is best for both the doctor and the patient.

— Dana Larsen, MD and Maria Brito, MD

ATA THYROID BROCHURE LINKS

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

Clinical **Thyroidology®** for the **Public** (from recent articles in *Clinical Thyroidology*)

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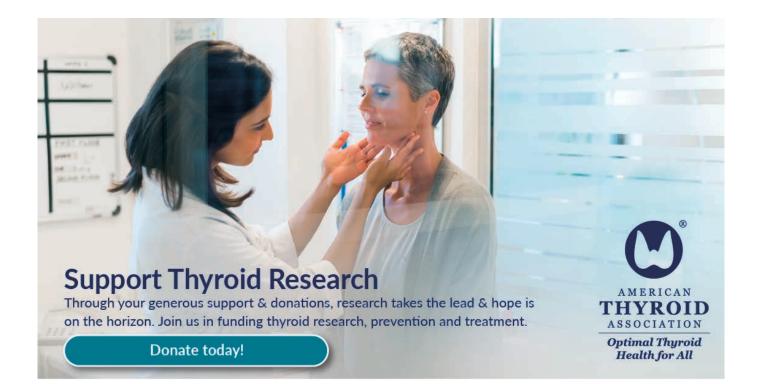


THYROID CANCER, continued



ABBREVIATIONS & DEFINITIONS

Active surveillance: the term for avoiding surgery for small thyroid cancers by monitoring them over time with ultrasound and physical exam **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.





ATA Alliance for Thyroid Patient Education

Foundation

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.





CANCER









Thyroid Cancer Canada Cancer de la thyroïde Canada

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

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

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