Volume 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

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 X (previously known as Twitter) at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association®, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association, 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.

September is Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- How scared are we of Thyroid Cancer?
- Can thyroid nodules known to be cancerous, or that are suspected to be cancerous, be safely watched over time instead of being removed with surgery?
- Is radiofrequency ablation superior to surgery for management of low-risk multifocal papillary thyroid microcarcinoma?
- Can AI help us to standardize ultrasound classification of thyroid nodules?
- Does levothyroxine treatment for subclinical hypothyroidism in pregnancy decrease risk of pregnancy loss?
- Can Teprotumumab help patients with chronic TED without evidence of active ongoing inflammation?

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 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

THYROID CANCER

How scared are we of Thyroid Cancer?

BACKGROUND

When someone is diagnosed with cancer, it often brings about a lot of negative emotions and fear. This fear happens largely because people don't always understand that there are differences between various cancer types and not all cancers are deadly. Patients with thyroid cancer experience fear similar to patients with more aggressive cancers, even though thyroid cancer usually has a very good outlook and has a good chance of being treated successfully.

Strong emotions like fear can affect how we behave and make decisions. Findings from past research suggest that fear related to cancer might lead some patients to choose more complicated treatments than necessary, just to be safe. This can sometimes cause more problems than if they had chosen a less aggressive treatment. To avoid making treatment decisions driven by fear, it is important to understand where this fear comes from and address it. This way, we can help reduce anxiety and make sure that treatment decisions are based on real risks associated with the specific type of cancer.

There hasn't been a study specifically focusing on fear related to thyroid cancer in the U.S. population. The researchers designed this study to find out how common this fear is among patients with thyroid cancer in the US and identify factors that might be contributing to higher levels of fear.

THE FULL ARTICLE TITLE

Taylor SR et al. Assessing Fear of thyroid cancer in the general U.S. population: A cross-sectional study. Thyroid 2024;34(2):234-242; doi: 10.1089/thy.2023.0479. PMID: 38115606.

SUMMARY OF THE STUDY

The researchers used an online survey platform. They included people over 17 that matched the US Census population in terms of age, gender, and race. Respondents with a history of cancer (other than certain skin cancers) were excluded from the study. The questions were about people's age, thyroid health, general health, cancer experiences, cancer risk factors, and knowledge about thyroid cancer. To measure fear of thyroid cancer, they used a special scale originally designed for breast cancer. Answers were scored and grouped into low (8-15), moderate (16-23), or high (24-40) levels of fear. The survey also had questions to make sure respondents were paying attention, and those who answered these incorrectly were not included in the results.

There were 1136 respondents who met the inclusion criteria. Half (50%) were women, most (74%) white, and many felt they didn't know much about thyroid cancer. Overall, 51% overestimated the average lifetime risk of developing thyroid cancer and most (89%) underestimated the overall survival of thyroid cancer.

About half of the respondents (47.5%) had a high level of thyroid cancer fear. These respondents were more likely to be women and younger than 40. They were more likely to feel that they couldn't do much to prevent thyroid cancer and to automatically think of death when thinking about thyroid cancer.

Respondents with a high level of thyroid cancer fear also tended to think that their risk of getting thyroid cancer was higher than it actually is and were more likely to underestimate how well patients with thyroid cancer actually do compared to respondents who had low or moderate levels of thyroid cancer specific fear.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that thyroid cancer-specific fear is common among US adults especially in women and those younger than 40. Most survey respondents had limited knowledge about thyroid cancer. Those who were generally more afraid of cancer tended to have higher

THYROID CANCER, continued

fear levels about thyroid cancer, which may be due to the mistaken belief that all cancers are equally dangerous. These findings are important because fear is a strong emotion that can lead to a fight or flight response and can affect how people choose their treatments. This can lead patients to select riskier treatments or even avoid getting checked altogether. Further studies are needed to understand common misconceptions about thyroid cancer, and educational programs are needed to improve thyroid cancer knowledge and to reduce fear before diagnosis.

— Ebru Sulanc, MD

ATA RESOURCES

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

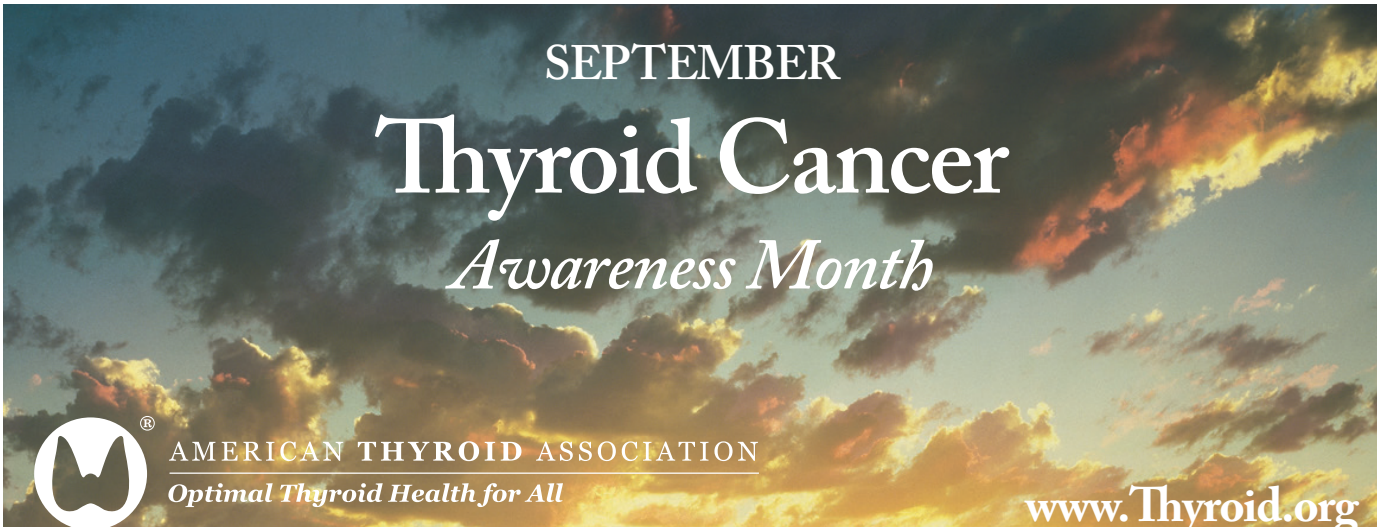
ABBREVIATIONS & DEFINITIONS

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

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

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.



AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

THYROID CANCER

Can thyroid nodules known to be cancerous, or that are suspected to be cancerous, be safely watched over time instead of being removed with surgery?

BACKGROUND

The development of nodules inside the thyroid gland, a butterfly-shaped organ in the front part of the neck that makes thyroid hormone, is very common. While the vast majority of thyroid nodules are benign (not cancerous), many thyroid nodules are biopsied to determine which may be cancerous. When these biopsies show thyroid cancer, or are suspicious for thyroid cancer, thyroid surgery is usually performed to remove at least that part of the thyroid containing the cancerous/possibly cancerous growth. This is done to prevent a thyroid cancer from growing and/or spreading to other parts of the body, which might cause significant illness or even death.

Several recent studies, however, suggest that when a thyroid cancer is very small (less than 1 cm in diameter, called microcarcinomas), most will never grow or spread to other parts of a person's body. For this reason, some doctors are now recommending watching these small thyroid cancers over time with ultrasound imaging (which is the best way to look at the thyroid), deferring surgery until the small cancer starts to grow. This is called active surveillance. Because most of these small cancers do not grow, or show evidence of trying to spread out of the thyroid over time, many people who have these small cancers might be able to avoid thyroid surgery.

Because of these findings, some researchers, are now interested in knowing if larger thyroid cancers, or larger nodules that are suspicious for cancer after a biopsy, may also be safely watched over time by ultrasound imaging. This study examined the results of active surveillance with nodules >1 cm that are either cancerous or suspicious for cancer.

FULL ARTICLE TITLE

Altshuler B et al. Non-operative, active surveillance of larger malignant and suspicious thyroid nodules. J Clin Endocrinol Metab. Epub 2024 Feb 13:dgae082. doi: 10.1210/clinem/dgae082. PMID: 38349208.

SUMMARY OF THE STUDY

The authors of this work identified 69 adults who were diagnosed with a thyroid nodule > 1 cm and for which a biopsy showed either thyroid cancer, was suspicious for cancer, between the years of 2001 and 2021. The people studied had not undergone thyroid surgery because of underlying health problems that might have made surgery too dangerous or because they voluntarily chose not to undergo thyroid surgery. Most of the people in the study were women (56 of 69). The thyroid nodule was >1 cm but <2 cm for 58 (84%) of the people studied, while the nodule was > 2 cm for the remaining 11 (16%) people in the group. The thyroid nodule biopsy showed thyroid cancer for 14 people in the study, with the remaining 55 having biopsies suspicious for thyroid cancer. The study group was monitored with repeated ultrasound imaging for an average of 55 months (about 5 years).

Over the average time of about 5 years, 15 people in the study were found to have significant increase in the size of their thyroid nodule (by at least 0.3 cm) and 17 study members had their nodules increase in volume by at least 50%. Overall, 13 people in the study ended up having thyroid surgery, and 9 of these proved to be cancerous when the removed thyroid was analyzed after surgery. None of the people in the study died of thyroid cancer or were found to have evidence of thyroid cancer spread to other parts of the body during the study period.

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that some thyroid cancers >1 cm in size may not need to undergo immediate surgical removal after being diagnosed by biopsy and can be followed by active surveillance. It is very important to understand that much bigger studies are needed to verify that thyroid cancers >1 cm can be safely watched over time instead of being removed surgically, which is generally safe and effective when performed by a surgeon who specializes in thyroid surgery. It is also very important to understand that there are no effective medicines for treating thyroid cancer and that thyroid cancer, if not removed with surgery, might grow and spread, ultimately causing significant illness or even death.

— Jason D. Prescott, MD PhD

ATA RESOURCES

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

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

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

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

ABBREVIATIONS & DEFINITIONS

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.

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

Suspicious thyroid biopsy: this happens when there are atypical cytological features suggestive of, but not diagnostic for malignancy. Surgical removal of the nodule is required for a definitive diagnosis.

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*.

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).

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

Active Surveillance: following small thyroid cancers by ultrasound rather than removing them by surgery

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

THYROID CANCER

Is radiofrequency ablation superior to surgery for management of low-risk multifocal papillary thyroid microcarcinoma?

BACKGROUND

Thyroid cancer has been one of the fastest rising cancer over the last 10 years. Fortunately, the prognosis for thyroid cancer is excellent as there are very effective treatments. The initial treatment for thyroid cancer is usually surgery. Many of the thyroid cancers diagnosed are small cancers (<1 cm), known as papillary microcarcinoma. Because of the excellent prognosis, the approach to the management of papillary microcarcinoma has shifted to deferring surgery and monitoring with ultrasound, known as active surveillance. However, due to an increase in worry and anxiety associated with a cancer diagnosis, active surveillance is not a option for many patients.

One way of treating recurrent thyroid cancer without surgery is to use heat to try and destroy the involved nodule(s). The most common option is using radiowave-based heat (radiofrequency ablation, RFA). This is done by inserting a fine needle through the skin into the nodule(s). The tip of this needle then delivers heat to the nodule, burning the nodule from the inside out and, as a result, hopefully destroying any cancer cells inside the nodule. In this study, the researchers evaluate RFA as an option to treat papillary microcarcinoma as an alternative to surgery in patients that are not interested in active surveillance.

THE FULL ARTICLE TITLE

Yan L et al Five-year outcome between radiofrequency ablation vs surgery for unilateral multifocal papillary thyroid microcarcinoma. J Clin Endocrinol Metab 2023;108(12):3230-3238; doi: 10.1210/clinem/dgad360. PMID: 37318878.

SUMMARY OF THE STUDY

This is a study of adult patients with thyroid microcarcinoma diagnosed on biopsy treated at Chinese PLA General Hospital between 2014 and 2017, with a minimum follow-up of 60 months. Worth mentioning, that the Chinese guidelines recommended surgery as the standard treatment for papillary microcarcinoma. Thus, RFA was only used if patients declined or were not candidates for surgery. The goal was to analyze growth of the cancer, either as persistent or recurring cancer, or development of spread of the cancer to the lymph nodes. Other goals included treatment variables, including procedure time and cost, treatment complications, and the need for delayed surgery after RFA.

A total of 44 patients that received RFA were compared to 53 patients that underwent surgery (lobectomy group). These patients were followed for an average of 73 months. The rate of cancer progression was the same in both groups, and no patient in either group developed spread of the cancer outside the neck. The RFA group had shorter hospitalization times, shorter procedure time, and lower associated costs than the lobectomy group while the lobectomy group had a higher procedure-related complications. However, no group had permanent complications.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that RFA of papillary microcarcinoma is comparable to lobectomy in terms of the low chances of cancer progression. RFA also had a lower procedure and hospitalization time, lower cost, and lower rates of treatment-related complications than lobectomy. This is a small study but suggests that RFA is safe and effective for treatment of papillary microcarcinoma. Larger studies are needed to confirm these findings.

— Joanna Miragaya, MD

THYROID CANCER, continued

ATA RESOURCES

Fine Needle Aspiration Biopsy of Thyroid Nodules: https://www.thyroid.org/fna-thyroid-nodules/
Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/
Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS & DEFINITIONS

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

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).

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

Radiofrequency ablation (RFA): using radiowave-based heat delivered by a needle to destroy abnormal tissue or lymph nodes containing cancer.

Lobectomy: surgery to remove one lobe of the thyroid.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

THYROID NODULES

Can AI help us to standardize ultrasound classification of thyroid nodules?

BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of individuals. The concern about any nodule is whether it is a cancer. Fortunately, only ~5-6% of nodules are cancerous. Ultrasound is the most common technique used to distinguish which nodules require further evaluation with biopsy or surgery and which can be watched. Features of the ultrasound images can be used to determine the risk that the nodule is a cancer and decide which should be biopsied. Clinicians look for different features of the nodules that are concerning for cancer, such as darkness (hypoechoic), a mostly solid composition, a taller-than-wide shape, irregular margins, or the presence of calcifications within the nodule. None of these features are individually diagnostic and thus several systems, combining these features, are described to determine the risk of a given nodule. The one developed by the American College of Radiology (American College of Radiology Thyroid Imaging and Reporting Data System - ACR TI-RADS) is frequently used and has been shown to helpful to avoid unnecessary biopsies. However, even in this well-developed system, there is variation within individual readings and, even more so, between readers.

This study was performed to evaluate a specific artificial intelligence (AI) decision-support system (DSS), called Koios DS, to determine if this would improve the diagnostic accuracy and consistency among different readers.

THE FULL ARTICLE TITLE

Fernández Velasco P et al. Clinical evaluation of an artificial intelligence-based decision support system for the diagnosis and American College of Radiology Thyroid Imaging Reporting and Data System classification of thyroid nodules. Thyroid 2024;34(4):510-518; doi: 10.1089/thy.2023.0603. PMID: 38368560.

SUMMARY OF THE STUDY

This was a study of the ultrasound imaging of all nodules with cytological and/or histological results from a thyroid nodule clinic referral unit of a university hospital. It included all consecutive patients over 18 years of age with thyroid nodules and at least two ultrasound images with cytologic and/or histologic findings evaluated from June 2021 to December 2022.

The Koios DS uses ACR TI-RADS descriptors and scoring and gives an AI-derived adaptor that downgrades or upgrades the initial score. Six experienced clinicians were trained in the use of Koios DS and evaluated the ultrasound images from 172 patients twice, both with and without the AI adjustment. The classifications were compared between the two readings and to the patients' histologic and/or cytologic findings.

A large number of nodules (81.3%) initially classified as ACR TI-RADS 3 (mildly suspicious) were reclassified as lower-risk. A quarter of those classified as ACR TI-RADS 4 (moderately suspicious) were also put into lower-risk categories. The AI-based DSS was better able to identify nodules that were suspicious that actually had suspicious cytology (improved from 14% to 16.1%) as well as those that were benign/not suspicious appearing and actually were benign (improved from 94.5% to 96.4%). In addition, the correlation between the observers improved significantly using AI-based DSS as compared to without. The AI system alone, without reader intervention, also showed good diagnostic performance.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that AI has the potential to improve some of problems with ultrasound evaluations of thyroid nodules, thus improving diagnostic accuracy and consistency. It may also be helpful in supporting less

THYROID NODULES, continued

experienced clinicians and improving the risk assessment process. Its limitations are that images were all obtained on a single ultrasound and read by two physicians with 20 years experience with only two images selected to be read by experienced physicians. In the real-world, thyroid ultrasounds are often obtained by technicians with varying experience, multiple images are evaluated by the reading physicians who also have varying experience. Thus, it would be important to continue to evaluate the system under different conditions. However, if in future studies, these results are confirmed, it represents the potential to minimize the number of nodules requiring biopsies while still capturing those patients who would benefit from biopsy and/or surgery.

— Marjorie Safran, MD

ATA RESOURCES

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.

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.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

THYROID AND PREGNANCY

Does levothyroxine treatment for subclinical hypothyroidism in pregnancy decrease risk of pregnancy loss?

BACKGROUND

Thyroid hormone plays an important role in baby's development during pregnancy. During the critical period of development in early pregnancy, the mother's thyroid gland provides all the thyroid hormone needed for the baby. Therefore, it is important for pregnant women to have normal thyroid hormone levels. The most common type of thyroid abnormalities in pregnancy is subclinical hypothyroidism, a mild form of low thyroid hormone levels where the thyroid stimulating hormone (TSH) level is high but the free thyroxine (FT4) level is normal. This affects 3.5-14.4% of pregnancies, depending on the region of the world. Although subclinical hypothyroidism has been linked adverse pregnancy outcomes such as miscarriage and preterm delivery, it is not clear whether treatment with levothyroxine is always helpful. The current American Thyroid Association guideline has different recommendations for treatment of subclinical hypothyroidism in pregnancy based on thyroid peroxidase antibody (TPOAb) status and TSH levels.

Therefore, the authors of this study investigated possible impact of levothyroxine treatment of subclinical hypothyroidism in pregnancy divided into different TPOAb status and TSH levels.

THE FULL ARTICLE TITLE

Gao S et al. Levothyroxine treatment in pregnant women with thyroid stimulating hormone levels ranging between 2.5 and 10 mIU/L: A propensity score matched analysis. Thyroid . Epub 2024 Apr 26; doi: 10.1089/thy.2023.0662. PMID: 38666684.

SUMMARY OF THE STUDY

Data from 4370 Chinese pregnant women from the China Birth Cohort Study were included. Women with pregnancies with a single baby and no history of thyroid disease were previously recruited between 6-14 weeks of pregnancy and had TSH, FT4, and TPOAb levels measured. The participants were divided into four subgroups according to TPOAb status and TSH level: *subgroup A* (TSH 2.5-4.0mIU/L and TPOAb negative), *subgroup B* (TSH 4.0-10.0mIU/L and TPOAb negative), *subgroup C* (TSH 2.5-4.0mIU/L and TPOAb positive), and *subgroup D* (TSH 4.0-10mIU/L and TPOAb positive).

Of the 4370 participants, 31% (1342) were treated with levothyroxine and 69% (3028) were not. In the whole group, less women treated with levothyroxine had pregnancy loss (miscarriage or stillbirth) compared to those who were not treated with levothyroxine (4.8% vs 8.8%). In analyses taking account of other potential factors, treatment with levothyroxine was associated with about 33% lower risk of pregnancy loss and about 60% higher risk of small-for-gestational age birth. When the impact of levothyroxine treatment was assessed separately for each subgroup, levothyroxine treatment was associated with about 43% lower risk of pregnancy loss in subgroup A and B. However, levothyroxine treatment was associated with about two-times higher risk of preterm birth in subgroup C.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The findings of this study suggest that levothyroxine treatment of subclinical hypothyroidism starting in the first trimester of pregnancy may be associated with a lower risk of pregnancy loss and a higher risk of small-for-gestational age birth. Treatment of mildly elevated TSH at 2.5-4mIU/L with levothyroxine was associated with an increased risk of preterm birth. This study shows potential benefit of levothyroxine treatment of subclinical hypothyroidism with TSH > 4mIU/L, which is the cutoff for abnormal TSH in pregnancy suggested by the current American Thyroid Association guideline. Determining the "right" level of TSH to treat is important to minimize harm from treatment, since

THYROID AND PREGNANCY, continued

this study also suggests that treatment of only slightly elevated TSH may be associated with increased risks of preterm birth or small-for-gestational age birth. Further studies are needed to clearly define the best TSH cutoff for treatment of subclinical hypothyroidism and safety of levothyroxine treatment in pregnancy.

— Sun Lee, MD

ATA RESOURCES

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

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.

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.

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.

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

Clinical Thyroidology® for the Public

THYROID EYE DISEASE

Teprotumumab (TempezzaTM) and thyroid eye disease

BACKGROUND

Graves' disease is an autoimmune condition in which patients produce antibodies (TSI or TRAb) that attack the thyroid, turning it on and causing an overactive thyroid gland. This condition can be associated with inflammation of the eyes and the muscles that move the eyes, known as Thyroid Eye Disease (TED). This inflammation can also lead to enlargement of the muscles that control eye movements and cause eye bulging (proptosis), eye swelling and double vision. Mild TED is common and does not require treatment. However, moderate to severe TED can be devastating. Fortunately, this is seen only in a few patients with Graves' disease.

Until recently, treatment for TED was limited to radiation therapy to the eye sockets and surgery. The game-changer has been a drug known as Teprotumumab (TempezzaTM) which blocks receptors in the eye muscles that are associated with inflammation. This drug was FDA approved in 2020 for TED treatment. Initial studies demonstrated that Teprotumumab improved the eye symptoms of patients with severe, active TED. It was unknown whether Teprotumumab would be effective in chronic TED patients without evidence of active eye inflammation. This study sought to determine if Teprotumumab would be beneficial to patients with chronic TED without evidence of active ongoing inflammation.

THE FULL ARTICLE TITLE:

Douglas RS, Couch S, Wester ST, et al. Efficacy and safety of teprotumumab in patients with thyroid eye disease of long duration and low disease activity. J Clin Endocrinol Metab 2023;109(1):25-35; doi: 10.1210/clinem/dgad637. PMID: 37925673.

SUMMARY OF THE STUDY:

The study was conducted at 11 sites in the United States. Patients with stable or inactive TED were enrolled in the study and randomly assigned to receive 8 infusions of teprotumumab or placebo once every 3 weeks. Stable/inactive disease was defined as a Clinical Activity Score (CAS) ≤ 1 in both eyes prior to screening for at least 1 year. Patients with prior eye surgery, radiation or treatment with steroids in the prior 3 weeks were ineligible to be in the study. Patients were evaluated at baseline and every 3 weeks with the final assessment at week 24 for eye symptoms and adverse reactions. The main study outcome was to assess the effect of the drug or placebo on proptosis (eye bulging) at week 24. A total of 62 patients (42 teprotumumab group, 20 placebo group) were enrolled in the trial.

At week 24, patients treated with teprotumumab had significantly less proptosis compared to placebo (average reduction of -2.41 mm vs -0.92 mm). More patients with teprotumumab had a response to therapy compared to placebo (61.9% vs. 25%). A total of 6 patients treated with Teprotumumab also had eye MRI imaging at baseline and 24 weeks. MRI imaging demonstrated a reduction in eye muscle volume with Teprotumumab. Teprotumumab patients also experienced greater improvements in eye disease related quality of life compared to controls. There were no differences in improvement in double vision between groups. There were no unexpected adverse effects for teprotumumab treated patients compared to prior studies. Teprotumumab treated patients experienced significantly more muscle spasms, headaches, high blood pressure, elevated glucose and hearing impairments compared to placebo treated patients.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

Thyroid eye disease (TED) can cause chronic eye symptoms for patients with Graves' disease, including patients with chronic mild and less active eye disease. This study demonstrated that teprotumumab treatment significantly improved proptosis in patients with long standing TED with low or no evidence of active inflammation. This suggests that medical therapy with Teprotumumab can be considered in patients with stable, less active but symptomatic chronic thyroid eye symptoms after full discussion of the potential risks and benefits.

— Whitney Woodmansee MD

THYROID EYE DISEASE, continued

ATA THYROID BROCHURE AND WEBSITE LINKS

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

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

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

ABBREVIATIONS & DEFINITIONS: FROM ACTIVE LIST

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).

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.

Proptosis: Bulging of the eyes, also known as exophthalmos. Proptosis is the medical term for when one or both eyes protrude forward from the natural eye position in the eye socket. A common component of Thyroid Eye Disease (TED).

TSH receptor: A molecule (protein) located on the thyroid cell surface that binds TSH and stimulates the production of the thyroid hormones within the thyroid cell.

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

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 9 | September 2024

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 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 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