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Banigé M et al 2022 Neonatal screening for hyperthyroidism proof of concept. J Clin Endocrinol Metab 107(4):e1374–e1381. PMID: 34894265.

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Rao M et al 2022 Thyroid autoimmunity is not associated with embryo quality or pregnancy outcomes in euthyroid women undergoing assisted reproductive technology in China. Thyroid. Epub 2022 Dec 26. PMID: 36571280.

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Total thyroidectomy improves quality of life in children and adolescents with Graves' disease

Pediatric Graves' disease is rare, but it is associated with hyperthyroid symptoms that may significantly affect psychosocial and physical functioning. As is the case in adults, thyroid surgery is an effective treatment option in children and adolescents, although less utilized than antithyroid drugs and radioactive iodine therapy. The goal of this study was to describe the impacts on quality of life of total thyroidectomy in children with Graves' disease.

Halada S et al 2022 Impact of definitive surgery for Graves' disease on adolescent disease-specific quality of life and psychosocial functioning. Thyroid. Epub 2022 Oct 17.

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The relationship between surgeon volume and outcomes of parathyroid surgery

High calcium levels from primary hyperparathyroidism and can lead to health problems such as thinning of the bones

and kidney stones. The main treatment for hyperparathyroidism is surgery to remove the overactive gland, called a parathyroidectomy. The goal of this study was to investigate the relationship between surgeon volume and patient outcome for parathyroid surgery.

Gray WK et al 2022 Volume-outcome associations for parathyroid surgery in England: Analysis of an administrative data set for the Getting It Right First Time program. JAMA Surg. 2022;157(7):581-588. PMID: 35507350.

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The goal of thyroid hormone therapy in thyroid cancer is to keep the TSH within a certain range to prevent any stimulation of growth of any remaining thyroid tissue by increased levels of TSH. The current American Thyroid Association provides treatment ranges/goals for TSH levels based on risk of the cancer returning. This study was done to evaluate whether patients with thyroid cancer who have undergone surgery for this disease and are now being treated with levothyroxine are meeting their goal TSH level as per current clinical guidelines.

Yavuz DG et al et al. 2022 Assessment of attainment of recommended TSH levels and levothyroxine compliance in differentiated thyroid cancer patients. Clin Endocrinol (Oxf). Epub 2022 May 31. PMID: 35639050.

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Molecular tests improve the detection of medullary thyroid cancer for patients with thyroid nodules

Diagnosing medullary thyroid cancer (MTC) on thyroid biopsies is challenging; more than 50% of MTCs are missed. Failure to identify MTC in a thyroid nodule prior to surgery can result in insufficient initial thyroid surgery with a lower chance of cure and the need for re-operations. The aim of this study is to report the development of and evaluate the performance of a commercially available MTC classifier.

Randolph GW et al 2022 Preoperative identification of medullary thyroid carcinoma (MTC): Clinical validation of the Afirma MTC RNA-sequencing classifier. Thyroid 32:1069–1076. PMID: 35793115.

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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](https://twitter.com/thyroidfriends) and on [Facebook](https://www.facebook.com/thyroidfriends). Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association®*, *Bite Me Cancer*, *the Graves' Disease and Thyroid Foundation*, *the Light of Life Foundation*, *MCT8 – AHDS Foundation*, *ThyCa: Thyroid Cancer Survivors' Association*, *Thyroid Cancer Canada*, *Thyroid Cancer Alliance* and *Thyroid Federation International*.

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association® (ATA®) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA® mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA® is a 501(c)3 nonprofit organization and your gift is tax deductible.

April is **[Hashimotos Disease Awareness Month](#)**.

In this issue, the studies ask the following questions:

- Should we be screening babies for neonatal hyperthyroidism?
- Is thyroid autoimmunity still a risk factor for women with normal thyroid function undergoing fertility treatments?
- Should thyroidectomy be more common for treatment of Graves' disease in children?
- Is there a relationship between surgeon volumes and parathyroidectomy outcomes?
- How often do thyroid cancer patients on levothyroxine reach their recommended TSH ranges?
- Can molecular markers on thyroid biopsy samples increase the diagnosis of medullary 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



HYPERTHYROIDISM

Neonatal screening for hyperthyroidism

BACKGROUND

Neonatal screening for hypothyroidism is universal in the United States because starting levothyroxine as soon as possible in babies diagnosed with hypothyroidism is extremely important in making sure the brain develops normally. In contrast, hyperthyroidism in newborns is seen in 1:5600 live births, although severe cases requiring treatment is much less common and is seen in 1:12,174 live births. The most common cause of neonatal hyperthyroidism is due to thyroid stimulating antibodies in the mother with a history of Graves' disease crossing over the placenta to affect the baby's thyroid. In mothers with thyroid stimulating antibodies, the chances of her passing on to her baby is 1% to 5%. Since the risk is low, relying only on the history of the mother having Graves' disease might not be enough to detect those babies that are at risk of developing hyperthyroidism. Also, relying on the history and blood measurements of antibodies in the mother would not help to identify babies with rare genetic causes of hyperthyroidism. Sadly, around 25% of neonatal hyperthyroidism leads to increased early death from congestive heart failure and premature birth. Therefore, it is important to diagnose and treat early by using a screening test.

This study examines samples from the neonatal TSH screening program in France to determine a threshold to identify patients with neonatal hyperthyroidism.

THE FULL ARTICLE TITLE

Banigé M et al 2022 Neonatal screening for hyperthyroidism proof of concept. *J Clin Endocrinol Metab* 107(4):e1374–e1381. PMID: 34894265.

SUMMARY OF THE STUDY

Past data in France from 48 cases of neonatal hyperthyroidism (31 moderate and 17 severe) and 24,862 controls (newborns with TSH born on the same days as the newborns with hyperthyroidism) was collected. Neonatal hyperthyroidism was defined based on clinical suggestion, such as elevated heart rate, heart failure, very excitable, and poor weight gain, but the presence of enlarged thyroid was not necessary. Moderate neonatal hyperthyroidism was described as neonatal hyperthyroidism requiring long stay in hospital but not needing anti-thyroid drugs (ATD) treatment. Severe neonatal hyperthyroidism was described as neonatal hyperthyroidism requiring admission to the neonatal ICU and ATD treatment. TSH levels were analyzed on day 3 after birth, and cases of neonatal hyperthyroidism were separated in three groups (all cases, moderate, and severe) and compared with control cases.

Results showed that, while the average TSH level (0.57 mIU/L) for all neonatal hyperthyroidism cases was lower than control cases, it was not enough to clearly separate babies with hyperthyroidism with babies that were normal. However, using a screening TSH level of <0.18 mIU/L detected 25% of neonatal hyperthyroidism cases and all of the cases with a genetic cause. This limit showed potential for detection of severe neonatal hyperthyroidism.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors determined a screening TSH level <0.18 mIU/L checked on day 3 post-delivery is ideal to diagnose severe neonatal hyperthyroidism. Combining this threshold, along with a history of the mother having Graves' disease, the vast majority of babies with neonatal hyperthyroidism can be identified.

— Joanna Miragaya, MD and Ebru Sulanc, MD

ATA RESOURCES

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



HYPERTHYROIDISM, 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.

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.

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





THYROID AND PREGNANCY

Is thyroid autoimmunity still a risk factor in women undergoing fertility treatment?

BACKGROUND

Thyroid autoimmunity, or autoimmune thyroid disease, includes a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies are the most common cause of both hyperthyroidism (Graves' disease) and hypothyroidism (Hashimoto's thyroiditis). The antibodies can also be present in individuals with normal thyroid function. Thyroid autoimmunity has for many years been considered associated with a poor outcome in women undergoing fertility treatment. As with spontaneous pregnancies, thyroid autoimmunity was associated with a higher pregnancy loss rate and lower live birth rate. However, many initial studies were done in women who were being treated for autoimmune thyroid disease, namely hypothyroidism. Recent studies now question this association in women who have normal thyroid function.

This study investigated the association of thyroid autoimmunity with fertility treatment and live birth rates in a group of infertile women with normal thyroid function and positive thyroid antibodies.

THE FULL ARTICLE TITLE

Rao M et al 2022 Thyroid autoimmunity is not associated with embryo quality or pregnancy outcomes in euthyroid women undergoing assisted reproductive technology in China. *Thyroid*. Epub 2022 Dec 26. PMID: 36571280.

SUMMARY OF THE STUDY

This was a study of couples undergoing fertility treatment (either in vitro fertilization or intracytoplasmic sperm injection) in a hospital setting in China between 2016 and 2022. All included women had concentrations of serum

thyroid function tests within the laboratory reference range prior to treatment. Thyroid autoimmunity was defined as elevated serum thyroid peroxidase antibodies (TPOAbs) or thyroglobulin antibodies (TgAbs).

The study included 3444 cycles from 2945 women without thyroid autoimmunity and 499 women with thyroid autoimmunity. Thyroid autoimmunity-positive women were significantly older (average age 31.6 vs. 30.9) and had a higher TSH at baseline (average 2.40 vs. 2.21 mIU/L) than thyroid autoimmunity-negative women. The proportions of thyroid autoimmunity positivity was 13.6% in women <35 years of age and 17.3% in those ≥35. There were no significant differences between women with and those without thyroid autoimmunity in any of the many investigated outcomes. The main effect on outcomes was the age of the mother and was similar in women with and those without thyroid autoimmunity: age <35 years 10% early loss rate vs 22.5% early loss rate in those >35 years and live birth rates 63.9% in women <35 years vs 37.1% in those >35 years.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that thyroid autoimmunity had no effect on pregnancy outcomes after fertility treatment as long as the mother has normal thyroid function. There was a significant difference in outcomes based on age, but this was unaffected by thyroid autoimmunity. This is welcome information for women that have positive thyroid antibodies but normal thyroid function that are undergoing fertility treatment.

— Alan P. Farwell, MD



THYROID AND PREGNANCY, continued

ATA RESOURCES

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

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

Hashimoto's Thyroiditis: <https://www.thyroid.org/hashimotos-thyroiditis/>

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).

In-vitro or intracytoplasmic sperm injection fertilization: a procedure when an egg is fertilized outside of the body and then implanted in a woman to achieve a pregnancy

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.



GRAVES' DISEASE

Total thyroidectomy improves quality of life in children and adolescents with Graves' disease

BACKGROUND

Autoimmune hyperthyroidism, or Graves' disease, affects 1 in 10,000 in the United States, mostly adults. Treatment options for Graves' disease include antithyroid drugs, radioactive iodine therapy and surgery (thyroidectomy). Pediatric Graves' disease is rare, but it is associated with hyperthyroid symptoms that may significantly affect psychosocial and physical functioning. The most common treatment option for Graves' disease in children and adolescents are antithyroid drugs, but the relapse rate can be as high as 30 to 35% even after 5 years of treatment. Radioactive iodine therapy is less attractive in children and young adults because of the risk of causing or worsening thyroid eye disease. As is the case in adults, thyroid surgery is an effective treatment option in children and adolescents, although less utilized than antithyroid drugs and radioactive iodine therapy.

Health-related quality of life (QoL) has been studied in adults with Graves' disease, but no data have been reported in children with Graves' disease. The goal of this study was to describe the impacts on QoL of total thyroidectomy in children with Graves' disease.

THE FULL ARTICLE TITLE

Halada S et al 2022 Impact of definitive surgery for Graves' disease on adolescent disease-specific quality of life and psychosocial functioning. *Thyroid*. Epub 2022 Oct 17.

SUMMARY OF THE STUDY

Patients 12 to 19 years old who were pursuing total thyroidectomy for Graves' disease, along with their parents, were recruited to complete surveys before and at least 6 months after undergoing the procedure. Total thyroidectomy was performed by a high-volume, pediatric thyroid surgeon (defined as a surgeon who has completed at least 25 thyroid surgeries annually). Surveys assessed the reasons for pursuing a total thyroidectomy, QoL

scores and satisfaction with the surgery. Prior to surgery, parents shared their perceptions on the severity of their child's condition and their thoughts about the potential treatments for Graves' disease. Parents also rated their reasons for considering surgery from a list of potential factors. Disease-specific QoL, psychosocial functioning, and appearance concerns were assessed using questionnaires completed before and after total thyroidectomy. Baseline surveys only were completed by 37 patient–parent pairs, whereas 20 patient–parent pairs completed both the before and after total thyroidectomy surveys. At baseline, patients reported the presence of symptoms, including tiredness, anxiety, and emotional susceptibility, via the ThyPRO QoL questionnaire.

Overall, disease-specific QoL significantly improved following total thyroidectomy, with notable improvements associated with resolution of the goiter, hyperthyroid symptoms, tiredness, anxiety and emotional lability. Physical functioning also significantly improved after total thyroidectomy. Reported Graves' disease–associated thyroid eye disease symptoms were the second-lowest-scoring ThyPRO subscore at baseline, but they improved following surgery. Overall, families reported recovery from the surgery by an average of 2 months, high satisfaction with the outcomes of total thyroidectomy, and minimal concerns over the scar appearance. No permanent surgical complications were noted.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that total thyroidectomy for Graves' disease in pediatric populations may have substantial beneficial effects on disease-specific QoL and psychosocial functioning scores. An important aspect of this study was the involvement of high-volume thyroid surgeons, who have been shown to have a much lower complication rate than low-volume surgeons. Indeed, no permanent surgical complications were noted.



GRAVES' DISEASE, continued

Further studies are needed to confirm these findings and to compare the impact of total thyroidectomy versus

other treatment options (radioactive iodine therapy or antithyroid drugs) on QoL in children.

— Alan P. Farwell, MD

ATA RESOURCES

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

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

ABBREVIATIONS & DEFINITIONS

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*.

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.



HYPERPARATHYROIDISM

The relationship between surgeon volume and outcomes of parathyroid surgery

BACKGROUND

The parathyroid glands are 4 pea-sized glands located next to the thyroid gland in the neck. The parathyroid glands control the body's calcium levels. Occasionally, one or more of the 4 parathyroid glands becomes overactive and calcium levels increase. This is called primary hyperparathyroidism and can lead to health problems such as thinning of the bones and kidney stones. The main treatment for hyperparathyroidism is surgery to remove the overactive gland, called a parathyroidectomy. In the United States, an estimated 17,000 parathyroidectomies are performed each year. Complications of a parathyroidectomy include low calcium levels and damage to the vocal cords.

Studies focused on non-parathyroid surgeries have consistently found an association between surgeon volume and patient outcome. For example, patients who undergo thyroid surgery are less likely to experience complications from the surgery if a surgeon performs the surgery frequently (high-volume surgeon) than if a surgeon only rarely performs the surgery (low-volume surgeon). Less is known about whether such a relationship between surgeon volume and patient outcome exists for parathyroidectomies.

The goal of this study was to investigate the relationship between surgeon volume and patient outcome for parathyroid surgery in a population of patients who were admitted to a hospital for parathyroid surgery in England between April 2014 and March 2019.

THE FULL ARTICLE TITLE

Gray WK et al 2022 Volume-outcome associations for parathyroid surgery in England: Analysis of an administra-

tive data set for the Getting It Right First Time program. JAMA Surg. 2022;157(7):581-588. PMID: 35507350.

SUMMARY OF THE STUDY

The authors included data from 17,494 patients who underwent parathyroidectomies. Most of the patients studied were female (79.0%) and the average age was 62 (range 53-71) years. The surgeons were categorized based on how many parathyroid surgeries they performed in the previous 12 months: <10, 10-19, 20-29, 30-39, 40-49, and 50 or more. The authors found that a higher surgeon volume was associated with lower rates of repeat parathyroid surgery within 1 year of the first parathyroid surgery. Patients who underwent parathyroid surgery with surgeons who performed less than 20 parathyroid surgeries a year (compared to at least 20 parathyroid surgeries per year) were 80% more likely to have vocal cord problem affecting voice, 63% more likely to have a repeat parathyroid surgery within 1 year, 59% more likely to stay in the hospital for more than 2 days following the initial parathyroid surgery, and 30% more likely to experience a complication from surgery.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study provides evidence that patients have better outcomes after parathyroid surgery when they have the procedure performed by a higher volume surgeon. A minimum volume threshold of 20 parathyroid surgeries per year appears to be a reasonable target.

— Debbie Chen, MD

ATA RESOURCES

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



HYPERPARATHYROIDISM, continued

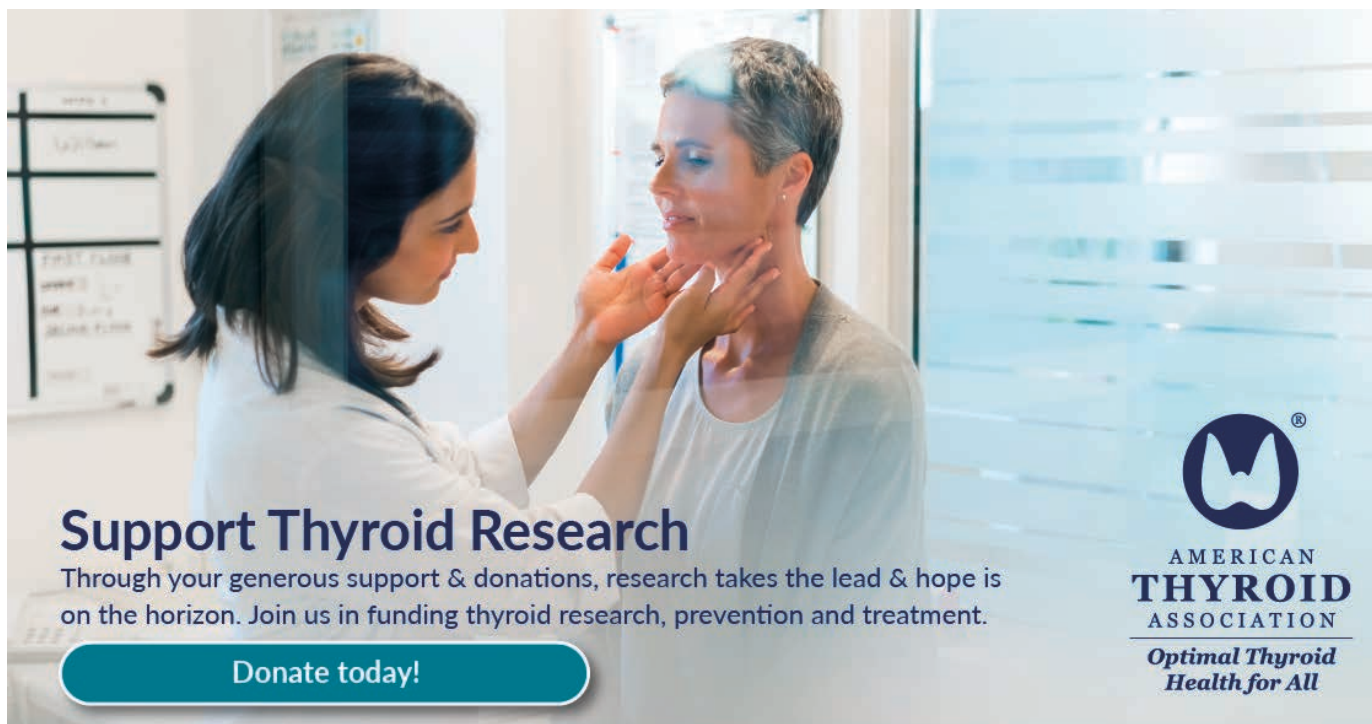
ABBREVIATIONS & DEFINITIONS

Hypoparathyroidism: low calcium levels due to decreased secretion of parathyroid hormone (PTH) from the parathyroid glands next to the thyroid. This can occur as a result of damage to the glands during thyroid surgery and usually resolves. This may also occur as a result of autoimmune destruction of the glands, in which case it is usually permanent.

Hypocalcemia: low calcium levels in the blood, a complication from thyroid surgery that is usually short-term and relatively easily treated with calcium pills. If left untreated, low calcium may be associated with muscle twitching or cramping and, if severe, can cause seizures and/or heart problems.

Parathyroid glands: usually four small glands located around the thyroid that secrete parathyroid hormone (PTH) which regulates the body's calcium levels.

Parathyroid hormone (PTH): the hormone that regulates the body's calcium levels. High levels of PTH cause hypercalcemia, or too much calcium in the blood. Low levels of PTH cause hypocalcemia, or too little calcium in the blood.



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THYROID CANCER

How many thyroid cancer patients on levothyroxine are meeting their treatment goals?

BACKGROUND

The first option to treat thyroid cancer is surgery to remove all or part of the thyroid. Based on the type and extent of cancer, treatment with radioactive iodine is the second option. The third option, which is often not thought of as a thyroid cancer treatment, is thyroid hormone therapy, usually in the form of levothyroxine. The goal of thyroid hormone therapy is to keep the TSH within a certain range to prevent any stimulation of growth of any remaining thyroid tissue by increased levels of TSH. The dose of thyroid hormone is decided based on maintaining the TSH level within a range based on the risk of the cancer returning. For example, the range in patients at high risk for the cancer returning is usually slightly low or low normal. In patients at low risk for the cancer returning, the range is usually within the normal range. The current American Thyroid Association guidelines provide treatment ranges/goals for TSH levels based on risk of the cancer returning.

This study was done to evaluate whether patients with thyroid cancer who have undergone surgery for this disease and are now being treated with levothyroxine are meeting their goal TSH level as per current clinical guidelines.

THE FULL ARTICLE TITLE

Yavuz DG et al et al. 2022 Assessment of attainment of recommended TSH levels and levothyroxine compliance in differentiated thyroid cancer patients. Clin Endocrinol (Oxf). Epub 2022 May 31. PMID: 35639050.

SUMMARY OF THE STUDY

This was a study of patients with thyroid cancer diagnosed at least 1 year prior to and following subtotal or total thyroidectomy across 21 centers in Turkey. Medical record review identified pertinent clinical data, including age, sex, cancer duration, medical problems, vital signs, surgical pathology, surgical type (total thyroidectomy or lobectomy), treatment with radioactive iodine, dose of levothyroxine, most recent thyroid function, and thyro-

globulin. Clinical parameters were used to establish cancer staging. Thyroid cancer risk was determined by American Thyroid Association guidelines and TSH targets were based on cancer risk and remission status. Participants were interviewed as to how often they were actually taking their levothyroxine and whether they missed any doses.

The group was composed of 1125 participants; average age was 50.7 years, the body-mass index (BMI) was 30.4, and 84% were women. The average levothyroxine dose of 132.4 µg (corresponding to a weight-based estimation of 1.7±0.5 µg/kg). Moderate to severe TSH suppression (<0.1 mU/L) was observed in 31%, mild suppression (0.1–0.5 mU/L) in 28%, normal range (0.5–4.0 mU/L) in 29%, and increased TSH (>4.0 mU/L) in 9%. Overall, only 29% of patients had TSH levels within their thyroid cancer risk-specific target range. Among the 50% of patients who were overtreated with levothyroxine, 80% had low-risk thyroid cancer.

Factors associated with greater TSH suppression between severely suppressed and nonsuppressed groups included shorter duration of cancer (3.8 vs. 5.6 years), lower BMI (28.5 vs. 31), higher levothyroxine dosing (138 vs. 127 µg and 1.9 vs. 1.6 µg/kg). Interestingly, patient age and thyroid cancer risk were not significant factors in TSH suppression. There were 83% of participants who had good or moderate adherence to therapy, and adherence to therapy was not associated with degree of suppression.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that most patients with thyroid cancer on levothyroxine take their medication regularly. However, a minority of patients actually achieved TSH levels within their target range. Further, many of the patients with suppressed TSH levels had low risk cancer. More awareness of the criteria and risks vs benefits of thyroid hormone treatment is needed.

—Vibhavasus Sharma, MD



THYROID CANCER, continued

ATA RESOURCES

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

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

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.

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

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



THYROID CANCER

Molecular tests improve the detection of medullary thyroid cancer for patients with thyroid nodules

BACKGROUND

Medullary thyroid cancer (MTC), a rare type of thyroid cancer, is usually more aggressive with higher death rates than the more common papillary or follicular thyroid cancers. To improve the outcome, it is important to detect and treat MTC early when the disease is confined to the thyroid gland, prior to the development of spread to the neck lymph nodes or distant metastases. Thyroid biopsy is an accurate and safe test available to differentiate between benign and suspicious or cancerous thyroid nodules; the results of this test have been used to guide treatment for thyroid nodules. However, diagnosing MTC on thyroid biopsies is challenging; more than 50% of MTCs are missed. In addition, according to the American Thyroid Association guidelines, routine screening for the presence of the MTC blood marker, calcitonin, is not recommended in patients with thyroid nodules, since MTC is very rare and other conditions not related to thyroid disease can result in falsely elevated levels. Because of frequent early neck lymph node involvement, more aggressive surgery is recommended at the time of the initial thyroid surgery for MTC. Failure to identify MTC in a thyroid nodule prior to surgery can result in insufficient initial thyroid surgery with a lower chance of cure and the need for re-operations.

The use of molecular testing in thyroid biopsies has improved the diagnosis for papillary and follicular thyroid cancer. These tests identify mutations in genes that are seen in thyroid cancer. If a thyroid biopsy has negative mutations, it is considered benign. However, initial molecular tests did not perform well for MTC. Veracyte Inc. has developed a novel algorithm to detect MTC in thyroid biopsies. The aim of this study is to report the development of and evaluate the performance of this commercially available MTC classifier.

THE FULL ARTICLE TITLE:

Randolph GW et al 2022 Preoperative identification of medullary thyroid carcinoma (MTC): Clinical validation

of the Afirma MTC RNA-sequencing classifier. Thyroid 32:1069–1076. PMID: 35793115.

SUMMARY OF THE STUDY:

Genes only expressed in MTC were identified using biopsy samples from 483 thyroid nodules and 97 surgical tissue samples. Among these, 21 biopsy specimens were from surgically confirmed MTC thyroid nodules and 462 specimens were from non-MTC thyroid nodules. A total of 8 different candidate gene groups were evaluated. The selected classifier included 108 genes.

The classifier was then validated using a separate group of 211 biopsy samples from patients with benign and cancerous thyroid nodules (21 MTC, 190 non-MTC) who underwent surgery and also had surgical tissue samples available. The classifier correctly identified as positive all 21 MTC samples and as negative all non-MTC samples. Of the MTC samples, 38% were initially diagnosed as atypical biopsy samples (Bethesda category III), 29% as indeterminate samples (Bethesda IV), and 33% as suspicious samples (Bethesda V). The non-MTC samples included benign thyroid nodules, malignant thyroid nodules (papillary, Hürthle, follicular, and poorly differentiated cancers), and chronic lymphocytic thyroiditis.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

A commercially available gene classifier showed excellent accuracy in diagnosing MTC in thyroid biopsy samples. The addition of molecular gene analysis can be useful in identifying this condition prior to the thyroid surgery. Given that MTC is rare, further studies will need to address how to select the patients with thyroid nodules who would benefit from this test.

— Alina Gavrilă, MD, MMSC



THYROID CANCER, continued

ATA RESOURCES

Medullary Thyroid Cancer: <https://www.thyroid.org/medullary-thyroid-cancer/>

Fine Needle Aspiration Biopsy of Thyroid Nodules: <https://www.thyroid.org/fna-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), 5-10% are cancerous (malignant).

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

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

Thyroid biopsy: 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.

Calcitonin: a hormone that is secreted by cells in the thyroid (C-cells). Calcitonin levels are increased in patients with medullary thyroid cancer.

Molecular markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and ThyroSeq™

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Mutation: A permanent change in one of the genes.

Indeterminate thyroid biopsy: this happens a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or Hurthle cell lesion. Follicular and Hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or Hurthle cell cancer from noncancerous nodules. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

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.



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Light of Life Foundation

www.checkyourneck.com

info@checkyourneck.com

MCT8 – AHDS Foundation

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Thyca: Thyroid Cancer Survivors' Association, Inc.

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