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Optimal Thyroid Health for All

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Burgos N et al 2020 Clinical outcomes after discontinuation of thyroid hormone replacement—A systematic review and meta-analysis. *Thyroid*. Epub 2020 Nov 9. PMID: 33161885

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van Trotsenburg AS et al. 2020 Congenital hypothyroidism: A 2020 consensus guidelines update An ENDO-European Reference Network (ERN) initiative endorsed by the European Society for Pediatric Endocrinology and the European Society for Endocrinology. *Thyroid*. Epub 2020 Dec 3. PMID: 33272083.

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Although many studies have shown that treating patients with subclinical hypothyroidism with thyroid hormone can improve some risk factors for heart disease, the data on whether this improves death from heart disease or death from any cause has not been clear. The authors of this study performed a large review of all the published studies done on this topic and combined the information from those studies to help answer this question.

Peng CC et al 2021 Association of thyroid hormone therapy with mortality in subclinical hypothyroidism: A systematic review and meta-analysis. *J Clin Endocrinol Metab* 106:292–303. PMID: 33107557.

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Chung SR et al 2020 Interobserver reproducibility in sonographic measurement of diameter and volume of papillary thyroid microcarcinoma. *Thyroid*. Epub 2020 Dec 7. PMID: 33287640.

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Endo M et al 2020 Features of cytologically indeterminate molecularly benign nodules treated with surgery. *J Clin Endocrinol Metab* 105:dga506. PMID: 32772084.

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Webb C et al 2020 Is thyroid cancer prognosis affected by solid organ transplantation? *Surgery*. Epub 2020 Aug 16. PMID: 32814633.

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

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

The Covid-19 pandemic has caused an unprecedented upheaval in our daily lives and presented extremely difficult challenges to our healthcare system. There is a lot of information circulating around. 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/>)

March is [Medullary Thyroid Cancer Awareness Month](#).

In this issue, the studies ask the following questions:

- Is thyroid hormone therapy lifelong for everyone?
- What is the best way to diagnose and manage congenital hypothyroidism?
- Does thyroid hormone therapy in subclinical hypothyroidism decrease the risk of death?
- How should significant growth of small thyroid cancers be measured during active surveillance?
- How can you predict which patients with indeterminate thyroid nodules with a 'benign' molecular test result actually have cancer?
- What is the risk of thyroid cancer after solid organ transplantation?

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,





HYPOTHYROIDISM

A third of patients treated for hypothyroidism may not require thyroid hormone therapy

BACKGROUND

Hypothyroidism is very common in the United States and patients are frequently diagnosed with hypothyroidism on routine lab tests. When including mild hypothyroidism, up to 25% of selected patient groups may meet this diagnosis. Indeed, thyroid hormone is one of the most commonly prescribed medications. The most common cause of hypothyroidism is Hashimoto's thyroiditis, an autoimmune disease where antibodies attack and destroy the thyroid. This usually results in lifelong treatment and, once started, patients often stay on thyroid hormone therapy indefinitely. There are also situations where the hypothyroidism may be short-lived and temporary, so long-term treatment is not needed. Thus, depending upon the circumstances of the initial diagnosis, patients may not need to stay on the medication. However, it is often difficult to determine which patients with hypothyroidism may actually be able to stop treatment.

This study was done to obtain information on when thyroid hormone can be successfully and safely stopped.

THE FULL ARTICLE TITLE

Burgos N et al 2020 Clinical outcomes after discontinuation of thyroid hormone replacement—A systematic review and meta-analysis. *Thyroid*. Epub 2020 Nov 9. PMID: 33161885

SUMMARY OF THE STUDY

This study reviewed 17 studies that examined the effect of stopping thyroid hormone. They excluded studies of patients with thyroid cancer, postpartum thyroiditis, and hypothyroidism from pituitary problems. Data included information on the patients (ie age, sex), reason for starting thyroid hormone, treatment duration, family history thyroid antibody status, TSH before and after stopping the medication, appearance on

thyroid ultrasound (if done) and clinical outcome. They determined the proportion of patients who remained euthyroid (not needing thyroid hormone replacement) after stopping thyroid hormone replacement.

Overall, 37% of patients remained euthyroid after stopping medication. When the reason for starting medication was analyzed it was apparent that patients who had overt (more significant) hypothyroidism at the onset were less likely to remain euthyroid off medication (only 11%) and most of these patients (82%) restarted thyroid hormone. Other things that predicted the need to restart thyroid medication in two of the studies were a heterogeneous appearance on ultrasound and a TSH greater than 8 mIU/L at initial presentation. In two other studies looking at the pediatric population, baseline TSH values above 9 mIU/L, younger age at diagnosis, and the presence of antithyroid antibodies were predictors of the need to resume thyroid hormone.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While this isn't a perfect study because of the variability between the various studies used for the meta-analysis, it does point out that, depending upon the reason for starting thyroid hormone replacement, as many as 1/3 of patients do not need to stay on it indefinitely. In particular, it appears that patients with normal thyroid ultrasounds and negative anti-thyroid antibodies can be given a trial off medication and many will not need to restart it.

This is important for patients to be able to discuss with their physicians whether they need to remain on thyroid hormone replacement indefinitely.

— Marjorie Safran, MD



HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

Euthyroid: a condition where the thyroid gland as working normally and producing normal levels of thyroid hormone.

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

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

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal.

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 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.



HYPOTHYROIDISM

A review of the 2020 guidelines for congenital hypothyroidism

BACKGROUND

Congenital hypothyroidism is a type of hypothyroidism that is present at birth either because the thyroid did not develop properly or because the thyroid has problems in making thyroid hormones. It occurs in 1:1700 newborns. Thyroid hormones play an important role to growth and development. In particular, normal brain development is dependent on thyroid hormone and the absence of thyroid hormone during the first 3 months of life results in marked decrease in intelligence. Newborn screening is helpful in identifying patients with congenital hypothyroidism. Screening allows for early diagnosis and treatment of congenital hypothyroidism to avoid severe developmental delay. Unfortunately, 70% of infants in the world are born in regions without newborn screening programs. The best test for detecting congenital hypothyroidism is measuring the thyroid stimulating hormone (TSH) level. TSH is a hormone that regulates thyroid function and the TSH level can help determine if the thyroid is working normally. Early treatment of congenital hypothyroidism and close monitoring to normalize the TSH level is important. The purpose of this study is to update the guidelines for the diagnosis and treatment of congenital hypothyroidism.

THE FULL ARTICLE TITLE

van Trotsenburg AS et al. 2020 Congenital hypothyroidism: A 2020 consensus guidelines update An ENDO-European Reference Network (ERN) initiative endorsed by the European Society for Pediatric Endocrinology and the European Society for Endocrinology. *Thyroid*. Epub 2020 Dec 3. PMID: 33272083.

SUMMARY OF THE STUDY

A total of 22 participants from the Endo-European Reference Network (ERN) and the European Society for Pediatric Endocrinology and the European Society for Endocrinology aimed to update the guidelines for the diagnosis and management of congenital hypothyroidism. A review of the literature was completed to identify important articles on neonatal screening, diagnosis and management of congenital hypothyroidism. The guidelines were based on evidence (evidence-based) and

were graded on the strength of the recommendations and quality of evidence. If evidence was lacking, recommendations were made based on expert opinion.

For abnormal congenital hypothyroidism screenings, the guidelines recommend measuring serum free thyroxine (FT₄) and TSH levels. Thyroxine is the major hormone made by the thyroid gland. Congenital hypothyroidism is categorized as mild (FT₄ levels of 10 – 15 pmol/L), moderate (FT₄ levels of 5 – 10 pmol/L), or severe (FT₄ levels < 5 pmol/L). Management of congenital hypothyroidism includes replacing the missing thyroid hormone with levothyroxine. The dose of levothyroxine is based on body weight per day and adjusted to keep thyroid hormone levels and TSH within normal. Treatment with levothyroxine should begin if the FT₄ is low and the TSH is elevated or if the TSH is > 20 mU/L even if FT₄ is normal. Treatment with levothyroxine should also begin if the TSH > 6 mU/L beyond 21 days of age. Genetic testing can help with make the diagnosis and can guide genetic counseling. All newborns with congenital hypothyroidism should be evaluated for birth defects such as cardiac defects and hearing loss. Preterm, low-birth-weight or very-low-birth weight infants, same-sex twin of an affected baby, and patients with Down syndrome have an increased risk for false-negative congenital hypothyroidism screening results (when screen results are negative, but patient actually has congenital hypothyroidism). For these newborns, a second screening test is recommended at approximately 10 to 14 days of age. In patients with congenital hypothyroidism, brain development progress and hearing should be regularly evaluated.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Early identification and appropriate treatment of congenital hypothyroidism is important in optimizing neurodevelopmental outcomes in these patients. Further studies are needed to understand the genetic causes and the increasing number of individuals who have congenital hypothyroidism.

— Priya Mahajan, MD





HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Congenital Hypothyroidism: <https://www.thyroid.org/congenital-hypothyroidism/>

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

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

ABBREVIATIONS & DEFINITIONS

Congenital hypothyroidism: hypothyroidism that exists at birth either because the thyroid did not develop properly (thyroid dysgenesis) or because the thyroid has problems in one of the needed steps to make thyroid hormones (thyroid dyshormonogenesis). Congenital hypothyroidism is estimated to occur in 1:1700 newborns.

Congenital: Condition that exists at birth.

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

Thyroid dysgenesis: a cause of congenital hypothyroidism where the thyroid did not develop properly

Thyroid dyshormonogenesis: a cause of congenital hypothyroidism where the thyroid has problems in one of the needed steps to make thyroid hormones. Thyroid dyshormonogenesis may be inherited in 25% of the children in a family.

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.

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





HYPOTHYROIDISM

Treating younger patients with subclinical hypothyroidism may decrease the risk of death from heart disease

BACKGROUND

Subclinical hypothyroidism is a mild form of underactive thyroid in which there is a high level of TSH (thyroid stimulating hormone) (usually <10) with a normal level of the thyroid hormone. Most often, patients with subclinical hypothyroidism do not have symptoms. This condition becomes more common as we age and some studies suggest that subclinical hypothyroidism may be associated with an increased risk of heart disease and death from any cause. Indeed, studies have shown that patients with subclinical hypothyroidism have more risk factors for heart disease than patients with normal thyroid tests, such as higher cholesterol levels. Although many studies have shown that treating patients with subclinical hypothyroidism with thyroid hormone can improve some risk factors for heart disease, the data on whether this improves death from heart disease or death from any cause has not been clear. The authors of this study performed a large review of all the published studies done on this topic and combined the information from those studies to help answer this question.

FULL ARTICLE TITLE

Peng CC et al 2021 Association of thyroid hormone therapy with mortality in subclinical hypothyroidism: A systematic review and meta-analysis. *J Clin Endocrinol Metab* 106:292–303. PMID: 33107557.

SUMMARY OF THE STUDY

The authors of this study looked through the databases of all published studies and included the ones that had adults

with subclinical hypothyroidism who were given thyroid hormone pills and measured whether those patients had heart disease or died from any cause. There were 21,055 patients in total and the highest level of TSH varied.

Overall, thyroid hormone treatment did not change the risk of death compared to those who did not take any treatment, regardless of the type of study, the amount of patients in the study, the baseline heart disease risk of the patients or the level of TSH. However, when looking at the age of the patients, there was a difference in the patients who took levothyroxine. Patients less than 65-70 years old who were treated with levothyroxine had a 54% decreased risk of death from heart disease when compared to those who did not take it. In patients older than 70 there was no such difference.

IMPLICATIONS OF THE STUDY

This study suggests that treatment of subclinical hypothyroidism in patients less than 70 years old leads to a significant decrease in the risk of death due to heart disease, while no such risk reduction was observed in older patients. Importantly, there was no evidence that treating increased the risk of death in any age group. Current American Thyroid Association guidelines recommend treating subclinical hypothyroidism only if the TSH is above 10, regardless of age. This review adds more evidence to favor treatment of subclinical hypothyroidism in younger patients but restrict treating older patients unless their TSH is >10.

— Dana Larsen, MD and Maria Brito, MD

ATA THYROID BROCHURE LINKS

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

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

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





HYPOTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

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.

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



AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

MARCH Medullary Thyroid Cancer Awareness Month





THYROID CANCER

Defining significant changes in ultrasound appearance during active surveillance of small papillary thyroid cancers

BACKGROUND

Thyroid cancer is the fastest rising cancer in the United States, with the most common type being papillary thyroid cancer. Many newly detected thyroid cancers are small (<1 cm) and many studies suggest that these small cancers may not have to be removed by surgery. Instead, they can be followed by thyroid ultrasound, known as active surveillance. Indeed, active surveillance of thyroid cancer has become more common as an alternative to surgery. Ultrasound is used to monitor for possible growth and change in either the longest diameter or the total volume of the small cancer. If the small cancer grows during active surveillance, then surgery is recommended.

The present study looks at how consistent and reliable measurements are between different operators of the ultrasound equipment. Since one definition of significant change is growth of as little as 3 mm in the longest dimension, the investigators want to know how consistent different ultrasound operators make the same measurement thyroid nodules.

THE FULL ARTICLE TITLE

Chung SR et al 2020 Interobserver reproducibility in sonographic measurement of diameter and volume of papillary thyroid microcarcinoma. *Thyroid*. Epub 2020 Dec 7. PMID: 33287640.

SUMMARY OF THE STUDY

This was a study of patients with small papillary thyroid cancers who had their ultrasound images reviewed by two experienced people and who performed measurements of the nodules where the papillary thyroid cancer was discovered. The main outcome was to see how consistent

the two ultrasound operators were at getting the same measurements of the nodules of interest. The description of the nodules (how light or dark they were, the presence of microcalcifications, etc) were compared between the operators as well.

Almost 200 nodules from 188 patients with an average size of just over 6 mm were evaluated. The measure of how consistent the nodules were measured between the two operators was almost 72% for total volume measurement and almost 24% for maximum nodule diameter. In other words, there was up to a 72% difference of measurement between the volume measurement between the two observers and up to a 24% difference between the maximum diameter measurements.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Even with experienced operators and a set of rules for how to measure thyroid nodules/cancers, there can a significant difference in measurements of thyroid nodules among two or more people. This is important for patients as small changes in thyroid nodule/cancer measurements may be due to differences in the measurement technique of the operator of the ultrasound and not a true change in the size of the nodule or cancer. This may inform patients of how worried (or not worried) they should be when there is a change in size of only a few millimeters when monitoring growth of known thyroid cancers. It is possible the changes reported are just due to the measurement technique. Further study is needed to clarify what is actual significant growth that would lead to a recommendation for surgery.

— Joshua Klopper, MD

ATA THYROID BROCHURE LINKS

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

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





THYROID CANCER, continued

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.

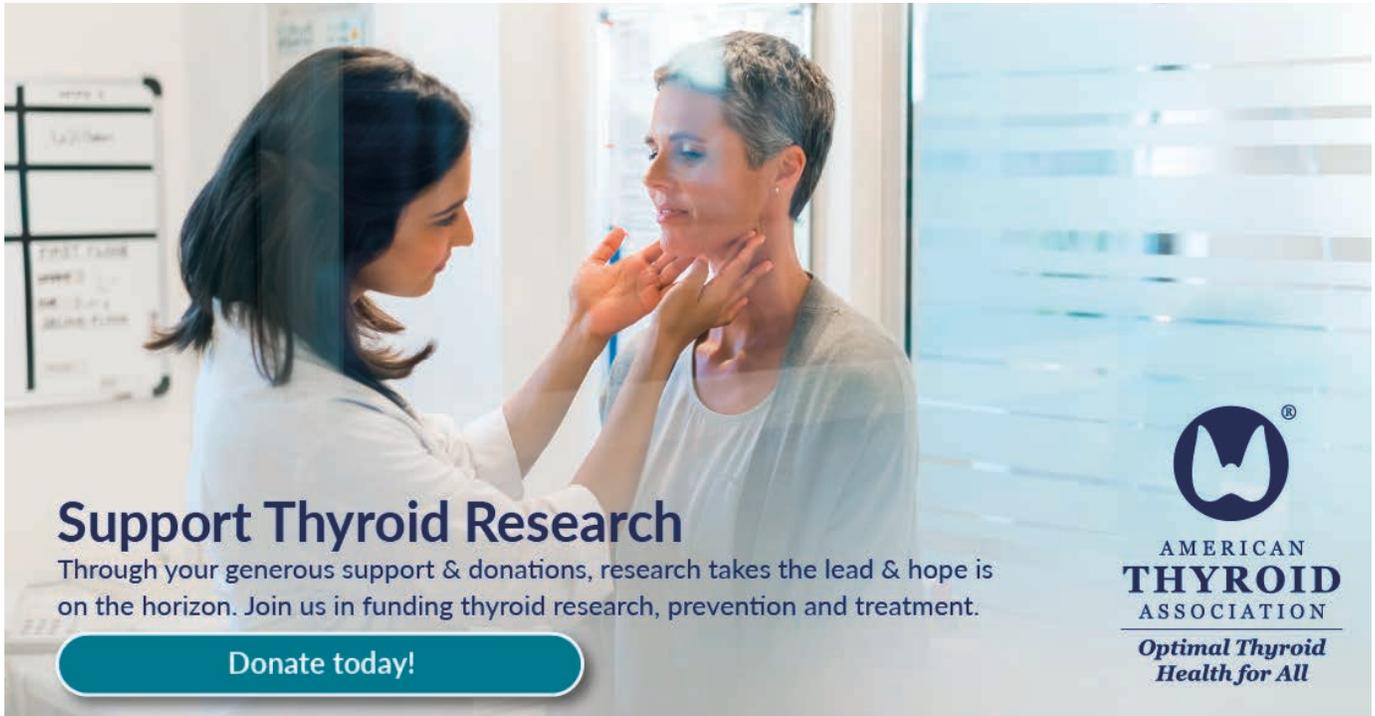
Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle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

Microcalcifications: Small flecks of calcium within a thyroid nodule, usually seen as small bright spots on ultrasonography. These are frequently seen in nodules containing papillary thyroid cancer.

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: the term for deferring surgery for small thyroid cancers by monitoring them over time with ultrasound and physical exam



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AMERICAN THYROID ASSOCIATION
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THYROID NODULES

Factors predicting thyroid surgery in patients with indeterminate thyroid nodules with a ‘benign’ molecular test result

BACKGROUND

Thyroid nodules are commonly found on imaging tests such as ultrasound and CT scans of the neck. Fine needle aspiration biopsy of thyroid nodules may be recommended based on the level of suspicion of cancer as a result of their appearance. However, sometimes, fine needle aspiration biopsies are inconclusive (i.e. indeterminate) and this may prompt molecular testing of the nodule in seeking additional information on the potential risk of cancer in the nodule. Some examples of molecular tests used for indeterminate thyroid nodules are the Afirma™ gene sequencing classifier and a previously developed Afirma™ gene expression classifier. The clinical implication of a ‘benign’ result of molecular testing would be that a nodule may be less likely to be a cancer and that thyroid surgery may potentially be avoided.

In this study, the authors examined how often patients with an indeterminate thyroid nodule biopsy result and a ‘benign’ result on an Afirma™ molecular test underwent thyroid surgery. The main analysis examined risk factors predicting the time from the biopsy to thyroid surgery.

THE FULL ARTICLE TITLE

Endo M et al 2020 Features of cytologically indeterminate molecularly benign nodules treated with surgery. *J Clin Endocrinol Metab* 105:dga506. PMID: 32772084.

SUMMARY OF THE STUDY

The authors reviewed the medical records of patients from Ohio State University Medical Center who had one or more thyroid nodules with an indeterminate biopsy result and who underwent an Afirma™ molecular test between

February of 2011 and December of 2018. The authors included in the study only the patients with a ‘benign’ result on molecular testing.

The authors examined data from 270 patients (including results of 289 nodules). During the study, 37 patients (13.7% of the 270) underwent thyroid surgery. These 37 patients had 38 nodules that were studied. For the 37 patients who underwent surgery, the range of time from biopsy to surgery was 0.4 to 45.7 months. Of the 37 patients who had surgery, 13.5% (5/37) of patients were found to have thyroid cancer.

In a statistical analysis adjusting for multiple possible features, the risk factors that were significantly related to ultimately having surgery included: presence of another nodule that had a ‘suspicious’ for cancer result on the molecular test, having compressive symptoms (in the neck), nodule size 3cm or larger and age younger than 40 years.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The main conclusion is that risk factors for thyroid surgery in patients who have an indeterminate thyroid biopsy with a ‘benign’ result on a molecular test include: presence of another nodule with a ‘suspicious’ molecular test result, compressive symptoms, larger nodule size, and younger age. These findings suggest that in spite of a ‘benign’ molecular test result, other factors may be important to patients and physicians in deciding whether to proceed with surgery for an indeterminate thyroid nodule.

— Anna Sawka, MD, PhD, FRCPC

ATA THYROID BROCHURE LINKS

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





THYROID NODULES, continued

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.

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.

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 adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

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™.

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



THYROID CANCER

Thyroid cancer in solid organ transplant recipients

BACKGROUND

As more patients are receiving organ transplants, it is important to understand the existence and risks of thyroid cancer in this patient population. The diagnosis of thyroid cancer has been shown to increase after transplantation, but the overall prognosis appears similar to that in the general population. Traditionally, patients with thyroid cancer diagnosed during screening before transplantation have waited up to 2 years after diagnosis before proceeding with transplantation. However, no clear data exist on the outcome of patients with a history of thyroid cancer who undergo subsequent solid organ transplantation. With expanding indications for transplantation, this variable waiting period between thyroid cancer diagnosis and transplantation has come into question. This study was performed to characterize the prognosis, recurrence, and survival of patients with thyroid cancer undergoing solid organ transplantation and to determine the risk and prognosis of thyroid cancer in transplant patients.

THE FULL ARTICLE TITLE

Webb C et al 2020 Is thyroid cancer prognosis affected by solid organ transplantation? Surgery. Epub 2020 Aug 16. PMID: 32814633.

SUMMARY OF THE STUDY

This study looked at patients who were undergoing solid organ transplantation at the Mayo Clinic in Phoenix, Arizona. It was based on a review of the medical charts. A detailed analysis was done to look at the prevalence of thyroid cancer in these patients before and after receiving

the transplants. Risk of recurrence was also studied. Approximately 13,000 chart reviews were conducted. The period of study was between the years 2000 to 2018 (18 years).

The results showed that even though the diagnosis of thyroid cancer can be made both before and after transplantation, the outcomes were quite similar in terms of recurrence and survival. The most common thyroid cancer in transplant patients was papillary thyroid cancer, as is seen in patients in the general population. For patients that were diagnosed before transplantation, there were no recurrences after the transplantation. The incidence of papillary thyroid cancer after a solid organ transplantation of the kidney, liver, pancreas, heart, or lung was 0.33%. About 1 in 5 of patients diagnosed with the thyroid cancer after the transplantation were diagnosed within the first year after receiving the transplant.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that may be useful to screen for thyroid cancer in patients undergoing or have had a solid organ transplant. Also, in patients who have not yet received the transplant and were diagnosed with thyroid cancer, proceeding with the transplant after the treatment of thyroid cancer is completed may be feasible. The recurrence rates before and after transplantation are similar. The outcomes of thyroid cancer in these patients is similar to the general population.

—Vibhavasu Sharma, MD, FACE

ATA THYROID BROCHURE LINKS

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





THYROID CANCER, continued

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).

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





ATA Alliance for Thyroid Patient Education

GOAL The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases. We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.



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



MCT8 - AHDS Foundation



American Thyroid Association

www.thyroid.org

ATA Patient Resources:

www.thyroid.org/thyroid-information/

Find a Thyroid Specialist: www.thyroid.org

(Toll-free): 1-800-THYROID

thyroid@thyroid.org

Bite Me Cancer

www.bitemecancer.org

info@bitemecancer.org

Graves' Disease and Thyroid Foundation

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

Light of Life Foundation

www.checkyourneck.com

info@checkyourneck.com

MCT8 – AHDS Foundation

mct8.info

Contact@mct8.info

Thyca: Thyroid Cancer Survivors' Association, Inc.

www.thyca.org

(Toll-free): 877-588-7904

thyca@thyca.org

Thyroid Cancer Alliance

www.thyroidcanceralliance.org

www.thyroidcancerpatientinfo.org

Rotterdam, The Netherlands

Thyroid Cancer Canada

www.thyroidcancer canada.org

416-487-8267

info@thyroidcancer canada.org

Thyroid Federation International

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JOIN US

PLEASE JOIN OUR JOURNEY TO ADVANCED DISCOVERIES AND TREATMENT FOR THYROID DISEASE AND THYROID CANCER



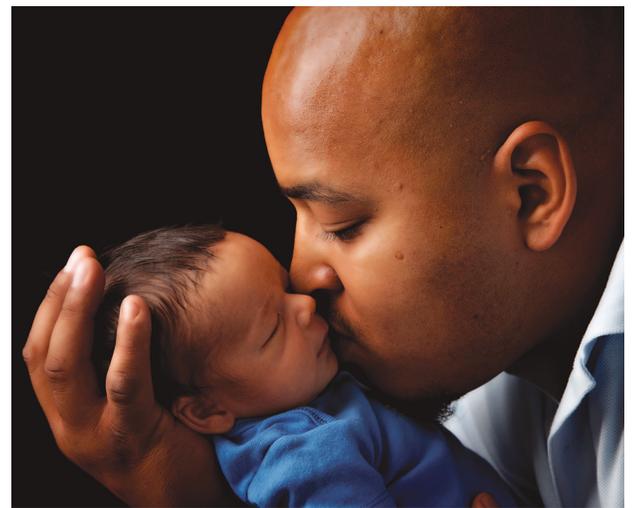
“ The ATA was a valuable resource for our family when my dad was diagnosed with Anaplastic Thyroid Cancer. When you’re faced with a detrimental diagnosis where even a few days can make the difference in life or death, understanding your options quickly is critical. The ATA website offers a one-stop shop for patients and caregivers to find specialists, current clinical trials, general thyroid cancer information, and links to other patient support groups and information.”

Mary Catherine Petermann

- Father who was diagnosed with Anaplastic Thyroid Cancer in 2006
- He was treated at Mayo Clinic
- He has clean scans as of October 2016

As patients with thyroid disease navigate the challenges to their quality of life and researchers and physicians look for more effective directions, we at the ATA have our own destination—**funding for critical thyroid research, prevention, and treatment.** For 94 years, the ATA has led the way in thyroidology. It’s a daily obstacle course to find new drugs, better treatments, advanced surgical methods, and more rapid diagnoses for the 20 million Americans who have some form of thyroid disease.

The ATA has paved the way with management guidelines for clinicians who diagnose and treat thyroid disease. For physicians treating pregnant women diagnosed with thyroid disease, our recent publication presents 97 evidence-based recommendations making sure that best practices are implemented with the latest, most effective treatment.



Through your generous support and donations, research takes the lead and hope is on the horizon. **Will you join us** in our campaign to raise **\$1.5 million** for thyroid research, prevention, and treatment? Your compassionate, tax-deductible gift will provide funds for:

- Research grants that pave the way for 1,700 ATA physicians and scientists who have devoted their careers to understanding the biology of and caring for patients affected by thyroid disease.
- Patient education for individuals and families looking for life-changing clinical trials, the best thyroid specialists, and cutting edge treatment and drugs.
- Professional education that offers a wealth of knowledge and leading-edge research for trainees and practitioners.
- A website that is the go-to resource for thyroid information for patients and practitioners alike. In 2016 alone, there were more than 3,700,000 website views of ATA’s library of online thyroid information patient brochures.

Donations **of all sizes** will change the future for thyroid patients. You will make a direct impact on patients like Mary Catherine’s father as he deals with Anaplastic Thyroid Cancer. You will help scientists like ATA Associate Member Julia Rodiger, Ph.D., a scientist at the National Institutes of Health, as she analyzes thyroid hormones for intestinal stem cell development.



Medullary Thyroid Cancer

WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

CANCER OF THE THYROID

Thyroid cancer is relatively uncommon compared to other cancers. In the United States it is estimated that in 2016 approximately 64,000 new patients will be diagnosed with thyroid cancer, compared to over 240,000 patients with breast cancer and 135,000 patients with colon cancer. However, fewer than 2000 patients die of thyroid cancer each year. In 2013, the last year for which statistics are available, over 630,000 patients were living with thyroid cancer in the United States. Thyroid cancer is usually very treatable and is often cured with surgery (see [Thyroid Surgery brochure](#)) and, if indicated, radioactive iodine (see [Radioactive Iodine brochure](#)). Even when thyroid cancer is more advanced, effective treatment is available for the most common forms of thyroid cancer. Even though the diagnosis of cancer is terrifying, the prognosis for most patients with [papillary and follicular thyroid cancer](#) is usually excellent.

MEDULLARY THYROID CANCER

Medullary Thyroid Cancer (MTC) accounts for 1%–2% of thyroid cancers in the United States. MTC is different from other types of thyroid cancers (which are derived from thyroid follicular cells – the cells that make thyroid hormone), because it originates from the parafollicular C cells (also called “C cells”) of the thyroid gland. These cells do not make thyroid hormone and instead make a different hormone called calcitonin.

MTC can, and frequently does, spread to lymph nodes and can also spread to other organs. MTC is likely to run in families (inherited forms) in up to 25% of diagnoses, and inherited forms can be associated with other endocrine tumors, in syndromes called Multiple Endocrine Neoplasia (MEN) 2A and MEN 2B. In addition to MTC, patients with MEN2A may have tumors of the adrenal glands called pheochromocytomas or in the parathyroid glands (parathyroid adenomas). Patients with MEN2B, have MTC, pheochromocytomas and neuromas (typically a benign growth or tumor of nerve tissue) in the lining of the mouth and/ or gastrointestinal tract.

Patients with an inherited form of MTC usually have a mutation in a gene called the RET proto-oncogene. This mutation is present in all of the cells in their body (a germline mutation) and these mutations cause the development of MTC. This is important because in family members of a person with an inherited form of MTC, a blood test for a mutation in the RET proto-oncogene can lead to an early diagnosis of MTC and, to curative surgery to remove it. However, in the majority of patients (~ 75%) a germline mutation is not found - indicating that MTC is not an inherited or inheritable condition. In these cases, MTC is called sporadic.

Whether MTC is sporadic or familial can be determined by a blood test for the RET proto-oncogene. Anyone diagnosed with MTC should have this test run to determine whether the MTC is familial (meaning other family members may also have MTC that has not yet been diagnosed) or sporadic.

Medullary Thyroid Cancer

WHAT ARE THE SYMPTOMS OF MEDULLARY THYROID CANCER?

Medullary thyroid cancer usually presents as a lump or nodule in the thyroid. It may be noted by the patient or discovered during routine neck examination by the doctor. Sometimes, the nodule is discovered incidentally by imaging studies done for other unrelated reasons (CT of the neck, PET scan, or carotid ultrasound). The nodule may cause no symptoms, but in some cases the tumor may have spread to lymph nodes in the neck, which may be enlarged on physical examination.

Patients with advanced MTC may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or the esophagus, it may cause difficulty with breathing or swallowing. Hoarseness can be present if the cancer invades the nerve that controls the vocal cords.

MTC is usually more aggressive than the other more common types of thyroid cancer (See *Thyroid Cancer- papillary and follicular- brochure*), and it is usually easier to treat and control if it is found before it spreads to lymph nodes in the neck or other parts of the body.

Thyroid function tests such as TSH are usually normal, even when MTC is present.

If you have a family history of MTC and have tested positive for the RET mutation, then you should see an endocrinologist to help determine how best to follow you or treat you.

HOW IS MEDULLARY THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer is usually made by a *fine needle aspiration (FNA) biopsy* of a thyroid nodule, or after the nodule is surgically removed. Patients in whom the results of an FNA biopsy (or histopathology) are suggestive or indicative of MTC should be further evaluated with measurement of the proteins calcitonin and carcinoembryonic antigen (CEA) in the blood, which are typically elevated in patients with MTC. These tests are useful to confirm the diagnosis of MTC which can help ensure the surgeon plans the correct surgery, and also serve as tumor markers during long-term follow-up to detect any remaining disease or recurrence of the cancer.

WHAT IS THE RET MUTATION?

The RET proto-oncogene is located on chromosome 10. A genetic mutation in the RET oncogene is seen in all cells in the body in patients with the hereditary forms of MTC. Mutations in RET can also be seen only in the tumor cells in patients with sporadic MTC. Since the discovery of the RET oncogene, more than 100 different mutations have been identified in the gene in patients with MTC.

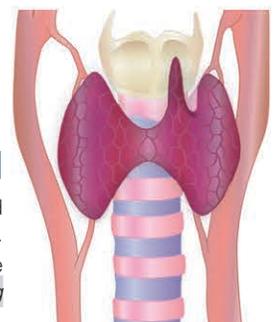
Genetic counseling and testing for RET gene mutations should be offered to patients diagnosed with MTC and first-degree relatives (parents, siblings and children of someone diagnosed with MTC) of all patients with proven germline mutations (hereditary MTC). If close relatives, especially children, are found to have the RET mutation on a blood test, the thyroid gland can be removed before MTC has a chance to develop or at least in its very early stages.

HOW IS MTC TREATED?

The primary treatment for MTC is surgery, and the currently accepted approach is to remove the entire thyroid gland (total thyroidectomy) (See *thyroid surgery brochure*). Often patients with MTC will have thyroid cancer present in the lymph nodes of the neck or upper chest. These lymph nodes are usually removed at the time of thyroid surgery or sometimes, at a later surgery if found subsequently. After surgery, patients need to take thyroid hormone replacement medication for life.

Unlike papillary and follicular thyroid cancer, medullary thyroid cancer does not take up iodine, and consequently radioactive iodine treatment is not a treatment option for patients with MTC.

Patients with MTC with very high levels of calcitonin should have imaging prior to surgery to determine whether the tumor has spread to sites outside the thyroid and/or outside the neck. If there is evidence of cancer outside the neck, surgery may be more palliative, aimed at reducing local complications caused by the tumor, rather than completely eliminating all tumor. Other treatment options (external beam radiation, or chemotherapy) may need to be used together with surgery after careful discussion with the patient.



FURTHER INFORMATION

Further details on this and other thyroid-related topics are available in the patient thyroid information section on the American Thyroid Association® website at www.thyroid.org.

For information on thyroid patient support organizations, please visit the *Patient Support Links* section on the ATA website at www.thyroid.org

Medullary Thyroid Cancer

New chemotherapeutic agents that have shown promise treating other advanced cancers are increasingly available for treatment of thyroid cancers. Two such agents, Vandetanib and Cabozantinib have been FDA approved for use by patients with MTC. These drugs do not cure advanced cancers that have spread widely throughout the body, but they can often slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and require care at specialized medical centers.

WHAT IS THE FOLLOW-UP FOR PATIENTS WITH MTC?

Periodic follow-up examinations are essential for all patients with MTC because the thyroid cancer can return, sometimes many years after successful initial treatment. These follow-up visits include a careful history and physical examination, with particular attention to the neck area. Neck ultrasound is also a very important tool to visualize the neck and look for nodules, lumps or enlarged lymph nodes that might indicate that the cancer has recurred.

Blood tests are also important in the follow-up of MTC patients. All patients who have had their thyroid glands removed require thyroid hormone replacement with levothyroxine. Thyroid stimulating hormone (TSH) should be checked periodically, and the dose of levothyroxine adjusted to keep TSH in the normal range. There is no need to keep TSH suppressed in patients with MTC.

Measurement of calcitonin and CEA are a necessary routine part of the follow-up of patients with MTC. Following thyroidectomy, it is hoped that calcitonin levels will be essentially undetectable for life. A detectable or rising calcitonin level should raise suspicion for possible cancer recurrence. Detectable calcitonin levels may require additional tests.

WHAT IS THE PROGNOSIS OF MEDULLARY THYROID CANCER?

The prognosis of MTC is usually not as favorable as differentiated thyroid cancers (*papillary and follicular cancer*). However, if discovered early, surgery can be curative. Even in cases where it is not caught early, MTC often progresses relatively slowly. Long-term survival depends on the stage of disease at the time of diagnosis. The blood levels of calcitonin or CEA over the first year after surgery can also be a predictor of a patient's survival.

ATA PARTNERING WITH MTC

The Medullary Thyroid Carcinoma (MTC) Registry Consortium* is partnering with the American Thyroid Association (ATA) to create a registry (list) of all new cases of MTC diagnosed in the United States over the next 10-15 years (the MTC Registry). The purpose of the MTC Registry is to help better understand what risk factors are associated with the development of MTC.

Click here for additional information:

<https://www.thyroid.org/professionals/partner-relations/medullary-thyroid-carcinoma-registry-consortium/>



FURTHER INFORMATION

Further details on this and other thyroid-related topics are available in the patient thyroid information section on the American Thyroid Association® website at www.thyroid.org.

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