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VOLUME 11 | ISSUE 3 | MARCH 2018

In the United States, thyroid blood tests are done 1-3 days after birth at the hospital as part of a national newborn screening program to detect congenital hypothyroidism. Each state determines which blood tests to perform and sets their own cutoffs for determining when the result should be interpreted as abnormal. This paper examines the differences in thyroid screening programs in newborns.

Kilberg MJ et al 2018 Newborn Screening in the U.S. May Miss Mild Persistent Hypothyroidism. J Pediatr 192:204-8.

There are many different tests available to evaluate the function of the thyroid gland. However, many tests are over utilized and/or may not be appropriate for the type of thyroid problem suspected. The objectives of this study were to compare patterns of thyroid testing ordered between different institutions, to assess the appropriateness of such testing, and to evaluate whether laboratory utilization protocols showed improvements in thyroid testing.

Lin DC et al and the Thyroid Benchmarking Group. Multicenter Benchmark Study Reveals Significant Variation in Thyroid Testing in the United States. Thyroid 2017;27:1232-45.

There has been recent interest on how factors in the mother during pregnancy may affect their children later in life. Thyroid problems are common in women and the association between the thyroid status of the mother during pregnancy and her child's health later in life has not been well studied. This study set up to study whether there is an association between thyroid autoimmunity and the child's risk to develop the cardiometabolic syndrome in later life.

Heikkinen AL et al. Maternal thyroid antibodies associates with cardiometabolic risk factors in children at the age of 16. J Clin Endocrinol Metab. September 11, 2017 [Epub ahead of print].

Thyroid nodules are very common. Although the majority of these nodules are non-cancerous, a small proportion do contain thyroid cancer. A thyroid ultrasound is an accurate test that can determine nodule characteristics and help physicians decide which nodules should be evaluated with a thyroid biopsy. The aim of this study was to evaluate the ultrasound appearance of thyroid nodules and correlate this with cytology and pathology results in order to validate the ultrasound risk-pattern categories proposed by the recent American Thyroid Association guidelines.

Tang, AL et al. Validation of American Thyroid Association Ultrasound Risk Assessment of Thyroid Nodules Selected for Ultrasound Fine-Needle Aspiration. Thyroid 2017;27:1077-82.

In 1–2% of PET scans performed for the diagnosis or staging of non-thyroid cancers, incidental uptake of a thyroid lesion is detected. Current American Thyroid Association guidelines recommends biopsy of all PET-positive nodules >1cm that are not definitively benign on a diagnostic thyroid ultrasound. However, there has not been a large study looking at the prognosis of these thyroid cancers that are identified incidentally on PET imaging.

Pattison DA et al. 18F-fluorodeoxyglycose-avid thyroid incidentalomas: the importance of contextual interpretation. J Nucl Med 2017;Oct 12:pii: jnumed.117.198085 [Epub ahead of print].

Up to 30% of patients treated with total thyroidectomy and radioactive iodine therapy have persistent metastatic thyroid cancer in the lymph nodes in the neck. Repeated doses of radioactive iodine therapy has proven to be beneficial in patients with thyroid cancer that has spread outside of the neck. This study was intended to determine whether a second radioactive iodine therapy in patients with thyroid cancer in the lymph nodes in the neck is beneficial.

Hirsch D et al. Second radioiodine treatment: limited benefit for differentiated thyroid cancer with locoregional persistent disease. J Clin Endocrinol Metab. November 3, 2017.

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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, 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.

March is Medullary Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Should US newborn thyroid screening programs be standardized?
- Should thyroid testing in the US be standardized?
- Does thyroid abnormalities in the mother after heart disease risk in their children?
- Are the ATA guidelines on ultrasound risk assessment of thyroid nodules valid?
- What is the prognostic significance of thyroid incidentalomas identified on PET scans?
- Is a 2nd radioactive iodine therapy helpful with patients with recurrent thyroid cancer in the neck?

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, FACE

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HYPOTHYROIDISM IN CHILDREN

U.S. newborn screening of congenital hypothyroidism

BACKGROUND

Congenital hypothyroidism is a condition in newborns in which the thyroid gland is underactive and does not produce sufficient thyroid hormone starting at birth. It occurs in 1 in every 2,000-4,000 live births, and approximately 1,400 newborns in the U.S. are diagnosed each year. It is an important disease to detect, since not having enough thyroid hormone as a newborn and during infancy can result in poor growth and abnormal brain development. When congenital hypothyroidism is found in a newborn, thyroid hormone medication is started immediately to prevent these severe problems and most children who are treated have an excellent prognosis.

Most infants at birth will show no clinical symptoms of low thyroid hormone levels. Thus, newborn screening of congenital hypothyroidism began in most developed countries during the early 1970s. In the United States, thyroid blood tests are done 1-3 days after birth at the hospital as part of a national newborn screening program to detect congenital hypothyroidism. However, there are many types of thyroid blood tests, and the specific type of that is done depends on each individual state's newborn screening practices. Each state also sets their own cutoffs for determining when the result should be interpreted as abnormal. For blood TSH, levels should normally be high in the first few days after birth, then fall to the adult range by two weeks of age. This paper examines the differences in thyroid screening programs in newborns.

THE FULL ARTICLE TITLE

Kilberg MJ et al 2018 Newborn Screening in the U.S. May Miss Mild Persistent Hypothyroidism. J Pediatr 192:204-8.

SUMMARY OF THE STUDY

In this study, the researchers contacted each of the newborn screening programs in all U.S. states and territories to gather information on what type of thyroid blood testing is used to detect congenital hypothyroidism and how results are interpreted and followed up. They found that all programs test for congenital hypothyroidism within 1-3 days of birth. Some states would still run samples if collected after day 3 and, although older babies should have a lower TSH level, many of these programs did not adjust the result for the age of the baby.

Some programs test babies with blood TSH tests, others with T_4 tests followed by TSH tests, and still others with both of these. Among all programs, there were differences of when a TSH value is considered abnormal. The authors concluded that state newborn screening programs for congenital hypothyroidism vary widely in the U.S. In many of the programs, mild cases of congenital hypothyroidism may be missed.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Newborn screening of congenital hypothyroidism is essential for diagnosing, treating and preventing the serious consequences of untreated congenital hypothyroidism. However, there are no national newborn screening standards in the United States and testing is done by each state. This study shows that states' newborn screening programs for congenital hypothyroidism in the United States vary widely and the testing approaches of some programs may potentially miss some cases of mild congenital hypothyroidism. The authors suggest that adopting the same approach in all congenital hypothyroidism screening programs across the United States would allow greater consistency of how babies with congenital hypothyroidism are diagnosed and treated.

— Angela M. Leung, MD, MSc

HYPOTHYROIDISM IN CHILDREN, continued

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/
Congenital Hypothyroidism: https://www.thyroid.org/congenital-hypothyroidism/
Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/

ABBREVIATIONS & DEFINITIONS

Congenital: A term that refers to diseases present at birth.

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

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.

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THYROID FUNCTION TESTS

Significant variations of thyroid testing in the US argue for improved standardization of practice patterns

BACKGROUND

Thyroid problems are common and the symptoms are often very nonspecific. This is especially true with hypothyroidism. There are many different tests available to evaluate the function of the thyroid gland. However, many tests are over utilized and/or may not be appropriate for the type of thyroid problem suspected. Over the past few decades, there has been a steady increase in the number of thyroid tests ordered and the estimated cost for the most commonly ordered tests (TSH and free T_4) totals $1.6 billion per year.

The objectives of this study were to compare patterns of thyroid testing ordered between different institutions, to assess the appropriateness of such testing, and to evaluate whether laboratory utilization protocols showed improvements in thyroid testing.

THE FULL ARTICLE TITLE

Lin DC et al and the Thyroid Benchmarking Group. Multicenter Benchmark Study Reveals Significant Variation in Thyroid Testing in the United States. Thyroid 2017;27:1232-45.

SUMMARY OF THE STUDY

This study was done with data obtained from 82 laboratories associated with 24 unique US healthcare organizations, of which 13 were academic medical centers. The sites were selected from a voluntary web-based survey. The volume of serum thyroid tests over the 2015 calendar year was determined for the following tests: TSH, free T_4, total T_4, free T_3, Total T_3, T_3 uptake and reverse T_3. Then, that volume was standardized against the frequency of complete blood count (CBC) testing, probably the most common blood test ordered. The prevalence of CBC testing was also used to determine the total testing volume of each laboratory so that comparisons regarding overall volume across health care centers could be done. Researchers divided data by inpatient vs. outpatient patient settings. The investigators also collected data related to health care utilization management initiatives at each center.

The results showed that across the 82 laboratories, there was a higher proportion of TSH testing among outpatients than inpatients. Based on median values, sites ordered 14 Free T_4, three total T_4, four free T_3, two total T_3, 0.1 rT_3 and 0.1 T_3 uptake for every 100 TSH orders. Tests for free T_4 were nine times as common as those for Total T_4, but free T_3 and Total T_3 were more evenly split. Comparing between sites, there were marked variations in whether an initial screening TSH was obtained and also in the order of tests ordered following an initial TSH. One of the most variable ordering behaviors for thyroid testing was whether a rT_3 level was obtained following an initial TSH. This happened even though there were general laboratory testing guidelines available to providers at 71% of the sites. At 38 % of the sites, some tests were restricted to specialists, but only 21% of centers had guidelines for when it is appropriate to obtain thyroid testing.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that there is significant practice variation in thyroid testing and suggests a need for better guidance in test selection to improve patient care and reduce testing costs. Although the study has limitations, including the lack of clinical information that would support a particular test over another, its strength is its relatively broad sample size which makes it likely to reflect practice patterns across the entire United States.

— Jessie Block-Galarza, MD

THYROID FUNCTION TESTS, continued

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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

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

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.

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THYROID DISEASE AND PREGNANCY

Thyroid antibodies in the mother are associated with cardiac and metabolic risk factors in the children at age 16

BACKGROUND

There has been recent interest on how factors in the mother during pregnancy may affect their children later in life. Approximately 17% of pregnant women have thyroid antibodies (a marker of autoimmune thyroid disease) and 2-3% of women have mild abnormalities in thyroid tests know as subclinical hypothyroidism. One study found that children of women with lower TSH and higher thyroid hormone levels during pregnancy were leaner at the age of 6 years. Another study found that children of women with subclinical hypothyroidism during pregnancy had higher blood pressure by the age of 20 than those whose mother's had normal thyroid blood tests during pregnancy. Obesity and high blood pressure are 2 of the components of the cardiometabolic syndrome, which is associated with the development of heart disease and diabetes. The other components are intolerance to glucose with resistance to insulin and abnormal lipid (fat) profile in the blood.

Despite these studies, the association between the thyroid status of the mother during pregnancy and her child's health later in life has not been well studied. This study set up to study whether there is an association between thyroid autoimmunity and the child's risk to develop the cardiometabolic syndrome in later life.

THE FULL ARTICLE TITLE

Heikkinen AL et al. Maternal thyroid antibodies associates with cardiometabolic risk factors in children at the age of 16. J Clin Endocrinol Metab. September 11, 2017 [Epub ahead of print].

SUMMARY OF THE STUDY

This study used the Northern Finland Birth Cohort, which includes a total of 9362 mothers and 9479 children (99% of the births in two provinces of Finland from July 1985 to June 1986). Mothers were enrolled at their first pregnancy visit between 8 and 24 weeks' of pregnancy and children have been followed since birth. Demographics, pregnancy and health histories, delivery information, and neonatal outcomes were obtained at routine clinic visits and by questionnaires. Child health and demographic data were obtained at clinic visits to free community child welfare clinics and using questionnaires and national registries. The study included 4176 mother–child pairs. The mother's serum TSH, free T_4, TPO antibodies, and Thyroglobulin (Tg) antibodies were measured around 10.7 weeks of gestation and reference ranges were determined for the study population. TSH reference ranges were between 0.07 and 3.1 mIU/L in the first trimester and between 0.10 and 3.5 mIU/L in the second trimester. Women with TPO antibodies above 167.7 IU/ml or Tg Ab ≥47.7 IU/ml were considered antibody-positive. Outcomes were available in 74% by the age of 16. Outcomes included weight, height, waist circumference, blood pressure, fasting serum glucose, insulin, lipids profile and information about puberty, smoking, and alcohol use. The cardiometabolic syndrome was defined as abdominal obesity with two or more of the following: elevated blood pressure, increased glucose, increased triglycerides, or low HDL cholesterol (good cholesterol).

Of the women with TSH measurements, 90% had normal thyroid function, 2% were hyperthyroid, 7% were hypothyroid, 1% had low T_4 levels with normal TSH. Of the women with TPO Ab measurements, 5% were antibody-positive. Of the women with Tg antibodies measurements, 5% were antibody-positive. Mother's thyroid function and Tg antibodies status were not associated with a child's lipids, fasting glucose, waist circumference, blood pressure, presence of metabolic syndrome, BMI, or resistance to insulin. Children of mothers who were TPO antibody-positive were more 1.6 times more likely to have a greater waist circumference, 1.56 times more likely to have a body mass index (BMI) in the overweight range and 2.57 times more likely to have the cardiometabolic syndrome.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study found that positive TPO antibodies in the mother were associated with a higher risk for the child to develop cardiometabolic syndrome. This suggests that

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THYROID DISEASE AND PREGNANCY, continued

women with positive TPO antibodies during pregnancy may need to be counseled regarding the importance of monitoring their children's diet, weight, blood pressure and metabolic parameters over time.

The results are surprising as there was no association with thyroid function or thyroglobulin antibodies. It is unclear whether this association is related to the thyroid antibodies per se or to other factors which may be present in women with positive TPO antibodies. Results need to be validated and more research is needed to better understand this relationship and possible ways to improve the outcome. Also, this information adds to the discussion about the usefulness of screening for thyroid disease in pregnant women, a controversial topic.

— Liuska Pesce, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/
Pregnancy and Thyroid Disease: https://www.thyroid.org/thyroid-disease-pregnancy/
Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/
Thyroid and Weight: https://www.thyroid.org/thyroid-and-weight/

ABBREVIATIONS & DEFINITIONS:

Antibodies: proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.

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).

Cardiometabolic syndrome: A combination of metabolic dysfunctions mainly characterized by insulin resistance with abnormal tolerance to glucose, abnormal fat concentrations in blood, high blood pressure and obesity

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.

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

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

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

Thyroglobulin antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

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THYROID NODULES

Validation of American Thyroid Association ultrasound risk assessment of thyroid nodules selected for biopsy

BACKGROUND

A thyroid nodule is an abnormal growth of thyroid cells that forms a lump within the thyroid gland. Thyroid nodules are very common. Although the majority of these nodules are non-cancerous, a small proportion do contain thyroid cancer. A thyroid ultrasound is an accurate test that can determine nodule characteristics and help physicians decide which nodules should be evaluated with a thyroid biopsy.

In 2015, the American Thyroid Association published updated guidelines regarding the evaluation and treatment of thyroid nodules and thyroid cancer. These new guidelines recommend using a combination of the thyroid nodules' appearance on ultrasound and their size to determine whether they should be evaluated with a biopsy. Depending on the thyroid nodule pattern seen on ultrasound, five categories were created with different risk of cancer. These include high (70–90%), intermediate (10–20%), low (5–10%), very low (<3%), and benign (<1%), with the percentages denoting risk for cancer. The aim of this study was to evaluate the ultrasound appearance of thyroid nodules and correlate this with cytology and pathology results in order to validate the ultrasound risk-pattern categories proposed by the American Thyroid Association.

THE FULL ARTICLE TITLE

Tang, AL et al. Validation of American Thyroid Association Ultrasound Risk Assessment of Thyroid Nodules Selected for Ultrasound Fine-Needle Aspiration. Thyroid 2017;27:1077-82.

SUMMARY OF THE STUDY

A total of 199 patients with suspicious or dominant thyroid nodules who had thyroid biopsy between March 2015 and May 2016 at a single institution were included in the study. For each patient a thyroid ultrasound was initially performed in the office and the nodule was classified in a risk category: high, intermediate, low, very low or benign, based on the guidelines mentioned above. Subsequently, biopsy of the nodules was performed. In total, 64 patients had thyroid surgery because of the biopsy result or because of the large size of the nodule.

The study showed that the nodules that were found to be cancer or suspicious for cancer by biopsy correlated with the following ultrasound risk pattern: high (77%), intermediate (6%), low (1%) and very low (0%). Among the 71 nodules that were indeterminate by biopsy, 52 were removed by surgery. Their cancer rates correlated with the following ultrasound risk pattern: high (100%), intermediate (21%), low (17%) and very low (12%). Overall, this study found a good correlation between the ultrasound risk pattern categories established by the 2015 American Thyroid Association guidelines and the pathology results in the patients studied.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This is an important study as it reinforces the validity of the recommendations made by the American Thyroid Association and helps to encourage physicians to use these guidelines when treating their patients with thyroid nodules. It is essential to consider the ultrasound appearance of thyroid nodules when determining the appropriate management for each patient. It is especially important to take into consideration that the high suspicion ultrasound pattern for thyroid nodules is highly predictive of thyroid cancer.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

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

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.

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.

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THYROID CANCER

FDG-PET-positive thyroid incidentalomas

BACKGROUND

Thyroid nodules are common. Further, it is common that thyroid nodules are found on imaging studies of the neck done for other reasons. PET scans are one common imaging study that identifies thyroid nodules when looking for other cancers. Nodules/masses that are PET-positive are concerning for cancer.

In 1–2% of PET scans performed for the diagnosis or staging of non-thyroid cancers, incidental uptake of a thyroid lesion is detected. Since 30-40% of these PET-positive lesions are found to be thyroid cancer, current American Thyroid Association guidelines recommends biopsy of all PET-positive nodules >1cm that are not definitively benign on a diagnostic thyroid ultrasound. However, there has not been a large study looking at the prognosis of these thyroid cancers that are identified incidentally on PET imaging.

THE FULL ARTICLE TITLE

Pattison DA et al. 18F-fluorodeoxyglycose-avid thyroid incidentalomas: the importance of contextual interpretation. J Nucl Med 2017;Oct 12:pii: jnumed.117.198085 [Epub ahead of print].

SUMMARY OF THE STUDY

The study assessed both overall survival and thyroid cancer specific survival in patients that had a thyroid cancer diagnosed incidentally on a PET scan. The authors performed a retrospective review of 45,000 PET scans performed for non-thyroid cancer at a single institution over a 10 year period. They identified 500 patients with a PET-positive thyroid incidentaloma and of these, 362 had follow-up data and were the population studied. Of the 131 patients that had a thyroid biopsy, 36% had a thyroid cancer (of which 4 were confirmed spread from the primary cancer). Of the 180 deaths during the study period with a median f/u of 24 months, only 1 was from a medullary thyroid cancer; the majority were from the primary cancer for which the PET-CT was performed initially.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

PET-positive thyroid nodules detected incidentally on scans performed for another primary malignancy have little impact on short-term (1–4 year) survival for these patients with more advanced non-thyroid malignancies. This suggests and affirms that when these lesions are detected incidentally, treatment of the primary cancer is more important. If there is concern for spread of the cancer to the thyroid that would change management of the primary cancer, then early biopsy of the thyroid nodule is warranted; if not, biopsy and treatment can likely wait until the patient is doing well from their primary cancer and active surveillance is a reasonable strategy for these lesions.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

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

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

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 CANCER, continued

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.

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

^{18}F-2-fluoro-2-deoxy-d-glucose-positron emission tomography (FDG-PET): a nuclear medicine imaging test that uses a small amount of radiolabeled glucose to identify cancer. Since cancer cells are more active than normal cells, the cancer cells take up more of the radiolabeled glucose and show up on the FDG-PET scan. FDG-PET scans are frequently combined with CT scans to accurately identify where the cancer is located. Its role in thyroid cancer is still being studied.

Incidentaloma: an abnormal finding on an imaging test that was not clinically identified prior to doing the test and that was unrelated to the reason the imaging test was performed. Examples of incidentalomas are thyroid nodules on neck imaging and adrenal nodules on abdominal imaging.

Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of **February** is **Medullary Awareness Month** and a bracelet is available through the **ATA Marketplace** to support thyroid cancer awareness and education related to thyroid disease.

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THYROID CANCER

A second radioactive iodine treatment alone is of little benefit in treating patients with thyroid cancer that has spread into the lymph nodes in the neck

BACKGROUND

Thyroid cancer is the fastest rising cancer in women. Current treatment including surgery (total thyroidectomy) followed by thyroid hormone therapy. Radioactive iodine therapy is used in patients with an intermediate or higher risk of persistent or recurrent thyroid cancer. Radioactive iodine works as a "magic bullet" by getting taken up by both normal and cancerous thyroid cells and destroying them. Similarly, radioactive iodine can be used to destroy thyroid cancer cells if the cancer returns.

Up to 30% of patients treated with total thyroidectomy and radioactive iodine therapy have persistent metastatic thyroid cancer in the lymph nodes in the neck. While surgery is the gold standard for treatment of large metastatic cancer, management of small, slowly progressive cancer in the neck remains unclear. Repeated doses of radioactive iodine therapy has proven to be beneficial in patients with thyroid cancer that has spread outside of the neck (ie into the lungs), however limited data is available on whether treatment of thyroid cancer in the lymph nodes in the neck with second administration of radioactive iodine therapy is effective. This study was intended to determine whether a second radioactive iodine therapy in patients with thyroid cancer in the lymph nodes in the neck is beneficial.

THE FULL ARTICLE TITLE

Hirsch D et al. Second radioiodine treatment: limited benefit for differentiated thyroid cancer with locoregional persistent disease. J Clin Endocrinol Metab. November 3, 2017.

SUMMARY

Authors selected for analysis 164 patients with thyroid cancer treated with total thyroidectomy and at least two doses of radioactive iodine therapy who had elevated thyroglobulin levels with or without evidence of metastatic cancer in the neck after the initial therapy. Patients were divided in three groups prior to a second dose of radioactive iodine therapy (which they all received): 1) elevated thyroglobulin levels only with no evidence of cancer in the neck by ultrasound imaging, 2) recurrent thyroid cancer in the neck treated with surgery, and 3) recurrent thyroid cancer in the neck treated that was not re-operated. Patients were followed for about 10 years after initial diagnosis and 7.3 years after a second radioactive iodine therapy. A total of 73% of the patients with a detectable thyroglobulin level (group 1) had persistently elevated thyroglobulin levels 1-2 years after radioactive iodine therapy; moreover, 16% of these patients developed metastatic cancer that was identified by ultrasound imaging. In group 2, who were re-operated prior to a second dose of radioactive iodine therapy, 48% of patients had persistent cancer. Almost all patients (94%) who did not have reoperation in the neck prior to a second radioactive iodine therapy (group 3) had persistent metastatic cancer at 1-2 years after the repeated radioactive iodine therapy treatment. After a second dose of radioactive iodine therapy, about 38% of patients received additional therapies.

In general, at final follow up 56/164 patients (34%) had no evidence of disease and 75 patients (45%) had imaging studies consistent with metastatic disease. Metastatic cancer in the neck was seen at the last follow up visit in 28% of patients with elevated thyroglobulin levels (group 1), in 40% of patients who were re-operated prior to a second dose of radioactive iodine therapy (group 2) and in 70% of patients who were not re-operated (group 3).

IMPLICATIONS

This study shows that only a modest decline in metastatic neck disease was noted after a second radioactive iodine therapy, unless this was also preceded by neck reoperation to remove metastasis. The patients who were re-operated prior to a second dose of the radioactive iodine therapy had the best outcomes achieving

THYROID CANCER, continued

cancer-free state. These results are attributed to surgery itself rather than to repeated radioactive iodine therapy. Furthermore, despite additional therapies that included radioactive iodine therapy, surgery and external beam radiation therapy about half of the patients had persistent metastatic disease in the neck at final follow up. Thus, it appears that patients with persistent thyroid cancer received little benefit from a second radioactive iodine therapy. Because of this, more studies are needed to evaluate the role of radioactive iodine therapy for recurrent cancer in the neck.

—Valentina Tarasova, MD

ATA WEB BROCHURE LINKS:

Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/
Radioactive Iodine: https://www.thyroid.org/radioactive-iodine/
Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS AND DEFINITIONS:

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies.

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid.

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

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

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 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
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Clinical Thyroidology® for the Public

VOLUME 11 | ISSUE 3 | MARCH 2018

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.

WHO WE ARE (in alphabetical order)

AMERICAN THYROID ASSOCIATION
www.thyroid.org
ATA Patient Resources:
http://www.thyroid.org/thyroid-information/
Find a Thyroid Specialist: www.thyroid.org
(Toll-free): 1-800-THYROID
thyroid@thyroid.org

BITE ME CANCER
http://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

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.
www.thyca.org
(Toll-free): 877-588-7904
thyca@thyca.org

THYROID CANCER CANADA
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416-487-8267
info@thyroidcancercanada.org

THYROID FEDERATION INTERNATIONAL
www.thyroid-fed.org
tfi@thyroid-fed.org

AMERICAN THYROID ASSOCIATION
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Light of Life Foundation
checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

BITE ME CANCER!

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

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FOUNDED 2005

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By subscribing to *Friends of the ATA Newsletter*, you will receive:

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- 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.

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Donate Now!

JOIN US

"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

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

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 track.

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.

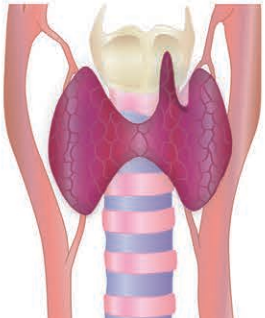
Genetic counseling and testing for RET gene mutations should be offered to patients diagnosed with MTC and first-degree relatives (parents, siblings and children of someone diagnosed with MTC) of all patients with proven germline mutations (hereditary MTC). If close relatives, especially children, are 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.

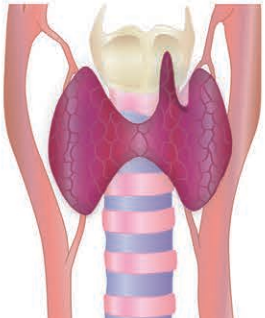
WHAT IS THE PROGNOSIS OF MEDULLARY THYROID CANCER?

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:
http://www.thyroid.org/media-main/partner-relations/medullary-thyroid-carcinoma-registry-consortium/



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