#### Volume 15 | Issue 4 | April 2022

## Clinical Thyroidology<sup>®</sup> for the Public

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

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There is a very complex association between hypothyroidism and depression. However, most hypothyroid patients do not develop depression and the majority of people with depression do not have hypothyroidism. This study aimed to investigate the existence and extent of an association between hypothyroidism, thyroid autoimmunity and clinical depression.

Bode H et al 2021 Association of hypothyroidism and clinical depression: A systematic review and meta-analysis. JAMA Psychiatry 78:1375-1383. PMID: 34524390.

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#### Is obesity is associated with increased fat cells in the thyroid?

Obesity has been associated with hypothyroidism and thyroid nodules. One possible link is inflammation, which is present in these disorders. This study evaluated thyroid tissue from normal-weight, overweight, and obese individuals to assess potential differences in inflammation that might contribute to altered thyroid function in obesity.

Basolo A et al 2021 Histological pattern and gene expression profiling of thyroid tissue in subjects with obesity. J Endocrinol Invest. Epub 2021 Aug 15. PMID: 34392500.

#### THYROID CANCER.....

#### Ultrasound appearance does not improve thyroid cancer risk predicted by molecular testing

Ultrasound of the thyroid is very useful in evaluating thyroid nodules to determine which need to be biopsied. If a biopsy is indeterminate, molecular tests can help identify those nodules that are benign and thus do not need surgery. This study examines whether combining results of molecular testing with ultrasound characteristics could improve the accuracy of risk stratification of indeterminate thyroid nodules even more than is currently achieved through molecular testing or ultrasound alone.

Figge JJ et al. 2021 Do ultrasound patterns and clinical parameters inform the probability of thyroid cancer predicted by molecular testing in nodules with indeterminate cytology? Thyroid. Epub 2021 Sep 1. PMID: 34340592.

#### THYROID NODULES ......9 The role of a computer-aided diagnosis system in the interpretation of thyroid nodules with challenging ultrasound features

Thyroid ultrasound is the best initial study to determine whether a nodule is a cancer. The use of CAD systems based on machine learning has emerged as a possible solution standardize the risk stratification of thyroid nodules based on ultrasound appearance. This small study aimed to evaluate the diagnostic accuracy of a CAD system in the evaluation of thyroid nodules deemed difficult by clinicians.

Reverter JL et al 2022 Reliability of a computer-aided system in the evaluation of indeterminate ultrasound images of thyroid nodules. Eur Thyroid J 11(1):e210023. PMID: 34981749.

#### THYROID CANCER......

#### The role of thyroglobulin testing in identifying cancer return after lobectomy

Monitoring for thyroid cancer recurrence in patients that had a lobectomy can be challenging. The goal of this study is to determine if there is a particular thyroglobulin and/or thyroglobulin antibody blood level, or rise in these levels over time, that can correctly predict thyroid cancer recurrence.

Siyuan Xu et al 2021 Predictive value of serum thyroglobulin for structural recurrence following lobectomy for papillary thyroid carcinoma. Thyroid 31:1391-1399.

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#### A 4-day preparation with a low-iodine diet may be enough before radioactive iodine therapy for thyroid cancer treatment

For some patients, radioactive iodine therapy is an option to decrease risk of recurrence. To make radioactive iodine therapy more effective, ATA guidelines recommend patients go on a low iodine diet for 1-2 weeks before treatment. Urinary iodine excretion (UIE) rate is commonly used to assess iodine status after LID. This study compared the UIE rates at 4 days and at 7 days after starting LID to determine the best duration of a LID before radioactive iodine therapy for thyroid cancer.

Dekker BL et al 2022 Low-iodine diet of 4 days is sufficient preparation for 131I therapy in differentiated thyroid cancer patients. J Clin Endocrinol Metab 107(2):e604-e611. PMID: 34534327.

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## Clinical Thyroidology<sup>®</sup> for the Public

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

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association (ATA) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.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. 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. (<u>https://www.thyroid.org/covid-19/</u>)

#### April is <u>Hashimoto's Disease Awareness Month</u>.

#### In this issue, the studies ask the following questions:

- Is there an association between hypothyroidism and depression?
- What are the links between obesity and thyroid disorders?
- Does ultrasound improve thyroid cancer risk predicted by molecular testing?
- Can computer-aided diagnosis systems help in the ultrasound evaluation of thyroid nodules?
- Can thyroglobulin be used to evaluate thyroid cancer recurrence after thyroid lobectomy?
- What is the best duration of a low iodine diet in preparing for radioactive iodine therapy for thyroid cancer?

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

— Alan P. Farwell, MD,

#### **HYPOTHYROIDISM**



Association of hypothyroidism with depression may depend on the severity of hypothyroidism and stronger in women

#### BACKGROUND

There is a very complex association between hypothyroidism and depression. Patients with hypothyroidism and those with depression can present with similar general symptoms. A depressed mood is a common symptom of hypothyroidism. Autoimmune thyroid disease, the most common cause of hypothyroidism in the United States, may also affect the brain and induce depression. Also, hypothyroidism, being a chronic disease, could result in depression, like other chronic illnesses. Indeed, symptoms of depression are not always resolved when hypothyroidism is corrected. Also, hypothyroidism and depression can also occur at the same time in the same person. However, most hypothyroid patients do not develop depression and the majority of people with depression do not have hypothyroidism.

Both hypothyroidism and depression are more frequent in women than in men; however, it is still unknown if depression is more common in women with hypothyroidism. Previous studies performed using different methods have reported various results, from no association to a strong association between hypothyroidism and depression. This study aimed to investigate the existence and extent of an association between hypothyroidism, thyroid autoimmunity and clinical depression.

#### THE FULL ARTICLE TITLE

Bode H et al 2021 Association of hypothyroidism and clinical depression: A systematic review and meta-analysis. JAMA Psychiatry 78:1375–1383. PMID: 34524390.

#### **SUMMARY OF THE STUDY**

The authors performed a search of large medical studies evaluating the association of hypothyroidism and depression from inception through May 2020. The study population for this study was representative of the general population. Of the 3372 articles identified in the initial search, 25 articles containing 348,014 participants were included in this study. Among these articles, 9 analyzed the association of depression with overt hypothyroidism, 17 with subclinical hypothyroidism, and 9 with positive TPO antibodies (TPOAb). A total of 15 studies assessed depressive symptoms using a standard depression score, and among these, 10 studies used the diagnostic coding of major depressive disorder by national criteria.

The average age of participants was 45 years, 56% of them being women. The study showed that there was a 1.3-fold increased risk to have depression with all degrees of hypothyroidism, ranging from a 1.13-fold risk in patients with subclinical hypothyroidism to 1.77-fold risk for patients with overt hypothyroidism. The risk was only seen in hypothyroid women (1.48-fold increase). TPOAb positivity was not associated with depression.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows a moderate association of overt hypothyroidism, and less so of subclinical hypothyroidism, with clinical depression. The association was only seen in hypothyroid women. Thus, the contribution of hypothyroidism to the development of depression may be smaller than previously thought.

— Alina Gavrila, MD, MMSc

#### **ATA THYROID BROCHURE LINKS**

Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u> Hashimoto's Thyroiditis: <u>https://www.thyroid.org/hashimotos-thyroiditis/</u>

#### HYPOTHYROIDISM, continued



#### **ABBREVIATIONS & DEFINITIONS**

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

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

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

**Thyroid-stimulating hormone (TSH)**: a 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.

Antithyroid peroxidase (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

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).

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#### **THYROID AND WEIGHT**

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Is obesity is associated with increased fat cells in the thyroid?

#### BACKGROUND

Obesity has been associated with hypothyroidism and thyroid nodules. To date, there is not a clear link between obesity and thyroid disorders other than this association. One possible link is inflammation, which is present in both disorders. In hypothyroidism and thyroid nodules, antibodies that attack the thyroid cause the inflammation. This is known as autoimmune thyroid disease. In obesity, inflammatory cells enter into fat tissues and cause low-grade inflammation. Findings of an association between obesity, thyroid inflammation and autoimmune thyroid disease have been inconsistent. This study evaluated thyroid tissue from normal-weight, overweight, and obese individuals to assess potential differences in inflammation that might contribute to altered thyroid function in obesity.

#### THE FULL ARTICLE TITLE

Basolo A et al 2021 Histological pattern and gene expression profiling of thyroid tissue in subjects with obesity. J Endocrinol Invest. Epub 2021 Aug 15. PMID: 34392500.

#### **SUMMARY OF THE STUDY**

Patients undergoing surgical treatment for thyroid nodules were included in this study. Patients with pre-existing autoimmune thyroid disease or a final diagnosis of thyroid cancer were removed from the study. The tissues were evaluated for the presence of fat cells inflammatory cells. In a subset of patients, the tissues were evaluated for genes that are associated with inflammation.

The study enrolled 98 patients (30 normal-weight, 34 overweight, 34 with obesity). Fat cells were seen within the thyroid gland in 55 individuals. Overall, fat cells in the thyroid were seen in 73.5% of the obese individuals, 52.9% of the overweight individuals and 40% in the normal weight individuals. The absolute number of fat cells within the thyroid increased directly with the increase in BMI. No differences in inflammatory cells in the thyroid was observed among groups, nor was there a significant association between fat cells and inflammatory cells within the thyroid. Further, there were some differences in gene expression in the thyroids from overweight and obese individuals as compared to normal weight individuals.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In individuals without autoimmune thyroid disease, obesity is associated with increased fat cells and altered gene expression in the thyroid. These findings suggest a role for the associated inflammation seen in obesity in causing changes in thyroid structure and function. Further studies are needed to clarify the contribution of obesity to clinically relevant thyroid disorders and the development of thyroid nodules.

— Alan P. Farwell, MD

#### **ATA THYROID BROCHURE LINKS**

Thyroid and Weight: <u>https://www.thyroid.org/thyroid-and-weight/</u> Thyroid Nodules: <u>https://www.thyroid.org/thyroid-nodules/</u> Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u>

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#### THYROID AND WEIGHT, continued



#### **ABBREVIATIONS & DEFINITIONS**

**Body-mass index (BMI):** a standardized measure of obesity calculated by dividing the weight in kilograms by the square of the height. A normal BMI is 18.5-24.9, overweight is 25-30 and obese is >30.

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

**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**



Ultrasound appearance does not improve thyroid cancer risk predicted by molecular testing

#### BACKGROUND

Thyroid nodules are commonly discovered in clinical practice, either during physical examination or incidentally during various imaging procedures. The purpose of evaluating thyroid nodules is to determine which nodules are cancerous and require surgery. Ultrasound of the thyroid is very useful in evaluating thyroid nodules. There are 2 major ultrasound-based algorithms are currently being used to help risk-stratify the nodules: the American Thyroid Association (ATA) risk stratification system and the American College of Radiology Thyroid Image Reporting system (ACR-TIRADS). These ultrasound algorithms identify high-risk nodules that require further assessment with a thyroid biopsy. Once a nodule is biopsied, the results are reported in 1 of 6 risk categories ranging from benign to indeterminate to cancer.

Indeterminate biopsy results means the thyroid cells do not look clearly normal or abnormal and occurs in 10-15% of nodules. The uncertainty associated with indeterminate biopsy results can lead to unnecessary thyroid surgery. Companies have developed molecular tests to detect genes often present in cancerous cells to address this dilemma. One test called ThyroSeq<sup>™</sup> can help identify those indeterminate nodules that are benign and thus do not need surgery.

This study examines whether combining results of molecular testing with ultrasound characteristics and other clinical variables could improve the accuracy of risk stratification of indeterminate thyroid nodules even more than is currently achieved through molecular testing or ultrasound alone.

#### THE FULL ARTICLE TITLE

Figge JJ et al. 2021 Do ultrasound patterns and clinical parameters inform the probability of thyroid cancer predicted by molecular testing in nodules with indeterminate cytology? Thyroid. Epub 2021 Sep 1. PMID: 34340592.

#### **SUMMARY OF THE STUDY**

The authors examined data from 257 nodules (from 232 patients) that a) were classified as indeterminate by thyroid biopsy, b) had molecular testing results with ThyroSeq<sup>™</sup> and c) were surgically removed. For each nodule, the authors went back and examined the initial ultrasound images and assigned scores using both the ATA ultrasound risk stratification system and the ACR-TIRADS. Finally, they recorded clinical variables such as sex, age and family history of thyroid cancer. All this data was compared with the final diagnosis after surgery to see which variables improve the ability to predict thyroid cancer.

In nodules classified as indeterminate by thyroid biopsy, a positive ThyroSeq<sup>™</sup> result was the strongest predictor of cancer. However, neither of the ultrasound scoring systems improved the ability to predict thyroid cancer, nor did any of the clinical variables that the authors examined. The results of this study suggest that, while ultrasound scoring systems are very helpful in identifying nodules that need to be biopsied, they cannot be used to decide if which nodules need to be surgically removed surgically when the result of the biopsy is indeterminate. When the biopsy result is indeterminate, the ThyroSeq<sup>™</sup> molecular test is the best test to predict thyroid cancer.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that thyroid ultrasound is best used to select the thyroid nodules that need thyroid biopsy. This is because ultrasound can accurately determine which nodules need surgery and which nodules can be monitored most of the time. However, with indeterminate thyroid biopsy results, a molecular test such as ThyroSeq<sup>™</sup> is the best test to predict which nodules are cancerous.

- Philip Segal, MD

#### THYROID CANCER, continued



#### ATA THYROID BROCHURE LINKS

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

#### **ABBREVIATIONS & DEFINITIONS**

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

**Thyroid nodule:** an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid biopsy: a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. 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<sup>™</sup> Gene Expression Classifier and Thyroseq<sup>™</sup>.



#### **THYROID NODULES**

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The role of a computer-aided diagnosis system in the interpretation of thyroid nodules with challenging ultrasound features

#### BACKGROUND

Thyroid nodules are very common, affecting up to half of the US population. The concern about a thyroid nodule is whether it is a cancer. Thyroid ultrasound is the best initial study to determine whether a nodule is a cancer. The ultrasound characteristics, including the size, the appearance, the margins, blood flow and calcifications, all contribute to the determination of which thyroid nodules can be followed and which need a biopsy. This is known as risk-stratification. There are 2 major ultrasound-based algorithms currently being used to help risk-stratify the nodules: the American Thyroid Association (ATA) risk stratification system and the American College of Radiology Thyroid Image Reporting system (ACR-TIRADS). These ultrasound algorithms identify high-risk nodules that require further assessment with a thyroid biopsy. An important consideration in clinical practice is the extent to which thyroid nodule risk stratification is consistent and reproducible across evaluators with variable degrees of expertise. This is particularly important, given that an inaccurate assigned ultrasound risk can lead to incorrect management recommendations.

The use of computer-aided diagnosis (CAD) systems based on machine learning has emerged as a possible solution standardize this process. Multiple CAD systems are available and are undergoing evaluation with the goal that they can support objective, accurate, and reproducible evaluation of thyroid cancer risk in practice and ultimately improve clinical outcomes for patients with thyroid nodules. An important part of this evaluation are thyroid nodules considered challenging by clinicians. This small study aimed to evaluate the diagnostic accuracy of a CAD system in the evaluation of thyroid nodules deemed difficult by clinicians.

#### THE FULL ARTICLE TITLE

Reverter JL et al 2022 Reliability of a computer-aided system in the evaluation of indeterminate ultrasound

images of thyroid nodules. Eur Thyroid J 11(1):e210023. PMID: 34981749.

#### **SUMMARY OF THE STUDY**

This study evaluated thyroid nodules deemed difficult to interpret by a single expert senior endocrinologist with experience in ultrasound assessment. Records and ultrasound images of patients age >18 years who underwent total thyroidectomy or thyroid lobectomy based on thyroid biopsy results were included in the study. The ultrasound classification of nodules deemed "difficult to interpret" was defined as thyroid nodules showing patterns of mixed benign and concerning components. Subsequently, the thyroid nodules deemed difficult to interpret were analyzed by a CAD system, as well as by five human experts with expertise in ultrasound examination for the assessment of malignancy risk, based on the ACR TI-RADS classification. The five reviewers were unaware of the final diagnosis after surgery. Nodules were further classified as agreeing if there was agreement between  $\geq 3$  human observers and disagreeing if  $\leq 2$ observers agreed. The diagnostic performances of the readers versus the CAD system were compared.

There were 300 thyroid nodules considered, each with one ultrasound image, from which 80 were considered difficult to interpret by the senior endocrinologist. After assessment by the five human reviewers, 37 (46.25%) nodules were classified as agreeing and 43 (53.75%) disagreeing. When analyzing the nodules in the agreeing group, both the clinician observers and the CAD system obtained similar levels of accuracy, as compared with the known surgical diagnosis (74.5% vs. 77%). However, when analyzing disagreeing nodules, both the experts and the CAD system had a lower degree of diagnostic accuracy when compared to the evaluation of agreeing images (57.1% vs 77.0% for experts and 70% vs 74.2% for the CAD system).



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#### THYROID NODULES, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The accuracy of cancer risk by clinical observers and a CAD system on thyroid nodules deemed difficult were similar when there was general agreement with the human reviewers. However, the CAD system was more reliable than reviewers for challenging images where there was disagreement among the human reviewers. While these data are promising, further studies are needed to determine the role of CAD in assisting ultrasound interpretation.

— Alan P. Farwell, MD

#### ATA THYROID BROCHURE LINKS

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

#### **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 CANCER**

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The role of thyroglobulin testing in identifying cancer return after lobectomy

#### BACKGROUND

Thyroid surgery is necessary to treat most cases of thyroid cancer. Often, removing just that part of the thyroid gland (called a thyroid lobectomy) that contains a thyroid cancer is enough to fully treat this disease. Unfortunately, thyroid cancer can come back after thyroid surgery, sometimes months or years later. For this reason, people diagnosed with thyroid cancer must be carefully monitored for cancer recurrence (return) after thyroid surgery. One way of doing this might be to regularly check the blood levels of a protein called thyroglobulin (Tg), which is only made by thyroid cells, including both normal and cancerous thyroid cells. In general, the more thyroid tissue (or thyroid cancer) present, the more Tg will be made. So, if a thyroid cancer recurs after thyroid surgery, the blood Tg levels may be elevated or may rise as the recurrent cancer grows. In addition, some people may develop an immune system response to Tg by making antibodies to this protein (TgAb). Like Tg, TgAb is detectable in the blood and, because the TgAb level should follow the Tg level (that is, higher Tg levels should mean higher TgAb levels), TgAb levels might also rise if thyroid cancer recurs.

Monitoring Tg levels works the best if the patient had a total thyroidectomy, where most of the thyroid tissue is removed. In patients that have had a lobectomy, they still have a lot of normal thyroid tissue left, all of which produces Tg. It is not clear how the high the Tg or TgAb levels must be, or how much these levels must rise after surgery, to correctly predict thyroid cancer recurrence in patients that had a lobectomy. In fact, several previous studies found that neither blood Tg nor TgAb levels predict thyroid cancer recurrence after thyroid lobectomy.

The research described here studied blood Tg and TgAb levels at specific time points after thyroid lobectomy among patients diagnosed with thyroid cancer. This was done to see if there is a particular Tg and/or TgAb blood level, or rise in these levels over time, that can correctly predict thyroid cancer recurrence.

#### **FULL ARTICLE TITLE**

Siyuan Xu et al 2021 Predictive value of serum thyroglobulin for structural recurrence following lobectomy for papillary thyroid carcinoma. Thyroid 31:1391–1399.

#### **SUMMARY OF THE STUDY**

The authors of this study looked at blood Tg and TgAb levels over time in 1852 people who underwent thyroid lobectomy to treat the most common type of thyroid cancer (papillary thyroid cancer). Blood Tg and TgAb levels were measured after surgery for each person twice each year for five years and then once yearly. Imaging studies were used to identify which people in the study developed cancer recurrence and mathematical/statistical testing was used to see if the blood Tg and/or TgAb levels could have predicted such recurrence. Overall, the authors found that the risk of thyroid cancer recurrence was significantly increased if the first blood Tg level tested was 5.3 mg/mL or higher, or if the last blood Tg level tested was 11mg/mL or higher. A sudden increase in blood Tg level was also associated with thyroid cancer recurrence. In contrast, thyroid cancer recurrence was not related to blood TgAb levels or changes in blood TgAb levels over time following surgery.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study authors found that blood Tg levels tend to be higher, or to rise more suddenly, when thyroid cancer recurs after treatment with thyroid lobectomy. These findings suggest that regular checks of the blood Tg level after thyroid lobectomy could help identify thyroid cancer recurrence. This could lead to earlier treatment for recurrent thyroid cancer, thus potentially preventing such cancer from growing and/or eventually spreading to other parts of the body. Additional studies involving many more patients are needed to confirm these findings and to better define if blood Tg levels can help predict thyroid cancer recurrence after thyroid lobectomy

— Jason D. Prescott, MD PhD

#### THYROID CANCER, continued



#### ATA THYROID BROCHURE LINKS

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

#### **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).

**Partial thyroidectomy:** surgery that removes only part of the thyroid gland (usually one lobe with or without the isthmus).

Lobectomy: surgery to remove one lobe of the thyroid.

**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. 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.

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.

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

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## Clinical Thyroidology<sup>®</sup> for the Public

#### **THYROID CANCER**

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### A 4-day preparation with a low-iodine diet may be enough before radioactive iodine therapy for thyroid cancer treatment

#### BACKGROUND

Most patients with thyroid cancer are low risk for recurrence of their cancer after surgery so do not require additional therapy. For patients with intermediate or high-risk thyroid cancers, radioactive iodine therapy is an option to decrease risk of recurrence. In order for radioactive iodine therapy to work, the remaining thyroid tissue needs to be "turned on" to take up the radioactive iodine and then to be destroyed. This is done by stimulating the remaining thyroid tissue with TSH, either by making the patient hypothyroid or treating with Thyrogen<sup>™</sup> (synthetic TSH).

To make radioactive iodine therapy more effective, American Thyroid Association guidelines recommend patients go on a low iodine diet (LID) to limit iodinecontaining food for 1-2 weeks before treatment. A low iodine state is thought to increase radioactive iodine uptake into the remaining thyroid tissue. While 1-2 weeks is recommended, it is not clear what the best length of time is for a LID before radioactive iodine therapy. Some studies did not show significant difference in the effectiveness of radioactive iodine therapy between 1-week and 2-week LID courses, while another study found that 1-week of LID did not result in enough decrease in iodine level in the urine.

Urinary iodine excretion (UIE) rate is commonly used to assess iodine status after LID, since iodine is excreted through urine and UIE reflects recent iodine intake. This study compared the UIE rates at 4 days and at 7 days after starting LID to assess to best duration of a LID before radioactive iodine therapy for thyroid cancer.

THE FULL ARTICLE TITLE

Dekker BL et al 2022 Low-iodine diet of 4 days is sufficient preparation for 1311 therapy in differenti-

ated thyroid cancer patients. J Clin Endocrinol Metab 107(2):e604–e611. PMID: 34534327.

#### **SUMMARY OF THE STUDY**

A total of 65 patients with intermediate risk thyroid cancer (63% women, 62% with papillary thyroid cancer) scheduled for radioactive iodine therapy were recruited from 2 hospitals in the Netherlands. All patients were asked to follow a LID with less than 50 micrograms of iodine a day for 7 days. Urine over 24-hour was collected on days 4 and 7 of the LID to calculate UIE in micrograms of iodine a day (mcg/day).

The average UIE was 36.1mcg/day at day 4 and 36.5mcg/ day at day 7, not significantly different between the two time points. Using 50mcg/day as a target, 72.1% of patients reached the target by day 4 and 82% of patients reached the target by day 7, although this was not significantly different. The number of patients who followed a LID did not differ between the group of patients who reached UIE target of 50mcg/day and those who did not.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors of this study concluded that there were no significant differences in UIE between 4-day and 7-day preparation with a LID prior to radioactive iodine therapy for thyroid cancer. Since a LID can be quite restricting for patients, a shorter duration is preferable. Indeed, this study suggests that a 4-day LID may be fine. While this data is promising, more studies with more patients are needed to establish the best duration of a LID , and its impact on the risk of thyroid cancer recurrence.

— Sun Y. Lee, MD, MSc

#### THYROID CANCER, continued



#### **ATA THYROID BROCHURE LINKS**

Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u> Low Iodine Diet: <u>https://www.thyroid.org/low-iodine-diet/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u>

#### **ABBREVIATIONS & DEFINITIONS**

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. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

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

**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.

**lodine:** an element found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. Common foods high in iodine include iodized salt, dairy products, seafood and some breads.

Thyroid Hormone Withdrawal (THW): this is used to produce high levels of TSH in patients by stopping thyroid hormone pills and causing short-term hypothyroidism. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan.

**Recombinant human TSH (rhTSH):** human TSH that is produced in the laboratory and used to produce high levels of TSH in patients after an intramuscular injection. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan. The brand name for rhTSH is Thyrogen<sup>™</sup>.



#### **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.





CANCER









Thyroid Cancer Canada Cancer de la thyroide Canada



### American Thyroid Association

Foundation

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.thyroidcancercanada.org 416-487-8267 info@thyroidcancercanada.org

#### Thyroid Federation International www.thyroid-fed.org

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