Volume 14 | Issue 10 | October 2021

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

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Editor's Comments

Welcome to another issue issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through Twitter at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International*.

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

While the Covid-19 pandemic is winding down, it 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. (https://www.thyroid.org/covid-19/)

October is Thyroid Nodule Awareness Month.

In this issue, the studies ask the following questions:

- Can a web-based tool help manage treatment decisions for thyroid nodules
- What are the predictors or cancer recurrence in patients with follicular thyroid cancer?
- Can repeat biopsies of indeterminate nodules decrease the risk of molecular marker testing?
- What is the major factor in treatment decision-making in Graves' disease?
- What is the best way to dose radioactive iodine for Graves' disease?
- Are liquid or gel-based formulations for levothyroxine better absorbed than tablets?

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,

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THYROID NODULES

A new thyroid nodule electronic tool to guide management decisions

BACKGROUND

Thyroid nodules are very common in the general population and increase with age. More than 90% of thyroid nodules are benign (non-cancerous) and do not result in any symptoms, while many of the nodules that prove to be cancer are low risk with an excellent prognosis requiring only thyroid surgery or no treatment. It is important to distinguish low-risk from high-risk thyroid nodules to appropriately diagnose and treat thyroid cancer and avoid excessive evaluation and unnecessary surgery for low risk nodules. Medical societies have provided recommendations to determine the cancer risk and improve the evaluation and treatment of thyroid nodules using a combination of variables, including the clinical presentation, blood thyroid tests, ultrasound features, biopsy results and molecular tests. Given the multiple variables involved, the evaluation of thyroid nodules is becoming increasingly complex and difficult to complete.

A task force of the American Association of Clinical Endocrinology (AACE) and Associazione Medici Endocrinologi (AME), including members from the United States and Europe met over a 3-year period to update the clinical practice guidelines for thyroid nodule care. The task force created a Web-based tool to provide guidance on the initial evaluation and treatment of patients with thyroid nodules. The article describes the development and details of this novel electronic tool.

THE FULL ARTICLE TITLE

Garber JR et al 2021 American Association of Clinical Endocrinology and Associazione Medici Endocrinologi thyroid nodule algorithmic tool. Endocr Pract 27:649–660. PMID: 34090820.

SUMMARY OF THE STUDY

The tool, termed TNAPP (Thyroid Nodule App, pronounced "tee nap") is available online at https://aace-thyroid.deontics.com. It provides recommendations for the initial treatment of a typical patient presenting with a thyroid nodule with an average risk for cancer. It was not designed to be used for patients at risk of having aggressive or advanced types of thyroid cancer. The tool uses 26 clinical factors, 36 ultrasound features, and 48 biopsy features associated with a greater or lesser risk of cancer.

A thyroid biopsy is the procedure of choice to identify suspicious thyroid nodules that require surgery. Clinical factors can be used to weigh for or against performing a biopsy. The ultrasound characteristics of thyroid nodules are the main variables used to determine the cancer risk and decide whether a biopsy is indicated. Each ultrasound feature has been assigned points based on the associated risk of cancer. Based on this numeric scoring system, thyroid nodules are categorized as having low, intermediate and high risk of cancer. A library of ultrasound images and cartoons was created to help with the ultrasound classification. The tool provides a recommendation to perform a biopsy or when to repeat ultrasound monitoring if necessary.

Cytologic features can also be entered in the algorithm if a biopsy was performed, to further determine the cancer risk. The six cytology categories (I-VI) of the Bethesda System for Reporting Thyroid Cytopathology are used with certain subcategories.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The AACE/AME TNAPP is a new, easy-to-use, electronic tool available online to provide recommendations for thyroid nodule management. The tool can be modified in the future as new information becomes available and guidelines change. The development of TNAPP represents an innovative way to disseminate evidence-based guidelines for thyroid nodule care. Future studies are needed to validate the accuracy of the TNAPP results.

— Alina Gavrila, MD, MMSc

THYROID NODULES, continued

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/

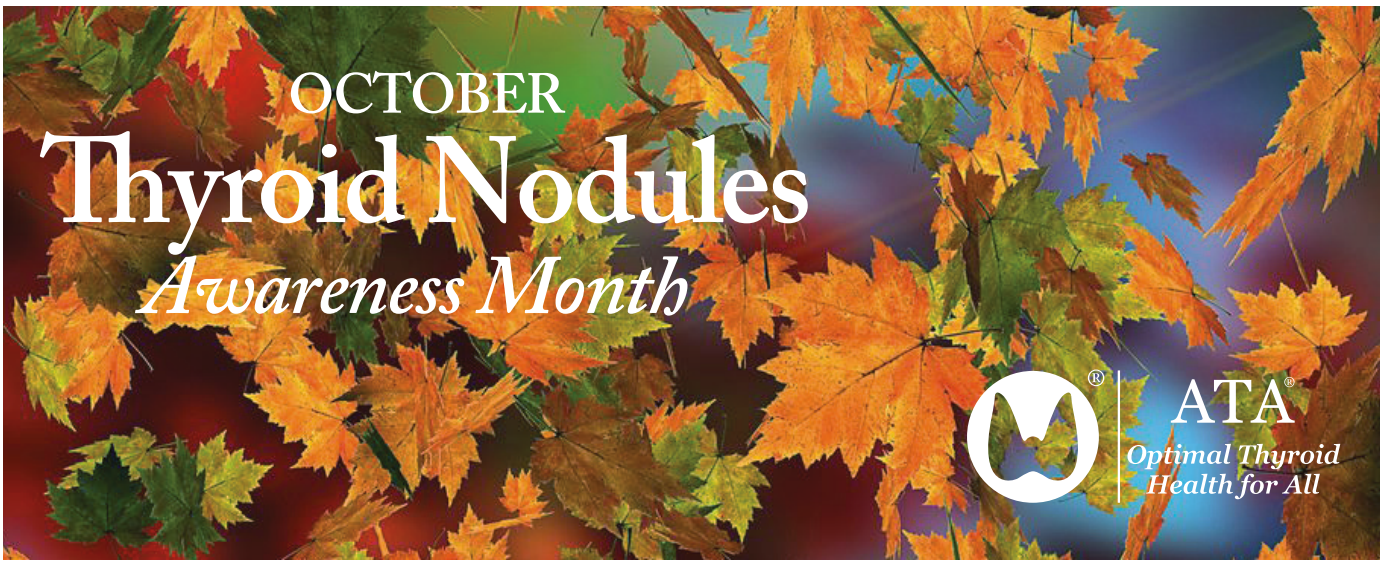
ABBREVIATIONS & DEFINITIONS

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5-10% are cancerous (Malignant).

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 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.

Thyroid cytology: the cells obtained from the FNA are prepared for optimal preservation and examined with a microscope to assess whether they are normal or show features of disease.



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THYROID CANCER

Risk factors for recurrence of follicular thyroid cancer

BACKGROUND

Thyroid cancer is the fastest rising cancer. Papillary thyroid carcinoma is the most common type of thyroid cancer and follicular thyroid carcinoma is the second most common. Together they make up 90+% of all thyroid cancer. Risks for recurrence (when the cancer comes back after treatment that was successful in destroying the cancer) of papillary thyroid carcinoma are well known. In contrast, follicular thyroid carcinoma is a lot less common than papillary thyroid carcinoma, and risk factors for recurrence of follicular thyroid carcinoma are not well defined. Papillary thyroid carcinoma and follicular thyroid carcinoma are often grouped together even though they differ in presentation and clinical behavior. In contrast to papillary thyroid carcinoma, follicular thyroid carcinoma recurs more frequently with distant metastases (where the cancer spreads to other organs far away from the thyroid) than involvement of neck lymph nodes (small organs found in the neck and also in other locations). The purpose of this study is to systematically review the risk factors for follicular thyroid carcinoma recurrence.

THE FULL ARTICLE TITLE

Grønlund MP et al Risk factors for recurrence of follicular thyroid cancer: A systematic review. Thyroid. Epub 2021 Jul 5. PMID: 34102860.

SUMMARY OF THE STUDY

A systematic literature search was performed in September 2020 of studies evaluating risk factors for follicular thyroid carcinoma recurrence. A total of 9 studies with a total of 1,544 patients from eight countries were included in this review. Risk factors examined in the studies included sex, age at diagnosis, primary cancer size, invasiveness (spread into the thyroid capsule and into blood vessels), positive resection margin (presence of leftover tumor after surgery), spread to the lymph nodes and spread outside the neck at diagnosis. The average follow-up time ranged from 5 to 23.7 years. The average rate of recurrence was 13.6% ranging from 2 to 29%. In 64.8% of recurrent cases, spread outside the neck was noted. Age greater than 45 years, primary cancer size greater than 4 cm, increased invasiveness, multiple nodules in the thyroid with the cancer, positive resection margin, spread to the lymph nodes in the neck and spread outside the neck were all identified as risk factors associated with follicular thyroid carcinoma recurrence.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Risk factors for recurrence of follicular thyroid carcinoma were identified. Age and multifocal disease had more of an impact on the risk of recurrence of follicular thyroid carcinoma than in papillary thyroid carcinoma. Future studies on follicular thyroid carcinoma are needed to better understand risk for cancer recurrence.

— Priya Mahajan, MD

ATA THYROID BROCHURE LINKS

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid Cancer: Includes papillary and follicular thyroid cancer

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

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

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

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

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

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THYROID NODULES

Repeated biopsies of thyroid nodules to perform molecular testing reduces need for thyroid surgery

BACKGROUND

Thyroid nodules are very common and, for the most part, develop for unknown reasons. The concern about any nodule is whether the nodule is cancerous. Only a small fraction (<6%) of thyroid nodules will turn out to be cancers. The American Thyroid Association has published guidelines as to which nodules are recommended to be evaluated for cancer, which requires a biopsy of the nodule.

Overall, ~5% of biopsies identify a cancer (papillary thyroid cancer) and 80-85% are benign (non-cancerous). However, 10-15% are indeterminate, which means that the cells are not either clearly abnormal or clearly normal. Because of this uncertainty, people who have indeterminate thyroid biopsies often undergo surgery to remove at least part of the thyroid to make sure that cancer is not present. Alternatively, the cells obtained in an indeterminate biopsy can be sent out for further analysis using molecular marker testing. If the molecular markers are positive, surgery is recommended. If they are negative, the nodule is considered benign. Molecular marker testing is an important clinical tool to provide additional cancer risk assessment, but it is expensive and their best use remains an area of ongoing study. It is unclear whether molecular testing should be used reflexively to test all categories of indeterminate nodules.

In this study, the authors analyze a unique clinical group of patients in whom repeat biopsy was obtained prior to molecular testing in almost all cases to evaluate the implications of performing a repeat biopsy before molecular diagnostic testing indeterminate nodules.

FULL ARTICLE TITLE

Nishino M et al 2021 Repeat fine needle aspiration cytology refines the selection of thyroid nodules for Afirma gene expression classifier testing. Thyroid. Epub 2021 Apr 3. PMID: 33813868.

SUMMARY OF THE STUDY

All of the patients included in this study not only had an indeterminate thyroid nodule biopsy, but all had a second biopsy to confirm the initial indeterminate result. Patients were 25 to 90 years of age and 80% of patients were female. A total of 370 nodules were included and all of these also had molecular marker testing using Afirma™. The study authors then went back and asked how many of the 370 indeterminate nodules actually benefited from Afirma™ testing.

Of the 370 nodules that were indeterminate with the first biopsy, the Afirma™ results were 148 suspicious and 222 negative (benign). A total of 182 second biopsies returned a different cytology result with the repeat biopsy (133 benign, 49 insufficient) and were considered low risk. The Afirma™ results were suspicious in 61 (33.2%) of these nodules. These 61 suspicious nodules were subsequently removed by surgery and revealed 4 cancers and 3 per-cancerous results (NFTP). Of the 188 nodules that were indeterminate on both biopsies, 87 were suspicious (46.3%) and 16 ended up being cancers with 12 pre-cancers (NFTP). Overall, if the decision was made to perform Afirma testing only if both biopsies were indeterminate, the number of tests would decrease by ~50% and result in missing 4 cancers. However, these 4 cancers were 20% of the total number of cancers in the entire group. Thus, the more nodules tested with Afirma™, the more cancers identified and the more surgeries were performed.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These data show that repeating a biopsy after an indeterminate result and testing with Afirma™ only if there were 2 inderminate results would decrease the number of Afirma™ tests by ~50%, decrease surgery by ~33% and miss 20% of the cancers. More data is needed to evaluate whether the missed cancers could otherwise be

THYROID NODULES, continued

identified. These data are important in the evaluation as to the best use of these molecular maker tests. Further, repeating this study with other molecular marker tests may be helpful to provide both the patient and the physician with the best data to make the best decision for treatment of inderminate nodules.

— Sarah R. Kaslow, MD, MPH and Jason D. Prescott MD PhD

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

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 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™ Gene Expression Classifier and Thyroseq™.

Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): a new term has been used to describe a type of papillary thyroid cancer which is non-invasive. These cancers behave less aggressively than typical papillary thyroid cancer and have been shown to have low risk for recurrence and low risk for spread outside of the thyroid.

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HYPERTHYROIDISM

Rate of remission is the most important determinant for treatment decision-making in Graves' disease

BACKGROUND

Graves' disease, the most common cause of hyperthyroidism or overactive thyroid, can be treated by one of three ways: antithyroid drugs (ATD), which are medications that slow the thyroid function), surgery or radioactive iodine therapy, a radioactive pill that targets the thyroid almost exclusively and slowly destroys thyroid cells. Each one of these treatments have different benefits and risks. For example, the chances of resolution of the hyperthyroidism (remission) for radioactive iodine therapy and surgery is more than 90%. In contrast, ATDs can produce a remission in only about 25-50% of the patients. On the other hand, the risks of complications are higher with surgery (low calcium, voice problems) and ATD (rash, liver problems). The choice of which treatment to use should be a shared one, between the clinician and the patient, and based on risks, benefits and patient's preferences. This study was done to try to understand which factors affect the treatment preferences in patients and clinicians and compare both of them.

THE FULL ARTICLE

van Kinschot CMJ et al 2021 Preferences of patients and clinicians for treatment of Graves' disease: A discrete choice experiment. Eur J Endocrinol 184:803–812.

SUMMARY OF THE STUDY

This study was conducted in the Netherlands in 2019. The researchers asked 286 patients with Graves' disease and 61 clinicians what treatment they would choose among two or more options offered. Each treatment given to the participants to choose from was associated with different characteristics: chances of remission, severe side effects, permanent voice changes and hypocalcemia (low calcium in blood). The responses were examined to find out which treatment characteristics influenced the most in making their final decision. Patients were in average 47 years old and 95% were women. The clinicians were in average 37 years old and 80% were internists.

The least chosen treatments were the ones characterized by having lower chances of remission and higher risks of severe side effects, hypocalcemia and permanent voice changes. In terms of how important those characteristics were for each group: *remission rates*: 37% for patients and 35% for clinicians; *risk of side effects*: 19% for patients and 24% for clinicians; *hypocalcemia*: 12% for patient and 16% for clinicians; *permanent voice changes*: 5% for patients and 11% for clinicians.

The ideal treatment choice was ATD for both, patients and clinicians. When choosing between surgery and radioactive iodine therapy, patients preferred surgery while clinicians preferred radioactive iodine therapy. A lower remission rate was acceptable as long as the choice was ATD over radioactive iodine therapy or surgery

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In the past few years, ATDs have become the preferred choice for the treatment of Graves' disease, even though the remission rates are significantly lower with this treatment as compared with both radioactive iodine therapy and surgery. This study shows that although remission rate was very important for the patients, other factors, such as avoidance of complications, were more valued when making their final decision. In this regard, it is important to communicate to the patients what their "individualized" chances of cure with ATD are in order for them to make a more informed decision. Even though radioactive iodine therapy has the lowest risk of complications, patients did not generally choose this treatment. This may be due to fear of radioactivity and its negative connotation. This is in contrast with the physician's positive view of radioactive iodine therapy. Physicians should be aware of their patient's attitudes and values towards the different treatments to better guide and counsel.

— Susana Ebner MD

HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/

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

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

ABBREVIATIONS & DEFINITIONS

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Total thyroidectomy: surgery to remove the entire thyroid gland.

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.

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GRAVES' EYE DISEASE

Effect of radioactive iodine therapy on thyroid eye disease

BACKGROUND

Radioactive iodine therapy has been used for many years to treat hyperthyroidism due to Graves' disease, which is the most common cause of hyperthyroidism in the United States. It is currently the most common treatment for Graves' disease in the United States. Radioactive iodine therapy works because the thyroid is the only organ that can take up and store iodine. Thus radioactive iodine is taken up by the overactive thyroid gland, stored and causes destruction of the gland to treat the hyperthyroidism.

Thyroid eye disease (TED) is a complex disease that causes inflammation of the eyes, eye muscles and the surrounding tissues. TED is most often seen in patients with Graves' disease. Radioactive iodine therapy has been associated with worsening of TED, particularly in smokers. Because of this, there are different treatment strategies currently in use to dose radioactive iodine in Graves' disease. Some methods use a fixed dose of radioactive iodine whereas others calculate a dose based on size of the gland and the activity as determined by a radioactive iodine uptake scan.

This study sought to determine if there were any differences in worsening of TED based on the radioactive iodine treatment strategy used. These investigators examined the effect of three different radioactive iodine dosing protocols on treatment of hyperthyroidism and thyroid eye symptoms due to Graves' disease.

THE FULL ARTICLE TITLE:

Ariamanesh S et al 2020 Effect of different ^{131}I dose strategies for treatment of hyperthyroidism on Graves' ophthalmopathy. Clin Nucl Med 45:514–518. PMID: 32433165.

SUMMARY OF THE STUDY:

This study is clinical trial of three different radioactive iodine dosing protocols for the treatment of Graves' disease. They recruited 92 patients (58 women and 34 men) with hyperthyroidism due to Graves' disease with no or inactive thyroid eye symptoms at baseline. The patients were randomized to one of three groups of RAI dosing: Fixed low dose - 7 mCi; Fixed high dose - 15 mCi and Calculated dose - 150 Ci per gram of thyroid tissue. All patients were assessed at baseline, 6 months, and 12 months after receiving a treatment dose of radioactive iodine. They measured thyroid function tests as well as performed measurements of eye disease activity, including degree of eye protrusion (proptosis) and a clinical activity score (CAS). Successful treatment response was defined as development of hypothyroidism, subclinical hypothyroidism, or normal thyroid function. Any patient with persistent hyperthyroidism or subclinical hyperthyroidism after radioactive iodine therapy was considered a non-responder.

At 12 months, the successful treatment of hyperthyroidism was higher in the Fixed High Dose (94.4%) and Calculated Dose (92.9%) groups compared to Fixed Low Dose group (66.7%). The treatment in the Calculated Dose group was as effective as the Fixed High Dose group despite administering lower overall radioactive iodine doses and thus exposing the patient to a lower amount of radioactivity. Eye exams were performed at baseline and 6 months. The patients in the Calculated Dose group had higher clinical activity scores at baseline. Radioactive iodine therapy was associated with a worsening of proptosis and CAS overall, however the CAS was more frequently increased in the Fixed High Dose group (34.4%) compared to the other groups (Fixed Low Dose 13.8%, Calculated Dose 6.4%).

In summary, this study demonstrated that Fixed High Dose and Calculated Dose effectively treat hyperthyroidism but that the Calculated Dose protocol was associated with fewer progressive thyroid eye symptoms.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

The calculated dose protocol was able to successfully treat Graves' hyperthyroidism with overall lower radioactive

GRAVES' EYE DISEASE, continued

iodine doses and was less likely to be associated with progressive thyroid eye symptoms than the fixed high dose treatment. Both of these treatment protocols were much better than the fixed low dose protocol in treating the hyperthyroidism. Clinicians who use radioactive iodine to treat Graves' hyperthyroidism may want to consider giving a calculated dose instead of a fixed high dose of radioactive iodine to minimize potential for worsening thyroid eye disease.

— Whitney W. Woodmansee MD

ATA THYROID BROCHURE AND WEBSITE LINKS

Graves' Disease: https://www.thyroid.org/graves-disease/
Graves' Eye Disease: https://www.thyroid.org/graves-eye-disease/
Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/

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*).

Radioactive iodine uptake (RAIU): this is a measurement of activity of the thyroid gland and is reported as the percent of a dose of radioactive iodine that is retained in the thyroid gland 24 h after the dose is given. An increase in RAIU usually indicates hyperthyroidism.

Thyroid eye disease (TED): also known as Graves ophthalmopathy. TED is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

CAS: Clinical Activity Score, a scoring system used to evaluate patients with Graves' ophthalmopathy, and is based on classical signs of inflammation (pain, redness, swelling and function) and that helps predict which patients will benefit from immunosuppressive treatment

Proptosis: abnormal protrusion or displacement of an eye or other body part.

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HYPOTHYROIDISM

New formulations of levothyroxine may benefit select patients

BACKGROUND

Hypothyroidism (underactive thyroid) is very common and affects >5% of the general population at some point in their life. The treatment of hypothyroidism requires thyroid hormone replacement, usually in the form of levothyroxine. Levothyroxine most commonly comes in the form of a tablet. Levothyroxine tablets contain thyroid hormone compressed into a tablet composed of lactose monohydrate, cornstarch, carboxymethyl starch, gelatin, and dyes, among other components. Before thyroid hormone is absorbed, it must be released from the tablet, which can be facilitated by crushing the tablets. In contrast, levothyroxine in liquid form is already in liquid. In gel from, the outer gelatin shell is readily dissolved in the stomach, allowing levothyroxine to remain in solution.

Missing doses and failing to take levothyroxine as recommended are common reasons for difficulty in treating hypothyroidism. However, erratic absorption of levothyroxine in the gut can make treatment of hypothyroidism difficult. This can be seen in patients with celiac disease or taking levothyroxine at the same time as certain foods or medications, such as calcium or iron that block the absorption of levothyroxine. This study was conducted to identify whether levothyroxine in liquid or gel forms provide a better intestinal absorption and more stable thyroid hormone levels in patients.

THE FULL ARTICLE TITLE

Nagy EV et al 2021 New formulations of levothyroxine in the treatment of hypothyroidism: Trick or treat? Thyroid 31:193–201. PMID: 33003978.

SUMMARY OF THE STUDY

The authors reviewed the published research and reviewed papers in medical journals to summarize data on the absorption differences between levothyroxine tablets with gel or liquid forms of the hormone. These studies used a standard levothyroxine absorption test. Study subjects were given a single dose of 600 mcg of Levothyroxine in each form (tablet, liquid and gel) and serum FT_4, and TSH levels were determined at several time points after administration. Overall, there was no difference in FT_4 levels between the different forms at any time point. However, the level of TSH was lower after liquid form.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that there is minimal difference between the absorption of levothyroxine in tablet, gel or liquid forms. The authors concluded that more study is needed to confirm these findings. However, they also suggest that selected patients may benefit from taking them, including those who take medications interfering with absorption of levothyroxine or those that have allergies to the dyes or other components in the tables.

— Shirin Haddady, MD MPH

ATA THYROID BROCHURE LINKS

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

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

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

HYPOTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal. *Replacement therapy* means the goal is a TSH in the normal range and is the usual therapy. *Suppressive therapy* means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.

Levothyroxine (T_4): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tirosint™ and generic preparations

Celiac disease: an autoimmune disorder of the small intestine that occurs in genetically predisposed people of all ages from middle infancy onward.

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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ATA Alliance for Thyroid Patient Education

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

ATA® *Optimal Thyroid Health for All*

GRAVES' DISEASE & THYROID FOUNDATION®

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

Light of Life Foundation checkyourneck.com

BITE ME CANCER!

MCT8 - AHDS Foundation

THYROID CANCER ALLIANCE

Thyroid Cancer Canada / Cancer de la thyroïde Canada

Thyroid Federation International

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

Bite Me Cancer
www.bitemecancer.org
info@bitemecancer.org

Graves' Disease and Thyroid Foundation
www.gdatf.org
(Toll-free): 877-643-3123
info@ngdf.org

Light of Life Foundation
www.checkyourneck.com
info@checkyourneck.com

MCT8 – AHDS Foundation
mct8.info
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Thyca: Thyroid Cancer Survivors' Association, Inc.
www.thyca.org
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Thyroid Cancer Alliance
www.thyroidcanceralliance.org
www.thyroidcancerpatientinfo.org
Rotterdam, The Netherlands

Thyroid Cancer Canada
www.thyroidcancercanada.org
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