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Clinical Thyroidology[®] for the Public



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

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Adherence to treatment guidelines improves outcomes in medullary thyroid cancer

Medullary thyroid cancer (MTC) is a rare form of thyroid cancer with a worse prognosis compared to the more common papillary thyroid cancer. The American Thyroid Association (ATA) published the first set of guidelines to standardize MTC management in 2009; revised guidelines were then released in 2015. The goal of this study was to evaluate national adherence to the ATA guidelines for MTC, identify factors that can affect adherence, and assess whether guideline adherence affects patient survival.

McMullin JL et al. Improved adherence to ATA medullary thyroid cancer treatment guidelines. Ann Surg Oncol 2023;30(12):7165-7171; doi: 10.1245/s10434-022-12734-3. PMID: 36367629.

Radioactive iodine treatment for children with low-risk thyroid cancer - to give or not to give? Most children with thyroid cancer do very well as there are effective treatments available. The most recent American Thyroid Association guidelines to treat thyroid cancer in children no longer recommend radioactive iodine therapy for those with low risk cancer. The researchers designed this study to find out if doctors changed how they treated the children with low-risk thyroid cancer after the change in the guidelines.

Bojarsky M, et al. Outcomes of ATA low-risk pediatric thyroid cancer patients not treated with radioactive iodine Therapy. J Clin Endocrinol Metab 2023;108(12):3338-3344; doi: 10.1210/clinem/dgad322. PMID: 37265226.

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Completion thyroidectomy may not always be necessary in the setting of cancer spreading to the lymph nodes

Since many of the thyroid cancers discovered are low risk, there has been an increase in removal of the lobe containing the cancer rather than removing the entire thyroid gland. When cancer is found in the lymph nodes, this may lead to additional surgery to remove the remaining lobe and to consider radioactive iodine therapy. The goal of this study was to examine the clinical course of patients with cancer found in the lymph nodes after a lobectomy for thyroid cancer.

Alameer E et al. Partial thyroidectomy with incidental metastatic lymph nodes. JAMA Otolaryngol Head Neck Surg 2024;150(1):49-56. doi: 10.1001/jamaoto.2023.3668. PMID: 37971746.

How good is ultrasound in the initial detection of thyroid nodules?

Thyroid ultrasound is the best study when a physician feels an abnormality on the patient's neck, the patient has a compressive neck symptoms like trouble swallowing, or to monitor a previously diagnosed thyroid nodule. However, some ultrasounds are also ordered due to vague complaints of fatigue, which contribute to the rise in the number of ultrasounds performed in the United States. This study was done to determine reasons for obtaining a thyroid ultrasound and determine under what circumstances nodules detected made a clinically significant difference in the patient's life.

Kennedy E et al. Rates of detecting thyroid nodules recommended for biopsy with ultrasound: are all indications equal? Thyroid 2023;33(12):1434-1440; doi: 10.1089/ thy.2023.0234. PMID: 37981778.

THYROID EYE DISEASE......II

Artificial intelligence as a screening tool to detect severity of thyroid eye disease

Thyroid Eye Disease (TED) is an autoimmune condition that can affect patients with Graves' disease. Making an early diagnosis of TED is very important so it can be monitored and treated before the disease permanently damages the eye. This study looks at how good artificial intelligence is in recognizing and assessing the severity of TED and compared it to ophthalmologists specialized in TED.

Lin LY et al. A deep learning model for screening computed tomography imaging for thyroid eye disease and compressive optic neuropathy. Ophthalmol Sci 2023;4(1):1000412; doi: 10.1016/j.xops.2023.100412. PMID: 38046559.

HYPOTHYROIDISM & HYPERTHYROIDISM ...13

The combined effect of immune checkpoint inhibitors and tyrosine kinase inhibitors on thyroid function

Thyroid abnormalities are frequent side effects of classes of drugs known as immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs) used to treat non-thyroid cancers. Initial reports indicate a potential increase in rates of thyroid abnormalities during combined ICI+TKI therapy. This study examines the effect of ICI+TKI therapy on thyroid function in cancer patients.

Tsai K et al. The combined effect of immune checkpoint inhibitors and tyrosine kinase inhibitors on thyroid function. Thyroid 2024;34(2):158-166; doi: 10.1089/thy.2023.0542. PMID: 38069567.

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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 X (previously known as Twitter) 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 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.

June is Differentiated Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Can guidelines improve outcomes in medullary thyroid cancer?
- Radioactive iodine treatment for children with low-risk thyroid cancer to give or not to give?
- Is completion thyroidectomy always necessary in the setting of cancer spreading to the lymph nodes?
- How good is ultrasound in the initial detection of thyroid nodules?
- Can artificial intelligence help in the detection of thyroid eye disease?
- Does the combination of ICI and TKI cancer drugs increase the development of thyroid abnormalities?

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



THYROID CANCER



Adherence to treatment guidelines improves outcomes in medullary thyroid cancer

BACKGROUND

Medullary thyroid cancer (MTC) is a rare form of thyroid cancer with a worse prognosis compared to the more common papillary thyroid cancer. MTC arises from the C-cells in the thyroid. Surgery is the main treatment since radioactive iodine is not effective for MTC as the C-cells do not take up iodine. More recently, targeted molecular therapy has been approved for advanced MTC cancer.

The American Thyroid Association (ATA) published the first set of guidelines to standardize MTC management in 2009; revised guidelines were then released in 2015. The goal of this study was to evaluate national adherence to the ATA guidelines for MTC, identify factors that can affect adherence, and assess whether guideline adherence affects patient survival.

THE FULL ARTICLE TITLE

McMullin JL et al. Improved adherence to ATA medullary thyroid cancer treatment guidelines. Ann Surg Oncol 2023;30(12):7165-7171; doi: 10.1245/s10434-022-12734-3. PMID: 36367629.

SUMMARY OF THE STUDY

The study included all MTC patients enrolled in the National Cancer Database (NCDB) between 2004 to 2015, with emphasis on data collected after 2009, when the initial ATA guidelines for MTC were released. The NCDB, which is jointly maintained by the American College of Surgeons Commission on Cancer (CoC) and the American Cancer Society, represents a comprehensive cancer database including data from patients followed at more than 1500 accredited cancer programs. More than 1 million cancer cases are added annually, which represent 70% of all newly diagnosed cancers in the US. Data used for this study included patient characteristics, demographics, socioeconomic status, and co-morbidities in addition to cancer-specific information, staging of the cancer, presence of invasion outside the thyroid and treatment type (thyroidectomy with/without central and lateral neck dissection). The primary study outcome was whether the use and extent of surgery were consistent with the 2009 ATA guidelines. Survival analysis was performed to assess the overall survival rates of patients who received treatment according to the guidelines in comparison to treatment that differed form guidelines.

The study included 3421 patients treated for MTC in 843 hospitals from 2009 to 2015. A total of 427 patients had spread of cancer outside of the neck (advanced cancer), while the rest had cancer limited to the neck region (low risk cancer). Among the 2994 patients with low risk cancer, 86% underwent total thyroidectomy and 68% lymph node dissection, as recommended by the ATA guidelines. In patients with advanced cancer, 51% underwent thyroid surgery and 54% lymph node dissection. Overall, 72% of patients received treatment according to the ATA guidelines. A small percentage of patients received treatment not recommended by the guidelines, such as chemotherapy (5.8%) and radioactive iodine therapy (2.3%).

A progressive increase in guideline adherence was noted over time, with an adherence rate of 67% before 2009 and 74% after 2009. Factors associated with non-adherence to guidelines included treatment at non-academic facilities, living within 50 miles to treatment facility, female gender, and older age. Adherence to treatment guidelines improved overall patient survival.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows a positive impact of the ATA guidelines for MTC management published in 2009, which resulted in improved adherence to treatment recommendations and overall patient survival. Thus, using standardized evidence-based treatment is critical for the best outcomes in patients with MTC. The identi-



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THYROID CANCER, continued



fication of factors that can affect guideline adherence, such as patient characteristics and treatment location is important for finding interventions to address these barriers. Additional research is needed to further increase adherence to the ATA guidelines and improve the quality of care for MTC patients.

— Alina Gavrila, MD, MMSC

ATA RESOURCES

Thyroid Cancer (Medullary): <u>https://www.thyroid.org/medullary-thyroid-cancer/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

ABBREVIATIONS & DEFINITIONS

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

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).

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.

Central neck dissection: surgical procedure to remove all lymph nodes in the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries

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

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

THYROID CANCER



Radioactive iodine treatment for children with low-risk thyroid cancer - to give or not to give?

BACKGROUND

Thyroid cancer is common in adults and children. Most patients do very well as there are effective treatments for thyroid cancer. Surgery is the first option and is often curative. For patients with high risk thyroid cancer, radioactive iodine therapy can be very helpful as it seeks out thyroid cancer cells remaining after surgery and destroys them. There are some potential long-term problems associated with radioactive iodine therapy, especially for children. For example salivary gland damage leading to dry mouth, getting other cancers later in life and possibly having trouble having kids in the future. Partly because of this, as well as the fact that patients with low risk thyroid cancer do well with surgery alone, the most recent American Thyroid Association guidelines to treat thyroid cancer in children no longer recommend radioactive iodine therapy for those with low risk cancer.

The researchers designed this study to find out if doctors changed how they treated the children with low-risk thyroid cancer after the change in the guidelines. They also wanted to find out if not giving radioactive iodine therapy had any effect on thyroid cancer recurrence in children.

THE FULL ARTICLE TITLE

Bojarsky M, et al. Outcomes of ATA low-risk pediatric thyroid cancer patients not treated with radioactive iodine Therapy. J Clin Endocrinol Metab 2023;108(12):3338-3344; doi: 10.1210/clinem/dgad322. PMID: 37265226.

SUMMARY OF THE STUDY

The study was done at Children's Hospital of Philadelphia. The researchers reviewed the medical records of patients who were less than 19 years old when they were treated for low-risk thyroid cancer between 2010 and 2020. Low risk patients had thyroid cancer only in their thyroid gland and not in the nearby lymph nodes, or if they had cancer in the lymph nodes it was a very small amount in less than 5 nodes. They looked at blood tests for a protein called thyroglobulin which only comes from thyroid cells, checked for antibodies related to it, and did ultrasound scans of the neck to see how well the treatments worked. They split the results into 4 groups: 1) excellent response if there was no sign of cancer with the blood tests or the ultrasound, 2) biochemical incomplete response if the thyroglobulin levels remain detectable, 3) structural incomplete response if the ultrasound found something abnormal and 4) indeterminate response if they were not sure yet. They also checked for some changes in the genes that might be linked to cancer especially more aggressive cancer. They analyzed the results to find out the things that had influenced whether patients got radioactive iodine therapy or if their cancer went away.

They looked at 95 patients who had low-risk thyroid cancer, 78 girls and 17 boys. Out of these, 53% got treatment with radioactive iodine therapy and 47% didn't. Radioactive iodine therapy was more commonly used before 2015, 82% of patients before 2015 and only 33% of patients after 2015 were treated with radioactive iodine therapy. Patients who had larger cancers, cancer in the lymph nodes and who were treated before 2015 were more likely to have radioactive iodine therapy. About 70% of patients who were treated with radioactive iodine therapy and 69% of those who didn't were doing very well after 1 year so there wasn't much difference. As time passed even more of them started to do well without any sign of cancer. None of the patients had persistent structural disease. There wasn't a big difference in the rate of improvement after one year and at the last check up between patients with genes that could make the cancer more aggressive and those with genes that are less likely to make it worse regardless of radioactive iodine therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that not giving radioactive iodine therapy to children with low-risk thyroid cancer doesn't



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THYROID CANCER, continued

affect their prognosis. One year after treatment is a good time to check how the cancer is doing to see if not giving radioactive iodine therapy has affected their chances of getting better. The findings of this study are important for patients because they support the recent recommendations in how we treat low-risk thyroid cancer in children and confirms that it is safe and equally effective to avoid radioactive iodine therapy in these patients. We still need the results from continuation of this and similar studies that follow the patients for longer periods to make sure cancer does not come back.

— Ebru Sulanc, MD

ATA RESOURCES

Pediatric Differentiated Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/</u>pediatric-differentiated-thyroid-cancer/

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.

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

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-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the nondestructive 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).

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

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.

THYROID CANCER



Completion thyroidectomy may not always be necessary in the setting of cancer spreading to the lymph nodes

BACKGROUND

Most patients diagnosed with thyroid cancer have an excellent prognosis. This is because there are excellent treatments available, with the first treatment almost always being surgery. An important guiding part of the management of thyroid cancer is an ongoing assessment of risk of the cancer persisting or returning after the initial therapy. This has resulted in incorporating higher thresholds for surgery and therapy with radioactive iodine and personalizing treatment options by factoring in patients' preferences. Since many of the thyroid cancers discovered are low risk, this means removal of the lobe containing the cancer rather than removing the entire thyroid gland.

When a lobe is removed, there is usually also removal of lymph nodes in the central neck behind the lobe. Traditionally, the presence of cancer in lymph nodes removed during surgery has been associated with higher cancer recurrence rates. When cancer is found in the lymph nodes, this may lead to additional surgery to remove the remaining lobe (completion thyroidectomy) and to consider radioactive iodine therapy.

The goal of this study was to examine the clinical course of patients with cancer found in the lymph nodes after a lobectomy for thyroid cancer.

THE FULL ARTICLE TITLE

Alameer E et al. Partial thyroidectomy with incidental metastatic lymph nodes. JAMA Otolaryngol Head Neck Surg 2024;150(1):49-56. doi: 10.1001/jamaoto.2023.3668. PMID: 37971746.

SUMMARY OF THE STUDY

This was a study performed at Memorial Sloan Kettering Cancer Center (MSKCC) reviewing patients undergoing surgery for thyroid cancer between 1985 and 2015. The authors included patients who had undergone thyroid lobectomy or isthmusectomy without lateral neck dissection and had cancer in lymph nodes identified on final pathology. The study group consisted of patients who did not proceed with immediate completion surgery and were followed clinically. They also identified a subgroup of patients who met the same inclusion criteria but who had undergone immediate completion thyroidectomy. Data on patients' demographics, surgical procedure, histopathology, cancer staging, and time to completion thyroidectomy were collected. Clinical outcomes, including recurrence of cancer and diseasespecific and overall survival, were reviewed.

The authors identified 1306 patients who had undergone thyroid lobectomy or isthmusectomy at Memorial Sloan Kettering Cancer Center between 1986 and 2015. Of these patients, 85 had cancer found in central lymph nodes; 74 of these were observed without immediate completion thyroidectomy. The remaining 11 patients opted for completion thyroidectomy. Average age at surgery was 39 years and 59% of patients were female. Lobectomy was performed in 64 patients and included isthmusectomy in 10. Classic papillary thyroid carcinoma (PTC) was the most common cancer type (46% of cases), followed by tall-cell PTC in 18%, follicular variants of PTC in 6.8%, solid/trabecular variants of PTC in 1.4%, and oncocytic carcinoma in 1.4%. Based on the American Thyroid Association (ATA) risk stratification, 70% of patients were characterized as intermediate risk for recurrence. The average diameter of metastatic lymph nodes was 3 mm (range, 0.7–12). Most patients had 1 positive node and 6 patients had 3-5 involved lymph nodes.

The 11 patients who proceeded directly to completion thyroidectomy were more likely to have additional aggressive cancer features in addition to cancer in the lymph nodes. The average follow-up for patients who were observed was ~48 months. The pathology of completion thyroidectomy showed benign nodules in two cases and a 2-mm microscopic PTC in the third. No radioactive



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THYROID CANCER, continued

iodine treatment was administered. Five-year disease specific survival was 100%, overall survival 96.2% and recurrence free survival 97.4%.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this study, patients undergoing lobectomy or isthmusectomy for thyroid cacner and found to have cancer in the central lymph nodes and not proceeding to routine completion surgery had excellent outcomes. This is an important study that will help continue to limit surgery to those that would most benefit from it and to spare extensive surgery in patients at low risk of cancer recurrence.

— Alan P. Farwell, MD

ATA RESOURCES

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

ABBREVIATIONS & DEFINITIONS

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

Lobectomy: surgery to remove one lobe of the thyroid.

Completion thyroidectomy: surgery to remove the remaining thyroid lobe in thyroid cancer patients who initially had a lobectomy.

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.

THYROID NODULES

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How good is ultrasound in the initial detection of thyroid nodules?

BACKGROUND

Thyroid ultrasound is the best study when a physician feels an abnormality on the patient's neck, the patient has a compressive neck symptoms like trouble swallowing, or to monitor a previously diagnosed thyroid nodule. The information generated by a thyroid ultrasound is used to determine whether any additional therapy is needed. However, it is not a good test for screening of thyroid abnormalities, as this can result in diagnosing too many small thyroid cancers that would otherwise not affect a patient's lifespan. Another big portion of small thyroid nodules are detected on other types of imaging tests that are done for other reasons, such as chect CT scans to evaluate problems in the lungs. In addition, some ultrasounds are also ordered due to vague complaints of fatigue, which contribute to the rise in the number of ultrasounds performed in the United States.

This study was done to determine reasons for obtaining a thyroid ultrasound and determine under what circumstances nodules detected made a clinically significant difference in the patient's life. With this study, physicians and patients might have a better understanding of appropriate use of the ultrasound machine.

THE FULL ARTICLE TITLE

Kennedy E et al. Rates of detecting thyroid nodules recommended for biopsy with ultrasound: are all indications equal? Thyroid 2023;33(12):1434-1440; doi: 10.1089/thy.2023.0234. PMID: 37981778.

SUMMARY OF THE STUDY

All adult patients who received a thyroid ultrasound at a United States academic medical center from 2017 to 2019 were studied, totaling 1739 patients. Of the patients, 86% were white, 76% were female, and 62% had private insurance. Patients with previous ultrasounds, no indication for the ultrasounds, or the ultrasounds performed to evaluate another anatomic structure than the thyroid gland were not included. The most common indication for the ultrasound was a suspected nodule on physical exam at 40%, and the next common indication was to further characterize a nodule previously diagnosed with another imaging test (28%). Of all the ultrasounds, only 62% of the ultrasounds performed showed a thyroid nodule, and only 27% of the nodules met criteria for further evaluation with a thyroid biopsy. When only considering the ultrasounds done to follow up a nodule diagnosed on another imaging test, the percentages of nodules and biopsies required increased to 94% and 55%, respectively. The percentage of nodules on the ultrasounds of patients whose physician felt a neck abnormality was 55%, and percentage of nodule on ultrasounds for patient with metabolic symptoms was 43%. Only 39% of the ultrasounds performed for compressive symptoms of patients showed nodules. Not only did this group have the smallest size of nodules (1.2 cm), but also the lowest portion of those nodules got biopsied (6%).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Non-ultrasound imaging tests resulted in the highest percentage of nodules found on subsequent ultrasounds and the highest rate of biopsies performed on these nodules. Other indications for ultrasound (nodules felt by physicians on exam, compressive symptoms felt by the patient, or metabolic symptoms) only revealed nodules at the same rate as the baseline population. While detection of thyroid cancer has increased, the death rates have remained the same. It is still appropriate to use ultrasound for nodules detected on other imaging tests and for a suspected nodule palpated by the physician based on physical exam, but it might not be appropriate to perform ultrasound based on nonspecific patient symptoms given high costs associated with monitoring or intervening on thyroid nodules or cancer.

— Pinar Smith, MD

THYROID NODULES, continued



ATA RESOURCES

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

ABBREVIATIONS & DEFINITIONS

Goiter: a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a nodular goiter; if there is more than one nodule it is called a multinodular goiter.

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 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.

Papillary microcarcinoma: a papillary thyroid cancer smaller than I cm in diameter.

THYROID EYE DISEASE



Artificial intelligence as a screening tool to detect severity of thyroid eye disease

BACKGROUND

Thyroid Eye Disease (TED) is an autoimmune condition that can affect patients with Graves' disease. TED occurs in about one in every three patients with Graves', with most cases being mild. In TED, there is inflammation of the tissues around the eyes (especially eye muscles and fat) causing the eye to be pushed forward (bulging), eye pain, tearing, swelling of the conjunctiva (the white part of the eye), double vision and, if severe, it can affect the optic nerve and cause loss of vision. Making an early diagnosis of TED is very important so it can be monitored and treated before the disease permanently damages the eye.

Artificial intelligence (AI) is a new technology that allows machines to think, learn and make decisions, like humans. For example, by providing information such as X-rays to the machine, it learns to recognize and diagnose certain conditions and can even tell how serious the condition maybe. Many fields in medicine are now utilizing AI to help with early diagnosis and identifying diseases. This study looks at how good AI is in recognizing and assessing the severity of TED and compared it to ophthalmologists specialized in TED (oculoplastic surgeons).

THE FULL ARTICLE TITLE

Lin LY et al. A deep learning model for screening computed tomography imaging for thyroid eye disease and compressive optic neuropathy. Ophthalmol Sci 2023;4(1):1000412; doi: 10.1016/j.xops.2023.100412. PMID: 38046559.

SUMMARY OF THE STUDY

The authors looked at patients who presented at the Massachusetts Eye and Ear Institute in Boston from 2011-2021. Patients who had CT scans of the orbits and eye exams done confirming TED were included in the study (total of 123 patients). Patient who had CT scan but did not have TED served as normal controls (31 patients). Based on their eye exam, patients were classified as normal, mild TED or severe TED (optic nerve damage). The average age of the patients was 71, and the majority were women (74%) and white (75%). The machine learned to recognize TED by first being taught (trained) on how CT images of patients with no disease, mild and severe TED look like. Once trained, when the machine looked at the CT scans of the orbits of the study patients, it correctly identified the diagnosis (normal, mild or severe TED) in almost 90%. Overall, 3 patients with severe TED were wrongly classified as mild, but none of the patients with severe TED were misclassified as normal. When eye specialist looked at the same CT scans, they correctly made a diagnosis in 70% of the cases.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that when using this design of machine learning, AI can correctly diagnose TED, including its severe form, in almost 90% of cases and does it better than experts. By being able to correctly diagnose severe TED in CT scans, it can alert the non-specialized physician to make an urgent referral to an oculoplastic surgeon. Timely treatment of severe TED can prevent vision loss.

— Susana Ebner MD

ATA RESOURCES

Graves' Disease: <u>https://www.thyroid.org/graves-disease/</u> Thyroid Eye Disease: <u>https://www.thyroid.org/thyroid-eye-disease/</u>

THYROID EYE DISEASE, continued



ABBREVIATIONS & DEFINITIONS

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

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





HYPOTHYROIDISM AND HYPERTHYROIDISM



The combined effect of immune checkpoint inhibitors and tyrosine kinase inhibitors on thyroid function

BACKGROUND

Recent advancements in cancer treatment include the introduction of immunotherapy and kinase inhibitors, which have significantly improved cancer prognosis among patients. However, these compounds are responsible for several adverse events that affect the endocrine glands. Endocrine-related adverse events, and specifically thyroid abnormalities, are now acknowledged as frequent side effects of classes of drugs known as immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs). Interestingly, thyroid abnormalities during treatment with ICIs has been shown to be a positive prognostic sign.

The favorable outcome achieved with ICI and TKI drugs individually have prompted clinical trials assessing combined ICI+TKI regimens. Initial reports indicate a potential increase in rates of thyroid abnormalities during combined ICI+TKI therapy. This study examines the effect of ICI+TKI therapy on thyroid function in cancer patients with normal thyroid function as determined by pretreatment TSH levels.

THE FULL ARTICLE TITLE

Tsai K et al. The combined effect of immune checkpoint inhibitors and tyrosine kinase inhibitors on thyroid function. Thyroid 2024;34(2):158-166; doi: 10.1089/ thy.2023.0542. PMID: 38069567.

SUMMARY OF THE STUDY

This study included adult patients treated with a combination of ICI and TKI therapy for solid cancers. ICIs used were pembrolizumab, nivolumab, and ipilimumab, and the TKIs used were lenvatinib, axitinib, sunitinib, pazopanib, cabozantinib, tivozanib, and imatinib. After receiving ICI+TKI, patients were identified as having no thyroid abnormalities if they had no changes in thyroid hormone levels. Thyroid disturbances were defined as follows: 1) hypothyroidism as elevated TSH and low FT4 levels; 2) subclinical hypothyroidism as elevated TSH with normal FT4 levels; 3) hyperthyroidism

as a low TSH and elevated FT4 levels; and 4) subclinical hyperthyroidism as low TSH with normal FT4 levels. Patients who needed an increase in thyroid hormone therapy after initiation of ICI+TKI were defined as having worsening of hypothyroidism.

A total of 106 patients with previous notmal thyroid function were included. Most patients were female (70.8%), the average age was 63.5 years and the most common cancer was uterine cancer (43.4%). The most common ICI+TKI therapy was pembrolizumab plus lenvatinib (73 patients, 68.9%). Of these patients, 67 (63.2%) developed new thyroid abnormalities after receiving ICI+TKI. In particular, 14 (13.2%) developed hypothyroidism, 42 (39.6%) developed subclinical hypothyroidism and 11 (10.4%) developed hyperthyroidism. No patients had subclinical hyperthyroidism. The onset of thyroid abnormalities occurred during the early phase of treatment with ICI+TKI. The average time from initiation of ICI+TKI treatment to hyperthyroidism was 7 weeks, to hypothyroidism 8.1 weeks and to subclinical hypothyroidism 8 weeks. All cases of hyperthyroidism resolved to a normal thyroid state or hypothyroidism in 12 weeks without intervention. Females had a 2.72-fold increased risk of developing thyroid abnormalities, after adjusting for age.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that changes in thyroid function are commonly observed during treatment with the combination ICI+TKI, typically starting within the initial weeks of therapy. Hypothyroidism is the most common result and is often long-term and requires treatment with levothyroxine. Hyperthyroidism is also common, but is short lived, resolving within 3 months and usually does not need to be treated. It is recommended to routinely monitor thyroid function from the initial stages of ICI+TKI therapy to promptly detect any abnormalities.

- Alan P. Farwell, MD



HYPOTHYROIDISM AND HYPERTHYROIDISM, continued



ATA RESOURCES

Hyperthyroidism (Overactive): <u>https://www.thyroid.org/hyperthyroidism/</u> Hypothyroidism (Underactive): <u>https://www.thyroid.org/hypothyroidism/</u>

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.

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.

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

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

Thyroxine (T4): the major hormone produced by the thyroid gland. T4 gets converted to the active hormone T3 in various tissues in the body.



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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

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