Volume 18 | Issue 8 | August 2025

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

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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 @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,* 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.

August is Thyroid Disease and Pregnancy Awareness Month.

In this issue, the studies ask the following questions:

- How long do pregnancy-related thyroid problems last?
- Does radioactive iodine treatment for Graves' disease increase the risk of thyroid cancer?
- How common is thyroid cancer in patients with Graves' disease?
- Is there an increased risk of depression with patients with hypothyroidism?
- How common are the salivary glands damaged after radioactive iodine therapy?
- Is molecular testing too expensive to help to plan treatment for indeterminate thyroid nodules?

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 AND PREGNANCY

How long do pregnancy-related thyroid problems last?

BACKGROUND

Disorders of the thyroid, including autoimmune disorders, can develop during pregnancy. These disorders may lead to problems in the mother and the baby. It is well known that thyroid hormone levels change during pregnancy and some of these changes may be interpreted as abnormal. This includes isolated low T4 levels (hypothyroxinemia), gestational thyrotoxicosis and overt hyperthyroidism. It is recognized that test results of thyroid function vary in pregnancy based on the pregnancy trimester.

This study aims to analyze thyroid function changes in different trimesters of pregnancy and compare these changes with pregnancy outcomes.

THE FULL ARTICLE TITLE

Yang Z, et al. The dynamic changes in maternal thyroid parameters across the three trimesters and their differential effects on the occurrence of adverse obstetric outcomes Endocr Metab Immune Disord Drug Targets. Epub 2025 Mar 4; PMID: 40045850.

SUMMARY OF THE STUDY

This study included 390 pregnant Chinese women between 2018 and 2022 from the Maternal-Fetal Cohort in Northeast China. The included participants were evaluated and had blood samples drawn to measure thyroid function tests through each trimester and after delivery.

The prevalence of thyroid dysfunction in the first, second, and third trimesters were, respectively, 0.3%, 2.0%, and 0.3% for subclinical hypothyroidism; 7.0%, 2.9%, and 2.0% for isolated hypothyroxinemia; 1.7%, 2.4% and 3.8% for subclinical hyperthyroidism, 2.9%, 0%, and 0% for overt hyperthyroidism (e.g., thyrotoxicosis); and 0% in all trimesters for overt hypothyroidism. The study showed that 1 out of 2 patients with isolated hypothyroxinemia in the first trimester improved to normal in the second trimester, while 2 out of 3 of these patients were normal in the third trimester. For those with overt hyperthyroidism in the first trimester, 7 of 10 were normal in the 2nd trimester, and the remaining 3 had levels improve to the level of subclinical hyperthyroidism in the second trimester. Serum FT4 and FT3 levels declined in all patients, while TSH levels increased from first to third trimester of pregnancy. Thyroid antibody levels decreased with time in those with thyroid autoimmunity.

In terms of outcomes, high blood pressure during pregnancy was higher in patients with thyroid autoimmunity and isolated hypothyroxinemia in the first trimester. Subclinical hypothyroidism was associated with postpartum hemorrhage, and subclinical thyrotoxicosis was associated with small for gestational age infants.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study shows that thyroid problems can resolve spontaneously as pregnancy progresses, indicating the necessity of repeated testing during different trimesters of pregnancy. While most of the thyroid problems do not require treatment, it is clear that some of these changes may have adverse outcomes during pregnancy. Finally, the ongoing questions as to what disorders are treated and which are simply watched are still unclear. Hence, it is worth further evaluation in monitoring thyroid function tests in pregnant patients presenting with thyroid dysfunction.

— Joanna Miragaya

ATA THYROID BROCHURE LINKS

Thyroid Disease in Pregnancy: https://www.thyroid.org/thyroid-disease-pregnancy/

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

THYROID AND PREGNANCY, continued

ABBREVIATIONS & DEFINITIONS

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.

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

Primary hypothyroidism: the most common cause of hypothyroidism cause by failure of the thyroid grand.

Transient hypothyroxinemia: temporary decrease in the blood level of thyroxine (T4) after delivery in pre-term infants, followed by the return of normal levels in the absence of any treatment.

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.

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

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

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

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GRAVES' DISEASE

Does radioactive iodine treatment for Graves' disease increase the risk of thyroid cancer?

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism. Radioactive iodine therapy is sometimes used for Graves' disease that has not responded to medication. There is a concern that radioactive iodine treatments might increase risk of thyroid cancer developing in the thyroid cells that are not destroyed. A group of patients were studied in the 1950s, and no increased risk of thyroid cancer with radioactive iodine treatments was found. However, when this same group was studied for an additional 24 years, an increase in thyroid cancers and other solid cancers was found. The criticism of the longer study is that the radioactive iodine doses were not accurate and that the hyperthyroidism itself can increase thyroid cancer risk. Nonetheless, after this study, fewer physicians have been ordering radioactive iodine treatments for their patients.

The goal of this study is to clarify if there is a link between radioactive iodine treatments and thyroid cancer and identify various characteristics of the thyroid cancers that occur in these patients treated with radioactive iodine.

THE FULL ARTICLE TITLE

Hiruma S, et al. Occurrence of newly diagnosed thyroid cancer is not increased after radioactive iodine therapy for Graves' disease. J Clin Endocrinol Metab. Epub 2025 Apr 11:dgaf231; doi: 10.1210/clinem/dgaf231. PMID: 40215268

SUMMARY OF THE STUDY

The medical charts of patients with Graves' disease from a specialized Japanese thyroid institute were analyzed from 2007 to 2016 to see if there was a link between receiving radioactive iodine for Graves' disease and thyroid cancer. After removing patients with pre-existing cancer, a total of 13,874 patients were studied. The patients were on average 30-50 years old and were followed for 5-10 years after the treatments. Separately, a second group of 23,179 patients who underwent radioactive iodine therapy for Graves' disease from April 1997 to December 2022 were studied.

A total of 2,284 Graves' patients were treated with radioactive iodine. A total of 12,418 patients were treated with antithyroid medications, and 287 patients had their thyroid glands surgically removed. New thyroid cancer was found in 8 patients who received the radioactive iodine treatment. In the group whose Graves' disease was only treated with medication, 39 patients developed cancer, with cancer found 0.43 times in a span of 1000 years of patients' lives. Over a total of 107,218 years of patient's lives studied, there was no significant difference in the incidence rates of thyroid cancer between the radioactive iodine group and the medication-only group. The sizes of the cancers were also not different between the two groups. Out of the 23,179 patients in the second group who underwent radioactive iodine for Graves' disease, 17 patients developed thyroid cancer. A total of 16 patients had the most common type of thyroid cancer, papillary thyroid carcinoma, and 15 were less than 1 cm in size. Only one patient who had received radioactive iodine developed anaplastic thyroid carcinoma, the most aggressive thyroid cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

For patients who received radioactive iodine, thyroid cancer occurred 0.53 times in a span of 1,000 years of patients' lives. This was not significantly different that the thyroid cancer incidence rates in patients who were treated with medication for their Graves' disease. The thyroid cancers found in patients who had received radioactive iodine were mostly in the category of American Thyroid Association low risk of recurrence, less than 1 cm, and with no concerning features of the cancer cells or genetic mutations. Patients and physicians can feel safe about using radioactive iodine treatment for Graves' disease that is not responding to medical therapy, as radioactive iodine does not seem to increase the risk of thyroid cancer significantly compared to medical therapies.

— Pinar Smith, MD

GRAVES' DISEASE, continued

ATA THYROID BROCHURE LINKS

Graves' Disease: https://www.thyroid.org/graves-disease/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/
Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/
Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/

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.

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).

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).

Anaplastic thyroid cancer: a very rare but very aggressive type of thyroid cancer. In contrast to all other types of thyroid cancer, most patients with anaplastic thyroid cancer die of their cancer and do so within a few years.

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GRAVES' DISEASE

Thyroid cancer in patients with Graves' disease

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States. Treatment options include antithyroid medication to control hyperthyroidism, surgery to remove the thyroid and radioactive iodine therapy to destroy the thyroid. All three treatments are effective options, but only surgery can determine if thyroid cancer be identified in patients with Graves' disease.

Since Graves' disease is caused by an antibody that attacks and turns on the thyroid, making it overactive, there has always been a concern that the antibody may increase the development of thyroid cancer. Fortunately, the presence of thyroid cancer in patients with Graves' disease has been reported to be very low (about 2%). However, the rate of diagnosis of thyroid cancer has increased in recent years in the general population. Because of this, these authors wanted to re-assess the rate of thyroid cancer among patients treated surgically for Graves' disease.

THE FULL ARTICLE TITLE

Moronta S, et al. Incidental thyroid cancer in patients with Graves' disease: not as rare as we previously believed. J Surg Res 2025;308:122-128; doi: 10.1016/j.jss.2025.02.024. PMID: 40101333.

SUMMARY OF THE STUDY

This study used a patient data set from the American College of Surgeons National Surgical Quality Improvement Program's (NSQIP) which anonymously collects information from multiple hospitals. Adult patients were selected who had a total thyroidectomy for Graves' disease and were excluded if they had preexisting thyroid cancer or were missing data needed for analysis. A total of 3,193 patients with Graves' disease were identified who underwent total thyroidectomy between 2013 and 2021. The average age was 42 years (range, 18–93); 82.3% of patients were female and 49.7% were White. Thyroid cancer was found in 406 patients (12.7%).

Almost all the patients were found to have papillary thyroid cancer (95%) or follicular thyroid cancer (3%), the most common types of thyroid cancer. Most patients had thyroid cancer limited to within the thyroid (343 patients (84.5%), and 26 had spread of the cancer to the lymph nodes in the neck (6.4%) disease. Cancers were solitary in 250 (61.6%), followed by 78 (19.2%) patients with multifocal cancer in both thyroid lobes followed by 51 (12.6%) with multifocal cancer only in 1 lobe. Patients with thyroid cancer tended to be older (average age, 47 years vs. 42 years) and had a higher body-mass index (28.9 vs. 27.8).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that the rate of undiagnosed thyroid cancer in patients with Graves' disease who undergo total thyroidectomy was much higher than previously reported and suggested that this information should be considered when counseling patients regarding treatment options for Graves' disease. However, there are several caveats to this recommendation. Since this is a database analysis based on patients that were already treated, so there is no data on why the patients underwent thyroidectomy for their Graves' disease or of the rate of thyroid cancer in those patients with Graves' disease who did not have surgery. All this needs to be considered when discussing treatment options for Graves' disease with patients. Hopefully future studies will shed more light on this issue.

— Marjorie Safran, MD

GRAVES' DISEASE, continued

ATA THYROID BROCHURE LINKS

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

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

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.

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.

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*.

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

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*).

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HYPOTHYROIDISM

Is there an increased risk of depression with patients with hypothyroidism?

BACKGROUND

Hypothyroidism is common and the rate of hypothyroidism is more common in women than men. Hypothyroidism and mood disorders often occur together, especially in women. The most common mood disorder seen in patients with hypothyroidism is depression. Low thyroid hormone levels may be in part responsible, especially when hypothyroidism is severe.

In patients with mild/subclinical hypothyroidism, a very mild form of hypothyroidism in which TSH levels are elevated but thyroid hormone levels are normal, the link with mood disorders is not clear. Treatment of subclinical hypothyroidism with thyroid hormone to improve depressive symptoms is still debatable. This study looks at the association of TSH levels and depressive symptoms in patients with and without mood disorders.

THE FULL ARTICLE TITLE

Singh B, et al. The association between thyrotropin and clinically relevant depression: a retrospective cross-sectional study. Thyroid
doi: 10.1089/thy.2024.0428. PMID: 39909475.

SUMMARY OF THE STUDY

This study was done at the University of Utah. The authors looked at 33,138 patients who had TSH levels and completed a health questionnaire between 2016 and 2021. The health questionnaire was used to assess clinically relevant depression in the individuals that responded. The average age was 42 and 69% were women.

Overall, 45% of individuals responding to the health questionnaire had a diagnosis of mood disorder, most often depression. Increasing TSH levels were linked to clinically relevant depression, particularly in women, those with hypothyroidism and those on thyroid hormone replacement. When divided by the TSH level, both subgroups with low and high TSH levels were linked to clinically relevant depression, but the link between high TSH and clinically relevant depression was stronger. Patients with subclinical hypothyroidism were more likely to have clinically relevant depression, in both groups with and without mood disorders.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study found that increasing TSH levels and clinically relevant depression are associated in patients with hypothyroidism and receiving thyroid hormone. This was true in patients with or without a diagnosis of mood disorders and those with mild hypothyroidism not on thyroid hormone. More studies are needed to evaluate this association and to determine the effect of treatment with thyroid hormone on patients with subclinical hypothyroidism with depressive symptoms.

— Susana Ebner MD

ATA THYROID BROCHURE LINKS

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.

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.

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

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

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THYROID CANCER

Oral health monitoring: a key part of thyroid cancer care after radioactive iodine treatment

BACKGROUND

Thyroid cancer is common, and, fortunately, has an excellent prognosis. This is because we have excellent treatments for thyroid cancer. Most patients initially get surgery to remove the thyroid. In patients at risk for the cancer recurring, or if all the cancer was not able to be removed, radioactive iodine therapy is the next step. Radioactive iodine therapy takes advantage of the fact that the thyroid is the only gland in the body that takes up, concentrates and retains iodine, which is used in making thyroid hormone. When patients are treated with radioactive iodine therapy, the remaining thyroid cells, both normal and cancer cells, take up the radioactive iodine and are destroyed.

Salivary glands also take up and concentrate iodine but do not store it. Because of this, the side effects of radioactive iodine therapy can include problems of the salivary gland. While these effects can be seen in all salivary glands, the parotid gland appears to be more susceptible to radioactive iodine. The complications can be immediate or long term and range from inflammation of the salivary gland and reduction in saliva production to gum and dental issues such as dental cavities.

This study reviews the potential impact of radioactive iodine therapy on salivary gland function and oral health in a patient population with thyroid cancer.

THE FULL ARTICLE TITLE

Terrazas JR, et al. Influence of radioiodine therapy on oral health and salivary production in patients with differentiated thyroid carcinoma. Endocr Pract. Epub 2025 Jan 10:S1530-891X(25)00019-9; doi: 10.1016/j.eprac.2025.01.001. PMID: 39800100.

SUMMARY OF THE STUDY

The study uses data from patients with a history of thyroid cancer who received radioactive iodine therapy. The amount of saliva produced was assessed using a standardized questionnaire answered by the patients and through an objective measurement of salivary flow. In addition to this, an assessment of oral health was done by a dental specialist.

A total of 67 patients were included in the study and a majority (81%) were female. The average age at the time of diagnosis of thyroid cancer was 43 years. The study data was collected on average of 69 months (5.8 years) after radioactive iodine therapy was administered and ranged from 1 month to 25 years.

Frequent decreased salivation was reported by 15%, dry mouth by 13% and difficulty eating by 12% of patients. The greater the number of radioactive iodine therapies and total dose, the more likely patients were to have a low salivary flow measurement. When evaluated by a specialist, 61% had good or very good and 17% of the study subjects had below average oral health. When assessing for plaque or bacterial biofilm visible on the teeth, 53% patients had slight film adherence and 15% had moderate to significant film adherence. Finally, 46% of patients had inflammation of the gums.

There are several factors that may influence the data seen in this study. In this particular study population, 24% of patients received neck external radiotherapy during their childhood which may have had an impact on salivary gland function. Given that the data was collected from a single hospital, the radioactive iodine therapy protocol and measures used to protect the salivary gland may influence outcomes and these may differ from other hospitals. Finally, comparison with a patient population that did not receive radioactive iodine would be helpful to understand the data better.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Similar to other studies, this study raises the concern about risk for changes in salivary gland function and oral health following radioactive iodine therapy given for

THYROID CANCER, continued

the treatment of thyroid cancer. The use of radioactive iodine therapy has changed over the years, from the practice where radioactive iodine therapy was part of the standard therapy recommended to all patients with thyroid cancer, to current recommendations to consider radioactive iodine for patients when there is a higher risk for recurrence or to treat thyroid cancer tissue present in the body. A discussion on the effect of radioactive iodine on the salivary gland and oral health should be part of the counseling provided to patients. It is also important for patients to have regular on-going visits with their dentist following radioactive iodine therapy to ensure any concerns can be addressed appropriately.

— Poorani Goundan, MD

ATA THYROID BROCHURE LINKS

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

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*).

Iodine: 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.

Salivary glands: These glands provide saliva to the mouth, both chronically and when eating. They are locates under the jaw. The parotid gland is one of the salivary glands located over the back part of the jaw.

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THYROID NODULES

Molecular testing could help to plan treatment for indeterminate thyroid nodules if the price was right

BACKGROUND

Thyroid nodules are present in up to 65% of the general population, however, only 5-10% are cancerous. Thyroid biopsy is the best test available to differentiate between benign and cancerous thyroid nodules. The thyroid biopsy results are usually reported using the Bethesda System. This is a standardized reporting system with six categories, each category having a different cancer risk and specific recommendations for patient management: Bethesda I (non-diagnostic); Bethesda II (benign); Bethesda III (indeterminate - atypia of undetermined significance/ AUS); Bethesda IV (indeterminate - follicular neoplasm); Bethesda V (suspicious for cancer), and Bethesda VI (cancer).

The two indeterminate categories for malignancy, Bethesda III and IV, include specimens with abnormal thyroid cells that have a risk of cancer between the benign and cancer categories (10 to 40%). In the past, these thyroid nodules required surgical removal for a definitive diagnosis. More recently, molecular tests to identify cancer-related genes in the biopsy cells have been developed to further clarify the cancer risk of indeterminate thyroid nodules and avoid unnecessary surgery. Molecular tests have been confirmed to be effective in reducing unnecessary surgeries and they are also cost-effective in the management of thyroid nodules in Western countries.

In many Asian countries, molecular tests are expensive and not commonly used since they are not covered by insurance. In addition, a more conservative approach is preferred for indeterminate thyroid nodules. This is frequently done with active surveillance on ultrasound (following the nodules by ultrasound instead of up-front thyroid surgery). Surgery is also less expensive in the Asian compared to Western countries. The goal of this study is to evaluate whether it would be cost-effective to routinely use a commercially available molecular test — Thyroseq V3 — for the management of indeterminate thyroid nodules in Hong Kong.

THE FULL ARTICLE TITLE

Fung MHM et al. High rates of unnecessary surgery for indeterminate thyroid nodules in the absence of molecular test and the cost-effectiveness of utilizing molecular test in an Asian population: a decision analysis. Thyroid 2005;35(2):166-176; doi: 10.1089/thy.2024.0436. PMID: 39835971.

SUMMARY OF THE STUDY

The study evaluated 1957 thyroid biopsies performed at a single endocrine surgery center in Hong Kong between January 2018 and December 2021. Among these, 365 biopsies (19%) showed indeterminate results (Bethesda III or IV) with 36% of these patients opting for up-front surgery, 42% for repeat biopsy, and 22% for active surveillance on ultrasound. Molecular tests were not available for these patients. Among the patients who underwent up-front surgery, 28% were diagnosed with thyroid cancer, while 72% had benign thyroid nodules, thus the surgical intervention was unnecessary for these patients. The same thyroid cancer rates were noted in patients who underwent surgery later after first undergoing repeat biopsy or active surveillance on ultrasound.

A decision analysis based on the simulation of 10,000 patients over a two-year period was then used to evaluate the cost-effectiveness of indeterminate thyroid nodule management with and without molecular tests and determine the impact of these on costs and reduction in unnecessary surgeries. The routine use of molecular tests increased effectiveness by avoiding 26% more unnecessary surgeries as compared to the current model without molecular tests. However, this came with a higher average cost. The routine use of molecular tests would be cost saving, only with a cost less than the equivalent of $1,031.

THYROID NODULES, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Despite a more conservative approach with a lower rate of initial surgery than in the Western countries, the proportion of unnecessary surgical interventions for indeterminate thyroid nodules (Bethesda III/IV) remains high (72%) in an Asian population. Routine use of molecular testing can reduce the rate of unnecessary surgeries by 26%, however it is currently limited due to high cost. Molecular tests use would become cost-effective if the cost was substantially reduced.

— Alina Gavrila, MD, MMSc

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% 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.

Indeterminate thyroid biopsy: this happens when a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance/AUS) or when the diagnosis is a follicular cell lesion. Follicular cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular cell cancer from non-cancerous 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 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™.

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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.

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GRAVES' DISEASE & THYROID FOUNDATION

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

Light of Life Foundation
checkyourneck.com

MCT8 - AHDS Foundation

BITE ME CANCER!

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
Contact@mct8.info

Thyca: Thyroid Cancer Survivors' Association, Inc.
www.thyca.org
(Toll-free): 877-588-7904
thyca@thyca.org

Thyroid Federation International
www.thyroid-fed.org
tfi@thyroid-fed.org

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