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Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION®
Optimal Thyroid Health for All

HYPERTHYROIDISM

Long-term safety of treatment options for hyperthyroidism: which is the best?

There are 3 treatment options for hyperthyroidism – antithyroid drugs, radioactive iodine therapy and thyroid surgery. There are various factors that go into deciding which treatment option to consider, including the underlying cause for hyperthyroidism, side effects of treatment and patient preferences. This study aimed to assess the long-term safety of each of the three options of treatment for hyperthyroidism.

Chiung-Hui Peng C et al. Mortality risks associated with antithyroid drugs, radioactive iodine, and surgery for hyperthyroidism: a systematic review and network meta-analysis. Thyroid. 2025 Sep 1; doi: 10.1177/10507256251372193. PMID: 40891035.

GRAVES' DISEASE

Is low-dose block-and-replace therapy as effective as high-dose block-and-replace therapy for treatment of Graves' disease?

In the 1990s, block-and-replace therapy had gained some popularity in the treatment of Graves' disease. However, this strategy was not shown to be quicker in resolving Gaves' disease than ATDs alone and resulted in more side effects, so it is not routinely used. Recent studies have suggested that block-and-replace therapy using lower ATD doses may be able to be effective with less side effects. This study compared high-dose and low-dose block-and-replace therapy in patients with first episodes of Graves' disease determine whether this would be as effective with possibly less side effects.

Smolders A et al High-dose versus low-dose block-and-replace treatment for a first episode of Graves' disease. Eur Thyroid J 2025;14:e250039; doi: 10.1530/ETJ-25-0039. PMID: 40172327.

THYROID CANCER

Less is more: is removing only the thyroid isthmus enough for some thyroid cancers?

In recent years, there has been a growing emphasis on reducing the extent of surgery for low-risk thyroid cancer, since the outcomes are similar while the complication rates are lower. Recent studies suggest that removing only the isthmus (isthmusectomy) may be an alternative for some patients when the cancer is limited to the isthmus. Researchers designed this study to look at which option works best for a single thyroid cancer located only in the isthmus.

Lee S et al. Comparative study of clinical outcomes for total thyroidectomy/lobectomy and isthmusectomy in patients with isthmic papillary thyroid carcinoma. Thyroid 2025;35:1322-1330; PMID: 41020703.

THYROID CANCER

A new blood test strategy may help find a medullary thyroid cancer earlier

Medullary thyroid cancer is a rare type of thyroid cancer that arises from the C-cells of the thyroid. Measuring levels of calcitonin, the hormone that C-cells make, can help diagnose medullary thyroid cancer, but results in the middle range are often unclear and may worry patients unnecessarily. The goal of this study was to see if using calcitonin along with procalcitonin together could improve the accuracy of diagnosing medullary thyroid cancer.

Schonebaum LE, et al. Progastrin-releasing peptide and pro-calcitonin as additional markers in the diagnostic workup for medullary thyroid carcinoma. Thyroid 2025;35(9):1030-1038; doi: 10.1089/thy.2024.0293. PMID: 40576708.

THYROID SURGERY

Protocol to decrease the risk of low calcium levels after total thyroidectomy

One of the complications of thyroidectomy is the development of low calcium levels after surgery due to damage/bruising of the parathyroid glands during surgery. Treatment of low calcium levels after surgery can include calcium pills and/or calcitriol. This study was done to evaluate a protocol that grouped patients according to their parathyroid hormone level after surgery to help predict which patients would benefit from supplemental calcium and calcitriol.

Chindris AM, et al. Hypocalcemia post total thyroidectomy: a ten-year, single institution experience with a parathyroid hormone-guided calcium and calcitriol supplementation protocol. Endocr Pract 2025;31(11):1399-1406; doi: 10.1016/j.eprac.2025.07.003. PMID: 40633692.

THYROID CANCER

From rare exceptions to common findings: implications for managing hereditary thyroid cancer risk

A small proportion of thyroid cancers are part of rare hereditary syndromes caused by distinct gene mutations. At present, thyroid cancer patients do not undergo genetic evaluation unless other relatives are diagnosed with these rare hereditary syndromes. The goal of this study is to evaluate mutations that cause thyroid cancer-associated hereditary syndromes by using two large, public, population-scale databases; the *All of Us* database from the US and the UK Biobank.

White SL et al. Population prevalence of the major thyroid cancer–associated syndromes. J Clin Endocrinol Metab. Epub 2025 Apr 15:dgaf236; doi: 10.1210/clinem/dgaf236. PMID: 40231587.

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Editor's Comments

Welcome to another issue of *Clinical Thyroidology for the Public* and Happy New Year! 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.

January is Thyroid Awareness Month.

In this issue, the studies ask the following questions:

- What is the best treatment option for hyperthyroidism?
- Is block-and-replace therapy coming back for treatment of Graves' disease?
- Is removing only the thyroid isthmus enough for some thyroid cancers?
- Can a standard protocol decrease the risk of low calcium levels after surgery?
- Is there a new test that can help diagnose medullary thyroid cancer?
- What is my risk of getting thyroid cancer if I have a thyroid cancer-associated gene?

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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HYPERTHYROIDISM

Long-term safety of treatment options for hyperthyroidism: which is the best?

BACKGROUND

Hyperthyroidism is a condition of increased thyroid hormone production by the thyroid gland. Symptoms include fast heart rate, heat intolerance, weight loss, insomnia, anxiety and tremors. The most common cause of hyperthyroidism is Graves' disease, where an antibody attacks and turns on the thyroid; followed by toxic nodular goiter, where the cells in a thyroid nodules start working on their own and do not shut down when thyroid levels increase. There are 3 treatment options for hyperthyroidism – antithyroid drugs (ATD) with either methimazole or propylthiouracil, radioactive iodine therapy (RAI) and thyroid surgery (thyroidectomy). There are various factors that go into deciding which treatment option to consider, including the underlying cause for hyperthyroidism, side effects of treatment and patient preferences.

This study aimed to assess the long-term safety of each of the three options of treatment for hyperthyroidism.

THE FULL ARTICLE TITLE

Chiung-Hui Peng C et al. Mortality risks associated with antithyroid drugs, radioactive iodine, and surgery for hyperthyroidism: a systematic review and network meta-analysis. Thyroid. 2025 Sep 1; doi: 10.1177/10507256251372193. PMID: 40891035.

SUMMARY OF THE STUDY

The study evaluated many published studies that compared long term outcomes in patients with hyperthyroidism who were treated with ATDs, RAI or surgery. The analysis included 12 studies with a total of 192,208 patients from Europe, North America, Asia and the Middle East.

The all-cause death rate in hyperthyroid patients was lower when comparing surgery to ATDs and when comparing surgery to RAI. Death due heart disease was lower when comparing surgery to ATDs and when comparing surgery to RAI. There was no significant difference in major adverse heart events (ie. heat attack, stroke and death due to heart disease) or death due to cancer among surgery, ATDs and RAI.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study found that patients with hyperthyroidism who underwent thyroid surgery had a lower all-cause risk of death and heart problems compared to ATDs and RAI. The reason this was the case is a bit unclear. It is possible that achieving better and more rapid control of thyroid hormone levels with surgery may contribute to the results seen. However, the studies included in the analysis do not take into account the baseline health status and other factors in the individual treatment groups that could result in better outcomes in patient undergoing surgery. The study also does not consistently differentiate between the different types of hyperthyroidism which is important when interpreting the results.

Further studies are required to understand the long-term outcomes of various treatment options available for the management of hyperthyroidism.

— Poorani Goundan, MD

ATA RESOURCES

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

HYPERTHYROIDISM, continued

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.

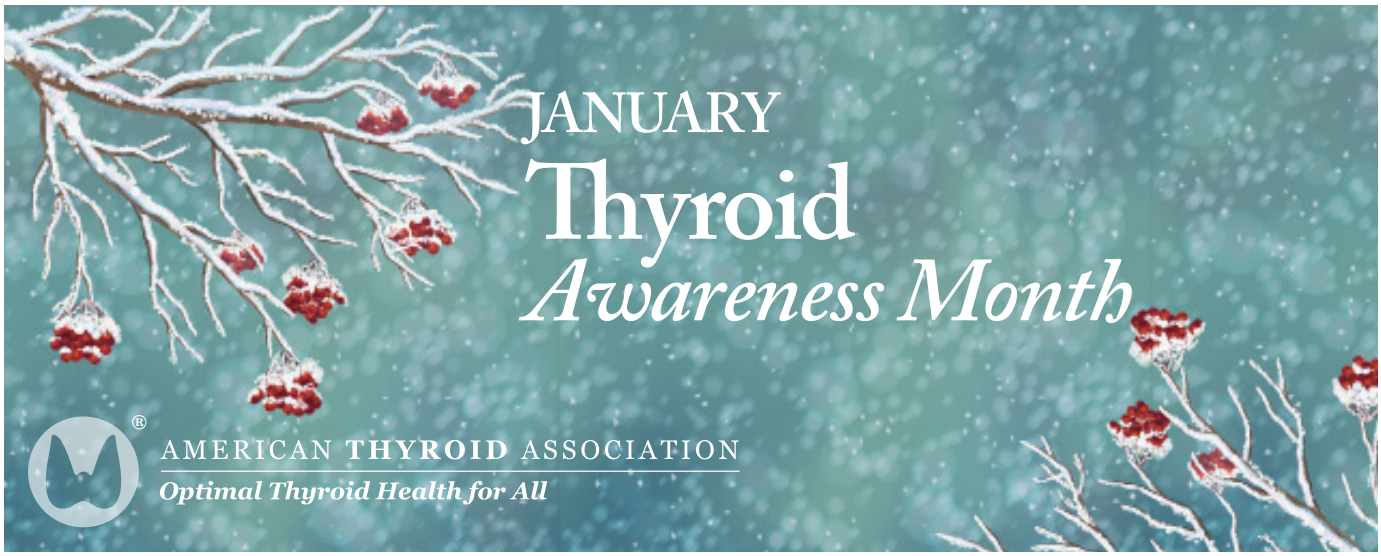
Toxic nodular goiter: characterized by one or more nodules or lumps in the thyroid that may gradually grow and increase their activity so that the total output of thyroid hormone in the blood is greater than normal.

Methimazole: an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease.

Propylthiouracil (PTU): an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

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 (hyperthyroidism).



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GRAVES' DISEASE

Is low-dose block-and-replace therapy as effective as high-dose block-and-replace therapy for treatment of Graves' disease?

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States. Graves' disease is caused by the body making an antibody (thyrotropin receptor antibody, TRAb) that attacks and turns on the thyroid gland, causing it to produce too much thyroid hormone. Antithyroid drugs (ATDs), such as methimazole or propylthioruacil, are the first-line treatment of Graves' disease to bring thyroid hormone levels back to normal and prevent harmful effects on various organ systems, including heart and bone.

In the 1990s, a treatment strategy using high-dose ATDs to completely shut down the thyroid gland along with levothyroxine to replace the thyroid hormones (known as "block-and-replace" therapy) had gained some popularity. High dose of ATDs used in this regimen was thought to decrease stimulating action of TRAb more rapidly while levothyroxine provides thyroid hormone replacement, compared to using ATDs alone. However, this strategy has not been shown to be quicker in resolving Gaves' disease than ATDs alone. There were also concerns about increased risks of side effects and overtreatment with high-dose ATDs. Therefore, block-and-replace therapy is currently not routinely used. However, recent studies have suggested that block-and-replace therapy using lower ATD doses (low-dose block and replace) may be able to be effective with less side effects.

This study compared high-dose and low-dose block-and-replace therapy in patients with first episodes of Graves' disease to determine whether lower ATDs dose would be as effective as higher ATDs dose with possibly less side effects.

THE FULL ARTICLE TITLE

Smolders A et al High-dose versus low-dose block-and-replace treatment for a first episode of Graves' disease. Eur Thyroid J 2025;14:e250039; doi: 10.1530/ETJ-25-0039. PMID: 40172327.

SUMMARY OF THE STUDY

Records of 120 patients with newly diagnosed Graves' disease treated between 1990 and 2022 in two hospitals in Belgium were used for this study. A total of 60 patients received high dose regimen, with 30 mg of methimazole and levothyroxine. The other 60 patients received low dose regimen, with methimazole starting at 20-40 mg a day and adjusted to 10-20 mg a day once free thyroxine (FT4) levels became normal. All patients were treated for at least 12 months and monitored for one year afterwards or until recurrence of Graves' disease off the medications.

The proportion of patients who had recurrence of Graves' disease after medications are discontinued were similar (63% in the high-dose group and 60% in the low-dose group), with similar time to recurrence (11 months in the high-dose group and 7 months in the low-dose group) between the two groups. TRAb became normal more frequently in the low-dose group than in the high-dose group (86% vs 65%). There were no significant differences in development of thyroid eye disease or frequency of medication side effects between two groups.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that the low-dose block-and-replace therapy achieved similar results in treatment of Graves' disease as the high-dose block-and-replace therapy with less medications and better normalization of TRAb levels, which can lead to remission of Graves' disease. Currently, block-and-replace therapy is rarely used in the United States. Based on findings of this study, block-and-replace therapy with low-dose ATDs may be an option with less concern for potential side effects in select cases, where thyroid function changes significantly on ATDs alone. However, we do not know whether low-dose block-and-replace therapy is more or similarly effective and safe to ATD alone in treating Graves' disease. Such studies are needed before block-and-replace therapy would be more routinely considered for treatment of Graves' disease.

— Sun Y. Lee, MD

GRAVES' DISEASE, continued

ATA RESOURCES

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

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

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.

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.

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.

Methimazole: an antithyroid medication that blocks the thyroid from making thyroid hormone. Methimazole is used to treat hyperthyroidism, especially when it is caused by Graves' disease.

Propylthiouracil (PTU): an antithyroid medication that blocks the thyroid from making thyroid hormone. Propylthiouracil is used to treat hyperthyroidism, especially in women during pregnancy.

Levothyroxine (T4): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tyrosint™ and generic preparations.

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THYROID CANCER

Less is more: is removing only the thyroid isthmus enough for some thyroid cancers?

BACKGROUND

Papillary thyroid cancer is the most common type of thyroid cancer. The vast majority of thyroid cancers are located in the right or left lobe of the thyroid. Only a small number of thyroid cancers are located in the isthmus, the thin middle part of the thyroid that connects the lobes on both sides. Cancers in this location may have have a higher risk of spreading beyond the thyroid. In recent years, there has been a growing emphasis on reducing the extent of surgery for low-risk thyroid cancer, since the outcomes are similar while the complication rates are lower. Traditionally, surgeons removed the entire thyroid (total thyroidectomy) for high risk cancers or one lobe (lobectomy) for small cancers that are limited to 1 lobe. However, there are no clear guidelines on how much thyroid tissue should be removed when the thyroid cancer is only in the isthmus.

Recent studies suggest that removing only the isthmus (isthmusectomy) may be an alternative for some patients when the cancer is limited to the isthmus. Researchers designed this study to look at which option works best for a single thyroid cancer located only in the isthmus.

THE FULL ARTICLE TITLE

Lee S et al. Comparative study of clinical outcomes for total thyroidectomy/lobectomy and isthmusectomy in patients with isthmic papillary thyroid carcinoma. Thyroid 2025;35:1322-1330; PMID: 41020703.

SUMMARY OF THE STUDY

Researchers reviewed records from 345 patients treated between 2013 to 2022 at 2 major hospitals in South Korea. These patients had a single, small, low-risk papillary thyroid cancer located in the isthmus and were treated with total thyroidectomy, lobectomy, or isthmusectomy. Patients with very aggressive cancer types, more than one cancer, or known extension of the cancer beyond the thyroid were excluded. Patients were considered candidates for isthmusectomy if the cancer was less than 4 cm and showed no clear extension beyond the thyroid gland. Researchers combined the patients who had total thyroidectomy or lobectomy into one group and compared them with the patients who had isthmusectomy. The groups were carefully matched, so the groups were very similar in age, sex, cancer type, size, and extent, as well as other factors that affect cancer behavior, such as BRAF gene mutation or Hashimoto thyroiditis. The main outcomes that were looked at were cancer return in the lymph nodes, thyroid, or other parts of the body. The study also looked at complications of surgery, such as low calcium levels, vocal cord paralysis, or the need to take thyroid hormone.

There were 345 patients with a single papillary thyroid cancer in the isthmus who met the inclusion criteria. After matching similar patients, 85 patients were included in each group. Patients were very similar at baseline between the groups. The average age was 48.5 vs 47.9 years; most patients were female (76.5% vs 77.7%); and the average cancer size was 0.8 cm. More than 60% had minimal extension beyond the thyroid, and about 10% had more than one cancer. These were patients who had hidden cancer in the lymph nodes or microscopic extension beyond the thyroid gland found after surgery. This situation is common in real-world practice, as these findings are sometimes too small to detect before surgery. Patients were followed for about 5 years.

There was no evidence of cancer return in either group during this time. However, patients who had a thyroidectomy or lobectomy had more complications after surgery. Temporary low calcium occurred in 14% and permanent low calcium in 1.2%, and temporary vocal cord paralysis in 3.5% while none of the patients who had isthmusectomy had these complications. The need for thyroid hormone replacement and the required dose were also higher in the total thyroidectomy/lobectomy group (90.6%) than in the isthmusectomy group (34%).

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The findings of this study show that isthmusectomy appears to be a safe and effective surgical option for carefully selected patients with small papillary thyroid cancers limited to the isthmus. This is important for patients since less surgery in the right situation can lower the risk of complications, improve quality of life without increasing the risk of cancer coming back. Longer follow-up is still needed to confirm these findings, and decisions about surgery should be tailored to each patient.

— Ebru Sulanc, MD

ATA RESOURCES

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of differentiated 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*.

Lobectomy: surgery to remove one lobe of the thyroid.

Isthmusectomy: surgery to remove only the isthmus, which is the thin middle part of the thyroid that connects the lobes on both sides.

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 CANCER

A new blood test strategy may help find a medullary thyroid cancer earlier

BACKGROUND

Medullary thyroid cancer is a rare type of thyroid cancer that can run in families. Medullary thyroid cancer arises from the C-cells of the thyroid. The C-cells secrete the hormone calcitonin. Importantly, the C-cells do not take up iodine. In contrast, the most common type of thyroid cancer, papillary thyroid cancer, arises from the thyroid follicular cells which take up iodine to make thyroid hormones. Because of this, papillary thyroid cancer can be treated with radioactive iodine to destroy the cancer cells. Radioactive iodine does not work to treat medullary thyroid cancer.

The main treatment for medullary thyroid cancer is surgery to remove the cancer. Finding medullary thyroid cancer early is important because treatment (mainly surgery) works best before the cancer spreads. However medullary thyroid cancer can be hard to find early. Ultrasound findings are often nonspecific, and thyroid biopsy misses medullary thyroid cancer in up to half of cases. This leads to delayed diagnosis and misses opportunities for curative surgery. Measuring levels of calcitonin, the hormone that C-cells make, can help, but results in the middle range are often unclear and may worry patients unnecessarily. Because of these problems, researchers wanted to find a better and more reliable way to use blood tests to detect medullary thyroid cancer early.

The goal of this study was to see if using calcitonin along with procalcitonin (a hormone that becomes calcitonin) together could improve the accuracy of diagnosing medullary thyroid cancer.

FULL ARTICLE TITLE:

Schonebaum LE, et al. Progastrin-releasing peptide and procalcitonin as additional markers in the diagnostic workup for medullary thyroid carcinoma. Thyroid 2025;35(9):1030-1038; doi: 10.1089/thy.2024.0293. PMID: 40576708.

SUMMARY OF THE STUDY

Researchers studied adults who had thyroid nodules and were being evaluated for possible thyroid cancer. The study included patients from hospitals in Europe between 2006-2025. First, doctors measured calcitonin levels in the blood. If calcitonin levels were slightly high, they then measured another procalcitonin levels. The researchers compared these test results with the patients' final diagnoses to see how accurate the tests were.

The study found that when calcitonin levels were only mildly high, procalcitonin helped clearly tell who had medullary thyroid cancer and who did not. Using calcitonin first and then procalcitonin correctly identified all patients with medullary thyroid cancer and correctly ruled out cancer in almost all patients who did not have it. This approach worked very well and reduced false alarms.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Using calcitonin first and adding procalcitonin when needed is a very accurate way to check for medullary thyroid cancer. This approach may help patients avoid unnecessary surgery, extra tests, and anxiety when calcitonin levels are only slightly elevated. At the same time, it helps doctors find medullary thyroid cancer earlier, when treatment is most effective.

— Maria Brito, MD, ECNU

THYROID CANCER, continued

ATA RESOURCES

Thyroid Cancer (Medullary): https://www.thyroid.org/medullary-thyroid-cancer/

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

ABBREVIATIONS & DEFINITIONS

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

C-cell hyperplasia: an abnormal growth of parafollicular (C-cells) cells that usually occurs before the development of familial forms of medullary thyroid cancer and is considered a pre-cancerous condition

Calcitonin: a hormone that is secreted by cells in the thyroid (C-cells) that has a minor effect on blood calcium levels. Calcitonin levels are increased in patients with medullary thyroid cancer.

Procalcitonin: a hormone that is produced by the C-cells in the thyroid that is a precursor to calcitonin

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THYROID SURGERY

Protocol to decrease the risk of low calcium levels after total thyroidectomy

BACKGROUND

Thyroidectomy is surgery to remove the entire thyroid gland. Thyroidectomy is done for treatment of both thyroid cancer and non-cancer thyroid problems such as Graves' disease and nodular goiter. While thyroidotomy is a safe and effective procedure, especially when done by experienced thyroid surgeons, there are potential complications. One of the complications of thyroidectomy is the development of low calcium levels after surgery, known as post-operative hypocalcemia. This low calcium often happens between 1-3 days after surgery and can occur in up to 1/3rd of patients. The parathyroid glands located next to the thyroid produce parathyroid hormone (PTH) that controls blood calcium levels. The cause of post-operative hypocalcemia is damage/bruising of the parathyroid glands during surgery leading to low PTH levels. Treatment of low calcium levels after surgery can include calcium pills and/or calcitriol, an active form of vitamin D.

Most of the time, post-operative hypocalcemia is mild to moderate (identified with blood tests, mild symptoms like numbness or tingling in fingers or lips or with abnormal twitching of muscles) and resolves in a few days. However, severe hypocalcemia can result in seizures, heart arrhythmias, mental status changes and often requires rehospitalization. Several methods have been suggested to treat patients after thyroid surgery. These include just waiting and watching patients for low calcium, treating all patients with standard doses of calcium and vitamin D after surgery or adjusting the dose for each patient. These run the risk of over-treating some patients and add to overall health care costs.

This study was done to evaluate a protocol that grouped patients according to their parathyroid hormone level after surgery to help predict which patients would benefit from supplemental calcium and vitamin D. This study used a parathyroid hormone level drawn 4 hours after surgery to guide calcium and vitamin D supplementations to see if this reduced the incidence of hypocalcemia and readmissions.

THE FULL ARTICLE TITLE

Chindris AM, et al. Hypocalcemia post total thyroidectomy: a ten-year, single institution experience with a parathyroid hormone-guided calcium and calcitriol supplementation protocol. Endocr Pract 2025;31(11):1399-1406; doi: 10.1016/j.eprac.2025.07.003. PMID: 40633692.

SUMMARY OF THE STUDY

This is a study of 882 consecutive patients who had total thyroidectomies at a single institution between January 2008 and December 2022. They were split into two groups – 148 who were treated prior to using the protocol (pre-protocol group) and 734 who were treated according to the protocol (protocol group). Patients who had previous parathyroid disease, parathyroid or thyroid surgery, untreated vitamin D deficiency or a prior diagnosis of hyperparathyroidism were excluded.

The patients in the pre-protocol group were managed with Ca carbonate (400 mg elemental Ca/tablet) 1-2 tablets every 4-6 h as needed, based on the postoperative serum Ca levels and/or symptoms of hypocalcemia, at the discretion of their surgeon. Patients in the protocol group had a 4-hour post operative PTH drawn and were split into 3 groups according to their hypocalcemia risk: low (PTH >30 pg/mL), intermediate (PTH 15-30 pg/mL), and high (PTH <15 pg/mL). Treatment was only calcium carbonate in low-risk group, calcium carbonate with low dose calcitriol in intermediate group and calcium carbonate with high dose calcitriol in high-risk group. Calcium levels were monitored weekly and if normal, doses of calcium and/or calcitriol gradually decreased. Hypocalcemia was defined as a serum calcium <8.0 mg/dl within 30 days of surgery. They looked at how often

THYROID SURGERY, continued

hypocalcemia was noted and whether hospital readmission for hypocalcemia was required as well as risk factors for developing hypocalcemia.

Hypocalcemia occurred in 20.9% of the pre-protocol subjects and was decreased to 9.5% in post-protocol subjects. Within this latter group, there was a low incidence of hypocalcemia in the low and medium risk groups (2.3 and 2.6% respectively) compared with the high-risk group in which the PTH was <15 pg/mL (23.4%). Other factors that increased the risk of hypocalcemia were lymph node dissection, parathyroid glands that were located within the thyroid gland and worsening kidney function .

Management of hypocalcemia differed between groups, with 40.0% of protocol patients treated as inpatients, 21.4% as outpatients, and 38.6% managed over the phone, compared with 80.6%, 16.1%, and 3.2% in the pre-protocol group.

Hypercalcemia (high calcium levels due to increase calcium pills) developed in 82 patients in the protocol group within 30 days post thyroidectomy. Only one of these patients required hospitalization.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study reinforced the previous information that measuring the PTH levels 4-h after surgery was helpful to predict the risk of low calcium levels after thyroidectomy. Along with the PTH-guided calcium and calcitriol treatment protocol, this reduced the incidence of hypocalcemia and hospital readmissions.
This is important to patients as it allows selection of patients who are good candidates for same-day surgery with resultant increase in patient satisfaction, and reduction in morbidity and health care costs.

— Marjorie Safran, MD

ATA RESOURCES

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

ABBREVIATIONS & DEFINITIONS

Hypocalcemia: low calcium levels in the blood, a complication from thyroid surgery that is usually short-term and relatively easily treated with calcium pills. If left untreated, low calcium may be associated with muscle twitching or cramping and, if severe, can cause seizures and/or heart problems.

Parathyroid hormone (PTH): the hormone that regulates the body's calcium levels. High levels of PTH cause hypercalcemia, or too much calcium in the blood. Low levels of PTH cause hypocalcemia, or too little calcium in the blood.

Calcitriol: the rapid acting, biologically active form of vitamin D.

Vitamin D: a vitamin that is important for maintaining calcium levels by increasing the absorption of calcium from the gut. Vitamin D is made in our sun after exposure to the sun.

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THYROID CANCER

From rare exceptions to common findings: implications for managing hereditary thyroid cancer risk

BACKGROUND:

Genes code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an individual's cells and pass genetic traits to offspring. All individuals have 2 sets of genes; 1 set from each parent. When different versions of a particular gene are passed down from each parent, it is termed heterozygous genes and is the most common pairing of genes. If the same version of a particular gene are passed down from each parent, it is termed homozygous.

A small proportion of thyroid cancers are part of rare hereditary (ie. tend to run in families) syndromes caused by distinct gene mutations. For example, medullary thyroid cancer (MTC) can be part of the multiple endocrine neoplasia (MEN) syndrome caused by a *RET* gene mutation. There are also hereditary syndromes associated with other types of thyroid cancer, such as PTEN hamartoma tumor syndrome (PHTS), familial adenomatous polyposis (FAP) and other rare syndromes, each syndrome being caused by specific gene mutations. At present, thyroid cancer patients do not undergo genetic evaluation unless other relatives are diagnosed with these rare hereditary syndromes.

More recent studies using large databases that include the genetic data of hundreds of thousands of individuals have shown that a considerable proportion of people have genetic mutations associated with thyroid cancer without developing cancer. It has been estimated that only ~53% of individuals who have associated genetic mutations will develop thyroid cancer.

The goal of this study is to evaluate mutations that cause thyroid cancer-associated hereditary syndromes by using two large, public, population-scale databases; the *All of Us* database from the US and the UK Biobank.

THE FULL ARTICLE TITLE:

White SL et al. Population prevalence of the major thyroid cancer–associated syndromes. J Clin Endocrinol Metab. Epub 2025 Apr 15:dgaf236; doi: 10.1210/clinem/dgaf236. PMID: 40231587.

SUMMARY OF THE STUDY:

This study included 245,394 participants from the *All of Us* research program founded by the US National Institutes of Health. The researchers analyzed genetic data as well as clinical data from electronic health records and self-reported surveys to determine the presence of possible mutations in genes associated with hereditary syndromes and their association with the development of thyroid cancer. The UK Biobank program which included 469,589 participants was used to validate the results from the *All of Us* program.

The *All of Us* database included 2,097 patients with a history of thyroid cancer. Overall, 3 genetic syndromes were significantly associated with thyroid cancer in this database: MEN type 2, PHTS, and FAP. A total of 113 individuals carried mutations of the *RET* gene that causes MEN type 2 syndrome. Mutations in the *PTEN* gene that causes PHTS were found in 28 individuals, while mutations in the *APC* gene characteristic for FAP were found in 29 individuals. Comparable results were noted for each syndrome in the UK database. All mutations were heterozygous, meaning that 1 form of the gene had the mutation while the other form of the gene was normal. Most mutations were known as having moderate risk for cancer development. No thyroid cancer patients were found to have mutations in other high-risk genes.

For all 3 syndromes, only a few (less than 20) individuals who carried the mutations known to raise the risk of thyroid cancer were diagnosed with thyroid cancer. The average age of thyroid cancer diagnosis was 56 years for MEN type 2, 28 years for PHTS, and 37 years for FAP. One surprising result was that none of the carriers of the most common MEN2-related mutations, representing 65% of all MEN2 cases in both the US and UK databases, had a thyroid cancer diagnosis in their records.

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This large, data-based study showed that genetic mutations characteristic for thyroid cancer-associated syndromes, such as MEN type 2, PTEN hamartoma tumor syndrome, and FAP, are more common than previously estimated. However, this study shows that most people that carry these mutations do not develop thyroid cancer. As genetic testing becomes more common in the general population, causing more individuals to be identified, we need to develop strategies to adequately monitor and treat these individuals, especially to prevent over-treatment.

— Elie Naous, MD and Alina Gavrila, MD, MMSc

ATA RESOURCES

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

ABBREVIATIONS & DEFINITIONS

Mutation: a permanent change in one of the genes.

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Heterozygous genes: having different versions of a particular gene from each parent.

Cancer-associated genes: these are genes that are normally expressed in healthy cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause cancer or are just associated with cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC, TERT and RAS.

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

Multiple endocrine neoplasia, type 2A (MEN 2A): A hereditary syndrome caused by *RET* mutations, in which medullary thyroid cancer is often seen in association with other endocrine tumors such as pheochromocytoma (a tumor of the adrenal glands) and hyperparathyroidism (elevated parathyroid hormone levels caused by tumors of the parathyroid glands).

PTEN Hamartoma Tumor Syndrome (PHTS): A hereditary syndrome caused by *PTEN* mutations, which is associated with thyroid cancer and other cancers or non-cancerous condition.

Familial Adenomatous Polyposis (FAP): A hereditary syndrome caused by *APC* mutations, which is primarily linked to colon cancer (affected individuals develop many abnormal growths/polyps in the colon, which can transform into cancer if not removed), but also thyroid cancer.

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Optimal Thyroid Health for All

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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-federation.org
tfi@thyroid-federation.org

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