Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

EDITOR'S COMMENTS 2

THYROID CANCER. 3

Quality-of-life changes after thyroidectomy for thyroid cancer

Despite an excellent prognosis, thyroid cancer patients are exposed to physical distress associated with treatment and the psychological stress induced by the cancer diagnosis. Indeed, thyroid cancer survivors report having fatigue, anxiety, depression, sleep problems and pain. The goal of this study was to evaluate changes in the quality of life of thyroid cancer patients starting prior to thyroid surgery and for up to 5 years after their initial treatment.

Kim BH, et al. Longitudinal changes in quality of life before and after thyroidectomy in patients with differentiated thyroid cancer. J Clin Endocrinol Metab 2024;109(6):1505-1516; doi: 10.1210/clinem/dgad748. PMID: 38141213.

THYROID SURGERY. 5

Patients undergoing thyroid surgery: Impact of body weight on postsurgical outcomes:

There has been considerable research evaluating surgical outcomes in obese patients with mixed results. Higher rates of postoperative complications are reported with a BMI in the overweight and obese range. The aim of this study was to examine the effect of increasing BMI on outcomes following thyroid surgery.

Armstrong VL et al Thyroidectomy outcomes in obese patients. J Surg Res 2024;295:717-722; doi: 10.1016/j.jss.2023.11.071. PMID: 38142574.

THYROID CANCER. 7

Are thyroid cancer gene mutations associated with the response to radioactive iodine therapy?

For patients with metastatic thyroid cancer, radioactive iodine acts as a "magic bullet" to destroy any thyroid cancer that has spread outside the thyroid to other parts of the body. Studies have shown that the ability of thyroid cancer cells to absorb radioactive iodine depends on specific genetic mutations in the cancer cells, known as the cancer's molecular signature. This study explores how a cancer's molecular signature affects its ability to absorb radioactive iodine.

Mu Z, Zhang X, Sun D, et al. Characterizing genetic alterations related to radioiodine avidity in metastatic thyroid Cancer. J Clin Endocrinol Metab 2024;109(5):1231-1240.

HYPERTHYROIDISM 9

What patients with Graves' disease should stay on methimazole longer?

Recently, more and more physicians have been preferring treating patients with Graves' disease with methimazole with the goal to treat until a remission occurs. Recent studies have shown that patients are more likely to have a remission from Graves' disease if they were on methimazole for a total of 60 months (long term) as compared to only 12-18 months (short term). This study was performed to assess predictors of relapse and to determine the rate of relapse of patients after short and long-term MMI therapy.

Azizi F et al. Risk of recurrence at the time of withdrawal of short- or long-term methimazole therapy in patients with Graves' hyperthyroidism: a randomized trial and a risk-scoring model. Endocrine 2024;84(2):577-588; doi: 10.1007/s12020-023-03656-5. PMID: 38165576.

THYROID EYE DISEASE. 11

Long-term effects of Teprotumumab for thyroid eye disease

Graves' disease can be associated with an eye complication called Thyroid Eye Disease (TED). A new drug called Teprotumumab has been shown to be very effective in the treatment of severe TED. This study looks at patients with TED who were part of the original trials of Teprotumumab and examines the effects of the drug over a longer period.

Kahaly GJ et al. Long-term efficacy of teprotumumab in thyroid eye disease: follow-up outcomes in three clinical trials. Thyroid. Epub 2024 Jun 2; doi: 10.1089/thy.2023.0656. PMID: 38824618.

THYROID HORMONE THERAPY. 13

Nonthyroidal illness in the setting of heart transplantation: is there a place for thyroid replacement?

The nonthyroidal illness syndrome (NTI) is seen in ~80% of patients in intensive care units. In the vast majority of these patients, thyroid hormone therapy is not indicated. In this study, the association between thyroid status and heart transplantation was explored in patients with end-stage heart failure. The benefit of administering thyroid hormone replacement was also evaluated.

Szécsi B et al. The perioperative period of heart transplantation is affected by thyroid hormone status. Thyroid 2024;34(6):774-784; doi: 10.1089/thy.2023.0628. PMID: 38613807.

ATA® ALLIANCE FOR THYROID PATIENT EDUCATION 15

Friends of the ATA 16

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

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, 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.

October is Thyroid Nodule Awareness Month.

In this issue, the studies ask the following questions:

- What quality-of-life changes are seen after thyroidectomy for thyroid cancer?
- Does obesity increase the risk on thyroid surgery?
- Are thyroid cancer gene mutations associated with the response to radioactive iodine therapy?
- What patients with Graves' disease should stay on methimazole longer?
- What are the long-term effects of Teprotumumab for thyroid eye disease?
- Is there a place for thyroid hormone replacement after heart transplantation?

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

THYROID CANCER

Quality-of-life changes after thyroidectomy for thyroid cancer

BACKGROUND

Thyroid cancer is common, and we currently have effective treatments that result in an overall excellent prognosis as very few thyroid cancer patients die from their cancer. Despite this excellent prognosis, thyroid cancer patients are exposed to physical distress associated with treatment and the psychological stress induced by the cancer diagnosis. Indeed, thyroid cancer survivors report having fatigue, anxiety, depression, sleep problems and pain. Thus, in addition to efforts to effectively treat thyroid cancer patients, there is now increased focus on improving the quality of life (QOL) of cancer survivors.

The goal of this study was to evaluate changes in the QOL of thyroid cancer patients starting prior to thyroid surgery and for up to 5 years after their initial treatment.

THE FULL ARTICLE TITLE

Kim BH, et al. Longitudinal changes in quality of life before and after thyroidectomy in patients with differentiated thyroid cancer. J Clin Endocrinol Metab 2024;109(6):1505-1516; doi: 10.1210/clinem/dgad748. PMID: 38141213.

SUMMARY OF THE STUDY

The study included 185 patients who underwent total thyroidectomy for thyroid cancer at a single medical center in Seul, Korea between 2013 and 2017 and completed a serial questionnaire survey for up to 5 years after their initial cancer treatment. The average age was 49 years, 81% of the patients being women. Most patients (97%) had papillary thyroid cancer, the rest having follicular cancer. One surgeon performed all surgical procedures, including 105 conventional thyroidectomies and 80 remote-access thyroidectomies via the axilla or behind the ear approaches. A total of 57% of patients underwent total thyroidectomy, the rest undergoing lobectomy; 84% of patients underwent central neck dissection, while 12% underwent lateral neck dissection. Surgical complications included vocal-cord paralysis in 12 patients (6.5%), which was permanent in 2 patients and hypoparathyroidism in 44 patients (24%), which was permanent in 4 patients. A total of 37% of the patients also received radioactive iodine therapy (RAI) treatment 2-3 months after the thyroid surgery.

The quality of life was assessed using the Korean versions of the University of Washington Quality of Life questionnaire (UW-QOL) designed for head and neck cancer patients and the City of Hope Quality of Life—Thyroid Version questionnaire (QOL-TV) designed for long-term thyroid cancer survivors. The UW-QOL provides three composite scores: physical function, social–emotional, and total composite scores, while the QOL-TV evaluates four aspects: psychological, physical, social, and spiritual well-being. The questionnaires were administered in the oncology clinic at seven time points: 1 day prior to surgery and then 3 months, 6 months, 1 year, 2 years, 3 years, and 5 years after the surgery.

The results of the two questionnaires showed worsening QOL immediately after surgery, with a progressive improvement after the first 3 months over a span of 5 years. Physical wellbeing scores were lower at all times after surgery in patients who underwent total thyroidectomy compared to lobectomy as well as conventional thyroidectomy compared to remote-access thyroidectomy. Patients undergoing remote-access thyroidectomy had higher scores for satisfaction with their appearance than those undergoing conventional surgery. Patients who received RAI therapy had lower taste scores, with those undergoing thyroid hormone withdrawal reporting more sleep, self-concept, and distress issues 3 months post-surgery as compared to those who received recombinant TSH preparation. Postsurgical hypoparathyroidism (short-lived or permanent) was associated with lower physical function scores in the first 3 years after surgery. Weight gain, cold/heat sensitivity, voice change, and fluid retention were reported after surgery, without subsequent recovery. The appearance-related concerns after the surgery did not improve over time. Anxiety and mood changes were significant prior to the surgery, and while there was a continuous improvement after surgery, they remained the most important concerns for thyroid cancer patients throughout the 5-year follow-up period.

THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that patients with thyroid cancer experience a significant worsening of their quality of life immediately after surgery followed by a progressive improvement over the next 5 years to surpass the pre-operative quality of life. More aggressive treatments can impair the quality of life of these patients. Therefore, total thyroidectomy and RAI ablation should be restricted for selected patients with more advanced/aggressive disease. Anxiety and mood changes are major clinical concerns in these patients, both before and after surgery. Psychological support should always be considered when indicated.

— Alina Gavrila, MD, MMSc

ATA RESOURCES

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

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

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

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer (DTC): the most common type of thyroid cancer, which includes papillary and follicular thyroid cancers.

Total thyroidectomy: surgery to remove the entire thyroid gland.

Remote access thyroidectomy: surgical removal the thyroid using approaches via the armpit or behind the ear to eliminate the scar in the middle of the neck

Lobectomy: surgery to remove one lobe of the thyroid.

Neck dissection: surgery to remove lymph nodes and surrounding tissues from the mid neck area close to the thyroid gland (central neck dissection) or from the lateral neck area (lateral neck dissection).

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

Hypoparathyroidism: low calcium levels due to decreased secretion of parathyroid hormone (PTH) from the parathyroid glands next to the thyroid. This can occur as a result of damage to the glands during thyroid surgery and usually resolves.

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. 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*).

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

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

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

THYROID SURGERY

Patients undergoing thyroid surgery: Impact of body weight on postsurgical outcomes:

BACKGROUND

The rates of obesity are increasing in the general population and many of these patients require surgery. There has been considerable research evaluating surgical outcomes in obese patients with mixed results. Higher rates of postoperative complications are reported with a high body-mass index (BMI) in the overweight and obese range. However, some studies have shown that patients with moderate obesity (BMI 25-35) may actually have better surgical outcomes as compared to patients with a BMI of <25 or >35.

In thyroid surgery, there have been conflicting results regarding outcomes in obese patients. The aim of this study was to examine the effect of increasing BMI on outcomes following thyroid surgery.

THE FULL ARTICLE TITLE

Armstrong VL et al Thyroidectomy outcomes in obese patients. J Surg Res 2024;295:717-722; doi: 10.1016/j.jss.2023.11.071. PMID: 38142574.

SUMMARY OF THE STUDY

The medical records of patients >18 years who underwent thyroid surgery between January 2015 and December 2018 were reviewed. The patients were divided into the following groups: Underweight (BMI, <18.5), normal (BMI, 18.5–24.9), pre-obesity (BMI, >25–29.9), class 1 obesity (BMI, 30–34.9), class II obesity (BMI, 35 to >39.5), and class III obesity (BMI, >40). Patients were also divided into two groups: those with a BMI ≥40 and those with a BMI <40.

A total of 465 patients were included; the majority were female. There was no significant difference regarding length of stay, operating room time or return to the operating room.

This study showed that BMI was not a factor in the rate of complications after thyroid surgery. However, the rate of postoperative infections, pneumonia and hospital readmission at a later date were higher in patients with a higher BMI. There was no difference in outcomes between patients undergoing total thyroidectomy or hemithyroidectomy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that thyroid surgery is safe for patients regardless of their BMI, although patients at the higher BMIs may be at risk for infections after surgery. A larger study may help us understand post-operative outcomes in patients undergoing thyroid surgery better.

—Vibhavasu Sharma, MD

ATA RESOURCES

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

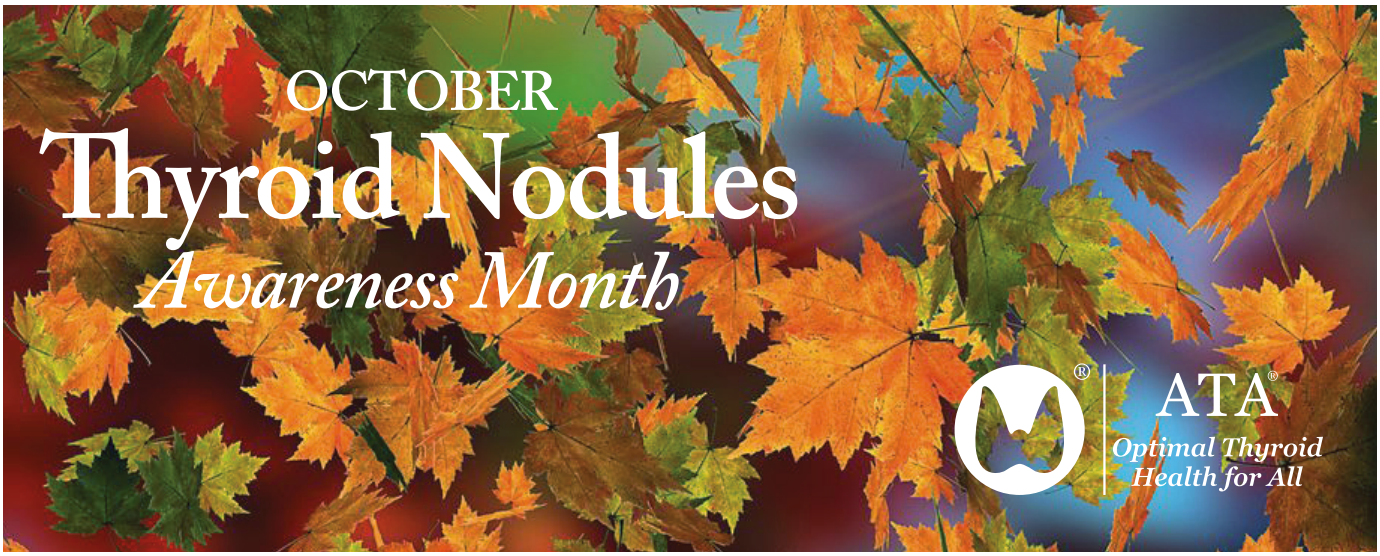
THYROID SURGERY, continued

ABBREVIATIONS & DEFINITIONS

Total thyroidectomy: surgery to remove the entire thyroid gland.

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

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



AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

THYROID CANCER

Are thyroid cancer gene mutations associated with the response to radioactive iodine therapy?

BACKGROUND

Thyroid cancer is common and there are effective treatments that result in an excellent prognosis for patients. Surgery is usually the initial treatment. If the cancer has spread outside the thyroid, then radioactive iodine is usually used. Radioactive iodine acts as a "magic bullet" to destroy any thyroid cancer that has spread outside the thyroid to other parts of the body, like the neck, lungs, or bones. Patients swallow a capsule containing a radioactive isotope of iodine, I-131. Once absorbed, the radioactive iodine will concentrate in the thyroid cancer cells. Over time, the radiation from radioactive iodine will destroy the cancer.

However, thyroid cancer cells must absorb the radioactive iodine for this treatment to work. The term radioiodine avidity refers to how well cancer cells can absorb the radioactive iodine. Cancer cells with high radioiodine avidity are better at taking in iodine, so the treatment will likely be effective. Studies have shown that the ability of thyroid cancer cells to absorb radioactive iodine depends on specific genetic mutations in the cancer cells, known as the cancer's molecular signature.

This study explores how a cancer's molecular signature affects its ability to absorb radioactive iodine.

THE FULL ARTICLE TITLE

Mu Z, Zhang X, Sun D, et al. Characterizing genetic alterations related to radioiodine avidity in metastatic thyroid Cancer. J Clin Endocrinol Metab 2024;109(5):1231-1240.

SUMMARY OF THE STUDY

The authors conducted genetic testing on 281 thyroid cancer samples from 214 patients with metastatic thyroid cancer (including papillary thyroid cancer, follicular thyroid cancer, or poorly differentiated thyroid cancer). Patients had undergone a thyroidectomy and received one or more doses of radioactive iodine at a single hospital in China between 2020 and 2022. The genetic tests focused on four types of mutations found in thyroid cancer cells: a) BRAF V600E, b) RAS, c) fusions (RET or NTRK), and d) other mutations. The researchers then analyzed the pattern of radioactive iodine uptake, categorizing each cancer as either radioactive iodine avid (I-RAIA) or radioactive iodine resistant (I-RAIR), in relation to each type of mutation.

A total of 80 patients had cancers classified as radioactive iodine resistant (I-RAIR), while 134 had cancers classified as radioactive iodine avid (I-RAIA). Compared to patients with I-RAIA disease, those with I-RAIR were older at the time of diagnosis (average age of 45.7 years vs. 36.8 years), had a higher number of genetic mutations, and were more likely to have poorly differentiated thyroid cancer. Notably, the BRAF V600E mutation was linked to a higher incidence of non-RAI-avid patterns (I-RAIR) compared to thyroid cancer with RAS variants, fusions, and other mutations (64.4% vs. 4.5% vs. 20.7% vs. 20.9%). Furthermore, cancers with BRAF V600E mutations and other related mutations such as TP53 and TERT that were initially radioiodine avid tended to lose there ability to absorb I-131 with subsequent treatments.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that thyroid cancers with BRAF V600E, TERT promoter, and TP53 mutations predominantly showed resistance to radioactoive iodine therapy. In contrast, cancers with RAS mutations and RET or NTRK fusions were likely to respond to radioactive iodine therapy. These findings suggest that cancer treatment can be individualized based on the molecular signature of each cancer. Perhaps patients with cancers that have a molecular profile predicting radioiodine avidity should receive radioactive iodine therapy, while those with a profile predicting radioiodine resistance should not.

— Phillip Segal, MD

THYROID CANCER, continued

ATA RESOURCES

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

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.

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.

Mutation: A permanent change in one of the genes.

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

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

HYPERTHYROIDISM

What patients with Graves' disease should stay on methimazole longer?

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States. Graves' disease is an autoimmune disease where the body makes an antibody directed against the TSH receptor that attacks and turns on the thyroid. This antibody is called thyroid stimulating immunoglobulin (TSI). Antithyroid medications (methimazole/MMI or PTU) are used to control the hyperthyroidism before definitive therapy or to treat until a remission occurs (ie when the TSI goes away). The definitive options that destroy the thyroid include radioactive iodine therapy and surgery. In the past, radioactive iodine therapy was the most common treatment for Graves' disease in the United States. Recently, more and more physicians have been preferring treating patients with anti-thyroid medications instead of with radioactive iodine ablation, with MMI the most common antithyroid medication used. The goal is to treat until a remission occurs.

Remission of Graves' disease with MMI has been reported anywhere from 3 – 48 months. However, recent studies have shown that patients are more likely to have a remission from Graves' disease if they were on methimazole for a total of 60 months (long term) as compared to only 12-18 months (short term). While factors that predict recurrence in short term MMI therapy have been previously reported, these may differ when considering long term MMI therapy. This study was performed to assess predictors of relapse and to determine the rate of relapse of patients after short and long-term MMI therapy.

THE FULL ARTICLE TITLE

Azizi F et al. Risk of recurrence at the time of withdrawal of short- or long-term methimazole therapy in patients with Graves' hyperthyroidism: a randomized trial and a risk-scoring model. Endocrine 2024;84(2):577-588; doi: 10.1007/s12020-023-03656-5. PMID: 38165576.

SUMMARY OF THE STUDY

A total of 302 patients with Graves' disease were treated for 18-24 months with MMI. Of these patients, 128 were monitored off medication after completing short-term treatment, and 130 patients were continued on MMI longer for a total treatment duration of 60-120 months. The primary end point was relapse into overt hyperthyroidism, and the secondary end points were hypothyroidism and subclinical hyperthyroidism.

Overt hyperthyroidism occurred in 56% (67 patients) of the short term MMI group and only 17% (20 patients) of the long term MMI group. Overall, 44% of the short term MMI group (53 patients) and 83% (98 patients) of the long term MMI group were still successfully in remission after 84 months. Even after adjusting for other factors that might affect the results, the short term MMI group was 16.2 x more likely than the long term MMI group have a Graves' recurrence after treatment. The patient's free T4 hormone level was a risk factor for recurrence in the short term MMI group, but not the long term MMI group. In both the short term and the long term MMI groups, the following factors were clinically significant for increasing chances of recurrence: male sex, T3 level, TSI level, and size of the goiter.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In patients experiencing their first Graves' disease episode, this data shows that long term MMI treatment of >60 months is more likely to ensure a remission than the short term MMI treatment of 18 months. This is important since the current 2016 American Thyroid Association guidelines recommend stopping methimazole after 12-18 months. To help determine the likelihood of remission, the authors are proposing a scoring system that will divide patients into risks of recurrence of 20% or 60%. This scoring system will need to be tested in larger studies but holds a lot of promise in helping to determine the best option for treatment of Graves' disease.

— Pinar Smith, MD

HYPERTHYROIDISM, continued

ATA RESOURCES

Goiter: https://www.thyroid.org/goiter/

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

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

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

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.

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

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.

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.

Thyroid stimulating immunoglobulin (TSI): antibodies often present in the serum of patients with Graves' disease that are directed against the TSH receptor, that cause stimulation of this receptor resulting in increased levels of thyroid hormones in the blood and hyperthyroidism.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

THYROID EYE DISEASE

Long-term effects of Teprotumumab for thyroid eye disease

BACKGROUND

Graves' disease is the most common cause of hyperthyroidism in the United States. Graves' disease can be associated with an eye complication called "Thyroid Eye Disease" (TED). TED is an autoimmune disorder caused by the same antibody that leads to Graves' hyperthyroidism. This condition is characterized by growth of fat, muscle and other tissues behind the eyes and can manifest as bulging (proptosis) of the eyes, tearing, redness, lid swelling, double vision and in severe cases -loss of vision. While TED can occur in up to half of the patients with Graves' disease, most of the time it is mild. For those patients with severe TED, steroids and/or radiation have been the standard medical treatment. However, the success of such treatments has been limited and short-lasting.

A new drug called Teprotumumab (Tepezza®) was recently developed to treat TED. This medication is an antibody that blocks a receptor (the insulin-like growth factor 1 receptor) located on fibroblast cells. By blocking this receptor, the growth of tissues behind the eyes is blunted. This drug is given as an intravenous infusion every three weeks for a total of eight infusions. The initial studies showed promising results: alleviation of symptoms and improvement of vision for patients with TED. Indeed, the American and European Thyroid Associations now recommend the use of teprotumumab for patients with moderate to severe TED. This study looks at patients with TED who were part of the original trials and examines the effects of the drug over a longer period.

THE FULL ARTICLE TITLE

Kahaly GJ et al. Long-term efficacy of teprotumumab in thyroid eye disease: follow-up outcomes in three clinical trials. Thyroid. Epub 2024 Jun 2; doi: 10.1089/thy.2023.0656. PMID: 38824618.

SUMMARY OF THE STUDY

This study looks at 121 patients with TED who were part of the original three clinical trials performed in the US and Europe. The patients were treated with either teprotumumab or placebo and followed over an extended period. The authors assessed the severity of the TED by using clinical scales called clinical activity scores (CAS). A decrease of 2 or more in CAS points was considered a good result. Authors also looked at the necessity for more treatments, such as steroids and surgery or repeat teprotumumab infusions due to either lack of effect or loss of initial response to the treatment. The authors also looked at the quality of life of the patients by administering a questionnaire.

CAS response to teprotumumab was high: 87% at week 24, 79% at week 48, 84% at week 60, and 91% at week 72. Quality of life, visual appearance and functional vision (ability to perform daily activities) were improved and stable over time. Of the patients who responded initially, 70-90% maintained the response at 72 weeks. Overall, 20% of the patients needed additional treatments for their TED, including eye surgery. There were some side effects on a few patients including high sugars and loss of hearing.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows: 1) that teprotumumab is very effective at treating TED, particularly in patients with proptosis and double vision, and 2) that the improvements are long lasting. Although, these studies did not directly compare the effects of the drug with that of steroids, it is fair to conclude based on previous data, that teprotumumab is superior to steroids. It is important to note that other smaller studies looking at this drug showed lower response rates. Longer follow up data is needed to better evaluate the overall effect of this drug in a wider variety of patients with TED.

— Susana Ebner MD

THYROID EYE DISEASE, continued

ATA RESOURCES

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

Thyroid Eye Disease: https://www.thyroid.org/thyroid-eye-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.

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.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

THYROID HORMONE THERAPY

Nonthyroidal illness in the setting of heart transplantation: is there a place for thyroid replacement?

BACKGROUND

In critically ill patients, especially those being treated in an intensive care unit, thyroid hormone levels are often altered, with low T3 and TSH values frequently observed. These abnormalities occur because of the response of the thyroid to the severe illness and not because of any specific thyroid function abnormality. This is called the nonthyroidal illness syndrome (NTI) and is seen in ~80% in of patients in intensive care units. In the vast majority of these patients, thyroid hormone therapy is not indicated.

While low T3 and TSH levels are common in NTI, low FT4 levels often indicate a bad prognosis, particularly when they persist after the acute period of the disease. There is still a large debate over the possible benefits of treatment of these NTI patients with low FT4 levels with thyroid hormones. One area where thyroid hormone therapy may have some benefit is in patients with heart failure or in heart donors before heart transplantation.

In this study, the association between thyroid status and heart transplantation was explored in patients with end-stage heart failure. The benefit of administering thyroid hormone replacement, as advocated by a standard donor protocol and treatment in the recipients, was also evaluated.

THE FULL ARTICLE TITLE

Szécsi B et al. The perioperative period of heart transplantation is affected by thyroid hormone status. Thyroid 2024;34(6):774-784; doi: 10.1089/thy.2023.0628. PMID: 38613807.

SUMMARY OF THE STUDY

This was a prospective single-center study of 283 patients who received heart transplantation (HTx) between February 2013 and November 2020 at the Heart and Vascular Center of Semmelweis University in Hungary. Thyroid status according to FT3, FT4, and TSH serum levels was evaluated before and after HTx. The effect of levothyroxine (LT4) administered to a subgroup of heart donors and recipients on death before transplantation and after 30 days (short-term) and 1 and 2 years (long-term) was assessed. The Index for Mortality Prediction After Cardiac Transplantation (IMPACT) score, a numerical measure to predict the risk of dying after HTx, was determined. Death was the primary outcome of this study.

The average age of the 283 patients was 54 years. Overt hypothyroidism was found in 12.4% and subclinical hypothyroidism in 2.1%, and 6.7% were diagnosed with thyrotoxicosis. Thyroid replacement was indicated in 37.8% of donors. Of recipients, 11.3% received levothyroxine prior to surgery and 19.4% received levothyroxine after surgery. Thyroid hormones and TSH significantly decreased after HTx except in patients who received levothyroxine. Short-term survival was higher if the donor had received levothyroxine. Long-term and short-term survival was higher in recipients who also received levothyroxine after transplantation.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirmed that thyroid tests after heart transplantation are consistent with NTI. Overt and subclinical hypothyroidism also occurred and was treated with levothyroxine. The study suggests that the use of levothyroxine in both donors and recipients improved survival after hear transplantation, especially in patient with pre-existing hypothyroidism. It is unclear how many patients were treated on the basis of NTI and not hypothyroidism. Even so, this is an important study that should result in larger studies to clarify the indications for treatment of these critically ill patients.

— Alan P. Farwell, MD

THYROID HORMONE THERAPY, continued

ATA RESOURCES

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

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

ABBREVIATIONS & DEFINITIONS

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

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

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.

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

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.

Nonthyroidal illness: alterations in thyroid hormone levels in critically ill patients that occur because of the response of the thyroid to the severe illness and not because of any specific thyroid function abnormality. Low T3 and TSH values are frequently observed and low T4 levels are associated with a bad prognosis. In the vast majority of these patients, thyroid hormone therapy is not indicated.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 17 | Issue 10 | October 2024

Clinical Thyroidology® for the Public

ATA® Alliance for Thyroid Patient Education

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

ATA®
Optimal Thyroid Health for All

Graves' Disease & Thyroid Foundation

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

Light of Life Foundation
checkyourneck.com

BITE ME CANCER!

MCT8 - AHDS Foundation

THYROID CANCER ALLIANCE

Thyroid 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 Cancer Alliance
www.thyroidcanceralliance.org
www.thyroidcancerpatientinfo.org
Rotterdam, The Netherlands

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

AMERICAN THYROID ASSOCIATION
ATA | *Founded 1923*

Friends of the ATA

FOUNDED 2005

Get the latest thyroid health information. You'll be among the first to know the latest cutting-edge thyroid research that is important to you and your family.

Become a Friend of the ATA!
Subscribe to *Friends of the ATA e-news*

By subscribing to *Friends of the ATA Newsletter*, you will receive:

- ✔ *Friends of the ATA e-news*, providing up-to-date information on thyroid issues, summaries of recently published articles from the medical literature that covers the broad spectrum of thyroid disorders, and invitations to upcoming patient events
- ✔ Updates on the latest patient resources through the ATA® website and elsewhere on the world wide web
- ✔ Special e-mail alerts about thyroid topics of special interest to you and your family

We will use your email address to send you *Friends of the ATA e-news* and occasional email updates. We won't share your email address with anyone, and you can unsubscribe at any time.

www.thyroid.org