EDITOR'S COMMENTS

THYROID CANCER
Fear of recurrence affects health-related quality of life in thyroid cancer patients, even a year after diagnosis
While the majority of patients with thyroid cancer do well and have an excellent prognosis, a diagnosis of cancer has many significant implications to patients. Previous studies have shown that thyroid cancer patients have decreased health-related quality of life (HRQoL) compared to the general population, and surprisingly similar to that of patients with more aggressive cancers. This study evaluated changes in HRQoL over time and the factors at diagnosis that may predict HRQoL at one-year follow up.

Hedman C et al. Fear of Recurrence and View of Life Affect Health-Related Quality of Life in Patients with Differentiated Thyroid Carcinoma: A Prospective Swedish Population-Based Study. Thyroid. 2018 Oct 26;28(12):1609-1617.

HYPOTHYROIDISM
Symptoms strongly drive the consideration of alternative thyroid hormone-replacement options in patients with hypothyroidism
The standard treatment for hypothyroidism is levothyroxine. However, some patients are dissatisfied with their treatment and request alternative therapies. The goal of this study was to assess the opinions of these doctors regarding the issue of treatment for hypothyroidism given the availability of the guidelines, reviews and other new publications on the topic of alternative thyroid hormone therapy.


GRAVES’ DISEASE
Which factors predict the outcome of radioactive iodine therapy of Graves’ Disease?
Graves’ disease is the most common cause of hyperthyroidism in the United States. Radioactive iodine therapy has become less popular recently with more patients started on anti-thyroid drugs. Since many people still feel that radioactive iodine therapy is a good treatment for hyperthyroidism, this study was done to review the response to radioactive iodine therapy as an initial treatment for Graves’ disease, including its usefulness and side effects.


HYPERTHYROIDISM
A mild risk of neonatal hyperthyroidism follows radioactive iodine therapy for Graves’ disease prior to pregnancy
Graves’ disease is caused by the patient making an antibody called TRAB that attacks and turns on the thyroid, making it overactive. TRAB is detectable in the blood of most patients with Graves’ disease and can pass through to the baby and cause hyperthyroidism after delivery in mothers with Graves’ disease. The goal of this study is to assess the risk of hyperthyroidism in newborns of mothers who were treated with radioactive iodine within 2 years before their pregnancy.

Yoshihara A et al, Incidence of neonatal hyperthyroidism among newborns of Graves’ disease patients treated with radioiodine therapy Thyroid; epub 2018 Nov-14

THYROID CANCER
Radioactive iodine dosing based on the radioiodine uptake and thyroglobulin levels is helpful in treating differentiated thyroid cancer
In more advanced cases of thyroid cancer, surgery is followed by a fixed dose of radioactive iodine therapy to destroy any remaining thyroid cancer cells. However, a fixed dose may be either insufficient to destroy the remaining cells or excessive, resulting in side effects. The goal of this study is to analyze the effectiveness of an individualized radioactive iodine doses on the amount of the remaining normal and cancerous thyroid tissue after the thyroid surgery.


HYPOTHYROIDISM
Patients with hypothyroidism adequately treated with levothyroxine have higher levels of cholesterol compared to healthy controls.
One of the objective signs in hypothyroidism is an increase in the level of cholesterol. This increase should be reversed during treatment with L-T₄, with a goal of therapy decreasing TSH levels back to the normal range. The objective of this study was to determine if normalization of TSH in patients with hypothyroidism treated with L-T₄ led to normalization of cholesterol levels.


ATA ALLIANCE FOR THYROID PATIENT EDUCATION
ATA Brochure: Medullary Thyroid Cancer

A publication of the American Thyroid Association®
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 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, ThyCa: Thyroid Cancer Survivors’ Association, Thyroid Cancer Canada, Thyroid Cancer Alliance and Thyroid Federation International.

The American Thyroid Association (ATA) extends its appreciation to all of the patients and their families that are part of the ATA community — our **Friends of the ATA**. It is for you that the 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.

As we think of all those who make a difference in our lives, we thank you for being part of the ATA family and for 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.

The editorial board of CTFP, the ATA Board of Directors, Members, and ATA Headquarters Staff, wish you the best and look forward to being part of your thyroid network in 2019.

March is Medullary Thyroid Cancer Awareness Month.

In this study, the studies ask the following questions:

- What affects quality of life in thyroid cancer patients?
- What drives patients with hypothyroidism to seek alternative therapies?
- What factors predict the outcome of RAI therapy in Graves’ disease?
- Does RAI therapy for Graves’ disease in women increase the risk of neonatal hyperthyroidism in their babies?
- Does individualized RAI therapy dosing have an effect on thyroid cancer outcomes?
- Does levothyroxine therapy normalize cholesterol levels in hypothyroid patients?

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, FACE
THYROID CANCER

Fear of recurrence affects health-related quality of life in thyroid cancer patients, even a year after diagnosis

BACKGROUND
The number of new cases of differentiated thyroid cancer, the most common endocrine cancer, has been increasing over the past several years. A diagnosis of cancer has many significant implications to patients, including concerns about death and the need for strong chemotherapy drugs that cause one to lose their hair. While thyroid cancer patients usually need to undergo surgery, the majority of patients do well and have an excellent prognosis. The risk of death due to differentiated thyroid cancer is very low and very few patients require strong chemotherapy drugs. Despite this, previous studies have shown that thyroid cancer patients have decreased health-related quality of life (HRQoL) compared to the general population, and surprisingly similar to that of patients with more aggressive cancers. This study evaluated changes in HRQoL over time and the factors at diagnosis that may predict HRQoL at one-year follow up.

THE FULL ARTICLE TITLE
Hedman C et al. Fear of Recurrence and View of Life Affect Health-Related Quality of Life in Patients with Differentiated Thyroid Carcinoma: A Prospective Swedish Population-Based Study. Thyroid. 2018 Oct 26;28(12):1609-1617.

SUMMARY OF THE STUDY
The study authors surveyed 487 Swedish patients diagnosed with differentiated thyroid cancer between 2012 and 2017. Information collected included patient characteristics, concurrent diseases, fear of the cancer coming back and view of life. Survey questions were included to assess HRQoL. Additionally, cancer characteristics, treatments and lab results were obtained from the patients’ medical records.

Overall, 72% of patients responded to the survey at diagnosis. Of the respondents that had at least one year follow up, 94% returned both surveys. Of the respondents, 70% were women and the mean age was 51 years old. The study found that HRQoL improved at the one-year follow up compared to diagnosis. Factors that were associated with decreased HRQoL at follow up included being older than 50 years old, lower education, living alone, having other concurrent diseases, a negative view of life and fear of recurrence at diagnosis. Report of lower HRQoL at diagnosis significantly predicted a lower HRQoL at the one-year follow up.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study found that even though the majority of thyroid cancer patients have a good prognosis and are cured of their cancer, they still may have a decreased health-related quality of life at diagnosis which somewhat improves one year later. A negative view of life and fear of the cancer coming back at diagnosis had a negative impact on quality of life. Physicians should make efforts to lessen worry in low risk disease-free thyroid cancer patients in order to improve their quality of life. Additionally, special attention and support should be given to those most vulnerable, such as older patients, as those patients that have decreased quality of life at the time of diagnosis and those that live alone.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS
Thyroid Cancer (Papillary and Follicular): https://www.thyroid.org/thyroid-cancer/
THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer: This is the most common type of thyroid cancer and includes papillary and follicular cancers.

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

MARCH Medullary Thyroid Cancer Awareness Month

www.thyroid.org/donate/
HYPOTHYROIDISM
Symptoms strongly drive the consideration of alternative thyroid hormone-replacement options in patients with hypothyroidism

BACKGROUND
Hypothyroidism is a common condition, and it is present in up to 5% of the general population. The symptoms attributed to hypothyroidism are many, but are not specific to the condition and therefore can be seen in patients with other health problems. Thyroxine (T4) is the main hormone secreted by the thyroid gland. T4 is converted to the active thyroid hormone, T3, in the liver, kidney and many target tissues where thyroid hormone acts.

The standard treatment for hypothyroidism is synthetic levothyroxine (L-T4) due to its’ long half-life and that it most closely mimics the thyroid production of T4. However, many doctors that treat thyroid conditions have patients who are dissatisfied with their treatment and who request combination therapy with either desiccated thyroid extract or combination therapy with liothyronine (L-T3).

The American Thyroid Association published its treatment guidelines for adults with hypothyroidism in 2014. These guidelines were devised after careful review of current scientific knowledge, and the committee concluded that there was not enough evidence to recommend using liothyronine (L-T3) on a routine basis. In 2017, the results of a patient survey showed a low level of satisfaction with their treatment and a greater satisfaction among patients taking desiccated thyroid extract. However, because of how this survey was distributed, it is possible that patients who had strong feelings about their therapy were most likely to respond and this could have very much influenced results reported.

This study reports the results of a survey of physician members of the American Thyroid Association about their choice of treatment for patients with hypothyroidism. The goal of the study was to assess the opinions of these doctors regarding the issue of treatment for hypothyroidism given the availability of the guidelines, reviews and other new publications on the topic of combination therapy with L-T4 and L-T3.

THE FULL ARTICLE TITLE

SUMMARY OF THE STUDY
Starting in February 2017, a link for the survey was sent to ATA members via e-mail, on several occasions. A total of 363 responses qualified for the study as these doctors indicated that they prescribed treatment for hypothyroidism.

The questions consisted of 13 theoretical scenarios, each describing a patient with hypothyroidism who had either no symptoms, various symptoms, low T3 concentration, and or had a genetic variant that could modify the metabolism of thyroid hormone. In each scenario, the physician could choose six treatment options, including continuing L-T4, adding L-T3 or replacement of L-T4 with desiccated thyroid extract.

Of the 363 responders, 86% were endocrinologists, 64% were from North America, and 53% had been in practice for more than 10 years. Once the answers were analyzed using statistical methods, it was seen that, although 98% of physicians opted to continue L-T4 for the standard patient (featured as a 29 year old female with Hashimotos’ thyroiditis, normal body weight, lack of suggestive symptoms, TSH of 2.2 and not contemplating pregnancy), there were situations in which the physicians would consider less conventional treatment. The patient characteristic that most influenced the prescribing of L-T3 was the presence of symptoms, but doctors also were more likely to prescribe it if patients requested it or if their measured T3 was low.

These results were surprising because as of now, most clinical trials have failed to show improvement in quality of life or in cognitive measures when a patient is treated for hypothyroidism with T3 containing treatments. It is also apparent that there has been a change in prescribing
HYPOTHYROIDISM, continued

patterns since 2013, when a similar study was carried out. In that study, only 3.6% of the physicians indicated that they would consider prescribing L-T₃ to a symptomatic patient, while in this study, a symptomatic patient would have been prescribed L-T₃ by 18% of the responders.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
In summary, this study indicates that doctors are increasingly prescribing treatments that include L-T₃ when encountering patients who complain of persistent symptoms of hypothyroidism in spite of standard L-T₄ treatment. This change in prescribing trends cannot be explained by new supporting evidence because only one trial was conducted since 2009 and it did not show superiority of combination therapy over standard therapy.

Therefore, it seems that doctors are listening to their patients and partnering with them with respect to management of their therapy. However, there is obviously a need to carry on clinical trials designed to assess the long term safety of treatments that add L-T₃, including the best dosing and monitoring strategies. A long term study and assessment is crucial because hypothyroidism is a life-long condition.

— Jessie Block-Galarza, MD

ATA THYROID BROCHURE LINKS
Hypothyroidism (Underactive): https://www.thyroid.org/hypothyroidism/

ABBREVIATIONS & DEFINITIONS

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

Hashimotos thyroiditis: the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

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

Triiodothyronine (T₃): the active thyroid hormone, usually produced from thyroxine, available in pill form as liothyronine (Cytomel™).

Desiccated thyroid extract: thyroid hormone pill made from animal thyroid glands.
GRAVES’ DISEASE

Which factors predict the outcome of radioactive iodine therapy of Graves’ Disease?

BACKGROUND
Graves’ disease is the most common cause of hyperthyroidism in the United States. Graves’ disease can be treated with medication (anti-thyroid drugs), surgery or radioactive iodine therapy. While the idealistic aim for treatment is to leave the patient with normal thyroid function long term, this is difficult to attain. In Europe and Asia, anti-thyroid drugs are frequently used as a first choice treatment. However, many patients will have a relapse of their hyperthyroidism after a course of anti-thyroid drugs. Because of this, in the US, many patients are treated with a goal of destroying the thyroid with radioactive iodine therapy, leaving the patient with stable hypothyroidism and using thyroid hormone as a replacement. Radioactive iodine therapy has become less popular recently with more patients started on anti-thyroid drugs. Since many people still feel that radioactive iodine therapy is a good treatment for hyperthyroidism, this study was done to review the response to radioactive iodine therapy as an initial treatment for Graves’ disease, including its’ usefulness and side effects.

THE FULL ARTICLE TITLE

SUMMARY OF THE STUDY
This study reviewed the records of 576 patients with Graves’ disease who received a total of 665 radioactive iodine therapy treatments over a 10 year period at the Edinburgh Centre of Endocrinology and Diabetes. Not surprisingly 75% of the patients were women, with an average age of 51. The group studied received their first dose of radioactive iodine therapy within 6 months of the diagnosis of Graves’ disease, although 12% required a second dose and 1% a third dose to cure their hyperthyroidism. Patients were treated with 10 mCi of radioactive iodine for the first dose but often received a higher dose for second or third doses. Nearly half of the patients received radioactive iodine therapy as their only treatment, while the remainder received anti-thyroid drugs either before, after or both receiving radioactive iodine therapy. A total of 45 patients had Graves’ eye disease and about half of these were treated with glucocorticoids, a medication that can help prevent any worsening of the eye disease. Thyroid hormone levels were monitored within 8 weeks after radioactive iodine therapy and then every 1-2 mo after.

The outcomes studied were treatment failure – meaning that hyperthyroidism persisted and a patient required another dose of radioactive iodine therapy or anti-thyroid drugs, weight change at 1 year after successful treatment, the presence or development of Graves’ eye disease, and patient satisfaction. Outcomes were determined at 1 year after the first dose of radioactive iodine therapy and at a mean follow up of 6.7 years.

At one year after the first dose of radioactive iodine therapy, 76.6% of patients were hypothyroid, 17% remained hyperthyroid and 5.7% had normal thyroid function. After 6.7 years an additional 11% were hypothyroid after 2 or 3 doses. Patients who remained hyperthyroid were either receiving anti-thyroid drugs (2.3%) or had thyroid surgery (0.9%).

They found that patients who had higher thyroid hormone levels, higher levels of a specific antibody associated with Graves’ disease (TRAB) or were treated with anti-thyroid drugs after their dose of radioactive iodine therapy were more likely to fail their first dose of radioactive iodine therapy. But failure was not associated with other features such as age, sex, smoking. Weight change was analyzed in only 228 patients and 84% gained weight by 1 year after radioactive iodine therapy. This seemed to be dependent on thyroid hormone levels before radioactive iodine therapy and the absence of anti-thyroid drug treatment prior to radioactive iodine therapy, but was not clearly related to thyroid hormone levels after treatment. New eye disease developed in
GRAVES’ DISEASE, continued

45 patients after radioactive iodine therapy. Of these, 13 patients required treatment with glucocorticoid, 4 needed radiation to the orbits and 6 required surgery. Higher thyroid hormone levels prior to radioactive iodine therapy treatment were associated with the development of new eye disease although increased levels of TRAB was not. While smoking was associated with the presence of eye disease prior to radioactive iodine therapy, it did not seem to be associated with development of eye disease after radioactive iodine therapy. Only 175 patients responded to a questionnaire regarding patient satisfaction. Most were satisfied about receiving radioactive iodine therapy and about their well being in the year after radioactive iodine therapy. Overall, 79% said they would recommend to a friend although 53% were unhappy about their weight gain.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This was a large study of patients who received radioactive iodine therapy for Graves’ disease and showed an overall favorable prognosis. While some patients will require more than one dose of radioactive iodine, by the end of the study over 97% were adequately treated by radioactive iodine therapy. Weight gain is common, but in this study was not measured against patients’ normal weight prior to the development of hyperthyroidism, which has previously been shown to be associated with weight gain after treatment. It appears there was little effect of radioactive iodine therapy on pre-existing Graves’ eye disease, although some will develop eye disease after radioactive iodine therapy. A majority of patients were satisfied with their treatment.

— Marjorie Safran, MD, FACE

ATA THYROID BROCHURE LINKS
Graves’ Disease: [https://www.thyroid.org/graves-disease/](https://www.thyroid.org/graves-disease/)
Hyperthyroidism (Overactive): [https://www.thyroid.org/hyperthyroidism/](https://www.thyroid.org/hyperthyroidism/)
Radioactive Iodine: [https://www.thyroid.org/radioactive-iodine/](https://www.thyroid.org/radioactive-iodine/)
Thyroid and Weight: [https://www.thyroid.org/thyroid-and-weight/](https://www.thyroid.org/thyroid-and-weight/)

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.

**Steroids/Glucocorticoids:** general anti-inflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation.

**TRAB:** antibodies often present in the serum of patients with Graves disease that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism.
HYPERTHYROIDISM

A mild risk of neonatal hyperthyroidism follows radioactive iodine therapy for Graves’ disease prior to pregnancy

BACKGROUND
Graves’ disease is an autoimmune condition and the most common cause of hyperthyroidism in women of childbearing age. It is caused by the patient making an antibody called TRAB (TSH Receptor Antibody) that attacks and turns on the thyroid, making it overactive. TRAB is detectable in the blood of most patients with Graves’ disease. TRAB can pass through to the baby and cause hyperthyroidism after delivery in mothers with Graves’ disease. This is called neonatal Graves’ disease. This is a risk for all babies that are born to mothers with Graves’ disease.

TRAB tends to decrease with treatment of Graves’ disease with anti-thyroid medications and, if it goes away or decreases low enough, the Graves’ disease goes into remission. TRAB also tends to decrease years after surgery. However, the amount of TRAB rises for several months after radioactive iodine therapy, but this effect may last longer in some individuals. This is likely due to the effect of the destruction of the thyroid by the radioactive iodine therapy. It is unknown of this increase in TRAB would have any effect on the thyroid function of babies or newborns of mother that have been previously treated with radioactive iodine. The goal of this study is to assess the risk of hyperthyroidism in newborns of mothers who were treated with radioactive iodine within 2 years before their pregnancy.

THE FULL ARTICLE TITLE
Yoshihara A et al, Incidence of neonatal hyperthyroidism among newborns of Graves’ disease patients treated with radioiodine therapy Thyroid; epub 2018 Nov-14

SUMMARY OF THE STUDY
This study was conducted in Ito Hospital in Tokyo, Japan, and included 145 pregnant women who had radioactive iodine therapy within 2 years before their pregnancy. Their newborns were born between April 2004 and December 2015. All newborns had been assessed for hyperthyroidism based on their symptoms and blood tests for thyroid function.

A total of 8 newborns were found to have hyperthyroidism. The mothers of the affected newborns had a higher levels of TRAB at the time of radioactive iodine treatment and in the first and third trimesters of pregnancy as compared to mothers with healthy newborns. There was not a difference between thyroid volume (checked by ultrasound) at the time of radioactive iodine therapy, radioactive iodine dose or the interval between radioactive iodine therapy and pregnancy between these two groups of mothers.

The most important factor predicting hyperthyroidism in newborns was the level of TRAB in their mothers in third trimester of pregnancy (especially when it was 4.9 times higher than the normal range).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?
This study suggests that the risk of hyperthyroidism in newborns whose mothers were treated with radioactive iodine within 2 years of their pregnancy was 5.5%. The level of TRAB at third trimester is a reliable factor to predict this risk. It is critical to treat hyperthyroidism in newborns early and this study provides valuable information to identify the babies at risk.

— Shirin Haddady, MD MPH
HYPERTHYROIDISM, continued

**ATA THYROID BROCHURE LINKS**

Graves' Disease: [https://www.thyroid.org/graves-disease/](https://www.thyroid.org/graves-disease/)
Hyperthyroidism (Overactive): [https://www.thyroid.org/hyperthyroidism/](https://www.thyroid.org/hyperthyroidism/)
Radioactive Iodine: [https://www.thyroid.org/radioactive-iodine/](https://www.thyroid.org/radioactive-iodine/)
Pregnancy and Thyroid Disease: [https://www.thyroid.org/thyroid-disease-pregnancy/](https://www.thyroid.org/thyroid-disease-pregnancy/)

**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.

**Autoimmune disorders:** A diverse group of disorders that are caused by antibodies that get confused and attack the body's own tissues. The disorder depends on what tissue the antibodies attack. Graves' disease and Hashimoto's thyroiditis are examples of autoimmune thyroid disease. Other Autoimmune disorders include: type 1 diabetes mellitus, Addison's disease (adrenal insufficiency), vitiligo (loss of pigment of some areas of the skin), systemic lupus erythematosus, pernicious anemia (B12 deficiency), celiac disease, inflammatory bowel disease, myasthenia gravis, multiple sclerosis, and rheumatoid arthritis.

**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.

**Antibodies:** proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.

**TRAB:** TSH receptor antibodies often present in the serum of patients with Graves disease that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism.

**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).
THYROID CANCER

Radioactive iodine dosing based on the radioiodine uptake and thyroglobulin levels is helpful in treating differentiated thyroid cancer

BACKGROUND

Treatment for most patients with differentiated thyroid cancer includes surgery first to remove the thyroid. In more advanced cases, surgery is followed by radioactive iodine therapy to destroy any remaining thyroid cells, both normal and cancerous cells. This is done to decrease the risk of recurrence of the cancer. It also helps the initial cancer staging and early detection of recurrent cancer with serum thyroglobulin levels and whole-body scanning.

Traditionally, a fixed-dose of radioactive iodine is administered. However, a fixed dose may be either insufficient to destroy the remaining cells or excessive, resulting in side effects. Normal and cancerous thyroid cells have the capacity to take up iodine and produce thyroglobulin proportional with the amount of remaining thyroid tissue after the thyroid surgery. Thus, an individualized radioactive iodine dose can be estimated based on the radioiodine uptake (RAIU) in the neck and the serum thyroglobulin level test measured after the thyroid surgery.

The goal of this study is to analyze the effectiveness of an individualized radioactive iodine doses on the amount of the remaining normal and cancerous thyroid tissue after the thyroid surgery.

THE FULL ARTICLE TITLE


SUMMARY OF THE STUDY

The study included 265 patients with differentiated thyroid cancer who underwent thyroidectomy and were referred for radioactive iodine therapy between 2013 and 2017 at a university hospital from Shanghai, China. Patients with local or distant spread of the cancer were excluded. Most patients were women (77%) with an average age of 43 and had papillary thyroid cancer (89%). The neck RAIU and serum thyroglobulin levels were measured after the thyroid surgery.

Patients were randomly assigned in a 4:1 ratio to receive radioactive iodine either based on their RAIU and serum thyroglobulin levels or as a fixed dose of 3.7 GBq (100 mCi). Those assigned to receive radioactive iodine therapy based on their RAIU and serum thyroglobulin levels were separated in four groups and took a radioactive iodine dose of 1.1, 1.85, 3.7, or 5.55 GBq based on the higher result of either the uptake (≤2%, 2–5%, 5–15%, and >15%) or thyroglobulin level (≤2 ng/mL, 2–5 ng/mL, 5–10 ng/mL, and >10 ng/mL). A total of 58 patients received a fixed radioactive iodine dose, while 52, 45, 57, and 53 patients received a calculated radioactive iodine therapy dose based on their RAIU/thyroglobulin levels. A complete response to the radioactive iodine therapy was defined as a serum thyroglobulin ≤1 ng/mL and the absence of visible RAIU after thyroid hormone withdrawal assessed six months or more (average of 12 months) after the radioactive iodine therapy.

A higher percentage of patients achieved a complete response to the radioactive iodine therapy in the calculated group than the fixed dose group (89% vs. 69%) with a similar response in the four RAIU/thyroglobulin-guided therapy subgroups. Additional radioactive iodine therapy was needed for less patients in the RAIU/thyroglobulin-guided therapy group than in the fixed-dose group (1% vs. 8%). Overall, a similar proportion of patients in the RAIU/thyroglobulin-guided and fixed-dose treatment groups had side effects (21% vs. 33%). However, less patients who received calculated radioactive iodine therapy developed a dry mouth as compared to those who received a fixed radioactive iodine therapy (9% vs. 19%). The risk of experiencing a dry mouth or dry eyes was higher in patients who received a higher radioactive iodine dose.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Patients with differentiated thyroid cancer who receive a calculated radioactive iodine therapy dose based on
THYROID CANCER, continued

the individual RAIU and serum thyroglobulin level have a higher complete response and success rate and less side effects as compared to patients who receive a fixed radioactive iodine therapy dose. An individualized radioactive iodine therapy administration could contribute to the improvement of care for thyroid cancer patients.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer: includes papillary and follicular cancer and overall has a favorable prognosis.

Thyroidectomy: surgery to remove the 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 (RAI treatment). 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).

Whole Body Scan: this radioactive iodine scan is performed under TSH stimulation, either after thyroid hormone withdrawal or after injections of recombinant human TSH (Thyrogen), and usually includes measuring serum thyroglobulin levels. The scan done after radioactive iodine treatment identifies what was treated and if there is any evidence of metastatic thyroid cancer.

Radioactive iodine uptake (RAIU): this is a measurement of the amount and activity of thyroid tissue and is reported as the percent of a dose of radioactive iodine that is retained in the neck 24 h after the dose is given.

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker.

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.
HYPOTHYROIDISM

Patients with hypothyroidism adequately treated with levothyroxine have higher levels of cholesterol compared to healthy controls.

BACKGROUND

Hypothyroidism is common, affecting up to 5% of people in the United States, with mild hypothyroidism affecting up to 20% of selected populations. Many of the symptoms of hypothyroidism are nonspecific and hard to quantify. The thyroid gland is controlled by thyroid stimulating hormone (TSH) secreted by the pituitary gland. TSH levels increase when the thyroid hormone levels fall in the patient who develops hypothyroidism. Treatment of hypothyroidism involves replacing the thyroid hormones, usually in the form of levothyroxine (L-T4).

Some of the objective signs in hypothyroidism include increases in the level of cholesterol, both total and LDL cholesterol. Decreases in brain function and energy expenditure are also seen. These changes all should be reverse during treatment with L-T4, with a goal of therapy decreasing TSH levels back to the normal range. Once the TSH is normal, cholesterol and creatine kinase levels, brain function and energy expenditure should also return to normal. The objective of this study was to determine if normalization of TSH in patients with hypothyroidism treated with L-T4 led to normalization of these thyroid hormone therapy markers. In this study, previously published data on that topic was systematically reviewed, combined and analyzed together.

THE FULL ARTICLE TITLE


SUMMARY OF THE STUDY

A systemic literature review identified 99 studies from 1970 to 2017 eligible for analysis. The analysis of 23 studies showed that hypothyroid patients treated with L-T4 to achieve normal serum TSH levels had significantly higher LDL and total cholesterol levels than healthy individuals with normal thyroid function. Similarly, analysis of 41 studies that lacked data from individuals with normal thyroid function reported that L-T4-treated hypothyroid patients had an average LDL level of 138.2 mg/dl and cholesterol level of 209.6 mg/dl, which are higher than recommended. Moreover, many patients with hypothyroidism were treated with cholesterol lowering medications. Kidney function was assessed in L-T4-treated patients and individuals with normal thyroid function in six studies; the results were consistent with restoration of normal renal function in L-T4-treated patients. L-T4-treated patients had lower energy expenditure than healthy controls in one study. Finally, brain test results also normalized following L-T4 therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that LDL and total cholesterol levels were higher in patients with hypothyroidism who achieved a normal TSH following L-T4 therapy than in individuals with normal thyroid function. This suggests that L-T4 alone is not sufficient to normalize cholesterol levels. The role of alternative therapies, such as combination therapy by adding L-T3 to L-T4, should be studied to determine if they improve the response of cholesterol levels over that seen with L-T4 alone. Finally, studies need to be done to determine if hypothyroid patients on L-T4 are at any increased risk of cardiac problems based on the increase in cholesterol levels.

— Valentina D. Tarasova, MD

ATA WEB BROCHURE LINKS:

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

ABBREVIATION AND DEFINITIONS:

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, available in pill form as Cytomel™.

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

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.

Levothyroxine (LT₄): the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyll™, 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.

www.thyroid.org/donate/
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.

**WHO WE ARE** (in alphabetical order)

**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**
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**
checkyourneck.com

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

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

**Thyroid Cancer Canada**
www.thyroidcancercanada.org
416-487-8267
info@thyroidcancercanada.org

**Thyroid Federation International**
www.thyroid-fed.org
tfi@thyroid-fed.org
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](http://www.thyroid.org)
JOIN US

PLEASE JOIN OUR JOURNEY TO ADVANCED DISCOVERIES AND TREATMENT FOR THYROID DISEASE AND THYROID CANCER

As patients with thyroid disease navigate the challenges to their quality of life and researchers and physicians look for more effective directions, we at the ATA have our own destination—funding for critical thyroid research, prevention, and treatment. For 94 years, the ATA has led the way in thyroidology. It’s a daily obstacle course to find new drugs, better treatments, advanced surgical methods, and more rapid diagnoses for the 20 million Americans who have some form of thyroid disease.

The ATA was a valuable resource for our family when my dad was diagnosed with Anaplastic Thyroid Cancer. When you’re faced with a detrimental diagnosis where even a few days can make the difference in life or death, understanding your options quickly is critical. The ATA website offers a one-stop shop for patients and caregivers to find specialists, current clinical trials, general thyroid cancer information, and links to other patient support groups and information.

Mary Catherine Petermann
- Father who was diagnosed with Anaplastic Thyroid Cancer in 2006
- He was treated at Mayo Clinic
- He has clean scans as of October 2016

The ATA has paved the way with management guidelines for clinicians who diagnose and treat thyroid disease. For physicians treating pregnant women diagnosed with thyroid disease, our recent publication presents 97 evidence-based recommendations making sure that best practices are implemented with the latest, most effective treatment.

Through your generous support and donations, research takes the lead and hope is on the horizon. Will you join us in our campaign to raise $1.5 million for thyroid research, prevention, and treatment? Your compassionate, tax-deductible gift will provide funds for:

- Research grants that pave the way for 1,700 ATA physicians and scientists who have devoted their careers to understanding the biology of and caring for patients affected by thyroid disease.
- Patient education for individuals and families looking for life-changing clinical trials, the best thyroid specialists, and cutting edge treatment and drugs.
- Professional education that offers a wealth of knowledge and leading-edge research for trainees and practitioners.
- A website that is the go-to resource for thyroid information for patients and practitioners alike. In 2016 alone, there were more than 3,700,000 website views of ATA’s library of online thyroid information patient brochures.

Donations of all sizes will change the future for thyroid patients. You will make a direct impact on patients like Mary Catherine’s father as he deals with Anaplastic Thyroid Cancer. You will help scientists like ATA Associate Member Julia Rodiger, Ph.D., a scientist at the National Institutes of Health, as she analyzes thyroid hormones for intestinal stem cell development.
Medullary Thyroid Cancer

WHAT IS THE THYROID GLAND?
The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid’s job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

CANCER OF THE THYROID
Thyroid cancer is relatively uncommon compared to other cancers. In the United States it is estimated that in 2016 approximately 64,000 new patients will be diagnosed with thyroid cancer, compared to over 240,000 patients with breast cancer and 135,000 patients with colon cancer. However, fewer than 2000 patients die of thyroid cancer each year. In 2013, the last year for which statistics are available, over 630,000 patients were living with thyroid cancer in the United States. Thyroid cancer is usually very treatable and is often cured with surgery (see Thyroid Surgery brochure) and, if indicated, radioactive iodine (see Radioactive Iodine brochure). Even when thyroid cancer is more advanced, effective treatment is available for the most common forms of thyroid cancer. Even though the diagnosis of cancer is terrifying, the prognosis for most patients with papillary and follicular thyroid cancer is usually excellent.

MEDULLARY THYROID CANCER
Medullary Thyroid Cancer (MTC) accounts for 1%–2% of thyroid cancers in the United States. MTC is different from other types of thyroid cancers (which are derived from thyroid follicular cells – the cells that make thyroid hormone), because it originates from the parafollicular C cells (also called “C cells”) of the thyroid gland. These cells do not make thyroid hormone and instead make a different hormone called calcitonin.

MTC can, and frequently does, spread to lymph nodes and can also spread to other organs. MTC is likely to run in families (inherited forms) in up to 25% of diagnoses, and inherited forms can be associated with other endocrine tumors, in syndromes called Multiple Endocrine Neoplasia (MEN) 2A and MEN 2B. In addition to MTC, patients with MEN2A may have tumors of the adrenal glands called pheochromocytomas or in the parathyroid glands (parathyroid adenomas). Patients with MEN2B, have MTC, pheochromocytomas and neuromas (typically a benign growth or tumor of nerve tissue) in the lining of the mouth and/or gastrointestinal track.

Patients with an inherited form of MTC usually have a mutation in a gene called the RET proto-oncogene. This mutation is present in all of the cells in their body (a germline mutation) and these mutations cause the development of MTC. This is important because in family members of a person with an inherited form of MTC, a blood test for a mutation in the RET proto-oncogene can lead to an early diagnosis of MTC and, to curative surgery to remove it. However, in the majority of patients (~ 75%) a germline mutation is not found - indicating that MTC is not an inherited or inheritable condition. In these cases, MTC is called sporadic.

Whether MTC is sporadic or familial can be determined by a blood test for the RET proto-oncogene. Anyone diagnosed with MTC should have this test run to determine whether the MTC is familial (meaning other family members may also have MTC that has not yet been diagnosed) or sporadic.
WHAT ARE THE SYMPTOMS OF MEDULLARY THYROID CANCER?

Medullary thyroid cancer usually presents as a lump or nodule in the thyroid. It may be noted by the patient or discovered during routine neck examination by the doctor. Sometimes, the nodule is discovered incidentally by imaging studies done for other unrelated reasons (CT of the neck, PET scan, or carotid ultrasound). The nodule may cause no symptoms, but in some cases the tumor may have spread to lymph nodes in the neck, which may be enlarged on physical examination.

Patients with advanced MTC may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or the esophagus, it may cause difficulty with breathing or swallowing. Hoarseness can be present if the cancer invades the nerve that controls the vocal cords.

MTC is usually more aggressive than the other more common types of thyroid cancer (See Thyroid Cancer-papillary and follicular- brochure), and it is usually easier to treat and control if it is found before it spreads to lymph nodes in the neck or other parts of the body.

Thyroid function tests such as TSH are usually normal, even when MTC is present.

If you have a family history of MTC and have tested positive for the RET mutation, then you should see an endocrinologist to help determine how best to follow you or treat you.

HOW IS MEDULLARY THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer is usually made by a fine needle aspiration (FNA) biopsy of a thyroid nodule, or after the nodule is surgically removed. Patients in whom the results of an FNA biopsy (or histopathology) are suggestive or indicative of MTC should be further evaluated with measurement of the proteins calcitonin and carcinoembryonic antigen (CEA) in the blood, which are typically elevated in patients with MTC. These tests are useful to confirm the diagnosis of MTC which can help ensure the surgeon plans the correct surgery, and also serve as tumor markers during long-term follow-up to detect any remaining disease or recurrence of the cancer.

WHAT IS THE RET MUTATION?

The RET proto-oncogene is located on chromosome 10. A genetic mutation in the RET oncogene is seen in all cells in the body in patients with the hereditary forms of MTC. Mutations in RET can also be seen only in the tumor cells in patients with sporadic MTC. Since the discovery of the RET oncogene, more than 100 different mutations have been identified in the gene in patients with MTC.

Genetic counseling and testing for RET gene mutations should be offered to patients diagnosed with MTC and first-degree relatives (parents, siblings and children of someone diagnosed with MTC) of all patients with proven germline mutations (hereditary MTC). If close relatives, especially children, are found to have the RET mutation on a blood test, the thyroid gland can be removed before MTC has a chance to develop or at least in its very early stages.

HOW IS MTC TREATED?

The primary treatment for MTC is surgery, and the currently accepted approach is to remove the entire thyroid gland (total thyroidectomy) (See thyroid surgery brochure). Often patients with MTC will have thyroid cancer present in the lymph nodes of the neck or upper chest. These lymph nodes are usually removed at the time of thyroid surgery or sometimes, at a later surgery if found subsequently. After surgery, patients need to take thyroid hormone replacement medication for life.

Unlike papillary and follicular thyroid cancer, medullary thyroid cancer does not take up iodine, and consequently radioactive iodine treatment is not a treatment option for patients with MTC.

Patients with MTC with very high levels of calcitonin should have imaging prior to surgery to determine whether the tumor has spread to sites outside the thyroid and/or outside the neck. If there is evidence of cancer outside the neck, surgery may be more palliative, aimed at reducing local complications caused by the tumor, rather than completely eliminating all tumor. Other treatment options (external beam radiation, or chemotherapy) may need to be used together with surgery after careful discussion with the patient.

FURTHER INFORMATION

Further details on this and other thyroid-related topics are available in the patient thyroid information section on the American Thyroid Association® website at www.thyroid.org. For information on thyroid patient support organizations, please visit the Patient Support Links section on the ATA website at www.thyroid.org.
New chemotherapeutic agents that have shown promise treating other advanced cancers are increasingly available for treatment of thyroid cancers. Two such agents, Vandetanib and Cabozantinib have been FDA approved for use by patients with MTC. These drugs do not cure advanced cancers that have spread widely throughout the body, but they can often slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and require care at specialized medical centers.

**WHAT IS THE FOLLOW-UP FOR PATIENTS WITH MTC?**

Periodic follow-up examinations are essential for all patients with MTC because the thyroid cancer can return, sometimes many years after successful initial treatment. These follow-up visits include a careful history and physical examination, with particular attention to the neck area. Neck ultrasound is also a very important tool to visualize the neck and look for nodules, lumps or enlarged lymph nodes that might indicate that the cancer has recurred.

Blood tests are also important in the follow-up of MTC patients. All patients who have had their thyroid glands removed require thyroid hormone replacement with levothyroxine. Thyroid stimulating hormone (TSH) should be checked periodically, and the dose of levothyroxine adjusted to keep TSH in the normal range. There is no need to keep TSH suppressed in patients with MTC.

Measurement of calcitonin and CEA are a necessary routine part of the follow-up of patients with MTC. Following thyroidectomy, it is hoped that calcitonin levels will be essentially undetectable for life. A detectable or rising calcitonin level should raise suspicion for possible cancer recurrence. Detectable calcitonin levels may require additional tests.

**WHAT IS THE PROGNOSIS OF MEDULLARY THYROID CANCER?**

The prognosis of MTC is usually not as favorable as differentiated thyroid cancers (papillary and follicular cancer). However, if discovered early, surgery can be curative. Even in cases where it is not caught early, MTC often progresses relatively slowly. Long-term survival depends on the stage of disease at the time of diagnosis. The blood levels of calcitonin or CEA over the first year after surgery can also be a predictor of a patient’s survival.

**ATA PARTNERING WITH MTC**

The Medullary Thyroid Carcinoma (MTC) Registry Consortium* is partnering with the American Thyroid Association (ATA) to create a registry (list) of all new cases of MTC diagnosed in the United States over the next 10-15 years (the MTC Registry). The purpose of the MTC Registry is to help better understand what risk factors are associated with the development of MTC.

Click here for additional information: [http://www.thyroid.org/media-main/partner-relations/medullary-thyroid-carcinoma-registry-consortium/](http://www.thyroid.org/media-main/partner-relations/medullary-thyroid-carcinoma-registry-consortium/)