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Optimal Thyroid Health for All

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Financial and health insurance status affect clinical management and quality of life in patients with thyroid cancer

Health insurance plays a significant role for Americans to access and receive care, and whether or not a patient has health insurance may affect cancer treatment and outcomes. Two recent studies addressed the impact of health insurance and financial status on thyroid cancer care. The first investigated the effect of health insurance status on diagnosis and treatment of patients with papillary thyroid cancer. The second evaluated the degree of financial difficulty among thyroid cancer survivors and its impact on quality of life.

- Ullmann TM et al 2019 Insurance Status Is Associated with Extent of Treatment for Patients with Papillary Thyroid Carcinoma. *Thyroid* 29(12):1784-1791.
- Mongelli MN et al 2020 Financial burden and quality of life among thyroid cancer survivors. *Surgery* 167(3):631-637.

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Patients who tend to prefer maximal medical care receive more intense thyroid cancer follow-up care

It has been recognized for a long time that individuals have different preferences for their medical care. Some are medical maximizers and others medical minimizers with quite different preferences for more or less medical care. The aim of this study was to better understand the role of patient preferences on the intensity of follow-up medical care in patients who became disease-free after initial treatment for thyroid cancer.

Evron JM 2019 role of patient maximizing-minimizing preferences in thyroid cancer surveillance. *J Clin Oncol* 37:3042–3049. PMID: 31573822

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Selenium supplements in pregnant women with thyroid disease

Selenium is a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid health. Two previous studies examining the effects of selenium supplementation in pregnant women had conflicting results. To address this, the current study examines the effect of selenium supplementation in pregnant women with autoimmune thyroid disease on the levels of TPO antibodies during and after pregnancy.

Mantovani, G., et al. "Selenium supplementation in the management of thyroid autoimmunity during pregnancy: results of the "SERENA study", a randomized, double-blind, placebo-controlled trial." *Endocrine* 66.3 (2019): 542-550.

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"Block-and-Replace" treatment in children with Graves' disease

Methimazole is an effective treatment for Graves' disease. However, some patients remain poorly controlled on methimazole alone. The block-and-replace method uses methimazole to completely block the thyroid gland and levothyroxine to bring the thyroid hormone levels back to normal. The current study examined a group of children with poorly controlled Grave's disease who were managed by the block-and-replace method with methimazole and levothyroxine.

Vigone MC et al 2019 "Block-and-replace" treatment in Graves' disease: experience in a cohort of pediatric patients. *J Endocrinol Invest*. Epub 2019 Nov 12. PMID: 31713721.

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Thyroiditis while receiving immune checkpoint inhibitor therapy for non-thyroid cancers is associated with improved overall survival

Immune checkpoint inhibitors are a new class of cancer chemotherapy agents that allow the body's own immune system to attack and destroy cancer cells. Since autoimmune thyroid disease is a common cause of thyroid problems, it is not surprising that one of the side effects of these drugs is both hyper- and hypothyroidism. This study examines the frequency, course and survival effects of newly diagnosed autoimmune thyroid disease after treatment with immune checkpoint inhibitors.

Kotwal A et al 2020 PD-L1 inhibitor-induced thyroiditis is associated with better overall survival in cancer patients. *Thyroid*. Epub Jan 9. PMID: 31813343.

THYROID CANCER 15

Controversies, consensus, and collaboration in the use of radioactive iodine therapy for the treatment of thyroid cancer

The latest ATA thyroid cancer guidelines encourage more conservative use of radioactive iodine therapy. These recommendations have been controversial and 2 prominent nuclear medicine organizations declined to endorse the guidelines. In order to promote better understanding of differences in perspective, leaders in the field met to develop recommendations/guiding principles for the use of radioactive iodine therapy.

Tuttle RM et al 2019 Controversies, consensus, and collaboration in the use of 131I therapy in differentiated thyroid cancer: a joint statement from the American Thyroid Association, the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the European Thyroid Association. *Thyroid* 29:461–470. PMID: 30900516.

Clinical Thyroidology® for the Public

www.thyroid.org

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EDITOR'S COMMENTS

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through [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 Canada*, *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.

May is International Thyroid Awareness Month.

Please see the [updated Statement on COVID-19](#) on page 3, and the [Comment on Thyroid Surgery During the Covid-19 Pandemic](#) on page 4.

In this issue, the studies ask the following questions:

- Does financial and health insurance status affect clinical management and quality of life in patients with thyroid cancer?
- Does patient preference affect the intensity of thyroid cancer surveillance?
- Does selenium supplementation during pregnancy affect thyroid function?
- Does “block and replace” have a role in the management of Graves’ disease in children?
- Do the new cancer chemotherapy agents affect thyroid function?
- What is the best use of radioactive iodine in the management of thyroid cancer?

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



STATEMENT ON COVID-19

The Covid-19 pandemic has caused an unprecedented upheaval in our daily lives and presented extremely difficult challenges to our healthcare system. There is a lot of information circulating around. As we try to do with *Clinical Thyroidology for the Public*, we at the American Thyroid Association would like to make sure that you all have access to the most accurate, reliable, fact-based and updated information.

We recommend the following websites:

- Centers for Disease Control (CDC) — <https://www.cdc.gov/coronavirus/2019-ncov/index.html>
- US Department of State — <https://www.state.gov/coronavirus/>
- World Health Organization — <https://www.who.int/>

For thyroid-specific information:

- American Thyroid Association — <https://www.thyroid.org/covid-19/>

We all can, and must, do our part to slow the spread of COVID-19 and to “flatten the curve”. COVID-19 is thought to spread mainly from person-to-person who are in close contact with one another. Because of this, we all have the power to attack this pandemic by:

- Practicing Social Distancing (6 feet apart) - This is the best way to avoid being exposed to, or spreading, this virus.
- Cleaning our hands often with soap or hand sanitizer. Avoid touching our eyes, nose and mouth.
- Avoiding close contact with people who are sick.
- Staying home if we are sick, except to get medical care.
- Cleaning AND disinfecting frequently touched surfaces daily.

Take care and stay safe — we will get through this, together.

Alan P. Farwell, MD
Editor, *Clinical Thyroidology for the Public*



SURGICAL AFFAIRS COMMITTEE — Comment on Thyroid Surgery During the Covid-19 Pandemic

Rosemarie Metzger and Michael Singer, Co-Chairs

The Covid-19 pandemic continues to influence all aspects of healthcare in the United States and abroad. Elective surgeries have been nearly universally postponed to minimize risk of disease transmission and also conserve resources.

As thyroid surgeons we appreciate the impact that this pause may have as nearly all of our patients who require surgical care will be expected to postpone or delay surgery and perhaps wait longer than usual to be seen by a surgeon for initial consultation. We recognize the anxiety this may provoke, particularly in those with a cancer diagnosis or nodules with indeterminate pathology. It is encouraging in these times to remember the generally favorable prognosis associated with well-differentiated thyroid cancer, its typical slow rate of growth, and even the role that non-operative management can play in select patients.

The leaders of national surgical societies including the American Association of Endocrine Surgeons, The American Head and Neck Society, and the Society of Surgical Oncology, have issued statements addressing the optimal approach to performing endocrine surgeries during this time. As the Surgical Affairs Committee of the ATA we would like to briefly summarize the common opinions of these groups as they pertain to the care of our patients with thyroid disease.

Urgent surgery (not to be delayed beyond 4 weeks) should be considered for:

- Thyroid cancers that are imminently life threatening, pose significant morbidity related to local invasion (trachea, recurrent laryngeal nerve), or exhibit aggressive tumor biology (short doubling times, rapid tumor growth or recurrence, or rapidly progressive local-regional disease)
- Life-threatening or severely symptomatic Graves' disease that cannot be medically controlled

- Goiter with symptomatic airway compromise or with risk for impending loss of airway
- Open biopsy for confirmation of clinically suspected anaplastic thyroid cancer or thyroid lymphoma when other diagnostic measures have been inconclusive
- Pregnant patients with thyroid related disorders that are dangerous to the health of the mother or fetus and cannot be controlled medically

These recommendations represent opinions from experts in the field, and it must be understood that all decisions should be made on a case-by-case basis considering individual patient factors and local hospital and regional resource capacity.

Referring physicians and patients should be assured that surgeons are committed to the prompt management of their thyroid diseases. As we move forward and begin to resume elective surgeries, we look to guidance from our national societies, who in concert with our hospitals and local and state authorities, have outlined general principles to be followed to ensure patient and healthcare worker safety and also continued preservation of resources. Individual surgeons will identify and prioritize patients whose surgeries are most time sensitive, such as those with more advanced thyroid cancer and medically labile hyperthyroidism. Patients with more indolent conditions, like compressive goiter, will likely be considered for surgery as operative capacity increases. Importantly, a range of other factors will also impact surgical timing: local community Covid-19 prevalence, regional and hospital supply status, preoperative testing requirements, and, perhaps most crucially, patient perception of risk and willingness and ability to proceed. As always, the safety and personal well being of our patients is paramount and should dictate the ultimate timing of surgery.

THYROID CANCER

Financial and health insurance status affect clinical management and quality of life in patients with thyroid cancer

BACKGROUND

Thyroid cancer affects more than 50,000 Americans each year, with the majority being young. In view of this, most patients diagnosed with thyroid cancer are working-age adults who do not yet qualify for government health insurance benefits. Health insurance plays a significant role for Americans to access and receive care, and whether or not a patient has health insurance may affect cancer treatment and outcomes. Additionally, it has been shown that thyroid cancer patients are at risk for financial difficulty and are at high risk for bankruptcy. Two recent studies addressed the impact of health insurance and financial status on thyroid cancer care. The first, by Ullmann et al, investigated the effect of health insurance status on diagnosis and treatment of patients with papillary thyroid cancer. The second, by Mongelli et al, evaluated the degree of financial difficulty among thyroid cancer survivors and its impact on quality of life.

THE FULL ARTICLE TITLES

Ullmann™ et al 2019 Insurance Status Is Associated with Extent of Treatment for Patients with Papillary Thyroid Carcinoma. *Thyroid* 29(12):1784-1791.

Mongelli MN et al 2020 Financial burden and quality of life among thyroid cancer survivors. *Surgery* 167(3):631-637.

SUMMARY OF THE STUDIES

Ullmann et al used the American College of Surgeons' National Cancer Database to identify 190,298 patients who had papillary thyroid cancer larger than 2 mm treated between 2004 and 2015. These patients were divided into four groups based on insurance stratus: privately insured, Medicare, Medicaid and no insurance. The majority of patients were women (76.1%) and had private insurance (73.4%). Patients with private insurance were the least likely to have thyroid cancer with high-risk features at diagnosis. Approximately twice the proportion of uninsured patients had spread of the

cancer outside of the neck compared with patients who were privately insured. Patients with any insurance were more likely to have small papillary cancers (microcarcinoma, <1 cm) at diagnosis compared to those without insurance, even when adjusting for other factors such as race/ethnicity, sex, age, income and education. Finally, patients with private insurance were also more likely to be treated with a total thyroidectomy, lymph node dissection and radioactive iodine therapy compared to those without insurance.

Mongelli et al conducted a survey administered to thyroid cancer patients aged 18-89 to collect information on financial difficulty and distress and quality of life. A total of 1,743 patients living in the United States completed the survey. The majority were women (88%), were white (95%), and had a diagnosis of papillary thyroid cancer (85%). Overall, patients who reported higher financial difficulty and distress were also more likely to report worse quality of life. At <5 years since thyroid cancer diagnosis, patients had higher financial difficulty and distress as compared with those at ≥5 years since diagnosis. Additionally, employment status was also found to be independently associated with quality of life in thyroid cancer survivors, such that those who reported being unable to get a new job or change jobs because of their thyroid cancer diagnosis had worse fatigue, pain and social functioning.

WHAT ARE THE IMPLICATIONS OF THESE STUDIES?

These studies highlight the significant impact health insurance status and finances have on thyroid cancer care and thyroid cancer survivors' quality of life in the United States. This is particularly important as thyroid cancer mostly affects younger individuals who are still working but don't necessarily qualify for government-subsidized health insurance benefits. The fact that patients with private insurance have less aggressive disease at the time of diagnosis and are also more likely to be treated more

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THYROID CANCER, continued

extensively, emphasizes the need for physicians to be mindful of these disparities when considering thyroid cancer treatment. It is also important for physicians to discuss cost of thyroid cancer care early in order to set realistic expectations. Finally, it is essential that proper

referral and follow-up is undertaken for uninsured and underinsured patients in order to improve care and quality of life.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

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

Papillary microcarcinoma: a papillary thyroid cancer smaller than 1 cm in diameter.

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

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

Lymph node dissection: careful removal of lymphoid tissue in the neck thought to be cancerous.

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.

THYROID CANCER

Patients who tend to prefer maximal medical care receive more intense thyroid cancer follow-up care

BACKGROUND

A cancer diagnosis is frequently associated with major illness and death in our minds and can be very frightening. However, we also know that some cancers, like thyroid cancer, have excellent long-term outcomes. There has been an increase in the number of small, low risk thyroid cancers diagnosed in recent years. Previous studies had shown that frequent follow-up tests after initial successful treatment may not have any benefit. In fact, this approach may cause harm by increasing medical costs and anxiety.

It has been recognized for a long time that individuals have different preferences for their medical care. Some are medical maximizers and others medical minimizers with quite different preferences for more or less medical care. The Medical Maximizer-Minimizer scale was developed to measure these treatment preferences.

The aim of this study was to better understand the role of patient preferences on the intensity of follow-up medical care in patients who became disease-free after initial treatment for thyroid cancer.

THE FULL ARTICLE TITLE

Evron JM 2019 role of patient maximizing-minimizing preferences in thyroid cancer surveillance. J Clin Oncol 37:3042–3049. PMID: 31573822

SUMMARY OF THE STUDY

Researchers identified adult patients who were diagnosed with thyroid cancer between January 2014 and December 2015. They used cancer registries from Georgia and Los Angeles County. Only patients who were effectively treated and considered cancer-free were included. Surveys were mailed between February 2017 and October 2018. The survey was designed to collect information such as ethnicity, other medical conditions, and about cancer related medical care such as frequency of clinic visits and

imaging tests in the previous year. Information about age, initial cancer staging was collected from the national SEER registries. Patient preference for medical care was assessed using the Medical Maximizer-Minimizer Scale. This scale consisted of 10 statements and identified 3 groups – minimizers, moderate maximizers and strong maximizers. Researchers analyzed the relationship between minimizer-maximizer group and the number of reported doctor visits and imaging tests.

Initially 4317 patients were identified and 2183 patients were disease-free and met the inclusion criteria. Of these, 63% of the patients responded to the survey. About 32% of patients were categorized as minimizers, 42% moderate maximizers, and 26% strong maximizers. Maximizers were more likely to live in Los Angeles county, were older, and had more advanced stage of disease. Significantly greater number of patients in the strong maximizer group reported 4 or more doctor visits (39%), 2 or more neck ultrasounds (30%), one or more radioactive iodine scans or more additional imaging studies in the past year. In the minimizer group only 25% reported 4 or more doctor visits and 2 or more neck ultrasounds in one year.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The findings of the study show that patient preference for more medical care was associated with more follow-up doctor visits and imaging tests.

This is important for patients since overtreatment can cause harm in several ways. In the worse-case scenario it can lead to unnecessary tests and treatment side effects. Both patients and physicians need to recognize the different tendencies in medical care preferences and have a careful and detailed discussion to develop an individual care plan.

— Ebru Sulanc, MD

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THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

Cancer registry: Information system designed for the collection, management, and analysis of data on patients with the diagnosis of a cancer

SEER: Surveillance, Epidemiology and End Results program, a nation-wide anonymous cancer registry generated by the National Cancer Institute that contains information on 26% of the United States population.
Website: <http://seer.cancer.gov/>

Thyroid cancer: Papillary and follicular thyroid cancers, which are the most common thyroid cancers. They tend to grow slowly and usually have an excellent prognosis.



AMERICAN THYROID ASSOCIATION
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THYROID AND PREGNANCY

Selenium supplements in pregnant women with thyroid disease

BACKGROUND

Selenium is a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid health. It is needed in small amounts by the body. Because it is needed in small amounts and is plentiful on our food and environment, selenium deficiency is rare in the United States. However, in areas of the world that do report selenium deficiency, there appears to be an association with an increase in positive thyroid peroxidase (TPO) antibodies, which is a marker for autoimmune thyroid disease.

Positive TPO antibodies in pregnancy are associated with increased risk for miscarriage and other poor outcomes such as preterm delivery. Further, there is an association between positive TPO antibodies and thyroid problems after delivery (post-partum thyroiditis). Two previous clinical trials examining the effects of selenium supplementation in pregnant women had conflicting results; one reported that selenium decreased the risk for postpartum thyroid problems and decreased TPO antibodies during pregnancy, while the other reported no effect on TPO antibody levels.

This study examines the effect of selenium supplementation in pregnant women with autoimmune thyroid disease on the levels of TPO antibodies and the development of thyroid problems after delivery.

THE FULL ARTICLE TITLE

Mantovani, G., et al. "Selenium supplementation in the management of thyroid autoimmunity during pregnancy: results of the "SERENA study", a randomized, double-blind, placebo-controlled trial." *Endocrine* 66.3 (2019): 542-550.

SUMMARY OF THE STUDY

This study was done in 10 endocrine and obstetric centers in Italy. Women 18 to 45 years of age, at week 4-8 of

pregnancy and who were TPO-positive were enrolled between 2011 and 2016. A total of 45 women with positive TPO antibodies were divided into 2 groups that were the same in terms of age, BMI, week of pregnancy, TPO antibody levels or baseline selenium level. Of these, 32 women (71%) were taking levothyroxine prior to the study and another three (7%) were started on levothyroxine at the start of the study as their TSH was >2.7. The women were randomly assigned to take an oral selenium supplement (L-selenomethionine 83 µg/day) or a non-selenium containing pill (placebo). Treatment was continued until 6 months after delivery.

TPO antibody levels decreased over the course of the pregnancy in both the placebo and the selenium group. At the postpartum visit, TPO antibody levels continued to decrease in the selenium group but had increased significantly in the placebo group. Thyroid-function tests did not differ between the groups at baseline or over the course of the study. Thyroid appearance and volume determined using ultrasound did not differ between groups at baseline or during the follow-up period. Similarly, there were no differences between the groups in health-related quality of life at baseline or during follow-up.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that selenium supplementation during and after pregnancy prevented postpartum increases in TPO autoantibody levels but was not associated with changes in thyroid function, thyroid volume, thyroid appearance, or health-related quality of life. This supports the recommendation from the American Thyroid Association against selenium supplementation during pregnancy.

—Vibhavasu Sharma, MD, FACE

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THYROID AND PREGNANCY, continued

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

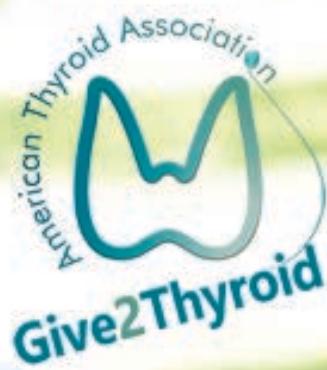
Selenium: a mineral found naturally in various foods that is important for making thyroid hormones and for normal thyroid function. It is needed in small amounts by the body.

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

TPO antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

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

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GRAVES' DISEASE

“Block-and-Replace” treatment in children with Graves’ disease

BACKGROUND

Grave's disease is a condition in which the thyroid gland is overactive and produces too much thyroid hormone (hyperthyroidism). It is caused by antibodies which attack the thyroid and turn it on. Graves' disease can be treated by antithyroid medication such as methimazole. Methimazole works by blocking the pathway that makes thyroid hormone within the thyroid gland. Unlike many other medications, methimazole is usually started at a higher dose to get the thyroid hormone levels back to normal quickly. The dose then is tapered down to a lower dose to maintain thyroid hormone levels in the normal range. Sometimes, the methimazole dose overshoots and decreases the thyroid hormone levels into the low range, then the dose is decreased and the levels return to the normal range.

Another, less common, way to dose methimazole is known as the block-and-replace method. The block-and-replace method continues the methimazole at the higher dose to completely block the production of thyroid hormone. When the thyroid hormone levels fall into the low range, levothyroxine is added to bring the thyroid hormone levels to back to normal. At one point, this method was thought to increase the remission rate of Graves' disease. Unfortunately, that has not been found to be true. However, this method can be effective in patients that are poorly controlled on methimazole alone.

There is limited data on the use of the block-and-replace method in children. The current study examined a group of children with poorly controlled Grave's disease who were managed by the block-and-replace method with methimazole in combination with levothyroxine.

THE FULL ARTICLE TITLE

Vigone MC et al 2019 “Block-and-replace” treatment in Graves’ disease: experience in a cohort of pediatric patients. J Endocrinol Invest. Epub 2019 Nov 12. PMID: 31713721.

SUMMARY OF THE STUDY

This was a study of children with Graves' disease over a 25-year period at a single center in Italy. All of the children were initially started on methimazole alone, but had poor control of their Graves' disease with wide changes in thyroid labs. These children were switched to the block-and-replace method and were managed by both methimazole and levothyroxine. Thyroid function was determined by fasting blood work at various times. The study included 28 pediatric patients diagnosed at an average age of 9.2 years. The children were initially treated with methimazole for an average duration of 1.5 years before changing to the block-and-replace method. At the time of analysis, patients had been on the block-and-replace method for an average of 2.85 years. The average methimazole dose was 0.3 mg/kg/day and the average levothyroxine dose was 1.12 µg/kg/day.

Only one patient (4%) achieved remission while treated with the block-and-replace method. Rates of normal thyroid hormone levels were significantly higher on the block-and-replace method than methimazole alone. A total of 15 patients (60%) underwent more definitive treatment for their Graves' disease with surgery (11 patients) or radioactive iodine therapy (4 patients). The block-and-replace method helped delay surgery by 2.9 years and radioactive iodine therapy by 4.9 years.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In cases in which it is difficult to manage Graves' disease in children, the block-and-replace method (a moderate dose of methimazole in combination of levothyroxine) may provide improved control of thyroid levels compared to methimazole treatment alone. The block-and-replace method may allow for definitive treatment (surgery or radioactive iodine therapy) of Graves' disease to be delayed until an older age, but does not appear to increase remission rates.

— Priya Mahajan, MD

Clinical Thyroidology® for the Public

GRAVES' DISEASE, continued

ATA THYROID BROCHURE LINKS

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

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

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

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

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.

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.

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

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

Euthyroid: a condition where the thyroid gland is working normally and producing normal levels of thyroid hormone.

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

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).

THYROIDITIS

Thyroiditis while receiving immune checkpoint inhibitor therapy for non-thyroid cancers is associated with improved overall survival

BACKGROUND

Cancers are capable of producing molecules to block generation and function of immune cells. On such molecule is programmed cell death ligand 1 (PD-L1) that binds to and inhibits immune cells. Immune checkpoint inhibitors are a new class of cancer chemotherapy agents that target and block molecules such as PD-L1, thus, allowing the body's own immune system to attack and destroy cancer cells. As expected, along with positive effects, these chemotherapy agents may also induce some unfavorable changes in the immune system processes. Since autoimmune thyroid disease is a common cause of thyroid problems, it is not surprising that one of the side effects of immune checkpoint inhibitors is both hyper- and hypothyroidism, which may happen up to 29% of cases. Interestingly, some previous publications reported a superior response to the cancer treatment when patients experience immune system related side effects.

This study examines the frequency, course and survival effects of newly diagnosed autoimmune thyroid disease after treatment with immune checkpoint inhibitors.

THE FULL ARTICLE TITLE

Kotwal A et al 2020 PD-L1 inhibitor-induced thyroiditis is associated with better overall survival in cancer patients. *Thyroid*. Epub Jan 9. PMID: 31813343.

SUMMARY OF THE STUDY

This study was conducted at the Mayo Clinic in Rochester, Minnesota. The medical records of adult cancer patients treated with one of the two PD-L1 inhibitors drugs (either atezolizumab or avelumab) were reviewed. Subjects who developed thyroid disease after starting the treatment were identified.

Of 91 patients who were treated with a PD-L1 inhibitor, the majority (86, ~95%) had received atezolizumab. The average age of the patients was 67.9 years, 47% were male, and nearly 2/3s of patients were being treated for primary lung cancer. Thyroid problems occurred in 23 subjects (25%); 61% developed hypothyroidism, 22% developed hyperthyroidism and 17% developed worsening of already existing hypothyroidism. Most patients developed the thyroid problem in about 6 weeks after starting the therapy.

On average, patients were followed for 6 months after the onset of the thyroid disease. During this time, 3 patients had spontaneous recovery.

After looking at mortality rate, the researchers found that a lower number of patients who developed thyroid disease died during the study period (43.5% of patients with a thyroid dysfunction versus 79.4% patients who did not develop thyroid disease).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In summary, this study showed that 25% of patients who had received a PD-L1 inhibitor drug also developed autoimmune thyroid disease. Interestingly the survival rate of patients who developed this type of side effect was better compared to the rest.

As more immune checkpoint inhibitors enter the market for treatment of cancer, this and similar studies will be instrumental to improve our knowledge about them.

— Shirin Haddady, MD MPH



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THYROIDITIS, continued

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): <https://www.thyroid.org/hypothyroidism/>

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

ABBREVIATIONS & DEFINITIONS

Autoimmune thyroid disease: a group of disorders that are caused by antibodies that get confused and attack the thyroid. These antibodies can either turn on the thyroid (Graves' disease, hyperthyroidism) or turn it off (Hashimoto's thyroiditis, hypothyroidism).

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

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.

Immune checkpoint inhibitors: a new class of cancer chemotherapy agents that target and block molecules produced by cancer cells to block generation and function of immune cells. This allows the body's own immune system to attack and destroy cancer cells.

Watch how your donations help find answers to thyroid cancer



The American Thyroid Association (ATA) – Searching for Answers to Thyroid Cancer
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11

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THYROID CANCER

Controversies, consensus, and collaboration in the use of radioactive iodine therapy for the treatment of thyroid cancer

BACKGROUND

The 2015 American Thyroid Association management guidelines for thyroid cancer encourage more conservative use of radioactive iodine therapy as compared with prior guidelines. Indeed, radioactive iodine therapy is no longer recommended for most low risk thyroid cancers. This was based in part on a greater number of studies about thyroid cancer outcomes that showed little or no improvement of radioactive iodine therapy on the otherwise excellent prognosis of low risk thyroid cancers. These recommendations have been controversial and 2 prominent nuclear medicine organizations, the European Association of Nuclear Medicine (EANM) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI), declined to endorse the guidelines.

In order to promote better understanding of differences in perspective, representatives from the American Thyroid Association (ATA) and the European Thyroid Association (ETA) met with representatives from the EANM and the SNMMI and to reach a more collaborative and consistent, evidence-based set of recommendations/guiding principles. This paper summarizes this groups efforts in reaching a consensus.

THE FULL ARTICLE TITLE

Tuttle RM et al 2019 Controversies, consensus, and collaboration in the use of ^{131}I therapy in differentiated thyroid cancer: a joint statement from the American Thyroid Association, the European Association of Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging, and the European Thyroid Association. *Thyroid* 29:461–470. PMID: 30900516.

SUMMARY OF THE STUDY

A 2-day meeting was held in Martinique in January 2018. A panel of 18 senior leaders and experts from 8 countries and 4 international organizations, including

the American Thyroid Association, convened to consider, debate, and exchange ideas regarding the use of radioactive iodine in the management of thyroid cancer. After much discussion and a review of 60 publications, in addition to expert opinion, the conference participants agreed on a set of nine principles, which are paraphrased as follows:

1. The best recommendations on thyroid cancer management requires cooperation between all of those involved in managing thyroid cancer patients, including endocrinologists, surgeons, nuclear medicine specialists and oncologists as well as the patients themselves.
2. Three goals of radioactive iodine therapy were defined as (a) destruction of remaining normal thyroid tissue, (b) therapy for suspected microscopic cancer or (c) treatment of known remaining cancer.
3. Proper patient selection for radioactive iodine therapy requires assessment of both pre-operative and postoperative thyroid cancer status.
4. Evaluation of postoperative thyroid cancer status should be standardized in terms of blood thyroglobulin levels and evidence of persistent cancer on imaging studies.
5. Proper patient selection for radioactive iodine therapy also requires evaluation of multiple factors, including patient preference, potential side effects, and availability and quality of medical resources.
6. The best administered dose of radioactive iodine for treating microscopic cancer cannot be determined from the available studies.

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THYROID CANCER, continued

7. Characteristics suggesting that patients may not respond to radioactive iodine therapy should be used to help determine the likelihood (or lack thereof) to respond but not to exclude them from consideration for radioactive iodine therapy.
8. The criteria for not responding to radioactive iodine therapy will continue to evolve, especially with progress in evidence-based studies, better standardized imaging, and other therapies.
9. Prospective studies are needed to address knowledge and evidence gaps with regard to radioactive iodine therapy.

ATA THYROID BROCHURE LINKS

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

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

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Defining the best use of radioactive iodine therapy in patients with thyroid cancer remains controversial, is subject to interpretation of evidence, and is influenced by many patient and health care delivery variables. Working together in the spirit of collaboration will help refine the use of radioactive iodine therapy within the patient-centered care of thyroid cancer.

— Alan P. Farwell, MD, FACE

ABBREVIATIONS & DEFINITIONS

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

Papillary thyroid cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Follicular thyroid cancer: the second most common type of thyroid cancer.

Evidence-based: any concept or recommendation that is derived from or informed by objective evidence, usually from the results of clinical trials

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ATA Alliance for Thyroid Patient Education

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



MCT8 - AHDS
Foundation



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

THYROID CANCER
ALLIANCE

Light of Life Foundation
checkyourneck.com



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

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

Bite Me Cancer

www.bitemecancer.org

info@bitemecancer.org

Thyroid Cancer Alliance

www.thyroidcanceralliance.org

www.thyroidcancerpatientinfo.org

Rotterdam, The Netherlands

Graves' Disease and Thyroid Foundation

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

Thyroid Cancer Canada

www.thyroidcancercanada.org

416-487-8267

info@thyroidcancercanada.org

Light of Life Foundation

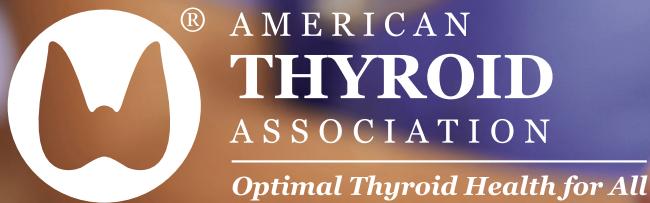
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Thyroid Federation International

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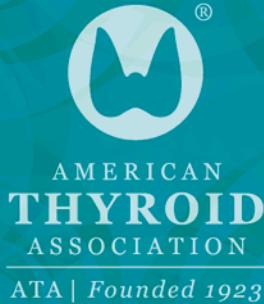
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We will use your email address to send you *Friends of the ATA e-news* and occasional email updates. We won't share your email address with anyone, and you can unsubscribe at any time.

www.thyroid.org



JOIN US



“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

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 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.