## Volume 16 | Issue 5 | May 2023

# Clinical Thyroidology® for the Public



AMERICAN **THYROID** ASSOCIATION **Optimal Thyroid Health for All** 

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EDITOR'S COMMENTS .....

## A healthy lifestyle may decrease genetic predisposition to thyroid cancer

Among the well-established thyroid cancer risk factors include a family history, exposure to ionizing radiation, and obesity. Lifestyle factors, such as physical activity, smoking, alcohol and diet have been proposed to affect thyroid cancer incidence. This study was done to explore the association between lifestyle, genetic factors and the risk for thyroid cancer, and also to address the question of whether lifestyle modification could reduce the risk for developing thyroid cancer.

Feng X et al 2022 Association Between Genetic Risk, Adherence to Healthy Lifestyle Behavior, and Thyroid Cancer Risk. JAMA Netw Open 5(12):e2246311.

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# Does radioactive iodine treatment for thyroid cancer increase the risk of developing other cancers?

Radioactive iodine therapy is an important treatment option for patients with thyroid cancer after undergoing surgery. One concern about radioactive iodine therapy has always been whether this treatment might be increasing patients' risk of developing other cancers. This study further investigated additional cancers involving other body organs after receiving radioactive iodine.

Kim KJ et al 2023 Linear association between radioactive iodine dose and second primary malignancy risk in thyroid cancer. J Natl Cancer Inst. Epub 2023 Feb 23. PMID: 36821433.

#### THYROID CANCER.....

## Predictors of outcomes in patients with medullary thyroid cancer

Studies show that the long-term prognosis of MTC depends on the calcitonin doubling time (CDT). Further, low-grade cancers are usually less aggressive and have a better prognosis while high-grade cancers are more aggressive and have a worse prognosis. This study aimed to investigate the differences in CDT between high and low-grade MTC.

Nigam A et al 2022. Tumor grade predicts for calcitonin doubling times and disease-specific outcomes after resection of medullary thyroid carcinoma. Thyroid 32:1193–1200. PMID: 35950622.

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Can serum calcitonin levels be used determine postoperative follow-up in medullary thyroid cancer?

Surgery is the mainstay of treatment for MTC. Follow-up of MTC after surgery uses imaging and measurement of calcitonin levels to determine if the disease is cured or if there are still cancer cells present. In this study, the authors measured calcitonin levels after thyroid surgery to assess cure.

Duval MAS et al 2023 An undetectable postoperative calcitonin level is associated with long-term disease-free survival in medullary thyroid carcinoma: Results of a retrospective cohort study. Thyroid 33:82–90. PMID: 36222615.

#### THYROID CANCER.....II

Treatment aggressiveness for thyroid cancers varies widely and is influenced by physician's attitude and local practice environment

Overall, thyroid cancer usually carries an excellent prognosis and treatment options have changed to less aggressive treatment strategies. However, the initial treatment approach chosen remains very variable due to several factors. This study was done determine the physicians' perceived risk with respect to the thyroid cancer progressing or recurring and their degree of aggressiveness exercised in choosing treatment options.

Schumm MA et al 2022 Perception of risk and treatment decisions in the management of differentiated thyroid cancer. J Surg Oncol 126:247–256. PMID: 35316538.

### THYROID EYE DISEASE......14

**Variation in treatment of thyroid eye disease** Thyroid eye disease (TED) is the result of inflammation of the eyes, the eye muscles and the surrounding tissues. Even mild symptoms can affect patients' well-being while severe cases can impact vision. This study was done to survey Endocrinologists from the US and Europe to compare diagnosis and treatment of TED.

Brito JP et al 2022 A survey on the management of thyroid eye disease among American and European Thyroid Association members. Thyroid 32:1535–1546. PMID: 35946071.

#### **ATA® ALLIANCE FOR THYROID**

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### www.thyroid.org

#### <u>Edi</u>tor

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## **Editor's Comments**

Welcome to another issue of *Clinical Thyroidology* <sup>®</sup> 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<sup>®</sup>, 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<sup>®</sup> (ATA<sup>®</sup>) 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<sup>®</sup> mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: <u>www.thyroid.org/donate</u> and all donations are put to good work. The ATA<sup>®</sup> is a 501(c)3 nonprofit organization and your gift is tax deductible.

### May is International Thyroid Awareness Month.

### In this issue, the studies ask the following questions:

- Can a healthy lifestyle decrease the genetic predisposition to thyroid cancer?
- Does radioactive iodine treatment for thyroid cancer increase the risk of developing other cancers?
- What are predictors of outcomes in patients with medullary thyroid cancer?
- Can serum calcitonin levels be used determine postoperative follow-up in medullary thyroid cancer?
- What influences treatment aggressiveness for thyroid cancers?
- Are there differences in the treatment of thyroid eye disease worldwide?

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

### **THYROID CANCER**

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# A healthy lifestyle may decrease genetic predisposition to thyroid cancer

### BACKGROUND

The incidence of thyroid cancer has increased approximately by 10% per year over the past 30 years, and according to Global Cancer Statistics, thyroid cancer ranks 9th among 36 cancers globally. Being diagnosed with thyroid cancer takes not only an emotional toll, but also a significant financial toll not just for individuals but for the whole US health care system. In fact, a thyroid cancer diagnosis and its long term management are the reasons for one of the highest bankruptcy rates among patients with cancer. It is likely that a combination of genetic and environmental factors increase the likelihood for a particular individual to develop thyroid cancer. Among the well-established thyroid cancer risk factors include a family history, exposure to ionizing radiation, and in recent data, an association with obesity. Lifestyle factors, such as physical activity, smoking, alcohol and diet have been proposed to affect thyroid cancer incidence, but published studies have shown mixed results.

This study was done to explore the association between lifestyle, genetic factors and the risk for thyroid cancer, and also to address the question of whether lifestyle modification could reduce the risk for developing thyroid cancer.

### THE FULL ARTICLE TITLE

Feng X et al 2022 Association Between Genetic Risk, Adherence to Healthy Lifestyle Behavior, and Thyroid Cancer Risk. JAMA Netw Open 5(12):e2246311.

### **SUMMARY OF THE STUDY**

This study used the UK Biobank data and included 264,956 participants aged 40-69 years who were followed

for approximately 11 years and for whom genetic data and clinical information were available. Applying statistical methods, a genetic risk score was generated. A lifestyle score was generated based on self-reported data for weight, diet, physical activity, smoking and alcohol consumption and categorized as unfavorable, intermediate or favorable. The associations between the genetic score, lifestyle, and thyroid cancer incidence as well as the interactions between them were tested.

During the follow up of 11.1 years, 423 cases of thyroid cancer were reported. The incidence rate was almost 3 fold higher in women than in men. The higher genetic score was associated with an increased risk for thyroid cancer. Independently, an unfavorable lifestyle was also associated with a higher risk of thyroid cancer. Individuals who had both the high genetic score and the unfavorable lifestyle score had the highest risk for thyroid cancer. Interestingly, among the patients who had the highest genetic score, a favorable lifestyle reduced thyroid cancer risk.

# WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that genetic and lifestyle factors are independently associated with thyroid cancer incidence, and that a healthy lifestyle can help reduce risk for developing thyroid cancer in patients who have a high genetic predisposition. This study is important for patients because it provides evidence that even when there is a strong genetic predisposition, they can help reduce their personal risk to develop thyroid cancer by engaging in a healthy lifestyle.

— Jesse Block-Galaraza, MD

### **ATA RESOURCES**

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

### THYROID CANCER, continued



#### **ABBREVIATIONS & DEFINITIONS**

**Ionizing radiation:** radiation that can damage cells, causing cell death or mutation. It can originate from radioactive materials, x-ray tubes or specialized machines. It is invisible and not directly detectable by human senses.

Genetic: relating to genes or heredity

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



Clinical Thyroidology® for the Public (from recent articles in Clinical Thyroidology)

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### **THYROID CANCER**

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Does radioactive iodine treatment for thyroid cancer increase the risk of developing other cancers?

### BACKGROUND

Radioactive iodine therapy is an important treatment option for patients with thyroid cancer after undergoing surgery. For many years, almost all patients with thyroid cancer received radioactive iodine therapy, often in high doses (100-150 mCi). However, more recently, the use of radioactive iodine therapy has markedly decreased as it was apparent that patients with low risk cancers did not gain much benefit in this treatment. Currently, the American Thyroid Association guidelines are recommending that radioactive iodine therapy be reserved for patients with cancers that have intermediate or high-risk features. Further, the doses used also have dropped to 50-75 mCi for intermediate risk cancers and dose of 100 mCi and higher reserved for the most aggressive/highest risk cancers.

One concern about radioactive iodine therapy has always been whether this treatment might be increasing patients' risk of developing other cancers. Previous large studies that included national populations have shown that radioactive iodine does slightly increase the risk of developing two blood cancers called acute myeloid leukemia and chronic myeloid leukemia. A "leukemia" is the uncontrolled growth of white blood cells that normally help the body combat infections.

This study further investigated additional cancers involving other body organs after receiving radioactive iodine.

### THE FULL ARTICLE TITLE

Kim KJ et al 2023 Linear association between radioactive iodine dose and second primary malignancy risk in thyroid cancer. J Natl Cancer Inst. Epub 2023 Feb 23. PMID: 36821433.

### SUMMARY OF THE STUDY

This study looked back at Korean patients diagnosed with thyroid cancers from 2014 to 2017 at least a year

after their diagnosis. All of the study participants had their whole thyroid glands surgically removed, did not receive any prior radiation therapy, and did not carry any other cancer diagnoses. Approximately 217, 000 patients from the Korean National Health Insurance Service–National Health Information Database (NHIS-NHID) met satisfactory criteria to be involved in the study. These patients were divided into groups that received radioactive iodine and those that did not receive radioactive iodine, and the rates of a second cancer development were analyzed.

In the group that received an average of 100 mCi of radioactive iodine, for every 1,000 years of human life, 7.3 people developed a second cancer. In the group that did not receive any radioactive iodine, for every 1,000 years of human life, 6.5 people developed a second cancer. Thus, the excess cancer caused by the high dose radioactive iodine therapy affected 0.8 people for every 1000 years of human life. In addition, patients developed the second cancer in about 52 months after the radioactive iodine therapy, a shorter time than in the group that did not receive radioactive iodine, which was 59 months. However, the difference could only be considered significant when the radioactive iodine dose in the treated group was greater than 100 mCi.

## WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that patients who receive more than 100 mCi of radioactive iodine following their surgery for thyroid cancer might be at a slightly increased risk of developing a second cancer. The risk of developing one of these second cancers increased with higher doses of radioactive iodine. These data support the use of lower doses of radioactive iodine in intermediate risk cancers. Further, these data show that the current ATA guidelines advocating no radioactive iodine therapy for patients with low risk cancers and lower dose radioactive



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### THYROID CANCER, continued



iodine therapy for intermediate risk cancers will decrease the risk of developing a second cancer related to the radioactive iodine. Finally, these data further support the recommendation that high dose radioactive iodine therapy should be reserved for the thyroid cancers that are most aggressive and at the highest risk of recurrence. — Pinar Smith, MD

### **ATA RESOURCES**

Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u>

### **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-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-I23 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*).

mCi: millicurie, the units used for I-131.

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).

### **THYROID CANCER**

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# Predictors of outcomes in patients with medullary thyroid cancer

### BACKGROUND

Medullary thyroid cancer (MTC) is a relatively rare type of thyroid cancer. While it is the 3rd most common type of thyroid cancer, it only comprises ~3% of all cases of thyroid cancer. MTC arises from the parafollicular cells of the thyroid, also known as C cells, which are responsible for producing the hormone calcitonin. The standard treatment for this cancer is removing the thyroid completely (total thyroidectomy) as well as the lymph nodes in the lateral neck (bilateral neck dissection). This treatment is considered the most effective way to cure the disease when it has not spread.

After surgery, physicians monitor for MTC recurrence by measuring serum calcitonin levels and performing imaging, most often neck ultrasound. If the cancer has been completely removed, calcitonin levels should be very low or undetectable. Undetectable calcitonin levels with negative neck imaging is evidence of a cure of MTC. For patients who are not cured, calcitonin levels steadily increase over time. Indeed, studies show that the long-term prognosis of MTC, the prediction of the course of the disease and the effectiveness of treatment depends on the rate at which the calcitonin level doubles (called the calcitonin doubling time (CDT). When the CDT is longer than two (2) years, overall survival, recurrence-free survival, and distant metastasis-free survival are significantly better.

Determining the grade of a cancer is also essential for predicting the prognosis. Cancer's grade reflects how abnormal the cancer cells appear when examined under a microscope compared to normal cells. Cancers with cells closely resembling normal healthy cells are categorized as low-grade, while those with more abnormal cells are classified as high-grade. Low-grade cancers are usually less aggressive and have a better prognosis. The *International Medullary Thyroid Cancer System* is a recent development that measures the grade of MTC and utilizes three different markers of cell division. High levels of these markers indicate a high-grade cancer.

This study aimed to investigate the differences in CDT between high and low-grade MTC. The authors hypothesized that high-grade cancers would have a faster CDT, leading to a worse clinical outcomes.

### THE FULL ARTICLE TITLE

Nigam A et al 2022. Tumor grade predicts for calcitonin doubling times and disease-specific outcomes after resection of medullary thyroid carcinoma. Thyroid 32:1193–1200. PMID: 35950622.

### SUMMARY OF THE STUDY

In this study, the authors investigated 117 patients who had undergone surgery for MTC between 1986 and 2017. Two pathologists evaluated the cancers and classified them as high or low grade based on the *International Medullary Thyroid Cancer Scoring System*. The patients' serum calcitonin levels were measured before and after surgery, at 6 and 12 months post-surgery, and every 6 months after that.

The analysis revealed that cancer grade and CDT were powerful indicators of clinical outcomes. By the end of the study, 70.5% of patients with low-grade MTC remained cancer-free, whereas only 9.1% of high-grade MTC patients remained cancer-free. Additionally, 2.1% of low-grade MTC patients died, compared to 45.4% of high-grade MTC patients. Among the 95 patients with low-grade MTC, 6 (6.3%) had a CDT of 1-2 years, 23 (24%) had a CDT of 2 or more years, and 65 (68.4%) did not experience a doubling of calcitonin levels. But of the 22 patients with high-grade MTC, 16 (72.7%) had a CDT of 1 year or less, 4 (18.2%) had a CDT of 1-2 years, and only 1 patient did not experience a doubling of calcitonin levels. Thus, high-grade MTC patients had significantly faster CDT than low-grade MTC patients. Furthermore, patients with high-grade MTC and CDT

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### THYROID CANCER, continued

of less than 2 years had the poorest overall survival and recurrence-free survival.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Cancer grade and CDT can help predict prognosis in MTC. Most patients with high-grade MTC have a CDT

of less than 2 years. This is why it is essential to frequently monitor calcitonin levels in MTC survivors since a rapid doubling of levels may predict cancer recurrence.

— Phillip Segal, MD

### **ATA RESOURCES**

Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u> Medullary Thyroid Cancer: <u>https://www.thyroid.org/medullary-thyroid-cancer/</u>

#### **ABBREVIATIONS & DEFINITIONS**

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

**Bilateral Neck Dissection:** Surgical removal of lymph node on both sides of the neck. This is done for cancers that are very likely to spread or have already spread to one or both sides of the neck.

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

**Calcitonin doubling time (CDT):** the rate at which the calcitonin level doubles, usually reported in years. The CDT is related to prognosis in medullary thyroid cancer.

**Recurrence-free survival:** the period of time during which a person with cancer remains free of any signs or symptoms of cancer recurrence in the area surrounding the original site of the tumor and the nearby lymph nodes.

Distant metastasis-free survival: the period of time during which a person with cancer remains free of any signs or symptoms of cancer recurrence in organs or tissues that are located far away from the original site of the cancer.

### **THYROID CANCER**



# Can serum calcitonin levels be used determine postoperative follow-up in medullary thyroid cancer?

### BACKGROUND

Medullary thyroid cancer (MTC) is a relatively rare type of thyroid cancer. While it is the 3rd most common type of thyroid cancer, it only comprises ~3% of all cases of thyroid cancer.

However, MTC is generally more aggressive than the most common type of thyroid cancer (papillary) and it is often found after it had already spread outside the thyroid. About 25% of all MTCs are genetic (ie run in families). A specific gene (RET) mutation can be detected in patients with the genetic forms of MTC and can be used to identify patients in a family that have MTC before it spreads outside the thyroid. Unlike the most common types of thyroid cancer (papillary and follicular thyroid cancer) which come from the thyroid follicular cells (which produce the thyroid. The C-cells produce the hormone calcitonin, which is also used as a marker of MTC.

Surgery is the mainstay of treatment for MTC. In early stage MTC, in which the cancer has not spread outside the thyroid, surgery can cure MTC. Follow-up of MTC after surgery uses imaging (ultrasound) and measurement of calcitonin levels to determine if the disease is cured or if there are still cancer cells present. In this study, the authors measured calcitonin levels after thyroid surgery to assess cure.

### THE FULL ARTICLE

Duval MAS et al 2023 An undetectable postoperative calcitonin level is associated with long-term disease-free survival in medullary thyroid carcinoma: Results of a retrospective cohort study. Thyroid 33:82–90. PMID: 36222615.

### **SUMMARY OF THE STUDY**

The authors studied 334 patients with MTC who underwent total thyroidectomy in two hospitals in Brazil, between 1997 and 2019. Calcitonin was initially measured 3-6 months after thyroid surgery and then every 6-12 months for an average of 7 years. Overall, 60% of patients were women and 40% were familial cancers. Half of the patients had spread of the cancer to the lymph nodes at the time of the surgery. About 40% of the patients had an undetectable calcitonin level after surgery. This group of patients, as compared to those who had detectable levels of calcitonin, were younger and their cancers were more likely to have been found by screening (due to family history). They had smaller cancers and less frequent spread to the lymph nodes. At their last follow-up, 90% of patients with undetectable calcitonin levels after surgery remained without evidence of MTC and 10% had stable levels without evidence of spread. There were no deaths in this group. On the other hand, in the group of patients who had detectable calcitonin levels after surgery, only 9% were free of cancer at their last visit, and 1/3 of the patients had died.

# WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirms that surgery is the best treatment to cure MTC. Finding an undetectable calcitonin level after surgery predicts cure. Many of the patients in the group with undetectable calcitonin level were those found by RET gene screening. This emphasizes the importance of genetic screening in patients at risk for the familial forms of MTC and recommending early thyroidectomy in those with the genetic mutation.

— Susana Ebner MD

### ATA RESOURCES

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

### THYROID CANCER, continued



### **ABBREVIATIONS & DEFINITIONS**

**Medullary thyroid cancer:** a relatively rare type of thyroid cancer that often runs in families. Medullary cancer arises from the C-cells in the thyroid. The familial form is caused by the RET gene mutation.

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

Mutation: A permanent change in one of the genes.

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

**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*.

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THYROID

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### **THYROID CANCER**

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Treatment aggressiveness for thyroid cancers varies widely and is influenced by physician's attitude and local practice environment

### BACKGROUND

The most common types of thyroid cancer are papillary and follicular cancer, which are also known as differentiated thyroid cancer (DTC). Overall, DTC usually carries an excellent prognosis. Indeed, when talking about low, intermediate and high risk thyroid cancer, the risk is the risk of cancer recurrence, not necessarily death due to cancer. Over the last decade, the treatment options for DTC have changed to less aggressive treatment strategies, especially for low to intermediate risk DTC. The American Thyroid Association guidelines recommend determining risk before deciding on the management of DTC. Management options include active surveillance (no surgery, watching a small cancer with regular ultrasound imaging), partial removal of the thyroid (lobectomy), complete removal of the thyroid (total thyroidectomy), and radioactive iodine therapy after total thyroidectomy.

In general, active surveillance and lobectomy are options for very low risk cancers, lobectomy and total thyroidectomy are options for low risk and intermediate risk cancers while radioactive iodine therapy after total thyroidectomy are options for intermediate and high risk cancers.

However, the initial treatment approach chosen remains very variable due to several factors, such as the physician's evaluation of risk of recurrence, benefits versus complications of treatment options as well as patient characteristics and patient preference. This study was done determine the physicians' perceived risk with respect to the DTC progressing or recurring and their degree of aggressiveness exercised in choosing treatment options. The aim was to find any association between the physicians' perception and management.

### THE FULL ARTICLE TITLE

Schumm MA et al 2022 Perception of risk and treatment decisions in the management of differentiated thyroid cancer. J Surg Oncol 126:247–256. PMID: 35316538.

#### **SUMMARY OF THE STUDY**

The study was conducted in 2020 using an online survey which was distributed amongst members of the ATA that comprised endocrinologists, endocrine surgeons, medical oncologists, and nuclear medicine physicians. The participants were presented with four clinical scenarios that included commonly encountered cases of low to intermediate-risk DTC. On a sliding scale score of 1 to 100, the respondent physicians estimated the perceived risk of complications after surgery, cancer recurrence, and cancer progression based on their judgment. The physicians were also asked to pick their choice of treatment for each scenario. Their treatment responses were either categorized into 'more aggressive' or 'less aggressive.' The investigators then assessed the perceived risk reduction in the recurrence of cancer between the more and less aggressive treatment options. Analysis was done to predict a physician's decision between the more and less aggressive approach while accounting for benefits/risk assessment.

The overall response rate to the survey was 13%. The respondents were predominantly male and 52% of participating physicians were endocrinologists. Most described their approach to DTC as 'moderate' with close with local clinical practice patterns. Interestingly, no single treatment option was recommended by >70% of respondents on any case example. The clinical scenario with very small papillary thyroid cancer was noted to have the most varied responses for treatment. The estimated risk for disease progression/recurrence when choosing 'less aggressive' versus 'more aggressive' approach showed a wide range across the clinical cases. No association was found between estimated operative risk and the planned treatment option. Most of the variation noted with respect to the degree of aggressiveness when managing DTC could not be correlated to the perceived risk of recurrence, with the likelihood of cancer recurrence accounting for only 10.3% of the observed variation in treatment aggressiveness.

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# Clinical Thyroidology<sup>®</sup> for the Public

## THYROID CANCER, continued

Physicians that self-identified to have less risk tolerance, that worked in a local practice environment and had a longer number of years in practice were more likely to recommend a more aggressive treatment approach.

# WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study helps understand that nonclinical factors influence the extent of aggressiveness employed when treating low to intermediate risk DTC. Self-identification by physicians as 'aggressive,' 'moderate,' and 'conservative' with respect to the local clinical practice influences the ultimate treatment approach to thyroid cancer. Physicians in academic settings were likely to be less aggressive while those with more years in practice were likely more aggressive in their approach. With frequent disagreement observed amongst thyroid specialists on the best course of treatment for thyroid cancer, this study serves as an insightful tool for the patients to understand where the differences in a physician's approach to their disease comes from. Also, this shows that, in a real-world scenario, consultations with different providers may give them a varied and broad range with respect to the risk of their cancer recurrence and progression. This would empower patients and help them understand that their input in shared decision-making is important and contributes to drafting a more effective management strategy.

— Sargun Singh, MD and Maria Brito, MD

### ATA RESOURCES

Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u> Thyroid Nodules: <u>https://www.thyroid.org/thyroid-nodules/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u>

### **ABBREVIATIONS & DEFINITIONS**

**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.

Lobectomy: surgery to remove one lobe of the thyroid.

**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*.

**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-I3I is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-I23 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, continued



### **ABBREVIATIONS & DEFINITIONS, continued**

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).

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

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

**Differentiated Thyroid Cancer:** includes both papillary and follicular thyroid cancer.

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

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Clinical Thyroidology<sup>®</sup> for the Public

### THYROID EYE DISEASE

## Variation in treatment of thyroid eye disease

### BACKGROUND

Thyroid eye disease (TED) is the result of inflammation of the eyes, the eye muscles and the surrounding tissues. It is called TED because it is most often associated with autoimmune thyroid disease, specifically Graves' disease. However, it can also be seen in patients with Hashimoto's thyroiditis and in patients with normal thyroid function but positive thyroid antibodies. While mild changes related to TED can be seen using sensitive imaging equipment in many patients with Graves' disease, clinical symptoms are only seen in ~5% of patients. Symptoms of TED can range from dry eyes and red eyes to significant bulging of the eyes and double vision and can be very disfiguring. Even mild symptoms can affect patients' well-being while severe cases can impact vision. Treatment varies according to both severity and treatments available and include steroids, immune suppressing drugs, selenium, radiation and surgery. A major advance in treatment is the new drug Tempezza (teprotumumab) which often results in marked improvement to resolution of symptoms. This study was done to survey Endocrinologists from the US and Europe to compare diagnosis and treatment of TED.

### THE FULL ARTICLE TITLE

Brito JP et al 2022 A survey on the management of thyroid eye disease among American and European Thyroid Association members. Thyroid 32:1535–1546. PMID: 35946071.

### SUMMARY OF THE STUDY

An electronic questionnaire was sent to members of the American and European Thyroid Associations in June, 2021. There were 227 respondents (58.1% from Europe, 27.3% from North America, and 14.5% from other locations). Questions included aspects of diagnosis and treatment of TED, using patient examples. Responses were grouped into three general areas (North America, Europe, and other regions including Central and South America, Asia and Asia Pacific). Results were separated according to severity of disease.

For mild disease, smoking cessation and artificial tears was recommended by over 65% of respondents. European respondents were more likely to use selenium for mild TED. For patients with moderate-to-severe TED, North American respondents tended to prefer Tempezza initially, while European clinicians preferred steroids (usually administered intravenously). Radiation therapy to the eyes or the use of the immune suppression drug rituximab was recommended by less than 5% of respondents for patients with moderate-to-severe TED. Over 50% of respondents did not have a multidisciplinary team of specialists to treat patients with TED. Overall, 80% said they would refer a patient to an ophthalmologist after diagnosing or suspecting TED. When treating moderate to severe TED, 30% would order an orbital MRI and 20% would use an orbital CT. One third said the financial cost of evaluation and treatment of TED was a major concern. Respondents preferred antithyroid medications for treatment of associated hyperthyroidism with surgery and radioactive iodine less often used.

# WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Treatment of TED varies by region. This can represent differences in guidelines from medical societies and insurance/governmental financial support. It points out the importance of multidisciplinary teams in caring for patients with TED. However, since most of the respondents were from academic institutions, results may not generalize to real-life clinical situations. For patients, it is important to recognize that there are multiple avenues to treatment of TED and to request consultation in moderate to severe cases.

— Marjorie Safran, MD





### THYROID EYE DISEASE, continued

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### **ATA RESOURCES**

Graves' Disease: <u>https://www.thyroid.org/graves-disease/</u> Thyroid Eye Disease: <u>https://www.thyroid.org/thyroid-eye-disease/</u>

### **ABBREVIATIONS & DEFINITIONS**

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.

Multidisciplinary team: a group of specialists, often including surgeons, radiologists, oncologists and endocrinologists, that work together to prove the best medical treatment to patients

**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 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).

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



## **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.













## American Thyroid Association®

Foundation

www.thyroid.org

ATA® Patient Resources: www.thyroid.org/thyroid-information/ Find a Thyroid Specialist: www.thyroid.org (Toll-free): 1-800-THYROID thyroid@thyroid.org

## **Bite Me Cancer**

www.bitemecancer.org info@bitemecancer.org

## Graves' Disease and Thyroid Foundation

www.gdatf.org (Toll-free): 877-643-3123 info@ngdf.org

## **Light of Life Foundation**

www.checkyourneck.com info@checkyourneck.com MCT8 – AHDS Foundation

mct8.info Contact@mct8.info

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

(Toll-free): 877-588-7904 thyca@thyca.org

## **Thyroid Cancer Alliance**

www.thyroidcanceralliance.org www.thyroidcancerpatientinfo.org Rotterdam, The Netherlands

## **Thyroid Cancer Canada**

www.thyroidcancercanada.org 416-487-8267 info@thyroidcancercanada.org

## Thyroid Federation International www.thyroid-fed.org

tfi@thyroid-fed.org

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