Clinical THYROIDOLOGY FOR THE PUBLIC

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

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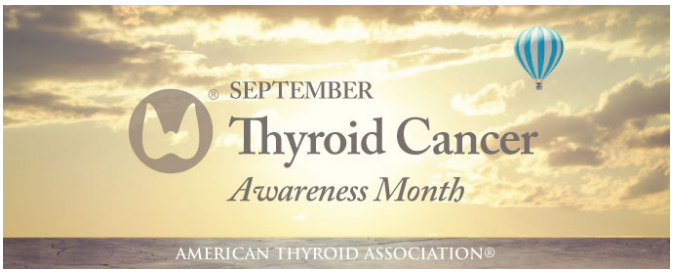
www.thyroid.org



Radioactive iodine is a very effective treatment for thyroid cancer and can be curative. It is well know that exposure to radiation is a risk factor for the development of leukemia. The current study by a Korean group involved over 200,000 patients with thyroid cancer and sheds new light on risk of leukemia after radioactive iodine therapy for thyroid cancer.

Seo GH et al. Increased risk of leukemia after radioactive iodine therapy in patients with thyroid cancer: a nationwide, population-based study in Korea. Thyroid. July 2, 2015 [Epub ahead of print].

A rare complication of radioactive iodine therapy for thyroid cancer in adult patients has been associated with a slightly increased risk of developing non-thyroid cancers later in life. There is concern that the risk may be higher in children and young adults, the data is currently limited. The goal of this study is to evaluate the risk of non-thyroid cancers in patients younger than 25 years of age who received radioactive iodine treatment for thyroid cancer.

Marti JL et al. Increased risk of second primary malignancy in pediatric and young adult patients treated with radioactive iodine for differentiated thyroid cancer. Thyroid 2015;25:681-7. Epub May 6, 2015.

While most patients are admitted to the hospital for at least one night following thyroid surgery, ambulatory thyroid surgery has become more common in the past decade. This study examined ambulatory surgery databases in various states to determine complication and readmission rates for ambulatory thyroidectomy.

Orosco RK. Ambulatory thyroidectomy: a multistate study of revisits and complications. Otolaryngol Head Neck Surg. March 31, 2015. pii: 0194599815577603 [Epub ahead of print].

Graves' orbitopathy (GO) is a significant problem in about 5% to 10% patients with Graves' disease. Glucocorticoids are the principal medical therapy for active moderate-to-severe GO but are not very effective in many patients. Rituximab is a selective immunosuppressive drug that has been reported to be effective in the treatment of GO. The current study is a clinical trial of rituximab (RTX) versus the glucocorticoid drug methylprednisolone (MP) in patients with moderate-to-severe GO.

Salvi M et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomized controlled study. J Clin Endocrinol Metab 2015;100(2):422-31. Epub December 15, 2014.

Almost 1/3rd of patients newly diagnosed with Graves' disease with have Graves' orbitopathy (GO) to some degree, with ~5-6% of patients having moderate-to-severe GO. Double vision is one of the features of moderate-to-severe GO and is the principal cause of an inability to work. In this study, the occurrence of double vision was examined in patients with moderate-to-severe GO and the results were correlated with the other symptoms of GO.

Laurberg P et al. Double vision is a major manifestation in moderate to severe Graves' orbitopathy, but it correlates negatively with inflammatory signs and proptosis. J Clin Endocrinol Metab. February 13, 2015 [Epub ahead of print].

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A publication of the American Thyroid Association
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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 will be providing summaries of research studies that were discussed in a recent issue of *Clinical Thyroidology*, a publication of the American Thyroid Association for physicians. These summaries are presented in lay language to allow the rapid dissemination of thyroid research to the widest possible audience. This means that you are getting the latest information on thyroid research and treatment almost as soon as your physicians. As always, we are happy to entertain any suggestions to improve *Clinical Thyroidology for the Public* so let us know what you want to see.

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 and Thyroid Federation International*.

Join us for a free thyroid patient forum at the Walt Disney World Swan and Dolphin hotel in Orlando, FL, on Sunday October 18 form 1–3 PM.

September is Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

1. What is the risk of leukemia in patients treated with radioactive iodine for thyroid cancer?
2. What is the risk of salivary cancer in young patients treated with radioactive iodine for thyroid cancer?
3. How safe is ambulatory thyroid surgery?
4. Are there any options other than steroids for active Graves' orbitopathy?
5. Is double vision in Graves' orbitopathy related to overall eye inflammation?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD

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THYROID CANCER

Radioactive iodine doses exceeding 100 mCi increase the risk for developing leukemia

BACKGROUND

In patients with advanced or high risk thyroid cancer, radioactive iodine is a very effective treatment and can be curative. It is well know that exposure to radiation is a risk factor for the development of leukemia, so patients treated with radioactive iodine have been followed since this therapy was started. It is clear that very high radioactive iodine doses (doses exceeding 600 mCi) were associated with an increased risk for developing leukemia. However, usual treatment doses of radioactive iodine were not believed to have this adverse effect. The current study by a Korean group involved over 200,000 patients with thyroid cancer and sheds new light on risk of leukemia after radioactive iodine therapy for thyroid cancer.

THE FULL ARTICLE TITLE

Seo GH et al. Increased risk of leukemia after radioactive iodine therapy in patients with thyroid cancer: a nationwide, population-based study in Korea. Thyroid. July 2, 2015 [Epub ahead of print].

SUMMARY OF THE STUDY

The authors obtained data from the National Health Insurance database of Korea, which includes the entire population of Korea. They identified 211,360 patients with thyroid cancer newly diagnosed between 2008 and 2013; there were 542,845 patient-years of follow-up. Patients were categorized into five groups based on their cumulative dose of radioactive iodine: 1 = no radioactive iodine, 2 = low-dose radioactive iodine (<30 mCi), 3 = moderate-dose radioactive iodine (31 to 100 mCi), 4 = high-dose radioactive iodine I (101 to 150 mCi), and 5 = very-high-dose radioactive iodine (>150 mCi). The number of patients with thyroid cancer per year increased from 25,437 in 2008 to 41,248 in 2013; 82% were female. The average age at diagnosis was 48 years. A total of 49% (103,741) underwent treatment with radioactive iodine, with an average total dose of 100 mCi. The average follow-up period was 29 months. During the study period, there were 72 cases of leukemia, 46 in the radioactive iodine group and 26 in the no- radioactive iodine group. The risk of leukemia was higher in those who received >100 mCi, as compared with those who received no radioactive iodine. Patients who received low- or moderate-dose radioactive iodine did not have a statistically significant risk for leukemia. The risk for development of leukemia in those who received >100 mCi of ^{131}I increased significantly as early as 9 months after radioactive iodine.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

While the overall risk of developing leukemia after radioactive iodine therapy for thyroid cancer is very low, it is clearly dose-related. Doses of radioactive iodine exceeding 100 mCi were strongly associated with the development of leukemia, but lower radioactive iodine doses were not. This is important when deciding the risks vs benefits of radioactive iodine therapy as well as determining a dose of radioactive iodine when treating thyroid cancer.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://www.thyroid.org/cancer-of-the-thyroid-gland

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

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).

mCi: millicurie, the units used for radioactive iodine.

Leukemia: cancer of the white blood cells

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THYROID CANCER

Radioactive iodine therapy for thyroid cancer increases salivary gland cancer in patients younger than age 25

BACKGROUND

Although children and young adults rarely develop thyroid cancer, the disease is often diagnosed at an advanced stage. After surgery, many of these patients are treated with radioactive iodine, which is very effective in treating advanced thyroid cancer. Because of this, the death rate due to thyroid cancer is low in young patients, despite of advanced disease at diagnosis. As in all patients with thyroid cancer, the benefit of radioactive iodine treatment is unclear in patients without advanced cancer.

A rare complication of radioactive iodine therapy for thyroid cancer in adult patients has been associated with a slightly increased risk of developing non-thyroid cancers later in life. There is concern that the risk may be higher in children and young adults because of increased sensitivity to radiation of tissues that are growing and because of longer life-span of this patient population. The data regarding this risk is currently limited. The goal of this study is to evaluate the risk of non-thyroid cancers in patients younger than 25 years of age who received radioactive iodine treatment for thyroid cancer.

THE FULL ARTICLE TITLE

Marti JL et al. Increased risk of second primary malignancy in pediatric and young adult patients treated with radioactive iodine for differentiated thyroid cancer. Thyroid 2015;25:681-7. Epub May 6, 2015.

SUMMARY OF THE STUDY

The study data was obtained from the Surveillance, Epidemiology, and End Results (SEER), a population-based cancer registry from the National Cancer Institute. The study included 3,637 patients followed in this registry who received initial treatment for thyroid cancer with or without radioactive iodine treatment between 0-24 years of age (1973-2008). Only 266 (7.3%) patients were diagnosed with thyroid cancer before age 15. At diagnosis, 1,569 (43.9%) patients had local lymph node metastases and 166 (4.7%) patients had distant metastases. A total of 1,587 (44%) patients received radioactive iodine treatment, the percentage increasing from 4% in 1973 to 62% in 2008, although the proportion of advanced stage thyroid cancer declined over time. The average follow-up period of the patients in the registry was 15.5 years. The overall survival at 20 years was similar in the patients who received (98.5%) and those who did not receive (97.3%) radioactive iodine treatment.

A total of 26 non-thyroid cancers were diagnosed in patients who received radioactive iodine treatment, as compared with an expected number of 18.3 cancers diagnosed in a the general population without history of thyroid cancer. The most common cancers were salivary gland cancers, noted in 3 patients compared to the expected 0.9 cancers noted in the reference population. The time for development of salivary gland cancer was 10 years after the radioactive iodine treatment. There was also a higher risk of leukemia (2 cases vs. 0.5 expected) and kidney cancer (1 case vs 0.32 expected) in thyroid cancer patients treated with radioactive iodine, however, there were only a few cases.

Over a decade, 1 in 227 young thyroid cancer patients treated with radioactive iodine will develop a non-thyroid cancer and 1 in 588 patients will develop salivary cancer attributable to the radioactive iodine treatment. The location of these cancers can be explained by the fact that the radioactive iodine is concentrated in the salivary glands, is toxic for the bone marrow and is excreted by the kidneys. The risk of developing non-thyroid cancers after from the radioactive iodine treatment for thyroid cancer was only slightly higher in young compared to adult patients. Young thyroid cancer patients who did not receive radioactive iodine treatment did not have an increased risk of non-thyroid cancers as compared to the general population without thyroid cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Children and young adults who receive radioactive iodine for thyroid cancer have an increased risk of developing non-thyroid cancers later in life, mainly salivary gland cancer. There has been an increasing proportion of young patients with thyroid cancer who receive radioactive iodine treatment over time, despite

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THYROID CANCER, continued

of the diagnosis being made in less advanced stages. Importantly, survival in the young patients with low risk thyroid cancer is not improved by the radioactive iodine therapy. Therefore, it is critical to carefully weigh the benefits and risks of the radioactive iodine treatment, including the small but real risk of developing other cancers later in life before recommending this treatment in children and young adults with thyroid cancer.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://www.thyroid.org/cancer-of-the-thyroid-gland

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

Thyroid Surgery: http://thyroid.org/patients/patient_brochures/surgery.html

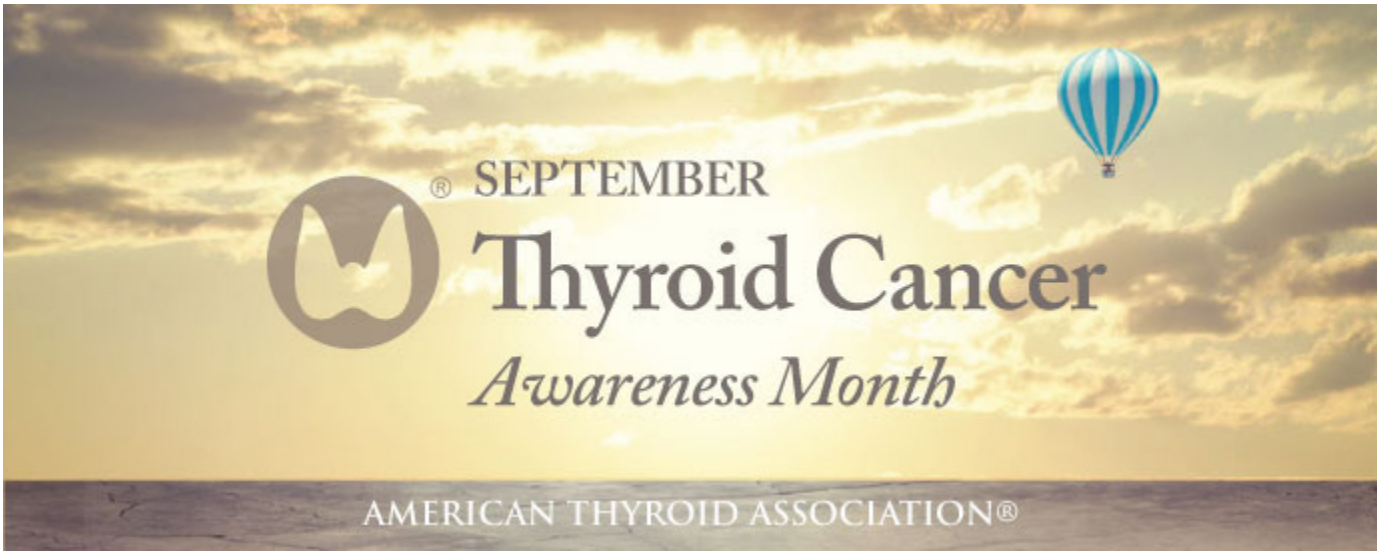
ABBREVIATIONS & DEFINITIONS

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.

Thyroidectomy: surgery to remove the thyroid gland.

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/

National Cancer Institute (NCI): a part of the National Institutes of Health in Bethesda, MD, the NCI is the federal government's primary agency for cancer research and training.



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THYROID SURGERY

Ambulatory thyroid surgery

BACKGROUND

Most patients are admitted to the hospital for at least one night following thyroid surgery. Ambulatory thyroid surgery, defined as patient discharge to home on the same day as surgery, has become more common in the past decade. For highly selected patients, ambulatory thyroid surgery is believed to be safe when the risk of complications is low and the patient can obtain additional medical care when necessary. This study examined ambulatory surgery databases in various states to determine complication and readmission rates for ambulatory thyroidectomy.

THE FULL ARTICLE TITLE

Orosco RK. Ambulatory thyroidectomy: a multistate study of revisits and complications. Otolaryngol Head Neck Surg. March 31, 2015. pii: 0194599815577603 [Epub ahead of print].

SUMMARY OF THE STUDY

Databases from California, Florida, New York, and Iowa were searched for ambulatory thyroidectomy cases in patients 18 years of age or older that were performed in the years 2010 and 2011. Cases were divided into two groups for comparison, broadly defined as either partial or total thyroidectomy. Any revisit to the hospital, emergency department, or ambulatory surgery center within 30 days was identified. A total of 25,634 ambulatory thyroidectomy cases were identified in the four databases during the study period; 44% of cases were total thyroidectomy and 56% were partial thyroidectomy. Overall, 24% of all surgeries were for thyroid cancer.

The authors identified 1858 revisits, representing 7.2% of the total; 1148 revisits were to the emergency department, and 22% of all revisits led to an admission. Revisits were most common on the second and third postoperative days, but the median number of days between surgery and revisit was 7. A total of 21% of revisits were for hypocalcemia (low calcium levels) and 7% of revisits were for bleeding, bruising/hematoma formation or seroma (lymphatic drainage). There was a significantly higher revisit rate in patients who had undergone total thyroidectomy as compared with those who had undergone partial thyroidectomy. Revisit due to hypocalcemia and hemorrhage were also significantly higher in the total thyroidectomy than in the partial thyroidectomy group. Three deaths were reported.

Revisit rates are higher for total thyroidectomy as compared with partial thyroidectomy and are mostly due to hypocalcemia. Hypocalcemia, hematoma, and bleeding usually develop within the first few days, but several patients presented at or beyond 7 days.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

As this study was based on a database search, it is likely that complications were underreported. While the study showed 7.2% of the patients revisited the care facility (emergency department, ambulatory surgical facility, or hospital) within 30 days after the procedure, other complications where patients presented to a clinic or a facility not included in the database were not reported. Three deaths were identified, but it is not known whether the deaths were due to the outpatient status of the patients.

While the authors concluded that ambulatory thyroid surgery has an acceptable safety profile, well-defined criteria and validated indicators for safe discharge are needed to ensure the safety of same-day discharge.

— Ronald B. Kuppersmith, MD, FACS

ATA THYROID BROCHURE LINKS

Thyroid Surgery: http://thyroid.org/patients/patient_brochures/surgery.html

ABBREVIATIONS & DEFINITIONS

Total thyroidectomy: surgery to remove the entire thyroid gland.

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

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THYROID SURGERY, continued

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

Hematoma: collection of blood under the skin from bleeding

Seroma: collection of lymphatic fluid under the skin

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GRAVES' DISEASE

Rituximab is better than corticosteroids for active Graves' orbitopathy

BACKGROUND

Graves' orbitopathy (GO) occurs in about 1/4th of patients with Graves' disease and is a significant problem in about 5% to 10% of these patients. Glucocorticoids are general antiinflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation but have many side effects. Glucocorticoids are the principal medical therapy for active moderate-to-severe GO but are not very effective in many patients. Rituximab is a selective immunosuppressive drug that is administered intravenously (IV) and which is directed against B lymphocytes (cells of the immune system) and has been reported to be effective in the treatment of GO. The current study is a clinical trial of rituximab (RTX) versus the glucocorticoid drug methylprednisolone (MP) in patients with moderate-to-severe GO.

THE FULL ARTICLE TITLE

Salvi M et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomized controlled study. J Clin Endocrinol Metab 2015;100(2):422-31. Epub December 15, 2014.

SUMMARY OF THE STUDY

The study included patients with Graves' disease who were affected by active GO based on a clinical activity score (CAS) of 4 or greater. The study was designed to include 60 patients but was stopped after 32 patients were treated (16 in each group). Patients in the RTX group received a single 500-mg IV infusion while patients in the MP group received 830 mg of MP IV weekly for 6 weeks followed by 415 mg weekly for another 6 weeks. The primary end point was a decrease in the CAS by 2 or more points.

The 32 patients included 26 women and 6 men; 19 were smokers. The duration of GO had been 4.5 months for patients in each group. Impressive decreases in CAS were similar in the two groups up to 12 weeks; after that, the CAS continued to improve with RTX but plateaued with MP, and the differences between the scores was significant at 16, 20, and 24 weeks, favoring RTX. A total of 5 of 16 patients in the MP group had reactivation of GO within 1 year, but none of the patients in the RTX group had reactivation. Ten patients in the MP group and 3 in the RTX group underwent a surgical procedure for GO. Based on the GO quality-of-life scale, RTX caused much greater improvement in quality-of-life than did MP. Adverse reactions occurred in 10 of 16 patients in the MP group, mainly high blood sugars and liver-function abnormalities. Adverse events occurred in 13 of 15 patients in the RTX group, mainly reactions of throat itching and nasal stuffiness during the IV infusion.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Treatment with rituximab results in a better therapeutic outcome for active moderate-to-severe Graves' orbitopathy than treatment with methylprednisolone with much fewr significant side effects. This is a great new drug to use in the unfortunate patient with Graves' disease and severe eye disease.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Graves' disease: http://www.thyroid.org/what-is-graves-disease

ABBREVIATIONS & DEFINITIONS

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Graves orbitopathy (GO): also known as Thyroid eye disease. GO is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. GO includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

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GRAVES' DISEASE, continued

Rituximab: a selective immunosuppressive drug that is administered intravenously and which is directed against B lymphocytes (cells of the immune system)

Steroids/Glucocorticoids: general antiinflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation

CAS: Clinical Activity Score, a scoring system used to evaluate patients with Graves' ophthalmopathy, and is based on classical signs of inflammation (pain, redness, swelling and function) and that helps predict which patients will benefit from immunosuppressive treatment

Thyroid Awareness Monthly Campaigns

The ATA will be highlighting a distinct thyroid disorder each month and a portion of the sales for Bravelets™ will be donated to the ATA. The month of September is **Thyroid Cancer Awareness Month** and a bracelet is available through the ATA Marketplace to support thyroid cancer awareness and education related to thyroid disease.

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GRAVES' DISEASE

Double vision is not related with overall inflammation in Graves' orbitopathy

BACKGROUND

Thyroid eye disease, also known as Graves' orbitopathy (GO), is one of the more disabling features of Graves' disease. Almost 1/3rd of patients newly diagnosed with Graves' disease with have GO to some degree, with ~5-6% of patients having moderate-to-severe and active GO. In the consensus statement of the European Group on Graves' Orbitopathy (EUGOGO) on management of GO, moderate-to-severe GO has a sufficient impact on daily life to justify the risks of powerful immune-suppressing drugs (if active) or surgery (if inactive). Double vision is one of the features of moderate-to-severe GO and is the principal cause of an inability to work. In this study, the occurrence of double vision was examined in patients with moderate-to-severe GO and the results were correlated with the other symptoms of GO.

THE FULL ARTICLE TITLE

Laurberg P et al. Double vision is a major manifestation in moderate to severe Graves' orbitopathy, but it correlates negatively with inflammatory signs and proptosis. J Clin Endocrinol Metab. February 13, 2015 [Epub ahead of print].

SUMMARY OF THE STUDY

The study included 210 patients diagnosed with moderate-to-severe GO who were seen in the Thyroid–Eye Clinic of Aalborg University Hospital in Denmark from 1992 to 2013. The duration of GO was determined based on the interview. At diagnosis, characteristics of GO were recorded by the same investigators, using standardized procedures. All patients had active GO at the time of referral. All patients had imaging of the orbit (CT or MRI).

Patients were stratified into four groups according to the degree of double vision: no double vision, 25%; double vision in up to 50% of the field, 22%; double vision in 55% to 80% of the field, 28% and double vision in ≥85 % of the field, 25%. Double vision was associated with a decrease in eye motility. In contrast, double vision was not related to the decree of inflammation. There were no correlations between double vision and patient's age, smoking habit, sex, body weight, type and duration of thyroid dysfunction, duration of GO, vision or previous radioiodine therapy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this series of patients with moderate-to-severe GO, double vision was very common and was the main reason for classifying GO as moderate-to-severe. Double vision was not related to the activity score of the disease or with the degree of eye bulging but was associated with decreased movement of the eyes. The authors suggest that eye-muscle restriction and degree of double vision be separately recorded in patients with GO as well as in controlled clinical studies of the disease.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Graves' disease: http://www.thyroid.org/what-is-graves-disease

ABBREVIATIONS & DEFINITIONS

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Graves orbitopathy (GO): also known as Thyroid eye disease. GO is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. GO includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

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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 towards the improvement of thyroid education and resources for patients.

WHO WE ARE (in alphabetical order)

- **American Thyroid Association**
- **Bite Me Cancer**
- **Graves' Disease and Thyroid Foundation**
- **Light of Life Foundation**
- **ThyCa: Thyroid Cancer Survivors' Association, Inc.**
- **Thyroid Cancer Canada**
- **Thyroid Federation International**

AMERICAN THYROID ASSOCIATION

www.thyroid.org
ATA Patient Resources: http://www.thyroid.org/patients/
Find a Thyroid Specialist: www.thyroid.org
Phone (toll-free): 1-800-THYROID
e-mail: thyroid@thyroid.org

ATA Mission: The ATA leads in promoting thyroid health and understanding thyroid biology.
ATA Vision: The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.
ATA Values: The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

To further our mission, vision and values the ATA sponsors "Friends of the ATA" online to advance the information provided to patients and the public such as this publication, *Clinical Thyroidology for the Public*. We welcome your support.

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GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

BITE ME cancer
attitude is everything

ATA Alliance for Thyroid Patient Education

Continued...

BITE ME CANCER

http://www.bitemecancer.org

Bite Me Cancer was formed as a nonprofit foundation in September, 2010, by Nikki Ferraro, who was 17-years old at the time. Nikki was diagnosed with a rare form of thyroid cancer in April 2010 when she was a junior at Chantilly HS in Virginia. Nikki was determined to lead a Relay for Life team just two weeks after her diagnosis. She named the team Bite Me Cancer and experienced immediate success. When Nikki decided to create a foundation a few months later, she wanted to continue the legacy of her team name and thus her foundation became the Bite Me Cancer Foundation.

e-mail: info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

Phone (toll-free): 1-877-NGDF-123 or 643-3123

e-mail: Gravesdiseasefd@gmail.com

Founded in 1990, the Graves' Disease Foundation offers support and resources to Graves' disease patients, their families, and health care professionals. Their mission is to find the cause of and the cure for Graves' thyroid disease through research, to improve the quality of life for persons with Graves' disease and their caregivers and to educate persons with Graves' disease, their caregivers, healthcare professionals, and the general public about Graves' disease and its treatment. The web site features a monitored bulletin board.

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com

email: info@checkyourneck.com

The Light of Life Foundation, founded in 1997, is a nonprofit organization that strives to improve the quality of life for thyroid cancer patients, educate the public and professionals about thyroid cancer, and promote research and development to improve thyroid cancer care.

continued on next page

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Light of Life Foundation checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

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

Thyroid Federation International

Thyroid Cancer Canada
Cancer de la thyroïde Canada

BITE ME cancer® attitude is everything.

ATA Alliance for Thyroid Patient Education

Continued...

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org
Phone (toll-free): 877 588-7904
e-mail: thyca@thyca.org

ThyCa: Thyroid Cancer Survivors' Association, Inc., founded in 1995, is an international nonprofit organization, guided by a medical advisory council of renowned thyroid cancer specialists, offering support and information to thyroid cancer survivors, families, and health care professionals worldwide.

THYROID CANCER CANADA

www.thyroidcancercanada.org
Phone: 416-487-8267
Fax: 416-487-0601
e-mail: info@thyroidcancercanada.org

Thyroid Cancer Canada is a non-profit organization founded in 2000. The organization works towards creating an environment in which people who are dealing with thyroid cancer, especially the newly diagnosed, are met with support and information. Their goals & objectives include facilitating communication among thyroid cancer patients, providing credible information about the disease, providing emotional support, and assisting thyroid cancer patients with voicing their needs to health care professionals and those who are responsible for health care policy.

THYROID FEDERATION INTERNATIONAL

http://www.thyroid-fed.org/
e-mail: tfi@thyroid-fed.org

Thyroid Federation International (TFI) was established in Toronto in 1995. Thyroid Federation International aims to work for the benefit of those affected by thyroid disorders throughout the world by providing a network of patient support organizations.

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Light of Life Foundation checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

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

Thyroid Federation International

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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 rare compared to other cancers. In the United States in 2010 an estimated 45,000 patients were diagnosed with thyroid cancer compared to over 200,000 patients with breast cancer and 140,000 patients with colon cancer. However, fewer than 2000 patients die of thyroid cancer each year. In 2008 when statistics were last collected, over 450,000 patients were alive and living with thyroid cancer. 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 and well-tolerated treatment is available for the most common forms of thyroid cancer. It is interesting that the number of individuals - both men and women - with newly diagnosed thyroid cancer is increasing at a rate faster than for other types of cancer. The reason for this is unclear. Even though the diagnosis of cancer is terrifying, the outlook for patients with thyroid cancer is usually excellent.

WHAT ARE THE SYMPTOMS OF THYROID CANCER?

Thyroid cancer often arises in a lump or nodule in the thyroid and does not cause any symptoms (see *Thyroid Nodule brochure*). Lab tests generally do not help to find thyroid cancer. Thyroid tests such as TSH are usually normal even when a cancer is present. The best way to find a thyroid cancer is to make sure that your thyroid gland does not have nodules and is not enlarged. Neck examination by your doctor is the best way to do that. Often, thyroid nodules are discovered incidentally on imaging tests like CT scans and neck ultrasound done for completely unrelated reasons. Occasionally, patients themselves find thyroid nodules by noticing a lump in their neck while looking in a mirror, buttoning their collar, or fastening a necklace. Rarely, thyroid cancers and nodules do cause symptoms. In these cases, patients may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the windpipe or esophagus, it may cause difficulty with breathing, swallowing, or cause a "tickle in the throat". Even less commonly, hoarseness can be caused if a cancer invades the nerve that controls the vocal cords.

The important points to remember are that cancers arising in thyroid nodules generally do not cause symptoms, thyroid tests are typically normal even when cancer is present, and the best way to find a thyroid nodule is to make sure your doctor checks your neck!

WHAT CAUSES THYROID CANCER?

Thyroid cancer is more common in people who have a history of exposure to high doses of radiation, have a family history of thyroid cancer, and are older than 40 years of age. However, for most patients, we do not know the specific reason why thyroid cancers develop.

High dose radiation exposure, especially during childhood, increases the risk of developing thyroid cancer in susceptible patients. Prior to the 1960s X-ray treatments were often used for conditions such as acne, inflamed tonsils, adenoids, lymph nodes, or to treat enlargement of a gland in the chest called the thymus. All these treatments have been associated with an increased risk of developing thyroid cancer later in life. Even X-ray therapy used to treat serious cancers such as Hodgkin's disease (cancer of the lymph nodes) or breast cancer has been associated with an increased risk for developing thyroid cancer if the treatment included exposure to the head, neck or chest. Routine X-ray exposure such as dental X-rays, chest X-rays, mammograms have not been shown to cause thyroid cancer.

Thyroid cancer can also be caused by radioactive iodine released during nuclear disasters such as the 1986 accident at the Chernobyl power plant in Russia or the 2011 nuclear disaster in Fukushima, Japan related to the tsunami. Children are usually the most affected and often develop cancers within a few years of exposure. However, even adults exposed during these accidents develop thyroid cancer with increased frequency, sometimes as many as 40 years later.

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You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see *Nuclear Radiation and the Thyroid brochure*). This prevents the absorption of radioactive iodine and has been demonstrated to reduce the risk of thyroid cancer. The American Thyroid Association recommends that anyone living within 200 miles of a nuclear accident be given potassium iodide. If you live in a state containing a nuclear reactor and want more information about potassium iodide, check the recommendations from your state at the following link: *http://www.thyroid.org/professionals/publications/statements/ki/02_04_09_ki_states.html.*

HOW IS THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer is usually made by a fine needle aspiration biopsy of a thyroid nodule or after the nodule is removed during surgery (see *Thyroid Nodule brochure*). Although thyroid nodules are very common, less than 1 in 10 harbors a thyroid cancer.

WHAT ARE THE TYPES OF THYROID CANCER?

PAPILLARY THYROID CANCER. Papillary thyroid cancer is the most common type, making up about 70% to 80% of all thyroid cancers. Papillary thyroid cancer can occur at any age. Papillary cancer tends to grow slowly and often spreads to lymph nodes in the neck. However, unlike many other cancers, papillary cancer has a generally excellent outlook even if there is spread to the lymph nodes.

FOLLICULAR THYROID CANCER. Follicular thyroid cancer, which makes up about 10% to 15% of all thyroid cancers in the United States, tends to occur in somewhat older patients than does papillary cancer. As with papillary cancer, follicular cancer first can spread to lymph nodes in the neck. Follicular cancer is also more likely than papillary cancer to grow into blood vessels and from there to spread to distant areas, particularly the lungs and bones.

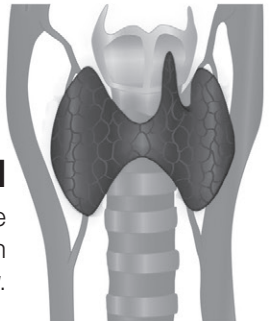
MEDULLARY THYROID CANCER. Medullary thyroid cancer, which accounts for 5% to 10% of all thyroid cancers, is more likely to run in families and be associated with other endocrine problems. In family members of an affected person, a test for a genetic mutation in the RET proto-oncogene can lead to an early diagnosis of medullary thyroid cancer and, subsequently, curative surgery to remove it.

ANAPLASTIC THYROID CANCER. Anaplastic thyroid cancer is the most advanced and aggressive thyroid cancer and is the least likely to respond to treatment. Fortunately, anaplastic thyroid cancer is rare and found in less than 2% of patients with thyroid cancer.

WHAT IS THE TREATMENT FOR THYROID CANCER?

SURGERY. The primary therapy for all forms of thyroid cancer is surgery (see *Thyroid Surgery brochure*). The generally accepted approach at the present time is to remove the entire thyroid gland in what is called a total thyroidectomy. Some patients will have thyroid cancer present in the lymph nodes of the neck or upper chest. These lymph nodes are removed at the time of thyroid surgery or sometimes, as a later procedure. After surgery, patients need to be on thyroid hormone for the rest of their life (see *Thyroid Hormone Treatment brochure*). Often, thyroid cancer is cured by surgery alone, especially if the cancer is small. If the cancer is larger, if it has spread to lymph nodes or if your doctor feels that you are at high risk for recurrent cancer, radioactive iodine may be used to destroy any remaining thyroid cancer cells after the thyroid gland is removed. Please read the Thyroid Surgery brochure to learn more details about the risks and benefits of surgery, and what kind of recovery can be expected.

RADIOACTIVE IODINE THERAPY. Thyroid cells and most thyroid cancers absorb and concentrate iodine very readily. That is why radioactive iodine can be used so effectively to destroy all remaining normal and cancerous thyroid tissue after thyroidectomy (see *Radioactive Iodine brochure*). The procedure to destroy or ablate thyroid tissue is called a radioactive iodine ablation. This produces high concentrations of radioactive iodine in thyroid tissues damaging the DNA in the thyroid cells, eventually causing the cells to die. Since other tissues in the body do not efficiently absorb or concentrate iodine, radioactive iodine used during the ablation procedure has little or no effect on tissues outside of the thyroid. Two risks are known to happen. In some patients, the radioactive iodine can affect the glands that produce saliva and lead to a having a dry mouth. In other patients, when high dose of radioactive iodine are necessary, there may be a small risk of developing other cancers later. These risks are small but increase as the doses of radioactive iodine increase. The potential risks of treatment can be minimized by using the smallest dose possible. Balancing potential risks against the benefits of radioactive iodine therapy is an important discussion that you should have with your doctor if radioactive iodine therapy is recommended.



FURTHER INFORMATION

Further details on this and other thyroid-related topics are available in the patient information section on the American Thyroid Association website at ***www.thyroid.org***.

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If your doctor recommends radioactive iodine therapy, your TSH will need to be elevated prior to the treatment. This can be done in two ways. The first is by stopping to take thyroid hormone pill (levothyroxine) for 4-6 weeks. This causes you to become hypothyroid and high levels of TSH will be produced by your body naturally. However, hypothyroidism causes fatigue that can sometimes be significant. To minimize the symptoms of hypothyroidism your doctor may prescribe T3 (Cytomel®, liothyronine) which is a short acting form of thyroid hormone that is usually taken after the levothyroxine is stopped until the final 2 weeks before treatment. Alternatively, TSH can be increased sufficiently without making you hypothyroid simply by injecting TSH into you! Recombinant human TSH (rhTSH, Thyrogen®) can be given as two injections in the several days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on thyroid hormone and do not become hypothyroid. You may also be asked to go on a low iodine diet for 1 to 2 weeks prior to treatment (see Low Iodine Diet FAQ). This will leave your body iodine depleted which improves absorption of radioactive iodine, and helps maximize the treatment effect.

Once the TSH level is high enough, a pretherapy iodine scan is often done by administering a small dose of radioactive iodine. This scan determines how much thyroid tissue needs to be destroyed and allows the doctor to calculate how large a dose of therapeutic radioactive iodine needs to be administered. When used correctly, radioactive iodine therapy has proven to be safe and well-tolerated and it has even been able to cure cases of thyroid cancer that have spread to other parts of the body like the lungs.

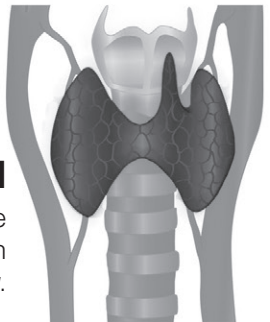
TREATMENT OF ADVANCED THYROID CANCER. Thyroid cancer that spreads (metastasizes) to distant locations in the body occurs rarely but can be a serious problem. Surgery and radioactive iodine remain the best way to treat such cancers as long as these treatments continue to work. However, for more advanced cancers, or when radioactive iodine therapy is no longer effective, other means of treatment are needed. External beam radiation directs precisely focused X-rays to areas that need to be treated—often metastases to bones or other organs. This can kill or slow the growth of specific tumors. Cancer that has spread more widely requires additional treatment.

New chemotherapy agents that have shown promise treating other advanced cancers are increasingly available for treatment of thyroid cancer. These drugs rarely cure advanced cancers that have spread widely throughout the body. However, they can often slow down or partially reverse the growth of the cancer. These treatments are usually given by an oncologist (cancer specialist) and often require care at a regional or university medical center.

WHAT IS THE FOLLOW-UP FOR PATIENTS WITH THYROID CANCER?

Periodic follow-up examinations are essential for all patients with thyroid cancer 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 inside of the neck and look for nodules, lumps or cancerous lymph nodes that might indicate the cancer has recurred. Blood tests are also important for thyroid cancer patients. All patients who have undergone thyroidectomy require thyroid hormone replacement with levothyroxine once the thyroid is removed (see *Thyroid Hormone Treatment brochure*). The dose of levothyroxine prescribed by your doctor will in part be determined by the extent of your thyroid cancer. More extensive cancers require higher doses of levothyroxine to suppress TSH. In cases of minimal or very low risk cancers, it's safe to keep TSH in the normal range. The TSH level is the most sensitive indicator of whether the levothyroxine dose is correctly adjusted and should be followed regularly by your doctor.

Another very important blood test is measurement of thyroglobulin. Thyroglobulin is a protein produced by thyroid tissue and most types of thyroid cancer and is usually checked at least once annually. Following thyroidectomy and radioactive iodine ablation, thyroglobulin levels should be undetectable for life. Therefore, a detectable thyroglobulin level should raise a suspicion for possible cancer recurrence. Detectable thyroglobulin levels may require additional tests and



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possible further treatment with radioactive iodine and surgery. Thyroglobulin is generally measured either when you're on thyroid hormone with a low or normal TSH, or after TSH is elevated either by stopping thyroid hormone for 3-6 weeks, or after injection of Thyrogen® (see section on radioactive iodine therapy above). Measurement of thyroglobulin may not be possible in up to 25% of patients who have interfering thyroglobulin antibodies present in their blood. In these patients, other means of follow up are often used.

In addition to routine blood tests, your doctor may want to periodically repeat a whole-body iodine scan to determine if any thyroid cells remain. Whole body scanning is also done after your TSH level is raised, either by stopping your thyroid hormone or by administering Thyrogen® injections. Increasingly, these scans are only done for high risk patients and have been largely replaced by routine neck ultrasound and thyroglobulin measurements that have a higher diagnostic sensitivity especially when done together.

WHAT IS THE PROGNOSIS OF THYROID CANCER?

Overall, the prognosis of thyroid cancer is excellent especially for patients younger than 45 years of age and those with small cancers. Patients with papillary thyroid cancer who have a primary tumor that is confined to the thyroid gland have an excellent outlook. 10 year survival for such patients is 100% and death from thyroid cancer anytime thereafter is extremely rare. For patients over 45 years of age, or those with larger or more aggressive tumors, the prognosis remains very good but the risk of cancer recurrence is higher. The prognosis is not quite as good in patients whose cancer cannot be completely removed with surgery or destroyed with radioactive iodine treatment. Nonetheless, these patients often are able to live a long time and continue to feel well despite the fact that they continue to live with cancer. It is important to talk to your doctor about your individual profile of cancer and expected prognosis. It will be necessary to have lifelong monitoring, even after successful treatment.

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