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Clinical Thyroidology for the Public

VOLUME 10 • ISSUE 7 • JULY 2017

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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 present 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*.

July is Graves' Disease Awareness Month.

In this issue, the studies ask the following questions:

1. Does bariatric surgery change levothyroxine requirements among hypothyroid patients?
2. How can treatment of hypothyroidism in older patients be improved?
3. How often do patients require thyroid hormone therapy after lobectomy?
4. What is the role of thyroglobulin testing and neck ultrasound in determining the need for radioactive iodine therapy?
5. Does low-dose vs high-dose radioactive iodine therapy change recurrence rates in thyroid cancer?
6. What is the role of surgery in thyroid cancer recurrence?

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

— Alan P. Farwell, MD, FACE

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HYPOTHYROIDISM

Does bariatric surgery decrease levothyroxine requirements among hypothyroid patients?

BACKGROUND

According to the American Society for Metabolic and Bariatric Surgery, 179,000 bariatric surgeries were performed in the United States in 2013. The two most common bariatric procedures are including Roux-en-Y gastric bypass, where part of the stomach is removed (34.2% of surgeries) and gastric sleeve procedures, where the stomach is constricted but remains intact (42.1% of surgeries). Obesity and hypothyroidism often occur in the same patient and ~18% of bariatric surgery patients require thyroid hormone therapy. It has previously been demonstrated in patients not taking thyroid hormone that both T_3 and TSH are elevated in obese individuals and that levels of TSH, T_3, or both tend to fall after either diet- or surgery-induced weight loss. A recent study demonstrated that average levothyroxine doses decreased proportionally with decreases in lean body mass in hypothyroid individuals following bariatric surgery. This study further examines the levothyroxine dose requirements after bariatric surgery in a population that received mainly gastric sleeve surgery.

THE FULL ARTICLE TITLE

Zendel A et al. The impact of bariatric surgery on thyroid function and medication use in patients with hypothyroidism. Obes Surg. March 2, 2017 [Epub ahead of print].

SUMMARY OF THE STUDY

The medical records of all patients who underwent bariatric surgery between 2009 and 2014 at a single center in Tel Aviv were reviewed. A total of 93 patients with a diagnosis of hypothyroidism made prior to their surgery (5.1% of all individuals in the database) were included. The diagnosis of hypothyroidism was made by primary care providers prior to referral for bariatric surgery and based on elevated serum TSH values on a minimum of two occasions. No patients had a history of thyroid surgery or radioactive iodine therapy. Body-mass index (BMI), TSH, free T_4, and levothyroxine doses were assessed at baseline and at 6 and 12 months after bariatric surgery. Thyroid hormone dosing was managed by clinical providers and was not done according to a study protocol.

Of the 93 study participants, 85 (91%) were women and the average age at surgery was 46.6 years. The majority of patients (77 (83%)) underwent gastric sleeve surgery. The remaining 16 patients underwent Roux-en-Y gastric bypass. The average baseline BMI was 43.7 and declined to 34.4 at 6 months and to 29.8 at 12 months. Most patients (89%) were treated with L-T_4 prior to surgery. The average baseline TSH was 3.9 mIU/L; this decreased to 3.0 mIU/L at 6 months and subsequently stabilized at 3.0 mIU/L at 12 months. The baseline average free T_4 was 13.7 pmol/L. This increased to 15 pmol/L at 6 months and to 14.9 pmol/L at 12 months. The average daily dose of L-T_4 at baseline was 98.4 µg. This decreased to 89.7 µg at 12 months. Ten patients (12%) required lowered levothyroxine doses and 11 patients (13%) stopped levothyroxine treatment altogether following their bariatric procedures. The likelihood of decreased levothyroxine dose requirement did not differ by age, sex, baseline BMI, or baseline levothyroxine dose.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirms that levothyroxine requirements in obese hypothyroid patients decreases after bariatric surgery, whether it is gastric bypass or gastric sleeve surgery. The average dose decreased ~9 mcg per day. This study shows that all hypothytoid patients need serial TSH monitoring after bariatric surgery.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): http://www.thyroid.org/hypothyroidism/

Thyroid and Weight: http://www.thyroid.org/thyroid-and-weight/

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

HYPOTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

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

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

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

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.

Thyroxine (T4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

Bariatric surgery: surgery where the stomach volume is decreased to assist in weight loss. Two general types are Roux-en-Y gastric bypass, where part of the stomach is removed and gastric sleeve surgery, where the stomach is constricted but remains intact.

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 **July** is **Graves' Disease 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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HYPOTHYROIDISM IN OLDER ADULTS

Sequential TSH determinations may help in assessing the adequacy of treatment for overt hypothyroidism in older patients

BACKGROUND

Hypothyroidism is a common problem and the risk of developing hypothyroidism increases with age. In some studies, an increased TSH levels is seen in up to 25% of individuals over the age of 75. Severe hypothyroidism can be fatal and less severe hypothyroidism can lead to an increased risk of death if not diagnosed or if inadequately treated. Further, it is known that there is an increased risk of death associated with an underactive thyroid. To determine whether thyroid hormone treatment is adequate, measurements of thyroid stimulating hormone (TSH) in the blood are done. However, the target level TSH in the blood is not clearly established in older patients. This study evaluated the association between a series of TSH and free T_4 levels and risk of death in older patients with hypothyroidism treated with thyroid hormone.

THE FULL ARTICLE TITLE

Akirov A et al. Elevated TSH in adults treated for hypothyroidism is associated with increased mortality. Eur J Endocrinol 2017;176:57-66. Epub October 19, 2016.

SUMMARY OF THE STUDY

The study included 611 patients 60-80 years old with overt hypothyroidism treated with levothyroxine who were admitted to a hospital between 2011 and 2014. Labs including TSH and free T_4 were collected periodically until the patients died or until the study ended in 2016. Patients were then grouped according to their TSH levels. A TSH level between 0.5-5.0 mIU/L was considered to be in the normal range. The authors found that overall death rate was 34% for all groups combined. More specifically, 28% died in the group with an average TSH of 0.5-2.5 mIU/L, 29% died in the group with an average TSH of 2.5-5.0 mIU/L and 54% died in the group with an average TSH of 5.0-10.0 mIU/L.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that older patients who still had an increased TSH despite being on thyroid hormone had a significantly higher risk of death than those whose TSH remained in the normal range. They also found that the free T_4 level did not influence risk of death. In older adults with hypothyroidism being treated with levothyroxine, physicians should aim for a TSH in the normal range in order to improve patients' survival.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

Hypothyroidism (Underactive): http://www.thyroid.org/hypothyroidism/

Thyroid Disease in the Older Patient: http://www.thyroid.org/thyroid-disease-older-patient/

ABBREVIATIONS & DEFINITIONS

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

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T_4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal.

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.

HYPOTHYROIDISM IN OLDER ADULTS, continued

Thyroxine (T4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

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

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THYROID SURGERY

Many patients who become hypothyroid after lobectomy will recover normal thyroid function

BACKGROUND

In the past, a total thyroidectomy was frequently the operation of choice for thyroid cancer. Currently, risk assessment of the potential of the cancer to recur can be done prior to surgery using the results of the thyroid biopsy and the ultrasound of the neck. Patients with small cancers and with no evidence of abnormal lymph nodes are generally considered low risk and may be managed with a lobectomy instead of a totally thyroidectomy, especially is the opposite lobe is normal. Thyroid lobectomy has advantages over total thyroidectomy in decreasing surgical complications and potentially avoiding the need for lifelong thyroid hormone therapy. The reported incidence of hypothyroidism (low thyroid hormone levels) after lobectomy is approximately 15%. Prior studies have not been uniform in their criteria for starting thyroid hormone therapy or duration of follow-up. This study examined the frequency and risk factors for hypothyroidism after lobectomy for papillary thyroid cancer.

THE FULL ARTICLE TITLES:

Park S et al. Clinical features of early and late postoperative hypothyroidism after lobectomy. J Clin Endocrinol Metab 2017;102:1317-24.

SUMMARY OF THE STUDY

This was a review of patients who underwent thyroid lobectomy for in Seoul, Korea, between 2008 and 2011. Thyroid function tests (TSH and free T_4) were measured 2 to 3 months after surgery. Patients with normal thyroid function had levels checked repeatedly every 6 to 12 months thereafter; patients diagnosed with hypothyroidism were reassessed every 3 to 6 months. Patients with hypothyroidism were treated with levothyroxine. The hypothyroidism group was separated into early (within 12 months after surgery) or late (>12 months after surgery) development. Pre-operative clinical factors including TSH and the presence of thyroid antibodies were assessed as potential predictors for postoperative hypothyroidism.

Of 335 patients who underwent lobectomy, 79.4% were female and the average age was 47.9 years. The average follow-up duration was 56.2 months. The rate of postoperative hypothyroidism was 64.2%. Overt hypothyroidism developed in only 5 patients, while the remaining 210 patients had subclinical hypothyroidism. The average time to diagnosis of hypothyroidism was 4.0 months. Early hypothyroidism developed in two-thirds of patients, while the remaining one-third had late hypothyroidism. Having a TSH level >3.1 mIU/L at 1 year after surgery was predictive of the development of late hypothyroidism. Patients in whom early hypothyroidism developed had higher preoperative TSH levels and an increased rate of positive thyroid peroxidase antibody compared with patients in whom late hypothyroidism developed. Patients who remained euthyroid (normal thyroid levels) had a lower preoperative TSH as compared with patients in whom postoperative hypothyroidism developed.

Of all patients in whom hypothyroidism developed, 40 were treated with levothyroxine. The remaining 175 patients had subclinical hypothyroidism with an average postoperative TSH in the 7 mIU/L range. These patients were followed without thyroid hormone treatment and 68.0% recovered normal thyroid function at an average time interval of 12.2 months. Despite a normal preoperative TSH level in the 2 mIU/L range, 64% of patients who underwent thyroid lobectomy experienced at least temporary post-surgical hypothyroidism. The majority of these patients had subclinical hypothyroidism, and two thirds recovered normal thyroid status. A preoperative TSH level >1.7 mIU/L was predictive of postoperative hypothyroidism and lack of recovery to normal thyroid hormone levels.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The benefits of lobectomy over total thyroidectomy include a decreased risk of surgical complications and the potential to avoid long-term thyroid hormone supplementation. Many patients are very interested in undergoing lobectomy to retain their own thyroid function and avoid the need for long-term medication. The current study will help to inform preoperative counseling about the risk of postoperative hypothyroidism in individual patients.

THYROID SURGERY, continued

This study shows that 64% of patients who undergo lobectomy will develop hypothyroidism, although in the vast majority these patients this will be mild with only a slightly increased TSH (subclinical hypothyroidism). Further, 68% of patients in whom subclinical hypothyroidism developed after surgery recovered normal thyroid function. Thus, patients with subclinical hypothyroidism after lobectomy may benefit from a prolonged period of observation without thyroid hormone therapy to determine whether the reamining lobe will eventually compensate and maintain normal thyroid function. An additional factor to consider is quality of life after surgery, particularly during a period of "subclinical" hypothyroidism. Hypothyroidism (even in the absence of overt symptoms) may contribute to this. Quality of life was not included in the current analysis but will be important to assess in future studies, particularly given the long time interval to recover the normal thyroid status.

— Ronald B. Kuppersmith, MD, FACS

ATA THYROID BROCHURE LINKS

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

Hypothyroidism (Underactive): http://www.thyroid.org/hypothyroidism/

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

ABBREVIATIONS & DEFINITIONS

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

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

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T_4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

Lobectomy: surgery to remove one lobe of the thyroid.

Total thyroidectomy: surgery to remove the entire thyroid gland.

Thyroxine (T4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

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

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THYROID CANCER

Thyroglobulin measurements and neck ultrasound findings in patients with thyroid cancer after total thyroidectomy

BACKGROUND

Thyroid cancer has an excellent prognosis due, in part, to very effective treatment options including surgery, thyroid hormone therapy and radioactive iodine therapy. Papillary and follicular thyroid cancer are the most common types of thyroid cancer and are typically treated initially with thyroidectomy followed by thyroid hormone therapy. After thyroid surgery, patients are divided into low, intermediate and high risk groups based on the severity of the thyroid cancer, whether there is any suspicion of persistent cancer, or whether there is a high risk of the cancer recurring. A thyroglobulin blood test (with thyroglobulin antibody) and neck ultrasound are generally performed to re-evaluate the status of the cancer as part of this risk evaluation and to look for any possible persistent cancer or remaining thyroid tissue. Most of the time, patients in the low risk group are simply monitored by ultrasound. Patients in the intermediate and high risk groups are usually selected to be treated with radioactive iodine. Those treated with radioactive iodine typically have a post-treatment whole body scan.

In this study, the authors reviewed the medical records of thyroid cancer patients who had a total thyroidectomy and radioactive iodine treatment, to evaluate the relationship between thyroglobulin levels, neck ultrasound and whole body radioactive iodine scan (performed after radioactive iodine treatment).

THE FULL ARTICLE TITLE

Matrone A et al. Postoperative thyroglobulin and neck ultrasound in the risk re-stratification and decision to perform 131I ablation. J Clin Endocrinol Metab 2016;Dec 8:jc20162860 [Epub ahead of print].

SUMMARY OF THE STUDY

The medical records of 505 low and intermediate risk thyroid cancer patients who were evaluated a few months after total thyroidectomy at the Endocrine Unit of the University Hospital of Pisa (during the years 2010 to 2011) were reviewed. All patients had a total thyroidectomy and underwent radioactive iodine therapy with 30 mCi of radioactive iodine after receiving recombinant human thyrotropin (rhTSH) preparation. Patients were excluded if they did not receive radioactive iodine (e.g. papillary microcarcinoma without adverse features) or had higher risk thyroid cancer (which was treated with higher dose activities of radioactive iodine). Patients with positive thyroglobulin antibodies (TgAb) (i.e. levels ≥20 U/ml) were also excluded, since thyroglobulin antibodies interfere with accurate measurement of thyroglobulin.

The study population characteristics were described as follows: 71.9% women, average age 47.4 years, 13.3% had central neck lymph node dissection, 53.9% American Thyroid Association Low Risk disease, 41.6% American Thyroid Association Intermediate Risk disease, 97% had surgery in Pisa. Following total thyroidectomy, the following surgical complication rates were reported: 5.7% temporary post-surgical hypoparathyroidism, 7.9% permanent hypoparathyroidism, 0.4% temporary post-surgical vocal cord injury, 1.4% permanent vocal cord injury. All patients took levothyroxine after total thyroidectomy. Following surgery, but before radioactive iodine treatment, the following percentages of patients were reported for each thyroglobulin measurement category (using a high sensitivity thyroglobulin blood test): 29.7% had thyroglobulin measurement <0.1 ng/ml (Group A), 56.8% had thyroglobulin measurement 0.1 to 1 ng/ml (Group B), and 13.5% had thyroglobulin measurement >1 ng/ml (Group C). Of the patients in Group A, 1/150 patients (0.7%) had apparent spread of cancer to the lymph nodes seen on neck ultrasound but not whole body radioactive iodine scan. Of the patients in Group B, 15/285 (5.2%) had apparent spread of cancer to the lymph nodes seen on neck ultrasound, 7 of which were detected only on whole body radioactive iodine scan. In group B, there were 4/285 (1.4%) of patients who had spread of the cancer outside of the neck seen on the whole body radioactive iodine scan. In Group C, 16.2% of patients had spread of cancer to the lymph nodes which were all detected on neck ultrasound.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that highly sensitive thyroglobu-

THYROID CANCER, continued

lin measurements and neck ultrasounds performed a few months after total thyroidectomy are useful in re-evaluating risk level (for persistent cancer) in patients with thyroid cancer. This study shows that patient that have a thyroglobulin <1 ng/ml after surgery have a <5% risk of having persistent thyroid cancer, while those with a thyroglobulin <0.1 ng/ml after surgery have a <1% risk of having persistent thyroid cancer. This study adds to the current knowledge of interpretation of sensitive thyroglobulin measurement after total thyroidectomy for thyroid cancer and helps further identify those patients that will benefit the most with the use of radioactive iodine therapy.

— Anna M. Sawka, MD, PhD

ATA THYROID BROCHURE LINKS

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

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

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

ABBREVIATIONS & DEFINITIONS

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).

Thyroidectomy: surgery to remove the 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, hemithyroidectomy, or lobectomy

Hypoparathyroidism: low calcium levels due to decreased secretion of parathyroid hormone (PTH) from the parathyroid glands next to the thyroid. This can occur as a result of damage to the glands during thyroid surgery and may be temporary, but sometimes it can be permanent. Hypoparathyroidism is generally treated with high dose calcium and vitamin D preparations, often taken multiple times per day.

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

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Thyroglobulin: a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker in patients that do not have thyroglobulin antibodies.

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

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 I-131.

Post- Radioactive iodine Whole Body Scan (post-RAI WBS): the scan done after radioactive iodine treatment that identifies what was treated and if there is any evidence of metastatic thyroid cancer.

THYROID CANCER, continued

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

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

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THYROID CANCER

Recurrence rates in patients with intermediate-risk thyroid cancer are similar after low-dose and high-dose radioactive iodine therapy

BACKGROUND

Current management of thyroid cancer involves a determination of the risk of relapse of the cancer when determining the best treatment plan. Low risk thyroid cancer is usually treated with surgery (total thyroidectomy or lobectomy) and thyroid hormone therapy. Standard treatment for intermediate and high risk thyroid cancer includes surgery, usually a total thyroidectomy, followed by radioactive iodine therapy and thyroid hormone therapy. The radioactive iodine treatment is used to remove any remaining thyroid tissue, both normal and cancerous tissue. The best radioactive iodine dose is still controversial. Prior studies have reported that low-dose radioactive iodine therapy may be just as effective as high-dose therapy in patients with intermediate risk thyroid cancer. However, these studies were different and most patients were followed only for a short period of time. The goal of this study was to evaluate the response to low-dose and high-dose radioactive iodine therapy, including the recurrence rate during long-term follow-up in patients with intermediate risk thyroid cancer.

THE FULL ARTICLE TITLE

Jeong et al. Clinical outcomes of low-dose and high-dose postoperative radioiodine therapy in patients with intermediate-risk differentiated thyroid cancer. Nucl Med Commun. 2017 Mar;38(3):228-233.

SUMMARY OF THE STUDY

This is a study of 204 thyroid cancer patients who had minimal invasion outside the thyroid gland or spread to the lymph nodes in the neck at the time of diagnosis. The patients underwent a total thyroidectomy with or without neck dissection followed by radioactive iodine therapy at two referral hospitals in an iodine-replete area in Korea from 2003 to 2004. A total of 90% of patients were women and the average age was 45 years. The majority (97%) of patients had papillary thyroid cancer while 3% had follicular thyroid cancer. Overall 34% of patients had cancers larger than 2 cm and 60% had spread to the lymph nodes. Of the 204 patients, 80 patients received low-dose radioactive iodine therapy at one center, while 124 patients received high-dose radioactive iodine therapy at the second center. The patients in the low-dose and high-dose groups had similar characteristics with the exception of a higher rate of minimal invasion outside the thyroid gland in the low dose group (90% vs. 76%). All patients underwent thyroid hormone withdrawal for at least 3 weeks and followed a low-iodine diet for 2 weeks before the radioactive iodine treatment. The patients were started on long-term thyroid hormone therapy after the radioactive iodine treatment.

The results of the radioactive iodine therapy were assessed within 2 years after the therapy. A successful treatment was defined as a thyroglobulin level of less than 0.2 ng/ml on thyroid hormone treatment or a stimulated thyroglobulin of less than 1 ng/ml after thyroid hormone withdrawal, a negative neck ultrasound and negative whole body scan (WBS). There was no difference in the radioactive iodine treatment success rate between the low-dose and high-dose groups based on the thyroglobulin measurement and neck ultrasound with a negative whole body scan (45% versus 55%) or without whole body scan results (63% and 61%). However, the rate of incomplete response to radioactive iodine treatment was higher in the low-dose as compared to the high-dose group (25% versus 11%). A total of 18 patients in the low-dose group and 8 patients in the high-dose group received additional radioactive iodine therapy.

The patients were monitored for recurrence with thyroglobulin tests, neck ultrasound and whole body scanning for a average of 10 years. During the follow-up period, 7 patients in the low-dose group (9%) and 7 patients in the high-dose group (6%) developed cancer recurrence. Importantly, all patients with a successful initial radioactive iodine treatment were disease-free during the entire follow-up.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Patients in the low-dose group had higher rates of incomplete response to the initial radioactive iodine

THYROID CANCER, continued

therapy requiring additional radioactive iodine therapy as compared to the high-dose group. The low-dose group may also have a slightly higher recurrence rate during long-term follow-up. These data show that the low-dose radioactive iodine therapy is not sufficient for the treatment of intermediate-risk thyroid cancer patients.

— Alina Gavrila, MD, MMSC

ATA THYROID BROCHURE LINKS

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

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

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

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancer: includes papillary (the most common) and follicular thyroid cancer.

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

Total thyroidectomy: surgery to remove the entire thyroid gland.

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

Thyroid hormone withdrawal: this is used to produce high levels of TSH in patients by stopping thyroid hormone pills and causing short-term hypothyroidism. This is mainly used in thyroid cancer patients before treating with radioactive iodine or performing a whole body scan.

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

Neck lymph node dissection: systematic removal of an entire group of lymph nodes from the neck to treat lymph node metastasis.

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

Stimulated thyroglobulin testing: this test is used to measure whether there is any cancer present in a patient that has previously been treated with surgery and radioactive iodine. TSH levels are increased, either by withdrawing the patient from thyroid hormone or treating the patient with recombinant human TSH (Thyrogen), then levels of thyroglobulin are measured. Sometimes this test is combined with a whole body iodine scan.

Diagnostic whole body scans: these radioactive iodine scans are performed under TSH stimulation, either after thyroid hormone withdrawal or after injections of recombinant human TSH, and usually include measuring serum thyroglobulin levels.

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THYROID CANCER

Surgery for neck recurrence of thyroid cancer can achieve complete remission in a majority of patients

BACKGROUND

Thyroid cancer is the fastest rising cancer in women. Because the overall prognosis in patients with thyroid cancer is excellent, management of thyroid cancer is based on the risk of cancer recurrence as opposed to the risk of dying of cancer. The most common site of cancer recurrence is in the lymph nodes in the neck. Frequently, surgery is the best treatment for cancer recurrence in the neck lymph nodes and offers many patients a chance for cure. The author's goals were to evaluate how good the initial operation was to prevent recurrence/persistence of cancer, to determine prognostic factors for who would have a cancer recurrence, and to look at the long-term outcomes of reoperation at a single institution in France.

THE FULL ARTICLE TITLE

Lamartina L et al Surgery for neck recurrence of differentiated thyroid cancer: outcomes and risk factors. J Clin Endocrinol Metab 2017;102:1020-31.

SUMMARY OF THE STUDY

All patients in this study had thyroid cancer, were treated with total thyroidectomy with or without neck dissection, and had post-operative radioactive iodine therapy. Each patient in the study later developed a recurrence of the cancer in the neck with no evidence of spread of the cancer outside of the neck and had a re-operation for that recurrence.

A total of 157 patients over an 18 year period had a neck re-operation for cure at a single institution in France. Many patients were young (average age was 35 years) and more than 60% were women. More than 2/3 (71%) had previously had a neck dissection as part of their initial operation and 25% of the cancers were of an aggressive type. Immediately after the re-operation, 63% had a complete response and the complication rates of reoperation were low. Of these, at least 25% experienced a second recurrence of their cancer within 5 years. Risk factors for non-cure at re-operation included age > 45 years, aggressive cancer type and a lymph node dissection as part of the initial surgery. Risk factors for a second recurrence included male sex, aggressive cancer type and >10 positive lymph nodes at rep-operation. At long-term follow-up, just overhalf of patients with a first recurrence were free of disease.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that after the first re-operation for persistent or recurrent thyroid cancer, just over 50% were free of disease and apparently cured. This study shows that surgery for an initial recurrence can produce long-lasting cures in many patients and therefore is a good approach to treatment. Moreover, certain risk factors for non-cure were identified that would be important for counseling patients about long-term prognosis.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

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

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

THYROID CANCER, continued

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

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

ATA Alliance for Thyroid Patient Education

GOAL

The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases.

We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.

WHO WE ARE (in alphabetical order)

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

BITE ME CANCER
http://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

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.
www.thyca.org
(Toll-free): 877-588-7904
thyca@thyca.org

THYROID CANCER CANADA
www.thyroidcancercanada.org
416-487-8267
info@thyroidcancercanada.org

THYROID FEDERATION INTERNATIONAL
www.thyroid-fed.org
tfi@thyroid-fed.org

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Light of Life Foundation
checkyourneck.com

GRAVES' DISEASE & THYROID FOUNDATION

Thyroid Federation International

BITE ME CANCER!

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

Thyroid Cancer Canada
Cancer de la thyroïde Canada

Graves' Disease

WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is located in the lower front of the neck. The thyroid makes thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormones help the body use energy, stay warm and keep the brain, heart, muscles, and other organs working appropriately.

WHAT IS GRAVES' DISEASE?

Graves' disease is an autoimmune disease that leads to a generalized overactivity of the entire thyroid gland (*hyperthyroidism*). It is the most common cause of hyperthyroidism in the United States. It is named after Robert Graves, an Irish physician, who described this form of hyperthyroidism about 150 years ago. It is 7-8 times more common in women than men.

WHAT CAUSES GRAVES' DISEASE?

Graves' disease is triggered by a process in the body's immune system, which normally protects us from foreign invaders such as bacteria and viruses. The immune system destroys foreign invaders with substances called antibodies produced by blood cells known as lymphocytes. Sometimes the immune system can be tricked into making antibodies that cross-react with proteins on our own cells. In many cases these antibodies can cause destruction of those cells. In Graves' disease these antibodies (called the thyrotropin receptor antibodies (TRAb) or thyroid stimulating immunoglobulins (TSI) do the opposite – they cause the cells to work overtime. The antibodies in Graves' disease bind to receptors on the surface of thyroid cells and stimulate those cells to overproduce and release thyroid hormones. This results in an overactive thyroid (*hyperthyroidism*).

WHAT ARE THE SYMPTOMS OF GRAVES' DISEASE?

- *Hyperthyroidism*

  The majority of symptoms of Graves' disease are caused by the excessive production of thyroid hormones by the thyroid gland (see *Hyperthyroidism brochure*). These may include, but are not limited to, racing heartbeat, hand tremors, trouble sleeping, weight loss, muscle weakness, neuropsychiatric symptoms and heat intolerance.

- *Eye disease*

  Graves' disease is the only kind of hyperthyroidism that can be associated with inflammation of the eyes, swelling of the tissues around the eyes and bulging of the eyes (called *Graves' ophthalmopathy or orbitopathy*). Overall, a third of patients with Graves' disease develop some signs and symptoms of Graves' eye disease but only 5% have moderate-to-severe inflammation of the eye tissues to cause serious or permanent vision trouble. Patients who have any suggestion of eye symptoms should seek an evaluation with an eye doctor (an ophthalmologist) as well as their endocrinologist.

  Eye symptoms most often begin about six months before or after the diagnosis of Graves' disease has been made. Seldom do eye problems occur long after the disease has been treated. In some patients with eye symptoms, hyperthyroidism never develops and, rarely, patients may be hypothyroid. The severity of the eye symptoms is not related to the severity of the hyperthyroidism.

  Early signs of trouble might be red or inflamed eyes, a bulging of the eyes due to inflammation of the tissues behind the eyeball or double vision. Diminished vision or double vision are rare problems that usually occur later, if at all. We do not know why, but problems with the eyes occur much more often and are more severe in people with Graves' disease who smoke cigarettes.

- *Skin disease*

  Rarely, patients with Graves' disease develop a lumpy reddish thickening of the skin in front of the shins known as pretibial myxedema (called Graves' dermopathy). This skin condition is usually painless and relatively mild, but it can be painful for some. Like the eye trouble of Graves' disease, the skin problem does not necessarily begin precisely when the hyperthyroidism starts. Its severity is not related to the level of thyroid hormone.

Graves' Disease

HOW IS THE DIAGNOSIS OF GRAVES' DISEASE MADE?

The diagnosis of hyperthyroidism is made on the basis of your symptoms and findings during a physical exam and it is confirmed by laboratory tests that measure the amount of thyroid hormones (thyroxine, or T4, and triiodothyronine, or T3) and thyroid-stimulating hormone (TSH) in your blood (see the *Hyperthyroidism brochure*). Clues that your hyperthyroidism is caused by Graves' disease are the presence of Graves' eye disease and/or dermopathy (see above), a symmetrically enlarged thyroid gland and a history of other family members with thyroid or other autoimmune problems, including type 1 diabetes, rheumatoid arthritis, pernicious anemia (due to lack of vitamin B12) or painless white patches on the skin known as vitiligo.

The choice of initial diagnostic testing depends on cost, availability and local expertise. Measurement of antibodies, such as TRAb or TSI, is cost effective and if positive, confirms the diagnosis of Graves' disease without further testing needed. If this test is negative (which can also occur in some patients with Graves' disease), or if this test is not available, then your doctor should refer you to have a radioactive iodine uptake test (RAIU) to confirm the diagnosis.

Also, in some patients, measurement of thyroidal blood flow with ultrasonography may be useful to establish the diagnosis if the above tests are not readily available.

HOW IS GRAVES' DISEASE TREATED?

The treatment of hyperthyroidism is described in detail in the *Hyperthyroidism brochure*. All hyperthyroid patients should be initially treated with beta-blockers. Treatment options to control Graves' disease hyperthyroidism include antithyroid drugs (generally methimazole [Tapazole®], although propylthiouracil [PTU] may be used in rare instances such as the first trimester of pregnancy), radioactive iodine and surgery.

Antithyroid medications are typically preferred in patients who have a high likelihood of remission (women, mild disease, small goiters, negative or low titer of antibodies). These medications do not cure Graves' hyperthyroidism, but when given in adequate doses are effective in controlling the hyperthyroidism.

If methimazole is chosen, it can be continued for 12-18 months and then discontinued if TSH and TRAb levels are normal at that time. If TRAb levels remain elevated, the chances of remission are much lower and prolonging treatment with antithyroid drugs is safe and may increase chances of remission. Long term treatment of hyperthyroidism with antithyroid drugs may be considered in selected cases.

If your hyperthyroidism due to Graves' disease persists after 6 months, then your doctor may recommend definitive treatment with either radioactive iodine or surgery.

If surgery (thyroidectomy) is selected as the treatment modality, the surgery should be performed by a skilled surgeon with expertise in thyroid surgery to reduce the risk of complications.

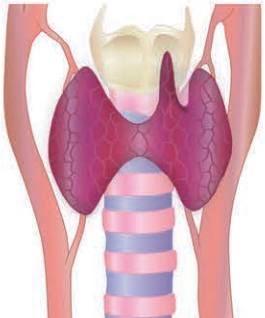
Your doctor should discuss each of the treatment options with you including the logistics, benefits and potential side effects, expected speed of recovery and costs. Although each treatment has its advantages and disadvantages, most patients will find one treatment plan that is right for them. Hyperthyroidism due to Graves' disease is, in general, controllable and safely treated and treatment is almost always successful.

WHAT WILL BE THE OUTCOME OF TREATMENT?

If you receive definitive treatment for your Graves' hyperthyroidism (such as radioactive iodine or surgery), you will eventually develop hypothyroidism (underactive thyroid). Even if you are treated with antithyroid drugs alone, hypothyroidism can still occur. Your doctor will check your *thyroid function tests* frequently to assess thyroid function following treatment. When hypothyroidism occurs, you will need to take a thyroid hormone tablet once a day at the right dose (see *Hypothyroidism brochure*).

OTHER FAMILY MEMBERS AT RISK

Graves' disease is an autoimmune disease and has a genetic predisposition. However, no specific gene has been identified for screening to date.



FURTHER INFORMATION

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

For information on thyroid patient support organizations, please visit the *Patient Support Links* section on the ATA website at *www.thyroid.org*