Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

EDITOR'S COMMENTS

Welcome to another issue of *Clinical Thyroidology for the Public*. In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through Twitter at @thyroidfriends and on Facebook. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the **Alliance for Thyroid Patient Education**. The **Alliance** member groups consist of: the *American Thyroid Association, Bite Me Cancer, the Graves' Disease and Thyroid Foundation, the Light of Life Foundation, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International*.

We invite all of you to join our **Friends of the ATA** community. It is for you that the American Thyroid Association (ATA) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA is a 501(c)3 nonprofit organization and your gift is tax deductible.

The Covid-19 pandemic has caused an unprecedented upheaval in our daily lives and presented extremely difficult challenges to our healthcare system. There is a lot of information circulating around. We at the American Thyroid Association would like to make sure that you all have access to most accurate, reliable, fact-based and updated information. (https://www.thyroid.org/covid-19/)

December is Thyroid and Development Awareness month.

In this issue, the studies ask the following questions:

- Are there racial disparities in thyroid surgery?
- Does RAI therapy affect the chances for future pregnancy?
- Are the current ATA guidelines for RAI therapy in thyroid cancer patients being followed?
- Do the ATA guidelines help identify missed cancers after a benign biopsy?
- Are routine pre-op chest CT scans needed?
- Does levothyroxine after a heart attack in patients who have mild hypothyroidism affect heart function?

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

THYROID SURGERY

Racial disparities in thyroid surgery

BACKGROUND

Recent protests over police brutality, as well as the COVID-19 pandemic, have brought to attention the systemic racism that pervades all sectors of our society, including the practice of medicine. No exception exists in endocrinology, where racial inequity is found in many areas, most notably in diabetes care and management.

Thyroid surgery is a commonly used treatment for many non-cancerous thyroid conditions such as goiter, thyroid nodules and Graves' disease. There is already evidence that there are gender, socioeconomic and racial disparities when looking at patients who had thyroid surgery for thyroid cancer or parathyroid disease, with non-white patients having worse outcomes than white patients. In this study, the authors sought to understand whether racial inequalities exist in outcomes after surgery for these conditions.

THE FULL ARTICLE TITLE

Maduka RC et al 2020 Racial disparities in surgical outcomes for benign thyroid disease. Am J Surg. Epub 2020 Jul 6. PMID: 32669203.

SUMMARY OF THE STUDY

This study was done by reviewing data collected by the American College of Surgeons National Surgical Quality Improvement Program. This is a database which collects information specific to outcomes after all types of surgery from multiple participating institutions. The population studied consisted of adults older than 17 years old, who had thyroid surgery for a condition other than cancer in the United States, from 2016 to 2017. Data collected regarding the patients demographics included race (Asian, Black, Hispanic, White and other/unknown), sex, age group, body-mass index, previous neck surgery, and the reason for surgery. Outcomes included neck hematoma, injury to the recurrent laryngeal nerve, low blood calcium levels causing symptoms and other general surgery complications.

There were 6187 patients included, the majority of whom were female (81.3%), non-Hispanic white (55%), 40-65 years of age (56.5%) and obese (48%). The majority (92.4%) did not have a previous neck surgery and presented with a goiter (65%). Overall, the rates of complications were low. The most common complication was injury to the recurrent laryngeal nerve in 357 patients (5.2%), followed by a low blood calcium which caused severe symptoms in 336 (4.9%), neck hematoma (2%) and other general complications not specific to thyroid surgery in 128 (1.9%).

Black patients had the highest incidence of neck hematoma (3.1% vs 1.3% in white patients, recurrent laryngeal nerve injury (8.7% vs 4.3%) and other surgical complications. These differences were statistically significant. Hispanic patients had the most incidence of a low blood calcium which caused severe symptoms, but the difference with other ethnicities was not statistically significant.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The conclusion of this study is that Blacks who have thyroid surgery for a non-cancerous condition have a higher risk for neck hematoma, recurrent laryngeal nerve injury and other general surgical complications than White patients. In addition, relative to Whites, Asians have a higher risk for recurrent laryngeal nerve injury.

The causes for these disparities are many, and include a more advanced disease at presentation, access to care, surgeon experience, health literacy and patient mistrust of the health care system. However, many studies have shown that differences in management of thyroid diseases may be contributing to these poorer outcomes in multiple ways. While there are limitations, the strength of this study is its large sample of more than 6800 patients. It highlights the work that needs to be done at understanding all causes of disparities and addressing them in order to improve delivery of health care that results in better outcomes for all patients, regardless of their race.

— Jessie Block-Galarza, MD

THYROID SURGERY, continued

ATA THYROID BROCHURE LINKS

Thyroid Surgery: https://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.

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.

Neck hematoma: surgical complication where there is bleeding at the site of the incision along with the formation of a blood clot. Most of the time, these are very small but occasionally they are large enough to require returning to the operating room to remove the hematoma.

Recurrent laryngeal nerve: this nerve serves to control the vocal cords and injury to this nerve causes hoarseness. This nerve is located right next to the thyroid on both sides and much of the time during thyroid surgery is spent trying to identify and protect the nerve from injury.

Goiter: a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a nodular goiter; if there is more than one nodule it is called a multinodular goiter.

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

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

THYROID AND PREGNANCY

Radioactive iodine therapy for the most common types of thyroid cancer does not decrease pregnancy chances in women

BACKGROUND

The number of patient diagnosed with thyroid cancer has been increasing worldwide over the last 10-20 years, including in young adults 15 to 39 years of age. The most common types of thyroid cancer are papillary and follicular thyroid cancers. These cancers are generally treated with surgery, and some patients may need radioactive iodine therapy to destroy any remaining thyroid tissue afterwards. Because patients with thyroid cancer generally do well without recurrence, and radioactive iodine therapy may have potential complications long-term, there is a trend to avoid radioactive iodine therapy unless cancer is aggressive. Indeed, current American Thyroid Association guidelines for the management of thyroid cancer do not recommend radioactive iodine therapy for low risk patient.

Radioactive iodine therapy can potentially affect a woman's fertility, or ability to become pregnant, long-term. A previous review of original studies in 2011 was limited because of small number of studies available. Blood anti-Müllerian hormone (AMH) levels are frequently used to assess ovarian reserve in women undergoing infertility treatment, as it is associated with the number of eggs obtained as a part of treatment. Recently, AMH levels have also been used to study how many eggs are available for future pregnancy in women treated for cancer. The current study reviewed original research studies to assess the potential effect of radioactive iodine therapy for thyroid cancer on fertility among young women.

THE FULL ARTICLE TITLE

Piek MW et al 2020 The effect of radioactive iodine therapy on ovarian function and fertility in female thyroid cancer patients: A systematic review and meta-analysis. Thyroid. Epub 2020 Nov 2. PMID: 33012254.

SUMMARY OF THE STUDY

A total of 22 original studies, including 36,215 patients, on the effects of radioactive iodine therapy treatment for thyroid cancer on female reproductive system were selected from a search of medical literature databases, including PubMed, Embase, and Web of Science. The effects of radioactive iodine therapy treatment on menstrual cycles and timing of menopause were reviewed. A meta-analysis, which combines the results of several studies, was done to assess the effects of radioactive iodine therapy on differences in pregnancy rate and AMH levels after radioactive iodine use.

A total of 4 studies showed that women who received radioactive iodine therapy were more likely to have irregular periods that would normalize within the first year, compared to women who did not receive radioactive iodine therapy (12-31% vs 15%). Women who received radioactive iodine therapy underwent menopause at slightly younger age than women who did not receive radioactive iodine therapy (49.5 vs. 51 years). The meta-analysis of these 4 studies showed that blood AMH levels decreased by an average of 1.5 ng/ml after 1 year of radioactive iodine therapy. If a patient was 35 years or older, she may have a higher degree of decrease in AMH level from baseline, compared to a patient younger than 35 years of age. However, the meta-analysis showed that there was no significant difference in pregnancy rates at 4-6 years of follow up between patients who received radioactive iodine therapy and those who did not.

In conclusion, this study showed that radioactive iodine therapy for thyroid cancer in young women appears to be associated with a short-term menstrual irregularities and decrease in blood AMH levels after 1 year. However, these do not appear to affect the pregnancy rates long-term.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Based on the findings of this study, radioactive iodine therapy for thyroid cancer in young women does not appear to affect the ability to become pregnant long-term. However, it is still recommended for women to wait 6

THYROID AND PREGNANCY, continued

to 12 months after radioactive iodine therapy before becoming pregnant due to the radiation exposure to the ovaries. This is also consistent with the decrease in AMH levels over 1 year after radioactive iodine therapy. This is more common in older women. Thus, women who are interested in pregnancy after treatment for thyroid cancer should have discussion regarding their pregnancy plans with their endocrinologists before radioactive iodine therapy.

— Sun Lee, MD

ATA THYROID BROCHURE LINKS

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

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

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

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).

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

Anti-Müllerian Hormone (AMH): a glycoprotein hormone that is made in the reproductive tissues of both males and females. In women, AMH levels can provide information about fertility, the ability to get pregnant. AMH level is often used to check a woman's ability to produce eggs that can be fertilized for pregnancy.

Meta-analysis: a study that combines and analyzes the data from several other studies addressing the same research hypothesis

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.

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.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

THYROID CANCER

Declining frequency and variability of radioactive iodine therapy for thyroid cancer suggests increasing adoption of evidence-based guidelines

BACKGROUND

Standard treatment for the most common types of thyroid cancer includes surgery to remove the thyroid (thyroidectomy) followed in some instances by radioactive iodine therapy. Early American Thyroid Association (ATA) guidelines recommended total thyroidectomy followed by radioactive iodine therapy in nearly all patients with thyroid cancer. Therefore, radioactive iodine therapy increased significantly from the 1970s to the early 2000s. The more recent ATA guidelines from 2006, updated in 2009 and then 2015, have recommended progressively a more selective use of radioactive iodine therapy, based on growing research evidence that many patients with thyroid cancer are at very low risk for complications and recurrence of the cancer. These low risk patients may not benefit from radioactive iodine therapy, which has its own risks and significantly increases health care costs. Currently, radioactive iodine therapy is not recommended for low risk thyroid cancer patients and is reserved for high risk patients after total thyroidectomy and for certain intermediate risk patients. The aim of this study was to analyze trends in radioactive iodine therapy use in the United States after the introduction of the new thyroid cancer treatment guidelines.

THE FULL ARTICLE TITLE

Jacobs D et al 2020 Changes in population-level and institutional-level prescribing habits of radioiodine therapy for papillary thyroid cancer. Thyroid. Epub 2020 Sep 22. PMID: 32811347.

SUMMARY OF THE STUDY

The study included 273,046 patients from the National Cancer Database who were diagnosed with papillary thyroid cancer and underwent total thyroidectomy between 2004 and 2016. The patients were divided in three groups: (i) patients for whom radioactive iodine therapy was recommended, (ii) patients for whom radioactive iodine therapy was not recommended and (iii) patients for whom selective use of radioactive iodine therapy was recommended, based on the 2009 ATA practice guidelines. According to these guidelines, radioactive iodine therapy treatment was recommended for patients with at least 1 of the following criteria: 45 years or older with a cancer size larger than 4 cm, extensive cancer extension outside the thyroid, residual cancer after surgery, or spread of cancer outside of the neck. Radioactive iodine therapy was not recommended for patients with thyroid cancer smaller than 1 cm without spread to the lymph nodes or other tissues in the neck or spread outside of the neck. Selective radioactive iodine therapy use was recommend for other patients outside of these criteria.

The overall radioactive iodine use in papillary thyroid cancer patients decreased from 61% between 2004 and 2007 to 44% in 2016. The use rate declined by 2% per year starting in 2007. In patients for whom radioactive iodine therapy was not recommended, two significant time points were noted: a 4.7% decrease in radioactive iodine use per year starting in 2008 and then a 2% decrease per year starting in 2011. A decline in radioactive iodine use was also noted in patients for whom the treatment was recommended and selectively recommended (0.53% fewer patients per year and 2.3% fewer patients per year, respectively). In 2015, radioactive iodine was administered to 72%, 53% and 9.5% of patients for whom radioactive iodine therapy was recommended, selectively recommended, and not recommended.

When analyzing individual hospitals, there was a greater reduction in radioactive iodine use for patients for whom radioactive iodine therapy was not recommended or was selectively recommended at high-volume institutions (>75th percentile) as compared to low-volume institutions (<25th percentile). The rate of radioactive iodine therapy use was lower at institutions on the East Coast of the

THYROID CANCER, continued

United States than other geographic areas. The variability in radioactive iodine therapy use between hospitals declined over time.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

National and individual hospital data show a progressive reduction in radioactive iodine therapy use in thyroid cancer patients and more consistent use across hospitals in the United States in the period 2004–2016. These findings suggest acceptance and clinical application of changing evidence and evidence-based guidelines for radioactive iodine therapy administration in thyroid cancer patients during this time.

— Alina Gavrila, MD, MMSc

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer (PTC): 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.

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).

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

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells. Thyroid cancer can spread in the lymph nodes located in the neck.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

THYROID NODULES

Initial ATA risk and subsequent growth helps identify missed cancers in initially benign thyroid nodules

BACKGROUND

Thyroid nodules are common, and it is important to separate those that are benign (noncancerous) from those that are cancerous. Neck ultrasound and thyroid aspiration biopsy are two techniques used to evaluate whether a given thyroid nodule could be a cancer. In 2015 the American Thyroid Association (ATA) published an ultrasound risk stratification system to identify concerning ultrasound features of thyroid nodules, which should be followed by a thyroid biopsy when present. Biopsy cytology results are classified into one of several categories, each of which is linked with a different risk of cancer. Cytology that is suspicious for cancer usually leads to surgery, whereas benign nodules are monitored with periodic neck ultrasound. However, since thyroid biopsy only samples a few cells within a thyroid nodule, there is a possible risk (<5%) of missing a cancer, even when the biopsy is benign. This concern is even more relevant when thyroid nodules grow in size since growth has traditionally been a warning for cancer. However, several recent studies question this assumption and suggest that a benign nodule's growth is not concerning for cancer. The 2015 ATA guidelines recommend repeating a biopsy in a benign nodule only when it grows or develops suspicious ultrasound characteristics.

In this study, the authors evaluate the accuracy of the ATA guidelines in monitoring benign thyroid nodules for growth and indications to repeat a biopsy.

THE FULL ARTICLE TITLE

Maino F et al 2020 Validation of American Thyroid Association ultrasound risk-adapted approach for repeating cytology in benign thyroid nodules. Thyroid. Epub 2020 Jul 27. PMID: 32718278.

SUMMARY OF THE STUDY

The authors studied 1010 thyroid nodules with benign cytology from 838 patients attending a single medical center in Italy (82.1% female and 17.9% male). All of the nodules had a second ultrasound and biopsy after an average follow-up of 3.8 years. They then compared the results from the first ultrasound and biopsy with the second. The repeat biopsy result was again benign in 976 cases (96.6%), while 31 (3.1%) were re-classified as indeterminate, and 3 (0.3%) were suspicious for cancer or cancer. Of the 976 cases with a second benign cytology, 71 eventually had surgery and only 1 of those (1.4%) was cancer. In contrast, 11 of the nodules that were re-classified as indeterminante had surgery, and 6 (54.5%) were cancer. All 3 of the nodules re-classified as suspicious for cancer had surgery and they were all cancer. A total of 69.7% of nodules had low-risk findings on the initial ultrasound, whereas 19.4% had intermediate and 10.9% had high-risk results. While the rate of missed cancer in the whole group of nodules was only 1.0%, it did increase according to the ultrasound risk (0.8% missed cancers in the with low-risk findings on initial ultrasound, 1.2% with intermediate and 3.1% with high-risk results).

Most importantly, when the authors compared nodules that grew over time with those that did not, the risk of missing a cancer was significantly more common in nodules with high-risk ultrasound findings to begin with (6.4%). Only 0.4% of nodules that grew in size were cancerous when the initial ultrasound findings were low-risk.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Overall, it is rare to miss a thyroid cancer when cytology from a thyroid cancer is benign, since it happened only 1.0% of the time in the current study. Even when nodules grow, it is only of concern in those with high-risk findings on the initial ultrasound. A second biopsy may be avoided when a thyroid nodule grows in size as long as it had low-risk results on the initial ultrasound.

— Philip Segal, MD

THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

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

Thyroid Nodules: https://www.thyroid.org/thyroid-nodules/

ABBREVIATIONS & DEFINITIONS

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.

Thyroid nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid fine needle aspiration biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Suspicious thyroid biopsy: this happens when there are atypical cytological features suggestive of, but not diagnostic for malignancy. Surgical removal of the nodule is required for a definitive diagnosis.

Indeterminate thyroid biopsy: this happens a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% of biopsies and often results in the need for surgery to remove the nodule.

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

THYROID CANCER

Routine preoperative chest CT does not identify distant metastases in papillary thyroid microcarcinoma

BACKGROUND

Thyroid cancer is one of the fastest rising cancers in the United States. A large part of this increase is a rise in the number of small thyroid cancers <1 cm, termed microcarcinomas. Imaging studies that include the neck region are a big reason these microcarcinomas are being identified. Importantly, not all of these microcarcinomas require surgery as it is increasingly recognized that patients with papillary microcarcinomas can be monitored with periodic ultrasound exams. This is called active surveillance. However, it is known that a very tiny number of patients with these microcarcinomas can spread outside of the thyroid. This study was done to see if there was any evidence that routine chest computerized tomography (CT) scans could identify patients with papillary microcarcinomas who develop spread of the cancer to the lungs.

THE FULL ARTICLE TITLE

Kawano S et al. 2020 Routine chest computed tomography at presentation does not identify distant metastasis in cT1aN0 papillary thyroid carcinoma. Thyroid. Epub 2020 May 27. PMID: 32368954.

SUMMARY OF THE STUDY

The study comes from a major thyroid center in Japan. They routinely do chest CT scans without contrast on patients with papillary thyroid cancer prior to surgery. They looked back on 1000 patients from January 2006 and May 2012 who had papillary thyroid cancer on biopsy and who were confirmed to have cancers <1 cm in size at the time of surgery – thus confirmed to have papillary thyroid microcarcinoma. While monitoring patients with papillary thyroid microcarcinoma was very common at this center, these patients had surgery for different reasons, including known suspicious lymph nodes, Graves' disease, an enlarging nodule while under active surveillance, patient or physician preference or co-existing hyperparathyroidism.

The study consisted of 885 females and 115 males with an average age of 55 years (range: 16–84 years). The average cancer size was 8 mm (range: 2–10 mm). Only 326 patients had any abnormality noted on CT. Of those, only 36 required any further evaluation and of those only 9 required surgical evaluation with the finding of 4 lung cancers and a pulmonary artery aneurysm requiring surgery. No one was found to have the spread of thyroid cancer to the lungs.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that for patients with papillary thyroid microcarcinoma, routine chest CT scans are not necessary prior to surgery or if they plan for active surveillance. The risk of developing spread to the lungs from papillary thyroid microcarcinoma is so low that patients should not be subjected to unnecessary costs, radiation exposure or unnecessary testing resulting from incidental findings.

— Marjorie Safran, MD

ATA THYROID BROCHURE LINKS

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

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

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

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

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.

Active surveillance: the term for avoiding surgery for small thyroid cancers by monitoring them over time with ultrasound and physical exam

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

HYPOTHYROIDISM

Levothyroxine does not affect heart function after a heart attack in patients who have mild hypothyroidism

BACKGROUND

Subclinical hypothyroidism is a milder form of hypothyroidism, when the TSH is elevated but the thyroid hormone levels are still normal. Patients with TSH levels less than 10 mIU/L have the mildest form. Even at these levels, prior studies suggest that patients with subclinical hypothyroidism are at higher risk for heart disease and they are more likely to die after a heart attack compared to someone without thyroid disease. However, we do not know whether treatment with thyroid hormone would decrease this risk.

The heart pumps blood to the rest of the body out of a large chamber called left ventricle. The left ventricular ejection fraction is the percentage of blood that leaves the left ventricle when it contracts. It is a good measure of heart function. Patients who have weaker left ventricle function after having a heart attack are more likely to die or to have difficulty recovering.

This study was designed to find out whether levothyroxine treatment would improve left ventricular function after having a heart attack in patients with subclinical hypothyroidism.

THE FULL ARTICLE TITLE

Jabbar A et al 2020 Effect of levothyroxine on left ventricular ejection fraction in patients with subclinical hypothyroidism and acute myocardial infarction: a randomized clinical trial. JAMA 324:249–258. PMID: 32692386.

SUMMARY OF THE STUDY

The study was done in United Kingdom at 6 hospitals. Patients who presented with a heart attack and had persistent mild hypothyroidism were studied. Inclusion criteria were age greater than 18 years and TSH levels more than 4 mIU/L and less than 10 mIU/L with normal thyroid hormone level on 2 occasions 7-10 days apart. Patients were given either levothyroxine or placebo (sugar/dummy pill) for 52 weeks. Levothyroxine was started within 21 days after the heart attack. Starting dose was 25 mcg and the dose was adjusted to keep the TSH between 0.4 to 2.5 mIU/L.

Left ventricular ejection fraction (LVEF) was measured with an MRI and the MRI was repeated after 52 weeks to see the effect of treatment. Researchers also assessed LV volume, size of the damage to heart muscle, health status, depression, and quality of life.

A total of 2147 patients were potentially eligible. Of these, 314 (16%) had subclinical hypothyroidism when they were admitted. Many of these patients had normal levels when the test was repeated 7- 10 days later. Ultimately, 95 patients qualified for the study and 39 levothyroxine-treated and 46 placebo-treated patients completed the study.

TSH levels were improved to a lower range in the levothyroxine-treated group. The LVEF improved in all patients at the end of 52 weeks without a difference in the treatment groups. Levothyroxine treatment did not improve any of the measured outcomes including quality of life and depression. One patient in each group died and there was no difference in adverse events between the groups.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In conclusion, levothyroxine treatment for 52 weeks did not help to improve LVEF in patients who had a heart attack and had mild subclinical hypothyroidism. Further studies are needed to find out whether treatment would help patients with more severe disease with TSH levels above 10 mIU/L or if treatment is started earlier.

Patients who have initial TSH elevation should have a repeat measurement in a few weeks since the levels frequently improve without treatment. It was also reassuring that treatment with levothyroxine did not increase the risk of any adverse event.

— Ebru Sulanc, MD

HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

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.

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

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

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

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

Volume 13 | Issue 12 | December 2020

Clinical Thyroidology® for the Public

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.

ATA® *Optimal Thyroid Health for All*

Graves' Disease & Thyroid Foundation

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

Light of Life Foundation
checkyourneck.com

Bite Me Cancer

MCT8 - AHDS Foundation

Thyroid Cancer Alliance

Thyroid Cancer Canada
Cancer de la thyroïde Canada

Thyroid Federation International

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

Bite Me Cancer
www.bitemecancer.org
info@bitemecancer.org

Graves' Disease and Thyroid Foundation
www.gdatf.org
(Toll-free): 877-643-3123
info@ngdf.org

Light of Life Foundation
www.checkyourneck.com
info@checkyourneck.com

MCT8 – AHDS Foundation
mct8.info
Contact@mct8.info

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

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

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

Thyroid Federation International
www.thyroid-fed.org
tfi@thyroid-fed.org

AMERICAN THYROID ASSOCIATION®

Optimal Thyroid Health for All

Connect with the ATA on Social Media

Facebook: American Thyroid Association, ATA Women in Thyroidology, American Thyroid Association Trainees

Twitter: @AmThyroidAssn, @thyroidfriends, @clinicalthyroid, @VEndocrinology, @thyroidjournal

LinkedIn: American Thyroid Association

Pinterest: americanthyroidassociation

Instagram: amthyroidassn

www.thyroid.org

AMERICAN THYROID ASSOCIATION
ATA | Founded 1923

Friends of the ATA

FOUNDED 2005

Get the latest thyroid health information. You'll be among the first to know the latest cutting-edge thyroid research that is important to you and your family.

Become a Friend of the ATA!
Subscribe to *Friends of the ATA e-news*

By subscribing to *Friends of the ATA Newsletter*, you will receive:

- *Friends of the ATA e-news*, providing up-to-date information on thyroid issues, summaries of recently published articles from the medical literature that covers the broad spectrum of thyroid disorders., and invitations to upcoming patient events
- Updates on the latest patient resources through the ATA website and elsewhere on the world wide web
- Special e-mail alerts about thyroid topics of special interest to you and your family

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

www.thyroid.org

AMERICAN THYROID ASSOCIATION
ATA | *Founded 1923*

Donate Now!

JOIN US

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

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

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

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

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

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

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

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

Hypothyroidism in Pregnancy

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 hormones help the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

WHAT ARE THE NORMAL CHANGES IN THYROID FUNCTION ASSOCIATED WITH PREGNANCY?

HORMONE CHANGES. Thyroid function tests change during normal pregnancy due to the influence of two main hormones: human chorionic gonadotropin (hCG) and estrogen. Because hCG can weakly stimulate the thyroid, the high circulating hCG levels in the first trimester may result in a low TSH that returns to normal throughout the duration of pregnancy. Estrogen increases the amount of thyroid hormone binding proteins, and this increases the total thyroid hormone levels but the "Free" hormone (the amount that is not bound and can be active for use) usually remains normal. The thyroid is functioning normally if the TSH and Free T4 remain in the trimester-specific normal ranges throughout pregnancy.

THYROID SIZE CHANGES. The thyroid gland can increase in size during pregnancy (enlarged thyroid = goiter). However, pregnancy-associated goiters occur much more frequently in iodine-deficient areas of the world. It is relatively uncommon in the United States. If very sensitive imaging techniques (ultrasound) are used, it is possible to detect an increase in thyroid volume in some women. This is usually only a 10-15% increase in size and is not typically apparent on physical examination by the physician. However, sometimes a significant goiter may develop and prompt the doctor to measure tests of thyroid function (see *Thyroid Function Test Brochure*).

WHAT IS THE INTERACTION BETWEEN THE THYROID FUNCTION OF THE MOTHER AND THE BABY?

For the first 18-20 weeks of pregnancy, the baby is completely dependent on the mother for the production of thyroid hormone. By mid-pregnancy, the baby's thyroid begins to produce thyroid hormone on its own. The baby, however, remains dependent on the mother for ingestion of adequate amounts of iodine, which is essential to make the thyroid hormones. The World Health Organization recommends iodine intake of 250 micrograms/day during pregnancy to maintain adequate thyroid hormone production. Because iodine intakes in pregnancy are currently low in the United States, the ATA recommends that US women who are planning to become pregnant, who are pregnant, or breastfeeding, should take a daily supplement containing 150 mcg of iodine.

HYPOTHYROIDISM & PREGNANCY

WHAT ARE THE MOST COMMON CAUSES OF HYPOTHYROIDISM DURING PREGNANCY?

Overall, the most common cause of hypothyroidism is the autoimmune disorder known as Hashimoto's thyroiditis (see *Hypothyroidism brochure*). Hypothyroidism can occur during pregnancy due to the initial presentation of Hashimoto's thyroiditis, inadequate treatment of a woman already known to have hypothyroidism from a variety of causes, or over-treatment of a hyperthyroid woman with anti-thyroid medications. Approximately, 2.5% of women will have a TSH of greater than 6 mIU/L (slightly elevated) and 0.4% will have a TSH greater than 10 mIU/L during pregnancy.

WHAT ARE THE RISKS OF HYPOTHYROIDISM TO THE MOTHER?

Untreated, or inadequately treated, hypothyroidism has increased risk of miscarriage, and has been associated with maternal anemia, myopathy (muscle pain, weakness), congestive heart failure, pre-eclampsia, placental abnormalities, and postpartum hemorrhage (bleeding). These complications are more likely to occur in women with severe hypothyroidism. Some risks also appear to be higher in women with antibodies against thyroid peroxidase (TPO). Women with mild hypothyroidism may have no symptoms or attribute symptoms they have to the pregnancy.

Hypothyroidism in Pregnancy

WHAT ARE THE RISKS OF MATERNAL HYPOTHYROIDISM TO THE BABY?

Thyroid hormone is critical for brain development in the baby. Children born with congenital hypothyroidism (no thyroid function at birth) can have severe cognitive, neurological and developmental abnormalities if the condition is not recognized and treated promptly. With early treatment, these developmental abnormalities largely can be prevented. Consequently, all newborn babies in the United States are screened for congenital hypothyroidism so they can be treated with thyroid hormone replacement therapy as soon as possible.

Untreated severe hypothyroidism in the mother can lead to impaired brain development in the baby. Recent studies have suggested that mild developmental brain abnormalities also may be present in children born to women who had mild untreated hypothyroidism during pregnancy. At this time, there is no general consensus of opinion regarding screening all women for hypothyroidism during pregnancy. However, the ATA recommends checking a woman's TSH as soon as pregnancy is confirmed in women at high risk for thyroid disease, such as those with prior treatment for hyper- or hypothyroidism, a family history of thyroid disease, a personal history of autoimmune disease, and those with a goiter.

Women with established hypothyroidism should have a TSH test as soon as pregnancy is confirmed. They also should immediately increase their levothyroxine dose, because thyroid hormone requirements increase during pregnancy. (See below for specific dosing recommendations.) If new onset hypothyroidism has been detected, the woman should be treated with levothyroxine to normalize her TSH values (see *Hypothyroidism brochure*).

WHO SHOULD BE TREATED FOR HYPOTHYROIDISM DURING PREGNANCY?

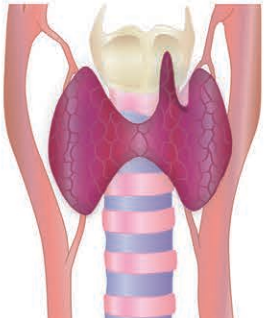
Women found to have a TSH level greater than 10 mIU/L in the first trimester of pregnancy should be treated for hypothyroidism. Conversely, women with a TSH of 2.5 or less, do not need levothyroxine treatment. For women with TSH measured between these (2.5-10), ATA recommendations for treatment vary and may depend on whether or not the mother has TPO antibodies. When TPO antibodies are positive, treatment is recommended when the TSH is above 4 and should be considered when the TSH is between 2.5-4.0. However, when there are no TPO antibodies (i.e. negative), current ATA recommendations are less strong and suggest that treatment 'may be considered' when TSH is between 2.5-10.0 mIU/L. These recommendations are based on the degree of evidence that exists that treatment with levothyroxine would be beneficial.

HOW SHOULD A WOMAN WITH HYPOTHYROIDISM BE TREATED DURING PREGNANCY?

The goal of treating hypothyroidism in a pregnant woman is adequate replacement of thyroid hormone. Ideally, hypothyroid women should have their levothyroxine dose optimized prior to becoming pregnant. Levothyroxine requirements frequently increase during pregnancy, usually by 25 to 50 percent. Hypothyroid women taking levothyroxine should independently increase their dose by 20%–30% as soon as pregnancy is diagnosed and should notify their doctor for prompt testing and further evaluation. One means of accomplishing the dose increase is to take two additional tablets weekly of their usual daily levothyroxine dosage. Thyroid function tests should be checked approximately every 4 weeks during the first half of pregnancy to ensure that the woman has normal thyroid function throughout pregnancy. As soon as delivery of the child occurs, the woman may go back to her usual pre-pregnancy dose of levothyroxine. It is also important to recognize that prenatal vitamins contain iron and calcium that can impair the absorption of thyroid hormone from the gastrointestinal tract. Consequently, levothyroxine and prenatal vitamins should not be taken at the same time and should be separated by at least 4 hours.

SPECIAL CONSIDERATIONS FOR WOMEN WITH A HISTORY OF GRAVES' DISEASE

In addition to the dosing and testing considerations explained in this brochure, women with a history of *Graves' disease* who were treated with radioiodine (RAI) or surgical thyroidectomy should also have Graves' antibodies (TRAb) tested early in pregnancy to assess the risk of passing antibodies on to the fetus. If antibodies are elevated, follow-up testing is recommended at weeks 18-22, and if antibodies are still elevated, additional follow-up is recommended at weeks 30-34 to evaluate the need for fetal and neonatal monitoring.



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*