

Clinical Thyroidology for the Public

VOLUME 9 • ISSUE 12 • DECEMBER 2016

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EDITOR'S COMMENTS2

THYROID CANCER......3

Estrogen status is not associated with increased thyroid cancer risk among postmenopausal women

Thyroid cancer is now the fifth most common cancer among women. Some laboratory studies suggest that estrogen might stimulate growth of cancerous thyroid cells. This study investigated the rate of thyroid cancer in women who had hysterectomy, oophorectomy or received treatment with estrogen.

Luo J et al. Hysterectomy, oophorectomy, and risk of thyroid cancer. J Clin Endocrinol Metab 2016;101:3812-9. Epub July 26, 2016.

THYROID DISEASE IN THE ELDERLY.....4

Abnormal thyroid function is associated with disability risk, but not with increased risk of death, in individuals 85 years of age or older

Adults in their 80s or older are more likely to have abnormal thyroid function than younger adults. Heart problems are also more common in elderly patients. However, it is unclear whether abnormal thyroid function is associated with increased risk of heart problems and death in these oldest individuals. The objective of this study was to determine whether abnormal thyroid function is associated with disability and death in a group of 85-year-olds.

Pearce SH et al Serum thyroid function, mortality and disability in advanced old age: the Newcastle 85+ study. J Clin Endocrinol Metab 2016. August 23, 2016 [Epub ahead of print].

Thyroid dysfunction and risk of death in patients receiving peritoneal dialysis

Individuals with chronic kidney disease have a greater risk of abnormal thyroid function for reasons that are not clear. Abnormal thyroid function is associated with higher risks of death in those receiving hemodialysis. This study was done to examine whether abnormal thyroid function is also associated with higher risks of death in those receiving peritoneal dialysis.

Rhee CM et al. Thyroid Functional Disease and Mortality in a National Peritoneal Dialysis Cohort. J Clin Endocrinol Metab. 2016 Nov;101(11):4054-4061.

THYROID CANCER.....8

Ultrasound monitoring of indeterminate neck lesions is safe in some cases of thyroid cancer

The rates of thyroid cancer are steadily increasing, especially in women, and 1 out of 3 patients may experience recurrence of thyroid cancer in the neck lymph nodes following surgery. Importantly, this does not change the otherwise excellent prognosis for most patients. Most thyroid cancer recurrences are slow-growing, and may not pose fast-approaching threats to the patient's health. This study examines the use of neck ultrasound as a monitoring tool for thyroid cancer recurrence.

Lamartina L et al. Risk stratification of neck lesions detected sonographically during the follow-up of differentiated thyroid cancer. J Clin Endocrinol Metab 2016;1013036-44. Epub May 17, 2016.

Prevalence of thyroid cancer found in autopsy studies has not increased since 1970

The incidence of thyroid cancer has reportedly been rising and it is the fastest rising cancer diagnosed in women in the last few years. However, it is unknown whether this increased incidence can be explained by better detection techniques or represents a true increase in the cancer across the world. This study reviewed all recently reported autopsy studies to determine if there is truly a rising incidence of thyroid cancer.

Furuya-Kanamori L et al. Prevalence of differentiated thyroid cancer in autopsy studies over six decades: a meta-analysis. J Clin Oncol. September 6, 2016 [Epub ahead of print].

THYROID CANCER.....

Sorafenib may offer benefits as a secondline treatment of metastatic medullary thyroid cancer

Medullary thyroid cancer (MTC) is a relatively rare type of thyroid cancer that can run in families. If the cancer can no longer be removed by surgery, some patients will be offered chemotherapy for metastatic MTC. This study tested a drug called Sorafenib for its ability to stop the growth of metastatic MTC. They also looked at side effects of the medication.

de Castroneves LA et al Sorafenib for the Treatment of progressive metastatic medullary thyroid cancer: efficacy and safety analysis. Thyroid 2016;26:414-9. Epub February 9, 2016.









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Clinical Thyroidology for the Public

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CLINICAL THYROIDOLOGY FOR THE PUBLIC

A publication of the American Thyroid Association

VOLUME 9 • ISSUE 12 • DECEMBER 2016

EDITOR'S COMMENTS

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

We also provide even faster updates of late-breaking thyroid news through Twitter at otherwise 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.

December is Thyroid and Development Month.

In this issue, the studies ask the following questions:

- 1. Is estrogen the reason why thyroid cancer is more common in women?
- 2. Is thyroid disease associated with increased mortality in the elderly?
- 3. Is thyroid disease more common in patient on dialysis?
- 4. What is the best way to manage abnormal neck nodes after surgery in patients with thyroid cancer?
- 5. Is the incidence of thyroid cancer actually increasing?
- 6. Is Sorafanib effective in patients with medullary thyroid cancer?

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

— Alan P. Farwell, MD, FACE









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THYROID CANCER

Estrogen status is not associated with increased thyroid cancer risk among postmenopausal women

BACKGROUND

The number of patients diagnosed with thyroid cancer has increased dramatically in the past few decades, especially in women. Thyroid cancer is now the fifth most common cancer among women. In addition, some experiments done in laboratories have shown that estrogen might stimulate growth of non-cancerous and cancerous thyroid cells. Based on these observations, some questioned the possibility of a connection between estrogen and thyroid cancer. To answer this question, clinical and population studies have been conducted to investigate the rate of thyroid cancer in women who had hysterectomy, oophorectomy or received treatment with estrogen. However, the results of these studies were mixed in regards to the effect of estrogen on thyroid cancer. In this current study the relationship between thyroid cancer and estrogen has been addressed again.

THE FULL ARTICLE TITLE

Luo J et al. Hysterectomy, oophorectomy, and risk of thyroid cancer. J Clin Endocrinol Metab 2016;101:3812-9. Epub July 26, 2016.

SUMMARY OF THE STUDY

The data presented in this study was obtained from Women's Health Initiative (WHI) study; a large population study of women of 50 to 79 years of age conducted in 40 U.S. clinical centers. Subjects in the current study were among participants of WHI who were enrolled during 1993 to 1998. The data from women who had cancer (except for non-melanoma skin cancer) at the time of enrollment in WHI and women who had only oophorectomy (without hysterectomy) was excluded.

A total of 127,566 women were included, about 37% had hysterectomy; 55% of women who had hysterectomy had also oophorectomy. After follow up for many years

(median of 14 years), 344 women were found to have thyroid cancer. Compared to women who did not have surgery, the rate of thyroid cancer diagnosis was higher in women who had hysterectomy alone or hysterectomy and oophorectomy. The increase in thyroid cancer was seen if the surgery was done before age of 50. When the surgery was done after age 50, no difference in thyroid cancer diagnosis was seen. In women who received treatment with estrogen after surgery, the rate of thyroid cancer was lower. The type, size and stage of thyroid cancer were not different among all women in the study regardless of surgery status.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Based on these results, it was concluded that estrogen does not increase the risk of thyroid cancer. The reason for the increased rate of thyroid cancer in women is still unclear. A possible reason could be increased rate of diagnosis, since women with surgery had more physical exams and more tests that could lead to a higher rate of diagnosis.

- Shirin Haddady, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer: http://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

Estrogen: The primary female sex hormone, produced primarily in ovaries

Hysterectomy: Surgery to remove uterus

Oophorectomy: surgery to remove ovaries

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THYROID DISEASE IN THE ELDERLY

Abnormal thyroid function is associated with disability risk, but not with increased risk of death, in individuals 85 years of age or older

BACKGROUND

It is clear that patients with overt hypothyroidism and hyperthyroidism (abnormal TSH and abnormal T_4 levels) are at increased risk of heart problems. It is less clear that subclinical hypothyroidism and hyperthyroidism (abnormal TSH and normal T_4 levels). In some studies, abnormal thyroid function has been associated with an increased risk of death related to heart problems.

Adults in their 80s or older are more likely to have abnormal thyroid function, especially higher TSH values, than younger adults. Heart problems are also more common in elderly patients. However, it is unclear whether abnormal thyroid function is associated with increased risk of heart problems and death in these oldest individuals. The objective of this study was to determine whether abnormal thyroid function is associated with disability and death in a group of 85-year-olds.

THE FULL ARTICLE TITLE

Pearce SH et al Serum thyroid function, mortality and disability in advanced old age: the Newcastle 85+ study. J Clin Endocrinol Metab 2016. August 23, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

This was a prospective study that used data from the Newcastle 85+ study. Participants in the study were all born in 1921 and recruited at the age of 85 in 2006-2007. A fasting blood draw, physical exam and health

questionnaires were conducted at baseline. Disability scores were based on assessments of daily living at baseline, 18, 36 and 60 months. Causes of death were obtained from the national registration system.

A total of 643 individuals participated in the study. Of these, 83% had normal thyroid function tests, 12.5% had subclinical hypothyroidism, 0.9% had overt hypothyroidism, 2.9% had subclinical hyperthyroidism and 0.8% had overt hyperthyroidism. Lower TSH levels were associated with greater degrees of disability in both men and women, but there was no association between thyroid status and risk for death in this group of individuals aged 85 years or older.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study provides reassurance that abnormal thyroid function was not associated with an increased risk for death in elderly patients. Moreover, the lower rates of disability associated with higher TSH levels seen in this study adds to the growing evidence that it may be inappropriate to treat mild TSH elevations in very elderly patients.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

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.

Subclinical Hyperthyroidism: a mild form of hyperthyroidism where the only abnormal hormone level is a decreased TSH.

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.

Prospective study: a research study in which a group of individuals who have one or more common characteristics are followed over time.

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THYROID DISEASE IN THE ELDERLY, continued



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

Overt Hyperthyroidism: clear hyperthyroidism with a decreased TSH and an increased T_4 level and/or T_3 level.



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HYPOTHYROIDISM AND HYPERTHYROIDISM

Thyroid dysfunction and risk of death in patients receiving peritoneal dialysis

BACKGROUND

The kidneys are very important in cleaning the blood of toxins. Patients with declining kidney function (chronic kidney disease, CKD) may have to go on dialysis to help cleanse the blood when their kidneys no longer work on their own. Dialysis can be done in different ways, depending on the individual's condition and other factors. Hemodialysis is when the patient's blood is run through a machine to help cleanse it several times a week and peritoneal dialysis is when a bag of fluid is inserted into the abdomen then drained several times a day are two different types of dialysis. In general, CKD is a very serious condition, as once a patient goes on dialysis, they are have an increased risk of dying.

Individuals with CKD have a greater risk of an underactive thyroid gland (hypothyroidism) for reasons that are not clear. Having abnormal thyroid function like hypothyroidism or hyperthyroidism (an overactive thyroid gland) is itself associated with higher risks of death, perhaps as a result of heart disease, which has been shown both in the general population with normal kidney function and in those receiving hemodialysis. What is not known is whether having abnormal thyroid function is also associated with higher risks of death in those receiving peritoneal dialysis. This study was done to examine this question using data from a large U.S. national dialysis organization.

THE FULL ARTICLE TITLE

Rhee CM et al. Thyroid Functional Disease and Mortality in a National Peritoneal Dialysis Cohort. J Clin Endocrinol Metab. 2016 Nov;101(11):4054-4061.

SUMMARY OF THE STUDY

This was a study of 1,484 adults receiving peritoneal dialysis between 2007–2011. Among this group, the researchers looked at the relationships between TSH levels and death from any cause. Patient with a low TSH were considered to be hyperthyroid while those with an increased TSH were considered to be hypothyroid. The patients in this study were primarily women (52%) and

non-Hispanic whites (67%) with an average age of 60 years.

The average TSH in this group was slightly increased, with an average serum TSH of 5. Overall, 7% of patients had a low TSH and were considered hyperthyroid and 18% had an increased TSH and were considered hypothyroid. Both groups had increased rates of death. Those with the more severe hyperthyroidism and hypothyroidism had at highest risks of death. Hyperthyroidism and hypothyroidism in this study was defined by blood TSH results alone, with those patients with an undetectable TSH have a 2-fold increased risk of death and those with a TSH >10 having a 3-fold increased risk of death.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that abnormal thyroid function, either hyperthyroidism or hypothyroidism, carries an increased risk of death in patients with CKD receiving peritoneal dialysis. The findings support those of similar studies done in patients receiving hemodialysis and even in those in the general population. The size of the study is large and thus represents its major strength. Overall, little is known regarding this topic, even though both thyroid dysfunction and CKD are relatively common conditions. Future research will help determine whether treatment of the thyroid dysfunction and normalization of TSH levels decreases the risk of death and will also help determine if there is a specific goal of what the TSH levels should be in patients with CKD.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

Hypothyroidism: http://www.thyroid.org/

hypothyroidism/

Hyperthyroidism: http://www.thyroid.org/

hyperthyroidism/

Thyroid Function Tests: http://www.thyroid.org/

thyroid-function-tests/

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HYPOTHYROIDISM AND HYPERTHYROIDISM, continued



ABBREVIATIONS & DEFINITIONS

Hypothyroidism: A condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. TSH levels are increased in most forms of hypothyroidism. Treatment requires taking thyroid hormone pills.

Hyperthyroidism: A condition where the thyroid gland is overactive and produces too much thyroid hormone. TSH levels are decreased in most forms of hyperthyroidism. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

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.

Chronic kidney disease (CKD): a condition of declining kidney function. When the kidneys no longer work on their own, patients need to go on diualysis to help clean the blood.

Hemodialysis: when the patient's blood is run through a machine to help cleanse it several times a week

Peritoneal dialysis: when a bag of fluid is inserted into the abdomen then drained several times a day to help clean the blood

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 December is **Thyroid Development 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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THYROID CANCER

Ultrasound monitoring of indeterminate neck lesions is safe in some cases of thyroid cancer

BACKGROUND

The rates of thyroid cancer are steadily increasing, especially in women. The good news is that patients with thyroid cancer have excellent long-term survival. In fact, treatment is based on the risk of recurrence rather than the risk of death. At the time of surgery, up to 30% of patients with have the cancer spread to the lymph nodes in the neck and this is the most likely place for the cancer to recur. Indeed, 1 out of 3 patients may experience recurrence of the cancer in the neck lymph nodes following surgery. Importantly, this does not change the otherwise excellent prognosis for most patients. Most thyroid cancer recurrences are slow-growing and may not pose fast-approaching threat to the patient's health. Further neck surgery after the initial thyroidectomy can be risky, so careful consideration is necessary to decide when a cancer recurrence needs surgery. Active monitoring is reasonable for many potential cancer recurrences that are in a lymph node smaller than 1 cm. Neck ultrasound is the most accurate imaging tool to detect recurrence in the thyroid bed or neck lymph nodes. This study examines the use of neck ultrasound as a monitoring tool for thyroid cancer recurrence.

THE FULL ARTICLE TITLES:

Lamartina L et al. Risk stratification of neck lesions detected sonographically during the follow-up of differentiated thyroid cancer. J Clin Endocrinol Metab 2016;1013036-44. Epub May 17, 2016.

SUMMARY OF THE STUDY

In this study, Lamartina et al. evaluated the European Thyroid Association ultrasound classification of neck lesions, which may be abnormal lymph nodes or masses in the thyroid bed, following thyroidectomy for predicting lesion growth during follow-up. This was a review of patients at a large teaching hospital in Italy between January 2005 and December 2014. Patients were included if they underwent surgery and had abnormal lesions detected on at least two ultrasounds. Lesions were retrospectively classified as suspicious or indeterminate. The main outcomes were lesion growth of >3 mm during follow-up or persistence of at least one abnormal lesion at last follow-up.

Of 637 patients, 58 had at least one abnormal lesion detected on ultrasound following surgery. The risk of recurrence according to American Thyroid Association guidelines was intermediate or high in 71% of cases. In total, there were 94 abnormal lesions (16 in the thyroid bed and 78 in lymph nodes of the neck). The average diameters of indeterminate and suspicious lesions were 8.2 mm and 9.8 mm respectively. Of the 49 suspicious lesions, 12% were in the thyroid bed, 10% were in the central neck lymph nodes, and the remainder were in the lateral lymph nodes of the neck.

Growth occurred in 36% of suspicious lesions as compared with only 8% of indeterminate lesions at an average follow-up of 3.7 years. Almost all suspicious lesions were still present at last follow-up, while half of indeterminate lesions resolved. All of the thyroid-bed lesions were still present during follow-up, while 17 of the abnormal lymph nodes had disappeared. The authors hypothesized that thyroid-bed lesions that did not represent tumor recurrence were frequently postoperative scarring or reaction to surgical suture material, which would be unlikely to resolve over time. Abnormal lymph nodes that were not cancer were likely reactive and could be expected to resolve with more time after surgery.

There were no local complications related to disease recurrence during the study period. A total of 8 of the 32 patients with persistent suspicious nodules were ultimately referred for additional surgery at the end of the study period on the basis of clinical factors including rising thyroglobulin levels and absence of distant spread as well as physician and patient preference, and each was confirmed to have recurrent thyroid cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Ultrasound is a critical tool in the diagnosis, surgical treatment, and follow-up of patients with thyroid cancer. The ultrasound appearance of neck lesions following thyroidectomy for differentiated thyroid cancer can help predict growth and persistence during follow-up. The majority of patients with indeterminate lesions and approximately two-thirds of those with suspicious lesions

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THYROID CANCER, continued

had no change during the study period. The authors suggest postponing additional workup including biopsy for most lesions with indeterminate characteristics on ultrasound as this may reduce additional surgery that may be risky and is unlikely to improve control of the disease or long-term survival.

Ronald B. Kuppersmith, MD, FACS

ATA THYROID BROCHURE

Thyroid Nodules: http://www.thyroid.org/

thyroid-nodules/

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

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

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.

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

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.



American Thyroid Association (ATA)
Spring 2017 Satellite Symposium

Hypothyroidism - Where Are We Now?

Friday, March 31, 2017, 1:00 PM - 5:30 PM (*Prior to the start of ENDO 2017*)

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THYROID CANCER

Prevalence of thyroid cancer found in autopsy studies has not increased since 1970

BACKGROUND

Thyroid cancer is the most common endocrine cancer. Unlike most other cancers, the incidence of thyroid cancer has reportedly been rising and it is the fastest rising cancer diagnosed in women in the last few years. However, it is unknown whether this increased incidence can be explained by better detection techniques or represents a true increase in the cancer across the world. Prior studies of autopsies done on people who died of non-thyroid-related causes have shown that thyroid cancer is a rather common finding. If the incidence of thyroid cancer has increased, recent autopsy studies should reflect this. This study reviewed all recently reported autopsy studies to determine if there is truly a rising incidence of thyroid cancer.

THE FULL ARTICLE TITLE

Furuya-Kanamori L et al. Prevalence of differentiated thyroid cancer in autopsy studies over six decades: a meta-analysis. J Clin Oncol. September 6, 2016 [Epub ahead of print].

SUMMARY OF THE STUDY

The authors looked at all recent thyroid cancer autopsy papers in the literature and combined their data to perform a meta-analysis. The final number of papers included was 35 and the final number of patients 12,834,

with 40% of the autopsies in females. The authors found that the rate of thyroid cancer in an autopsy specimen was dependent on how thoroughly a thyroid specimen was examined. The more thorough a thyroid was examined the more likely it was to have a thyroid cancer found in it. The overall incidence of thyroid cancer in autopsy specimens ranged from 4-11%. There was no difference in the rate of thyroid cancer found in autopsy specimens over time, meaning there was a constant rate of thyroid cancer and an "increase" was not seen.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that, since the rate of thyroid cancer found on autopsy over the years has been stable, the incidence of thyroid cancer is really not increasing around the world. Instead, this study indicates that the increasing rate of diagnosis of thyroid cancer is most likely due to better detection techniques. This study also shows that thyroid cancer is a common finding at autopsy and that the closer you look, the larger the chance that you will find it. Further, this study suggests that it is relatively rare for most thyroid cancers to become clinically important.

- Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer: http://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: the most common type of thyroid cancer. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

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

Autopsy: a detailed examination of all of the tissues and organs of the body after a person dies to determine why that person died

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AMERICAN THYROID ASSOCIATION FOUNDED 1923 www.thyroid.org

THYROID CANCER

Sorafenib may offer benefits as a second-line treatment of metastatic medullary thyroid cancer

BACKGROUND

Medullary thyroid cancer (MTC) is a relatively rare type of thyroid cancer that can run in families. Most patients with MTC are cured after surgery, but about 15% can have metastatic spread of MTC to distant organs such as the bone, liver, and lung. Unlike other types of thyroid cancer, MTC does not respond to radioactive iodine therapy. If the cancer can no longer be removed by surgery, some patients will be offered chemotherapy for metastatic MTC. There are 2 drugs, Vandetanib and Cabozantanib, approved for the treatment of metastatic MTC. These drugs work by blocking the stimulators of growth of the cancer and are called targeted kinase inhibitors (TKI). The drugs are taken by mouth each day.

Some MTC patients do not respond to the current TKI options and therefore, there is a need to find more treatments for this group of patients. This study from a hospital in Brazil tested a drug called Sorafenib also a TKI (already approved for treating metastatic papillary thyroid cancer) for its ability to stop the growth of metastatic MTC. They also looked at side effects of the medication.

THE FULL ARTICLE TITLE

de Castroneves LA et al Sorafenib for the Treatment of progressive metastatic medullary thyroid cancer: efficacy and safety analysis. Thyroid 2016;26:414-9. Epub February 9, 2016.

SUMMARY OF THE STUDY

This study included 12 adults (7 men and 5 women)

who were treated with Sorafenib (400mg twice a day). Most of the patients were followed for just over a year. The patient's tumors were assessed using the standard scoring system known as RECIST criteria. A total of 10 of the patients did not have growth of their cancer for almost 12 months and 9 patients did not have growth of the cancer for 6 months or more after starting Sorafenib. Only 2 patients had growth of their cancer and 3 patients overall died within 3 months of starting Sorafenib. The MTC marker calcitonin did decrease in 92% of patients after starting Sorafenib. The majority (9 patients) had side effects to the drug and had to lower the dose of medication but were able to continue the drug. The most common side effects were skin rashes, weight loss and fatigue).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that Sorafenib can decrease the growth of metastatic MTC. However, we have to look at this in perspective because it included a small number of patients. In addition, the majority of patients (75%) had side effects from the medication which often can limit its use. More studies of sorafenib for metastatic MTC will need to be done to assess its ability to treat metastatic MTC.

-Wendy Sacks, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer: http://www.thyroid.org/thyroid-cancer/

ABBREVIATIONS & DEFINITIONS

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

Cancer metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

Papillary thyroid cancer: the most common type of thyroid cancer. There are 3 variants of papillary thyroid cancer: classic, follicular and tall-cell.

RECIST: Response Evaluation Criteria in Solid Tumors — this is a set of published rules that define when cancer patients improve ("respond"), stay the same ("stable") or worsen ("progression") during treatments.

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THYROID CANCER, continued

Sorafenib: an anticancer drug that has been shown to be effective in thyroid cancer.

Tyrosine kinases: proteins that are overactive in many of the pathways that cause cells to be cancerous.

Tyrosine kinase inhibitors: chemotherapy drugs that inhibit tyosine kinases and slow the growth of certain metastatic cancers

Calcitonin: a hormone that is secreted by cells in the thyroid (C-cells) that has a minor effect on blood calcium levels. Calcitonin levels are increased in patients with medullary thyroid cancer and serve as a marker for this type of thyroid cancer.



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THYROID ASSOCIATION www.thyroid.org

ATA Alliance for Thyroid Patient Education

GOAL

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

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

WHO WE ARE (in alphabetical order)

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

AMERICAN THYROID ASSOCIATION

www.thyroid.org

ATA Patient Resources: http://www.thyroid.org/patients-portal/

Find a Thyroid Specialist: www.thyroid.org Phone (toll-free): I-800-THYROID e-mail: thyroid@thyroid.org

ATA Mission: The ATA leads in promoting thyroid health and understanding thyroid biology.

ATA Vision: The ATA is the leading organization focused on thyroid biology and the prevention and treatment of thyroid disorders through excellence and innovation in research, clinical care, education, and public health.

ATA Values: The ATA values scientific inquiry, clinical excellence, public service, education, collaboration, and collegiality.

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

continued on next page















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

A publication of the American Thyroid Association



ATA Alliance for Thyroid Patient Education

Continued...

BITE ME CANCER

http://www.bitemecancer.org

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

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

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

e-mail: Gravesdiseasefd@gmail.com

e-mail: info@bitemecancer.org

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

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com

email: info@checkyourneck.com

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

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Volume 9 • ISSUE 12 • DECEMBER 2016 • 14

A publication of the American Thyroid Association



ATA Alliance for Thyroid Patient Education

Continued...

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org

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

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

THYROID CANCER CANADA

www.thyroidcancercanada.org

Phone: 416-487-8267 Fax: 416-487-0601

e-mail: info@thyroidcancercanada.org

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

THYROID FEDERATION INTERNATIONAL

www.thyroid-fed.org

e-mail: tfi@thyroid-fed.org

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













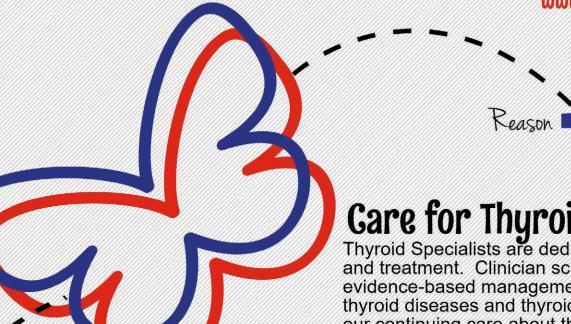


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American Thyroid Association www.thyroid.org/donate

WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

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

HORMONE CHANGES. A normal pregnancy results in a number of important physiological and hormonal changes that alter thyroid function. These changes mean that laboratory tests of thyroid function must be interpreted with caution during pregnancy. Thyroid function tests change during pregnancy due to the influence of two main hormones: human chorionic gonadotropin (hCG), the hormone that is measured in the pregnancy test and estrogen, the main female hormone. HCG can weakly turn on the thyroid and the high circulating hCG levels in the first trimester may result in a slightly low TSH (called subclinical hyperthyroidism). When this occurs, the TSH will be slightly decreased in the first trimester and then return to normal throughout the duration of pregnancy (see Table 1). Estrogen increases the amount of thyroid hormone binding proteins in the serum which increases the total thyroid hormone levels in the blood since >99% of the thyroid hormones in the blood are bound to these proteins. However, measurements of "Free" hormone (that not bound to protein, representing the active form of the hormone) usually remain normal. The thyroid is functioning normally if the TSH, Free T4 and Free T3 are all normal throughout pregnancy.

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, which is thought to be relatively iodine-sufficient. 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.

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

For the first 10-12 weeks of pregnancy, the baby is completely dependent on the mother for the production of thyroid hormone. By the end of the first trimester, 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 200 micrograms/day during pregnancy to maintain adequate thyroid hormone production. The normal diet in the United States contains sufficient iodine so additional iodine supplementation is rarely necessary.

HYPERTHYROIDISM & PREGNANCY

WHAT ARE THE MOST COMMON CAUSES OF HYPERTHYROIDISM DURING PREGNANCY?

Overall, the most common cause (80-85%) of maternal hyperthyroidism during pregnancy is Graves' disease (see *Graves' Disease brochure*) and occurs in 1 in 1500 pregnant patients. In addition to other usual causes of hyperthyroidism (see *Hyperthyroidism brochure*), very high levels of hCG, seen in severe forms of morning sickness (hyperemesis gravidarum), may cause transient hyperthyroidism. The diagnosis of hyperthyroidism can be somewhat difficult during pregnancy, as 123I thyroid scanning is contraindicated during pregnancy due to the small amount of radioactivity, which can be concentrated by the baby's thyroid. Consequently, diagnosis is based on a careful history, physical exam and laboratory testing.

WHAT ARE THE RISKS OF GRAVES' DISEASE/ HYPERTHYROIDISM TO THE MOTHER?

Graves' disease may present initially during the first trimester or may be exacerbated during this time in a woman known to have the disorder. In addition to the classic symptoms associated with hyperthyroidism, inadequately treated maternal hyperthyroidism can result in early labor and a serious complication known as pre-eclampsia. Additionally, women with active Graves' disease during pregnancy are at higher risk of developing very severe hyperthyroidism known as thyroid storm. Graves' disease often improves during the third trimester of pregnancy and may worsen during the post partum period.

WHAT ARE THE RISKS OF GRAVES' DISEASE/ HYPERTHYROIDISM TO THE BABY?

The risks to the baby from Graves' disease are due to one of three possible mechanisms:

- 1)UNCONTROLLED MATERNAL HYPERTHYROIDISM: Uncontrolled maternal hyperthyroidism has been associated with fetal tachycardia (fast heart rate), small for gestational age babies, prematurity, stillbirths and possibly congenital malformations. This is another reason why it is important to treat hyperthyroidism in the mother.
- 2)EXTREMELY HIGH LEVELS OF THYROID STIMULATING IMMUNOGLOBLULINS (TSI): Graves' disease is an autoimmune disorder caused by the production of antibodies that stimulate thyroid gland referred to as thyroid stimulating immunoglobulins (TSI). These antibodies do cross the placenta and can interact with the baby's thyroid. Although uncommon (2-5% of cases of Graves' disease in pregnancy), high levels of maternal TSI's, have been known to cause fetal or neonatal hyperthyroidism. Fortunately, this typically only occurs when the mother's TSI levels are very high (many times above normal). Measuring TSI in the mother with Graves' disease is often done in the third trimester.

In the mother with Graves' disease requiring antithyroid drug therapy, fetal hyperthyroidism due to the mother's TSI is rare, since the antithyroid drugs also cross the placenta. Of potentially more concern to the baby is the mother with prior treatment for Graves' disease (for example radioactive iodine or surgery) who no longer requires antithyroid drugs. It is very important to tell your doctor if you have been treated for Graves' Disease in the past so proper monitioring can be done to ensure the baby remains healthy during the pregnancy.

3)ANTI-THYROID DRUG THERAPY (ATD). Methimazole (Tapazole) or propylthiouracil (PTU) are the ATDs available in the United States for the treatment of hyperthyroidism (see *Hyperthyroidism brochure*). Both of these drugs cross the placenta and can potentially impair the baby's thyroid function and cause fetal goiter. Historically, PTU has been the drug of choice for treatment of maternal hyperthyroidism, possibly because transplacental passage may be less than with Tapazole. However, recent studies suggest that both drugs are safe to use during pregnancy. It is recommended that the lowest possible dose of ATD be used to control maternal hyperthyroidism to minimize the development of hypothyroidism in the baby or neonate. Neither drug appears to increase the general risk of birth defects.

Overall, the benefits to the baby of treating a mother with hyperthyroidism during pregnancy outweigh the risks if therapy is carefully monitored.

WHAT ARE THE TREATMENT OPTIONS FOR A PREGNANT WOMAN WITH GRAVES' DISEASE/HYPERTHYROIDISM?

Mild hyperthyroidism (slightly elevated thyroid hormone levels, minimal symptoms) often is monitored closely without therapy as long as both the mother and the baby are doing well. When hyperthyroidism is severe enough to require therapy, anti-thyroid medications are the treatment of choice, with PTU being the historical drug of choice. The goal of therapy is to keep the mother's free T4 and free T3 levels in the high-normal range on the lowest dose of antithyroid medication. Targeting this range of free hormone levels will minimize the risk to the baby of developing hypothyroidism or goiter. Maternal hypothyroidism should be avoided. Therapy should be closely monitored during pregnancy. This is typically done by following thyroid function tests (TSH and thyroid hormone levels) monthly.

In patients who cannot be adequately treated with anti-thyroid medications (i.e. those who develop an allergic reaction to the drugs), surgery is an acceptable alternative. Surgical removal of the thyroid gland is only very rarely recommended in the pregnant woman due to the risks of both surgery and anesthesia to the mother and the baby.

Radioiodine is contraindicated to treat hyperthyroidism during pregnancy since it readily crosses the placenta and is taken up by the baby's thyroid gland. This can cause destruction of the gland and result in permanent hypothyroidism.

Beta-blockers can be used during pregnancy to help treat significant palpitations and tremor due to hyperthyroidism. They should be used sparingly due to reports of impaired fetal growth associated with long-term use of these medications. Typically, these drugs are only required until the hyperthyroidism is controlled with anti-thyroid medications.

FURTHER INFORMATION



WHAT IS THE NATURAL HISTORY OF GRAVES' DISEASE AFTER DELIVERY?

Graves' disease typically worsens in the postpartum period, usually in the first 3 months after delivery. Higher doses of anti-thyroid medications are frequently required during this time. At usual, close monitoring of thyroid function tests is necessary.

CAN THE MOTHER WITH GRAVES' DISEASE, WHO IS BEING TREATED WITH ANTI-THYROID DRUGS, BREASTFEED HER INFANT?

Yes. PTU is the drug of choice because it is highly protein bound. Consequently, lower amounts of PTU cross into breast milk compared to Tapazole. It is important to note that the baby will require periodic assessment of his/her thyroid function to ensure maintenance of normal thyroid status.

TABLE 1:			
	1st Trimester	2ND TRIMESTER	3RD TRIMESTER
TSH	Normal or Decreased	Normal	Normal
Free T4	Normal	Normal	Normal
	Normal		
Total T4	High	High	High
Total T3	High	High	High
T3 Resin Uptake . (Inverse measure of protein	LOW N BINDING)	Low	Low
Free T4 Index (FT4	I, FTI) Normal	Normal	Normal

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 slightly elevated TSH of greater than 6 and 0.4% will have a TSH greater than 10 during pregnancy.

WHAT ARE THE RISKS OF HYPOTHYROIDISM TO THE MOTHER?

Untreated, or inadequately treated, hypothyroidism has been associated with maternal anemia (low red blood cell count), myopathy (muscle pain, weakness), congestive heart failure, pre-eclampsia, placental abnormalities, low birth weight infants, and postpartum hemorrhage (bleeding). These complications are more likely to occur in women with severe hypothyroidism. Most women with mild hypothyroidism may have no symptoms or attribute symptoms they may have as due to the 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. These developmental abnormalities can largely be prevented if the disease is recognized and treated immediately after birth. 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.

The effect of maternal hypothyroidism on the baby's brain development is not as clear. Untreated severe hypothyroidism in the mother can lead to impaired brain development in the baby. This is mainly seen when the maternal hypothoidism is due to iodine deficiency, which also affects the baby However, recent studies have suggested that mild brain developmental abnormalities 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, some physician groups recommend checking a woman's TSH value either before becoming prenant (pre-pregnancy counseling) or as soon as pregnancy is confirmed. This is especially true in women at high risk for thyroid disease, such as those with prior treatment for hyperthyroidism, a positive family history of thyroid disease and those with a goiter. Clearly, woman with established hypothyroidism should have a TSH test once pregnancy is confirmed, as thyroid hormone requirements increase during pregnancy, often leading to the need to increase the levothyroxine dose. If the TSH is normal, no further monitoring is typically required. This issue should be discussed further with your health care provider, particularly if you are contemplating pregnancy. Once hypothyroidism has been detected, the woman should be treated with levothyroxine to normalize her TSH and Free T4 values (see Hypothyroidism brochure).

FURTHER INFORMATION



HOW SHOULD A WOMAN WITH HYPOTHYROIDISM BE TREATED DURING PREGNANCY?

The treatment of hypothyroidism in a pregnant woman is the same as for a man or non-pregnant woman, namely, adequate replacement of thyroid hormone in the form of synthetic levothyroxine (see *Hypothyroidism* brochure). It is important to note that levothyroxine requirements frequently increase during pregnancy, often times by 25 to 50 percent. Occasionally, the levothyroxine dose may double. Ideally, hypothyroid women should have their levothyroxine dose optimized prior to becoming pregnant. Women with known hypothyroidism should have their thyroid function tested as soon as pregnancy is detected and their dose adjusted by their physician as needed to maintain a TSH in the normal range. Thyroid function tests should be checked approximately every 6-8 weeks during pregnancy to ensure that the woman has normal thyroid function throughout pregnancy. If a change in levothyroxine dose is required, thyroid tests should be measured 4 weeks later. 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 2-3 hrs.



FURTHER INFORMATION