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Griffen A et al. Applying criteria of active surveillance to low-risk papillary thyroid cancer over a decade: How many surgeries and complications can be avoided? *Thyroid* 27:518-523.

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The rate of diagnosis of thyroid cancer has increased in the past several decades. A cut off age of 45 had traditionally been used to separate patients with a higher possibility of recurrence and death (>45) from those with higher possibility of cure (<45). The aim of this study was to evaluate whether cutoff age of 45 is still appropriate.

Adam MA et al Exploring the relationship between patient age and cancer-specific survival in papillary thyroid cancer: rethinking current staging systems. *J Clin Oncol* 2016;34:4415-20. Epub October 28, 2016.

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Childhood radiation and thyroid cancer

Exposure to radiation occurs with many imaging studies and medical treatments. When this involves the head and neck areas directly, the thyroid is exposed and there is an increased risk for the development of thyroid cancer in the future. Children exposed to radiation are particu-

larly vulnerable to these thyroid cancer health risks. This study was done to further understand what the risks are regarding radiation exposure among children and its potential effect on getting thyroid cancer.

Lubin JH et al Thyroid cancer following childhood low dose radiation exposure: a pooled analysis of nine cohorts. *J Clin Endocrinol Metab* 2017 Mar 8. doi: 10.1210/jc.2016-3529. [Epub ahead of print]

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Survivors of pediatric thyroid cancer have good quality of life

Adult survivors of thyroid cancer have reported low health-related quality of life, while studies done in adolescents have reported no difference as compared to controls. This study was done to study the quality of life of adult survivors who were diagnosed with thyroid cancer between the ages of 7 and 18 years.

Nies M et al. Long-term quality of life in adult survivors of pediatric differentiated thyroid carcinoma. *J Clin Endocrinol Metab* (2017) 102 (4): 1218-1226.

THYROID CANCER.....9

Low-risk thyroid cancer that spreads outside of the neck has mutations in cancer-related genes

Spread of thyroid cancer outside of the neck is rare (<10% of patients) and is associated with significantly worse prognosis. In rare instances, thyroid cancer otherwise lacking any high-risk features present with spread of the cancer outside of the neck. The current study examined the features and molecular markers of thyroid cancer that initially appeared low risk but developed spread of the cancer outside of the neck.

Xu B et al. Primary thyroid carcinoma with low-risk histology and distant metastases: clinicopathologic and molecular characteristics. *Thyroid*. February 1, 2017 [Epub ahead of print].

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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 10 • ISSUE 6 • JUNE 2017

EDITOR'S COMMENTS

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

We also provide even faster updates of late-breaking thyroid news through **Twitter** at [@thyroidfriends](https://twitter.com/thyroidfriends) and on **Facebook**. Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room.

Also check out our friends in the **Alliance for Thyroid Patient Education**. The Alliance member groups consist of: the *American Thyroid Association*, *Bite Me Cancer*, the *Graves' Disease and Thyroid Foundation*, the *Light of Life Foundation*, *ThyCa: Thyroid Cancer Survivors Association*, *Thyroid Cancer Canada* and *Thyroid Federation International*.

June is **Differentiated Thyroid Cancer Awareness Month**.

In this issue, the studies ask the following questions:

1. Do all patients with thyroid cancer require surgery?
2. Should 45 years of age still be a cutoff to determine more aggressive thyroid cancer?
3. What is the thyroid cancer risk in adults after radiation exposure as a child?
4. Does getting thyroid cancer as a child affect long term quality of life?
5. Why do some patients with low risk thyroid cancer have aggressive disease?

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

Some patients with low-risk papillary thyroid cancer may not need surgery

BACKGROUND

Thyroid cancer is increasing, with the majority of this increase coming in patients with small papillary thyroid cancers. These patients have been shown to have a low risk (<2) of recurrence of their cancer after the initial surgery. In fact, some studies have actually followed some patients with regular ultrasound exams rather than recommending surgery and found no difference in long-term outcomes in patients as compared to similar patients that have surgery. With this in mind, the recent guidelines by the American Thyroid Association has suggested that active surveillance (following with ultrasound) be considered as an alternative to surgery in patients with low risk papillary thyroid cancer.

It is also known that most surgeries for thyroid cancer are done by surgeons who do few thyroid surgeries per year. We know that the higher the volume of thyroid cancer surgery done by an individual surgeon decreases the risk of complications, such as nerve injury/hoarseness and low calcium levels. Thus, if avoiding surgery is a reasonable option, we can avoid exposing patients to surgical complications.

This study was done to explore how many patients diagnosed with papillary thyroid cancer would meet criteria for active surveillance without surgery and how many surgical complications could be avoided.

THE FULL ARTICLE TITLE

Griffen A et al. Applying criteria of active surveillance to low-risk papillary thyroid cancer over a decade: How many surgeries and complications can be avoided? *Thyroid* 27:518-523.

SUMMARY OF THE STUDY

The records of 681 patients with papillary thyroid cancer who had thyroid surgery from January 2003 through December 2012 at a single center the US were reviewed. Patients were divided into 3 groups based upon ultrasound findings (size of the cancer, presence of abnormal lymph nodes, location of the cancer within the thyroid), patient characteristics (age, other medical problems), and medical

team characteristics (experience). Categories for surveillance included ideal, appropriate, and inappropriate. Many of the patients inappropriate for surveillance had abnormal lymph nodes on ultrasound, for example.

A total of 418 of the 681 patients had pathology showing papillary thyroid carcinoma and 243 of these (58%) had a biopsy before surgery showing papillary cancer. A total of 77 of these patients had nodules smaller than 1.5 cm on ultrasound before surgery with 27 under 1 cm and 50 ranging in size from 1.1-1.5 cm. A total of 15 of the 27 nodules under 1 cm were appropriate for surveillance, 12 were inappropriate, and none were ideal. Of the 50 nodules measuring 1.1-1.5 cm in size, 36 were appropriate, 9 were inappropriate, and 5 were ideal for active surveillance.

The patients with nodules less than 1cm who would have met the criteria for surveillance were treated with total thyroidectomy with central lymph node dissection in 13 of 15 patients, all with negative lymph nodes. Complications in this group included a chipped tooth and breast hematoma. No patients died or had recurrence.

The patients with nodules of 1.1-1.5cm who met criteria for active surveillance had total thyroidectomy 95% of the time (39/41 patients). A total of 33 of the patients had central lymph node dissection with 14 with spread to lymph nodes (largest 4mm). No patients had death or recurrence. One patient had permanent vocal cord paralysis and one patient had permanent hypocalcemia. The total rate of permanent complications was ~5%.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

If we apply active surveillance as an option for treatment of papillary thyroid cancer up to 1.5cm, 25% of patients may be able to participate in surveillance. Offering patients active surveillance is safe and would allow avoidance of surgery and its possible complications. Additionally, active surveillance would avoid the need for thyroid hormone replacement.

— Julie Hallanger Johnson, MD


THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

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

Thyroidectomy: surgery to remove the 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.

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

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

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.

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 **June** is **Differentiated Thyroid Cancer Awareness Month** and a bracelet is available through the ATA Marketplace to support thyroid cancer awareness and education related to thyroid disease.



**THYROID CANCER****The age cutoff of 45 years may not be appropriate for papillary thyroid cancer staging****BACKGROUND**

The rate of diagnosis of thyroid cancer has increased in the past several decades. There are different types of thyroid cancers but the most common type is Papillary thyroid cancer. Papillary thyroid cancer is a curable disease in the majority of cases and 90% of patients with Papillary thyroid cancer are still alive 10 years after the diagnosis. Older patients are at higher risk of developing a more aggressive type of Papillary thyroid cancer with higher chance of cancer recurrence and death. A cut off age of 45 had traditionally been used by American Joint Committee on Cancer to separate patients with a higher possibility of recurrence and death (>45) from those with higher possibility of cure (<45). Recent studies suggest this is not a hard cut off age. As this cutoff is important for staging of thyroid cancer and naturally the type of treatment that one would receive, the aim of this study was to evaluate whether cutoff age of 45 is still appropriate.

THE FULL ARTICLE TITLE

Adam MA et al Exploring the relationship between patient age and cancer-specific survival in papillary thyroid cancer: rethinking current staging systems. *J Clin Oncol* 2016;34:4415-20. Epub October 28, 2016.

SUMMARY OF THE STUDY

A total of 31,802 patients with Papillary thyroid cancer were found in United State SEER cancer registry for the period of 1998 to 2012. The rate of death from Papillary

thyroid cancer was calculated at different age groups among these patients.

As expected, majority of patients were women (about 79%) and the average age at the time of diagnosis of cancer was 45. A total of 331 patients died of thyroid cancer; the rate of death was found to be higher with increasing age, without finding a specific age that could serve as a cutoff for separating patients at higher risk of death from the others.

This study has shown that the chance of dying from Papillary thyroid cancer is indeed higher with increasing age. However, no age cutoff was found to distinguish patients with a better outcome from the others.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The finding of this study may change the staging system for thyroid cancer. This study suggests that an age >45 does not necessarily indicate a significantly higher risk of thyroid cancer recurrence and it may not be appropriate to recommend more aggressive treatment options. More studies are needed to clarify these findings.

— Shirin Haddady, MD

ATA THYROID BROCHURE LINKS

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

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).

SEER: Surveillance, Epidemiology and End Results program, a nation-wide anonymous cancer registry generated by the National Cancer Institute that contains information on 26% of the United States population. Website: <http://seer.cancer.gov/>



THYROID CANCER

Childhood radiation and thyroid cancer

BACKGROUND

Exposure to radiation occurs with many imaging studies (like CT scans) and medical treatments (like radiation therapy for cancer). When radiation exposure involves the head and neck areas directly, the thyroid is exposed and there is an increased risk for the development of thyroid cancer in the future. Children exposed to radiation are particularly vulnerable to these thyroid cancer health risks.

This study was done to further understand what the risks are regarding radiation exposure among children and its potential effect on getting thyroid cancer. The study specifically assessed very low doses of radiation exposure. To determine the potential thyroid cancer health risks, the authors pooled data from nine individual previously published studies of children who had a history of radiation exposure. These individuals included children with a history of radiation treatment for other cancers, children exposed to radiation during the treatment of non-cancerous diseases, and children who survived the atomic bombs in Japan during WWII.

THE FULL ARTICLE TITLE

Lubin JH et al Thyroid cancer following childhood low dose radiation exposure: a pooled analysis of nine cohorts. *J Clin Endocrinol Metab* 2017 Mar 8. doi: 10.1210/jc.2016-3529. [Epub ahead of print]

SUMMARY OF THE STUDY

From these data, the authors found that thyroid cancer was more common in the individuals who had a history of radiation exposure as children. The increased thyroid cancer risks were seen even in the children who received as

little as 0.1 Gray (ie one chest x-ray). Furthermore, there was a direct dose-response relationship between the dose of the radiation and the thyroid cancer risk, meaning that the higher the amount of radiation the child received, the higher the risk of thyroid cancer.

The risk for developing thyroid cancer as a result of childhood radiation exposure was present even more than 45 years later. The risk was greatest in those who received the radiation at particularly younger ages, except for the children who were irradiated at less than one year of age. There were no differences in the thyroid cancer risk between males and females.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study provides data that radiation exposure among children is not without risks. Although radiation may be required for certain medical procedures, the risk of developing thyroid cancer supports use of only the lowest amount of radiation needed, particularly when the child is very young. Finally, children who have known radiation exposure should continue to be monitored for the development of thyroid nodules or thyroid cancer for the rest of their lives.

— Angela M. Leung, MD, MSc

ATA THYROID BROCHURE LINKS

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

Thyroid nodules: <http://www.thyroid.org/thyroid-nodules>

ABBREVIATIONS & DEFINITIONS

Ionizing radiation: Radiation that can damage cells, causing cell death or mutation. It can originate from radioactive materials, x-ray tubes or specialized

machines. It is invisible and not directly detectable by human senses.



THYROID CANCER

Survivors of pediatric thyroid cancer have good quality of life

BACKGROUND

Most thyroid cancer arises from cells that make thyroid hormone, known as follicular thyroid cells. When it occurs in people younger than 18 years, is considered pediatric thyroid cancer. The number of cases of thyroid cancers is increasing, although the survival is excellent. Initial treatment usually involves the removal of the thyroid gland. As the thyroid concentrates iodine, if additional treatment is needed, it usually involves the administration of radioactive iodine to destroy the remaining cancer cells. Patients then need life-long follow up. The surgery may have complications.

Adult survivors of thyroid cancer have reported low health-related quality of life (QoL), while studies done in adolescents have reported no difference as compared to controls. Little is known about the long term quality of life of survivors of pediatric thyroid cancer. This study was done to study the quality of life of adult survivors who were diagnosed with thyroid cancer between the ages of 7 and 18 years.

THE FULL ARTICLE TITLE

Nies M et al. Long-term quality of life in adult survivors of pediatric differentiated thyroid carcinoma. *J Clin Endocrinol Metab* (2017) 102 (4): 1218-1226.

SUMMARY OF THE STUDY

This study included patients treated for thyroid cancer in the Netherlands between 1970 and 2013 who had a diagnosis of thyroid cancer made when they were younger than 18 years. Each participant was asked to recruit one person of similar age and sex without history of cancer, to be a control participant, best if of similar socio-economic status. If this was not possible, they were instructed to recruit a brother or sister. The participants answered four questionnaires of quality of life. One of the questionnaires (THYCA-QoL) was answered only by the patients with history of cancer as it is designed for survivors of thyroid cancer. Questionnaires assessed physical functioning, limitations due to physical problems, bodily pain, general health, vitality, social functioning, limitations due to emotional problems, and mental aspects of mental aspects of fatigue, motivation, and activity, depression and anxiety.

There were 170 patients with a history of pediatric thyroid cancer who were identified in the survey and 105 patients were available for the present study. Of these, only 67 were included for a variety of reasons. The average age of the patients was 34.2 years (range 18.8- 61.7 years) and they were followed for ~18 years. All patients had their thyroid removed completely and almost all (97%) received radioactive iodine therapy. Of these, 82% of patients were in remission of their cancer during their follow-up, with 10% having recurrent thyroid cancer and 7% having persistent thyroid cancer. Most patients were women (87%), were employed or were full-time students (90%) and were married or in a relationship (65%).

On most scales, survivors and controls did not differ; however, survivors reported more physical problems and limitations due to physical problems and mental fatigue. No differences were noted in anxiety and depression. The THYCA-QoL questionnaire identified that 84% of survivors did not have problems with their thyroid scar, 51-70% denied problems with symptoms related to low thyroid levels and 12% indicated not having interest in sex. Male survivors had higher levels of reduced motivation and depression as compared to females. Patients with recurrent or persistent thyroid cancer reported more symptoms and headaches were associated with higher doses of radioactive iodine. Unemployment was also associated with less QoL.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study confirms the good prognosis of pediatric thyroid cancer after 18 years of follow up, as only 1 out of 170 patients had died,. Although the study has some limitations, the data is encouraging as most patients were studying or working and were in relationships. It is also reassuring that there were no differences in anxiety or depression, social functioning, bodily pain, mental health, emotional problems or vitality, although some survivors reported less physical functioning and limitations due to physical functioning. It is unclear whether this could be associated with under-treatment or over-treatment of low thyroid hormone levels or low calcium levels. This study helps the providers caring for patients with pediatric thyroid cancer to reassure them about their future.

— Liuska Pesce, MD



THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

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

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

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

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

ABBREVIATIONS & DEFINITIONS

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

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.

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

the goal is a TSH in the normal range and is the usual therapy. Suppressive therapy means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.

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).

Parathyroid glands: usually four small glands located around the thyroid that secrete parathyroid hormone (PTH) which regulates the body's calcium levels.





THYROID CANCER

Low-risk thyroid cancer that spreads outside of the neck has mutations in cancer-related genes

BACKGROUND

Most thyroid cancers have an excellent prognosis even though spread of the cancer to lymph nodes in the neck are common, with a 10-year survival >90%. Spread of the cancer outside of the neck is rare (<10% of patients) and is associated with significantly worse prognosis. Older patients with spread of the cancer outside of the neck have a 5-year survival of 60% to 80%. Risk factors for spread of the cancer outside of the neck can be determined by examining the tissue after surgery and include extension of the cancer through the thyroid capsule, invasion into blood vessels and aggressive cancer subtypes, especially poorly differentiated cancer. In rare instances, thyroid cancer lacking any high-risk features present with spread of the cancer outside of the neck. Recent studies have identified mutations in cancer-related genes that are also associated with more aggressive cancers. Molecular marker analysis can identify these gene mutations, both on biopsy samples and after remove to the cancer by surgery. The current study examined the features and molecular markers of thyroid cancer that initially appeared low risk but developed spread of the cancer outside of the neck.

THE FULL ARTICLE TITLE

Xu B et al. Primary thyroid carcinoma with low-risk histology and distant metastases: clinicopathologic and molecular characteristics. *Thyroid*. February 1, 2017 [Epub ahead of print].

SUMMARY OF THE STUDY

This was an analysis of patients with thyroid cancer treated at Memorial Sloan-Kettering Cancer Center between 1983 and 2009. Patients with thyroid cancer were identified through a search of the institutional databases and included patients with spread of the cancer outside of the neck either at presentation or during follow-up. Patients were considered to have low-risk cancer if they did not have a poorly differentiated component, gross extension of the cancer through the thyroid capsule or extensive spread into blood vessels and had <5 lymph nodes involved with cancer. Next-generation sequencing for detection of mutations was performed on a subset of patients

Of 123 patients identified, 60% had spread of the cancer outside of the neck at the time of presentation while in 40% the spread developed during follow-up period. Only 15 patients (12%) had low-risk features and all had spread of the cancer outside of the neck at the time of initial presentation. Of these, 11 were female and the average age was 63 years. The average size of the primary cancer was only 1.8 cm, and the smallest cancer was 2 mm. Also 8 patients had encapsulated follicular variant papillary thyroid cancer with invasion, 2 had infiltrative follicular variant papillary thyroid cancer, 2 had encapsulated Hürthle-cell carcinoma and there was 1 patient each with papillary microcarcinoma infiltrative follicular variant, encapsulated papillary thyroid cancer classical variant and encapsulated follicular carcinoma (n = 1 for each). The majority of these cancers had extensive fibrosis and calcifications.

Molecular analysis with next-generation sequencing was performed in 8 cases; RAS mutations were identified in 5 of these cases and TERT promoter mutations in 6 while a combination of TERT plus BRAF V600E or RAS mutations occurred in 4 cases. Overall, 4 of the 15 patients had died within 32 months of diagnosis. Distant cancer spread was most frequently present in the bone.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that patients with thyroid cancer that lack high-risk features have a very low rate of spread of the cancer outside of the neck. Those low-risk patients that do have spread of their cancer most frequently have spread of the cancer to bone at presentation and often have RAS and TERT promoter mutations in their cancer. This study suggests that TERT mutations may help to predict aggressive cancer in the absence of other risk factors and suggests that molecular markers be done on all patients with thyroid cancer.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

**THYROID CANCER**, continued**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).

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

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

Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): a new term has been used to describe a type of papillary thyroid cancer which is non-invasive. These cancers behave less aggressively than typical papillary thyroid cancer and have been shown to have low risk for recurrence and low risk for spread outside of the thyroid.

Molecular markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular

markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and Thyroseq™

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

Mutation: A permanent change in one of the genes.

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC, TERT and RAS.

Watch this video to learn how you can support the ATA's ongoing research on Differentiated Thyroid Cancer!

ATA: Searching for Answers to Thyroid Cancer



00:05

vimeo



ATA Alliance for Thyroid Patient Education

GOAL

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

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

WHO WE ARE (in alphabetical order)

AMERICAN THYROID ASSOCIATION

www.thyroid.org

ATA Patient Resources:

<http://www.thyroid.org/thyroid-information/>

Find a Thyroid Specialist: www.thyroid.org

(Toll-free): 1-800-THYROID

thyroid@thyroid.org

BITE ME CANCER

<http://www.bitemecancer.org>

info@bitemecancer.org

GRAVES' DISEASE AND THYROID FOUNDATION

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

LIGHT OF LIFE FOUNDATION

www.checkyourneck.com

info@checkyourneck.com

THYCA: THYROID CANCER SURVIVORS' ASSOCIATION, INC.

www.thyca.org

(Toll-free): 877-588-7904

thyca@thyca.org

THYROID CANCER CANADA

www.thyroidcancer canada.org

416-487-8267

info@thyroidcancer canada.org

THYROID FEDERATION INTERNATIONAL

www.thyroid-fed.org

tfi@thyroid-fed.org



AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923



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



Thyroid Cancer Canada
Cancer de la thyroïde Canada



Thyroid Cancer

(Papillary and Follicular)

WHAT IS THE THYROID GLAND?

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

CANCER OF THE THYROID

Thyroid cancer is relatively uncommon compared to other cancers. In the United States it is estimated that in 2016 approximately 64,000 new patients will be diagnosed with thyroid cancer, compared to over 240,000 patients with breast cancer and 135,000 patients with colon cancer. However, fewer than 2000 patients die of thyroid cancer each year. In 2013, the last year for which statistics are available, over 630,000 patients were living with thyroid cancer in the United States. Thyroid cancer is usually very treatable and is often cured with surgery (see [Thyroid Surgery brochure](#)) and, if indicated, radioactive iodine (see [Radioactive Iodine brochure](#)). Even when thyroid cancer is more advanced, effective treatment is available for the most common forms of thyroid cancer. Even though the diagnosis of cancer is terrifying, the prognosis for most patients with papillary and follicular thyroid cancer is usually excellent.

WHAT ARE THE TYPES OF THYROID CANCER?

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

Follicular thyroid cancer. Follicular thyroid cancer makes up about 10% to 15% of all thyroid cancers in the United States. Follicular cancer can spread to lymph nodes in the neck, but this is much less common than with papillary cancer. Follicular cancer is also more likely than papillary cancer to spread to distant organs, particularly the lungs and bones.

Papillary and follicular thyroid cancers are also known as **Well-Differentiated Thyroid Cancers (DTC)**. The information in this brochure refers to the differentiated thyroid cancers. The other types of thyroid cancer listed below will be covered in other brochures

Medullary thyroid cancer. Medullary thyroid cancer (MTC), accounts for approximately 2% of all thyroid cancers. Approximately 25% of all MTC runs in families and is associated with other endocrine tumors (see [Medullary Thyroid Cancer brochure](#)). In family members of an affected person, a test for a genetic mutation in the RET proto-oncogene can lead to an early diagnosis of medullary thyroid cancer and, as a result, to curative surgery.

Anaplastic thyroid cancer. Anaplastic thyroid cancer is the most advanced and aggressive thyroid cancer and the least likely to respond to treatment. Anaplastic thyroid cancer is very rare and is found in less than 2% of patients with thyroid cancer. (See [Anaplastic thyroid cancer brochure](#).)

WHAT ARE THE SYMPTOMS OF THYROID CANCER?

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



Thyroid Cancer

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The important points to remember are that cancers arising in thyroid nodules generally do not cause symptoms, thyroid function tests are typically normal even when cancer is present, and the best way to find a thyroid nodule is to make sure that your doctor examines your neck as part of your periodic check-up.

WHAT CAUSES THYROID CANCER?

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

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

Exposure to radioactivity released during nuclear disasters (1986 accident at the Chernobyl power plant in Russia or the 2011 nuclear disaster in Fukushima, Japan) has also been associated with an increased risk of developing thyroid cancer, particularly in exposed children, and thyroid cancers can be seen in exposed individuals as many as 40 years after exposure.

You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see [Nuclear Radiation and the Thyroid brochure](#)). This prevents the absorption of radioactive iodine and has been shown to reduce the risk of thyroid cancer. The American Thyroid Association recommends that anyone living within 200 miles of a nuclear accident be given potassium iodide to take prophylactically in the event

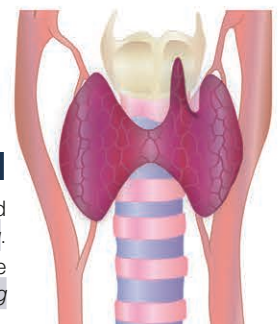
of a nuclear accident. If you live near a nuclear reactor and want more information about the role of potassium iodide, check the recommendations from your state at the following link: www.thyroid.org/web-links-for-important-documents-about-potassium-iodide/.

HOW IS THYROID CANCER DIAGNOSED?

A diagnosis of thyroid cancer can be suggested by the results of a fine needle aspiration biopsy of a thyroid nodule and can be definitively determined after a nodule is surgically excised (see [Thyroid Nodule brochure](#)). Although thyroid nodules are very common, less than 1 in 10 will be a thyroid cancer.

WHAT IS THE TREATMENT FOR THYROID CANCER?

Surgery. The primary therapy for all types of thyroid cancer is surgery (see [Thyroid Surgery brochure](#)). The extent of surgery for differentiated thyroid cancers (removing only the lobe involved with the cancer- called a lobectomy- or the entire thyroid – called a total thyroidectomy) will depend on the size of the tumor and on whether or not the tumor is confined to the thyroid. Sometimes findings either before surgery or at the time of surgery – such as spread of the tumor into surrounding areas or the presence of obviously involved lymph nodes – will indicate that a total thyroidectomy is a better option. Some patients will have thyroid cancer present in the lymph nodes of the neck (lymph node metastases). These lymph nodes can be removed at the time of the initial thyroid surgery or sometimes, as a later procedure if lymph node metastases become evident later on. For very small cancers (<1 cm) that are confined to the thyroid, involving only one lobe and without evidence of lymph node involvement a simple lobectomy (removal of only the involved lobe) is considered sufficient. Recent studies even suggest that small tumors – called micro papillary thyroid cancers – may be observed without surgery depending on their location in the thyroid. After surgery, most patients need to



FURTHER INFORMATION

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be on thyroid hormone for the rest of their life (see [Thyroid Hormone Treatment brochure](#)). Often, thyroid cancer is cured by surgery alone, especially if the cancer is small. If the cancer is larger, if it has spread to lymph nodes or if your doctor feels that you are at high risk for recurrent cancer, radioactive iodine may be used after the thyroid gland is removed.

Radioactive iodine therapy. (Also referred to as I-131 therapy). Thyroid cells and most differentiated thyroid cancers absorb and concentrate iodine. That is why radioactive iodine can be used to eliminate all remaining normal thyroid tissue and potentially destroy residual cancerous thyroid tissue after thyroidectomy (see [Radioactive Iodine brochure](#)). The procedure to eliminate residual thyroid tissue is called radioactive iodine ablation. This produces high concentrations of radioactive iodine in thyroid tissues, eventually causing the cells to die. Since most other tissues in the body do not efficiently absorb or concentrate iodine, radioactive iodine used during the ablation procedure usually has little or no effect on tissues outside of the thyroid. However, in some patients who receive larger doses of radioactive iodine for treatment of thyroid cancer metastases, radioactive iodine can affect the glands that produce saliva and result in dry mouth complications. If higher doses of radioactive iodine are necessary, there may also be a small risk of developing other cancers later in life. This risk is very small, and increases as the dose of radioactive iodine increases. The potential risks of treatment can be minimized by using the smallest dose possible. Balancing potential risks against the benefits of radioactive iodine therapy is an important discussion that you should have with your doctor if radioactive iodine therapy is recommended.

If your doctor recommends radioactive iodine therapy, your TSH will need to be elevated prior to the treatment. This can be done in one of two ways.

The first is by stopping thyroid hormone pills (levothyroxine) for 3-6 weeks. This causes high levels of TSH to be produced by your body naturally. This results in hypothyroidism, which may involve symptoms such as fatigue, cold intolerance and others, that can be significant. To minimize the symptoms of hypothyroidism

your doctor may prescribe T3 (Cytomel®, liothyronine) which is a short acting form of thyroid hormone that is usually taken after the levothyroxine is stopped until the final 2 weeks before the radioactive iodine treatment.

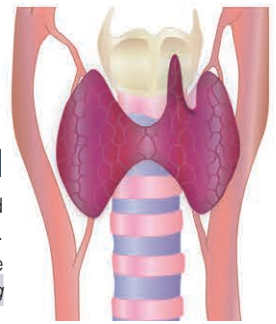
Alternatively, TSH can be increased sufficiently without stopping thyroid hormone medication by injecting TSH into your body. Recombinant human TSH (rhTSH, Thyrogen®) can be given as two injections in the days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on thyroid hormone and avoid possible symptoms related to hypothyroidism.

Regardless of whether you go hypothyroid (stop thyroid hormone) or use recombinant TSH therapy, you may also be asked to go on a low iodine diet for 1 to 2 weeks prior to treatment (see [Low Iodine Diet FAQ](#)), which will result in improved absorption of radioactive iodine, maximizing the treatment effect.

TREATMENT OF ADVANCED THYROID CANCER.

Thyroid cancer that spreads (metastasizes) outside the neck area is rare, but can be a serious problem. Surgery and radioactive iodine remain the best way to treat such cancers as long as these treatments continue to work. However, for more advanced cancers, or when radioactive iodine therapy is no longer effective, other forms of treatment are needed. External beam radiation directs precisely focused X-rays to areas that need to be treated—often tumor that has recurred locally or spread to bones or other organs. This can kill or slow the growth of those tumors. Cancer that has spread more widely requires additional treatment.

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



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

Periodic follow-up examinations are essential for all patients with thyroid cancer because the thyroid cancer can return—sometimes several years after successful initial treatment. These follow-up visits include a careful history and physical examination, with particular attention to the neck area. Neck ultrasound is an important tool to view the neck and look for nodules, lumps or cancerous lymph nodes that might indicate the cancer has returned. Blood tests are also important for thyroid cancer patients. Most patients who have had a thyroidectomy for cancer require thyroid hormone replacement with levothyroxine once the thyroid is removed (see [Thyroid Hormone Treatment brochure](#)). The dose of levothyroxine prescribed by your doctor will in part be determined by the initial extent of your thyroid cancer. More advanced cancers usually require higher doses of levothyroxine to suppress TSH (lower the TSH below the low end of the normal range). In cases of minimal or very low risk cancers, it's typically safe to keep TSH in the normal range. The TSH level is a good indicator of whether the levothyroxine dose is correctly adjusted and should be followed periodically by your doctor.

Another important blood test is measurement of thyroglobulin (Tg). Thyroglobulin is a protein produced by normal thyroid tissue and thyroid cancer cells, and is usually checked at least once a year. Following thyroidectomy and radioactive iodine ablation, thyroglobulin levels usually become very low or undetectable when all tumor cells are gone. Therefore, a rising thyroglobulin level should raise concern for possible cancer recurrence. Some patients will have thyroglobulin antibodies (TgAb) which can make it difficult to rely on the Tg result, as this may be inaccurate.

In addition to routine blood tests, your doctor may want to repeat a whole-body iodine scan to determine if any thyroid cells remain. Increasingly, these scans are only done for high risk patients and have been largely replaced by routine neck ultrasound and thyroglobulin measurements that are more accurate to detect cancer recurrence, especially when done together.

WHAT IS THE PROGNOSIS OF THYROID CANCER?

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



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