AMERICAN THYROID ASSOCIATION
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Clinical Thyroidology® for the Public

VOLUME 11 | ISSUE 9 | SEPTEMBER 2018

Treatment-free survival, which is living without the need for treatment for recurrent cancer, is an important outcome for thyroid cancer patients. The goal of this study was to understand factors associated with treatment-free survival in the general population, because this will enable the care teams to tailor long term follow up to a particular situation, and, many times, help decrease patient worry.

Banerjee M, Reyes-Gastelum D and Haymart MR 2018 Treatment-free survival in patients with differentiated thyroid cancer. J Clin Endocrinol Metab. Epub 2018 May 16. PMID: 29788217.

Ultrasound is the imaging method of choice for evaluating thyroid nodules. TIRADS is a 5 point classification to determine the risk of cancer in thyroid nodules based on ultrasound characteristics. The aim of this study was to compare the biopsy rate and diagnostic accuracy before and after applying TIRADS risk stratification to patients with thyroid nodules.

Hoang JK et al 2018 Reduction in thyroid nodule biopsies and improved accuracy with American College of Radiology Thyroid Imaging Reporting and Data System. Radiology 287:185–193. Epub 2018 Mar 2. PMID: 29498593.

Thyroid ultrasound is important in identifying a nodule and the appearance on ultrasound in addition to size are the key factors determining the need for biopsy. TIRADS is a 5 point classification to determine the risk of cancer in thyroid nodules based on ultrasound characteristics. This study explores the accuracy of TIRADS to predict cancer in thyroid nodules that are ≤ 1 cm.

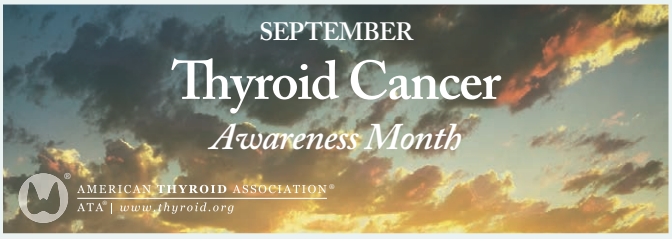
Mendes GF et al 2018 Fine needle aspiration biopsy of thyroid nodule smaller than 1.0 cm: accuracy of TIRADS classification system in more than 1000 nodules. Br J Radiol 91:20170642. Epub 2017 Dec 22. PMID: 29182368.

Patients diagnosed with thyroid cancer usually have an excellent prognosis. This is due to both surgery and, when needed, radioactive iodine therapy. There is currently no agreement regarding the best timing of administration of radioactive iodine. The objective of this study was to evaluate the response to treatment when giving radioactive iodine within 3 months of thyroidectomy versus ≥3 months after surgery.

Li H et al 2018 Delayed initial radioiodine therapy related to incomplete response in low- to intermediate-risk differentiated thyroid cancer. Clin Endocrinol (Oxf) 88:601–606. Epub 2018 Feb 18. PMID: 29338092.

Up to 50% of patients with intermediate-high risk thyroid cancer have clinically meaningful cancer that has spread to the lymph nodes at the time of surgery. Further, persistent or residual cancer in lymph nodes is the most common cause of recurrent thyroid cancer. This study's aim was to identify the most common location of persistent lymph node cancer as well as the primary reason why there remained cancer in patients with intermediate and high risk thyroid cancer.

Miller JE et al 2018 Location and causation of residual lymph node metastases after surgical treatment of regionally advanced differentiated thyroid cancer. Thyroid 28:593–600. Epub 2018 Apr 23. PMID: 29562827.



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EDITOR'S COMMENTS

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

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

September is Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Can we predict the length of treatment-free survival in patients with thyroid cancer?
- Can the TIRADS imaging criteria decrease the number of thyroid nodule biopsies without missing any cancers?
- Can the TIRADS imaging criteria be applied to small thyroid nodules?
- Does the timing of radioactive iodine therapy after surgery affect outcomes in patients with thyroid cancer?
- What are the implications of residual cancer in lymph nodes after surgery for patients with intermediate to high risk 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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Clinical Thyroidology® for the Public

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THYROID CANCER

Analysis of clinical factors 1 year after surgery for thyroid cancer enables prediction of treatment-free survival

BACKGROUND

Thyroid cancer is the fastest rising cancer in women. Fortunately, effective treatments exist and most patients have an excellent prognosis and death from thyroid cancer is rare. Persistent or recurrent cancer is more common and suspected or confirmed thyroid cancer recurrence is associated with psychological distress and increased cancer related worry. Treatment of cancer recurrence increases risk for complications such as hoarseness due to vocal cord paralysis (with recurrent surgery) and dry mouth due to salivary gland problems (with recurrent radioactive iodine therapy)

Treatment-free survival, which is living without the need for treatment for recurrent cancer, is an important outcome for patients. However, data regarding treatment-free survival in the general population does not exist. What there is known about this outcome in general is limited to data from single institutions. The goal of this study was to understand factors associated with treatment-free survival in the general population, because this will enable the care teams to tailor long term follow up to a particular situation, and, many times, help decrease patient worry.

THE FULL ARTICLE TITLE

Banerjee M, Reyes-Gastelum D and Haymart MR 2018 Treatment-free survival in patients with differentiated thyroid cancer. J Clin Endocrinol Metab. Epub 2018 May 16. PMID: 29788217.

SUMMARY OF THE STUDY

Data for this study was obtained from a large national registry called Surveillance, Epidemiology and End Results (SEER) and Medicare data. A total of 9273 patients who were diagnosed with thyroid cancer between 1998 and 2012, who had a documented initial thyroid surgery and who did not have another diagnosis of a non-thyroid cancer , were selected for the study. Their outcomes formed the basis for the analysis. Clinical characteristics that were recorded included age, race, household income, tumor stage, tumor size and type of treatment received.

A treated recurrence was defined as additional treatment done 1 year or more after diagnosis. Treatment-free survival was the time interval between diagnosis and treatment of recurrent/persistent cancer or to the time of analysis. Disease-specific survival was defined as the time interval from diagnosis to death from thyroid cancer or time of analysis. A complex statistical analysis was employed to analyze data obtained.

The average follow up time was 6.4 years. Women comprised 75% of patients and the average age was 69 years. Of the 9273 patients, 1332 (14.4%) had a recurrence, 301 patients (3.3%) had additional surgery, 978 (10.6%) were treated with radioactive iodine and 435 (4.7%) received external radiation.

Five groups were defined with progressively reduced recurrence-free survival based on history of additional neck surgery, use of radioactive iodine or external radiation done at 1 or more years after initial diagnosis. Group 1 consisted of patients with the lowest risk for recurrence: they had localized cancer stage, cancer size less or equal to 1 cm and no therapy with radioactive iodine. Group 2 added therapy with radioactive iodine and female sex. Group 3 added larger cancers and male sex. Group 4 included patients spread of the cancer into the neck lymph nodes. Group 5 was comprised of patient with spread of the cancer outside of the neck.

The 5-year treatment-free survival rates of groups 1-5 were 96%, 91%, 85%, 72% and 52% respectively. The 10-year treatment-free survival rates were 94%, 87%, 80%, 64% and 39%. The 10-year disease-specific survival rates were 99%, 98%, 96%, 89% and 59%.

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THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The results of this study verify the factors that have previously been shown to carry worse prognosis: male sex, spread of the cancer to the lymph nodes, cancer extending outside of the thyroid and especially spread of the cancer outside of the neck. They also confirm that the majority of thyroid cancer patients continue to do very well. The limitation of this study mainly is that the use of Medicare data excludes most patients younger than 65 and therefore the average age of 69 in this study is older than most people diagnosed with differentiated thyroid cancer.

— Jessie Block-Galarza, MD

ATA THYROID BROCHURE LINKS

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

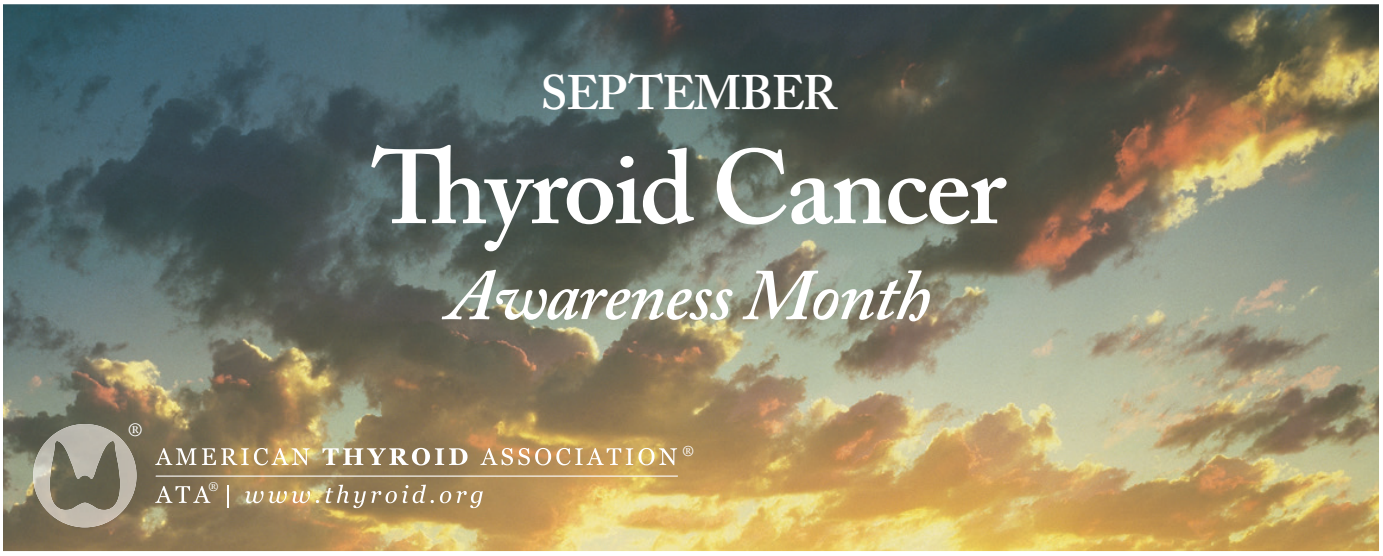
ABBREVIATIONS & DEFINITIONS

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

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

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.



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THYROID NODULES

Using the Thyroid Imaging Reporting and Data Systems (TIRADS) will decrease the number of thyroid nodule biopsies while improving diagnostic accuracy

BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of people in the United States. The concern of any nodule is whether it is a thyroid cancer. Fortunately, ~95% of thyroid nodules are benign. At present, the only way to make a diagnosis of thyroid cancer prior to surgery is with a thyroid biopsy. Ultrasound is the imaging method of choice for evaluating thyroid nodules and the appearance on ultrasound in addition to size are the key factors determining the need for biopsy. The more suspicious features thyroid nodule has the lower is the threshold for thyroid biopsy. In rare cases, the appearance on ultrasound alone can be diagnostic of either cancerous or benign nodules. A lot of research is being done to expand the characteristics of a nodule on ultrasound into a risk assessment of the likelihood of thyroid cancer.

The American College of Radiology Thyroid Imaging Reporting and Data Systems (TIRADS) is a 5 point classification to determine the risk of cancer in thyroid nodules based on ultrasound characteristics. The aim of this study was to compare the biopsy rate and diagnostic accuracy before and after applying TIRADS risk stratification to patients with thyroid nodules.

THE FULL ARTICLE TITLE

Hoang JK et al 2018 Reduction in thyroid nodule biopsies and improved accuracy with American College of Radiology Thyroid Imaging Reporting and Data System. Radiology 287:185–193. Epub 2018 Mar 2. PMID: 29498593.

SUMMARY OF THE STUDY

The study consisted of 100 nodules in 92 patients who underwent thyroid biopsy and/or surgical resection between April 2009 and May 2010 at a single institution. All biopsied nodules had dedicated video imaging reviewed. The ultrasound images were reviewed by 11 radiologists from 9 different institutions. The radiologists were blinded to the cytology and pathology results. Of these, 3 radiologists were considered experts, as they were part of the committee that developed the TIRADS criteria. Their consensus reports of the US findings were used as the "truth" for the nodule features. The other 8 radiologists—2 radiologists in academic practice and 6 in private practice—were test readers and had no knowledge of TIRADS guidelines. All the radiologists reviewed the ultrasound images and evaluated the nodules for the five features used in TIRADS, including composition (what the nodule looked like), echogenicity (darkness), shape, margin, and echogenic foci (bright spots on the images). The test readers assigned each nodule a cancer risk category that matched the five risk-stratification levels used in TIRADS (highly suspicious, moderately suspicious, mildly suspicious, not suspicious, and benign). The test readers also noted whether they would recommend a biopsy for each nodule. A comparison was made between the test readers' recommendations with and without TIRADS guidelines.

The average age of the patients was 52 years. Of the 100 nodules that were evaluated, the average size was 2.7 cm. There were 15 cancers (15%) identified, with an average size of 2.2 cm, including 11 classic papillary thyroid cancer (73%) and 4 follicular variant of papillary thyroid cancer (27%). The average number of biopsies recommended by the 8 test readers was 80 with their own practice pattern and 57 with TIRADS guidelines. After applying TIRADS guidelines, the readers of each test had a reduction in the number of biopsies that ranged from 5% to 41%. After the TIRADS guidelines were applied, 5 cancers were not recommended for biopsy by some of the test radiologists and 3 cancers were not recommended for follow-up or biopsy because of incorrect categorization of ultrasound features by 2 of the 8 test readers.

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THYROID NODULES, continued

If test readers had used guidelines from other societies (the American Thyroid Association, Korean TIRADS, or French TIRADS), the average number of nodules recommended for biopsy would have been 77, 85, and 74, respectively, as compared with 57 nodules with TIRADS. The 2 cancerous nodules that did not meet the criteria for biopsy according to TIRADS guidelines also did not meet criteria for biopsy with any of the other guidelines.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

By using the TIRADS guidelines from the American College of Radiology, one can see a significant reduction in the number of thyroid nodules recommended for biopsy and an improvement in the accuracy of recommendations for nodule management. With this system, the vast majority of the cancerous nodules will be recommended for biopsy or follow-up ultrasound.

— Alan P. Farwell, MD, FACE

ATA THYROID BROCHURE LINKS

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

Fine Needle Aspiration Biopsy of Thyroid Nodules: https://www.thyroid.org/fna-thyroid-nodules/

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

ABBREVIATIONS & DEFINITIONS

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

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

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

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).

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THYROID NODULES

Thyroid Imaging Reporting and Data Systems (TIRADS) accurately determine the risk of cancer in small thyroid nodules

BACKGROUND

Thyroid nodules are very common, occurring in up to 50% of people in the United States. The concern of any nodule is whether it is a thyroid cancer. Fortunately, ~95% of thyroid nodules are benign. At present, the only way to make a diagnosis of thyroid cancer prior to surgery is with a thyroid biopsy. Thyroid ultrasound is important in identifying a nodule and the appearance on ultrasound in addition to size are the key factors determining the need for biopsy. The more suspicious features thyroid nodule has the lower is the threshold for thyroid biopsy. In rare cases, the appearance on ultrasound alone can be diagnostic of either cancerous or benign nodules. A lot of research is being done to expand the characteristics of a nodule on ultrasound into a risk assessment of the likelihood of thyroid cancer.

The American College of Radiology Thyroid Imaging Reporting and Data Systems (TIRADS) is a 5 point classification to determine the risk of cancer in thyroid nodules based on ultrasound characteristics. This system has been mainly used for thyroid nodules that are ≥1 cm. This study explores the accuracy of TIRADS to predict cancer in thyroid nodules that are ≤ 1 cm.

FULL ARTICLE TITLE

Mendes GF et al 2018 Fine needle aspiration biopsy of thyroid nodule smaller than 1.0 cm: accuracy of TIRADS classification system in more than 1000 nodules. Br J Radiol 91:20170642. Epub 2017 Dec 22. PMID: 29182368.

SUMMARY OF THE STUDY

A total of 1116 thyroid nodules < 1 cm in 951 patients who had a thyroid biopsy were selected for analysis. Thyroid nodules were classified according to TIRADS based on their US features. In the TIRADS, the following four ultrasound features were scored 1 point each: irregular margins, hypoechogenicity (darkness), taller-than-wide shape, and microcalcifications; marked hypoechogenicity scored 2 points. TIRADS 1 was defined as normal thyroid, 2 as the presence of benign features such as a cystic or spongiform nodule, 3 as the absence of suspicious features, and 4A as 1 point, 4B as 2 points, 4C as 3 to 4 points, and 5 as 5 points, respectively.

Cancer rates were 0.9% in TIRADS 2, 2.9% in TIRADS 3, 12.3% in TIRADS 4A, 34.4% in TIRADS 4B, 66.6% in TIRADS 4C, and 86% in TIRADS 5.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

A simple 5-category TIRADS analysis was able to accurately assess the risk of cancer in thyroid nodules <1 cm. This is the first study validating TIRADS in thyroid nodules that are ≤ 1 cm. We are not yet at the point where a diagnosis of cancer can be made with ultrasound alone without a thyroid biopsy. However, better understanding of the characteristics of benign nodules may help decrease the need for a biopsy in some patients. Understanding the risk of cancer in these small thyroid nodules can guide the management in selected patients.

—Valentina D. Tarasova, M.D.

ATA THYROID BROCHURE LINKS

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

Fine Needle Aspiration Biopsy of Thyroid Nodules: https://www.thyroid.org/fna-thyroid-nodules/

THYROID NODULES, continued

ABBREVIATIONS AND DEFINITIONS

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

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

Microcalcifications: Small flecks of calcium within a thyroid nodule, usually seen as small bright spots on ultrasonography. These are frequently seen in nodules containing papillary thyroid cancer.

Thyroid Awareness Monthly Campaigns

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

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THYROID CANCER

Giving radioactive iodine within 3 months after thyroidectomy results in better responses than delaying therapy beyond 3 months after surgery

BACKGROUND

Patients diagnosed with thyroid cancer usually have an excellent prognosis. This is due to effective therapies, including surgery and, when needed, radioactive iodine therapy. Radioactive iodine works like a "magic bullet", as it is taken up and destroys only thyroid cells, both normal and cancerous. The process of destroying residual thyroid tissue is called radioactive iodine ablation. In patients who have an indication to undergo radioactive iodine ablation, there is currently no agreement regarding the best timing of administration. The objective of this study was to evaluate the response to treatment when giving radioactive iodine within 3 months of thyroidectomy versus ≥3 months after surgery.

THE FULL ARTICLE TITLE

Li H et al 2018 Delayed initial radioiodine therapy related to incomplete response in low- to intermediate-risk differentiated thyroid cancer. Clin Endocrinol (Oxf) 88:601–606. Epub 2018 Feb 18. PMID: 29338092.

SUMMARY OF THE STUDY

A total of 235 patients with low-to -intermediate risk thyroid cancer were included in the study. These patients were treated with radioactive iodine between December 2008 and May 2015 following a total thyroidectomy at the Peking Union Medical College Hospital. They were divided into two groups: Group 1 included 187 patients who received radioactive iodine ablation <3 months following surgery and Group 2 included 43 patients who received it ≥3 months after surgery. The two groups were similar in regard to age, sex, type of cancer and cancer stage. Response to therapy was categorized as excellent, indeterminate or incomplete (persistent disease by imaging or blood tests).

The authors found that there was a significant difference between the two groups in terms of response to therapy when excluding the impact of other factors such as patient age, sex, cancer type, cancer stage and radioactive iodine dose. Overall, 78.1% of patients in group 1 had an excellent response compared to 62.5% in group 2. Additionally, only 4.3% of patients in group 1 had an incomplete response compared to 18.8% patients in group 2.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study found that giving radioactive iodine ablation within 3 months after surgery resulted in better outcomes than waiting for >3 months in patients with low-to-intermediate risk thyroid cancer. This is helpful when planning the best treatment plan. However, it is possible that some of the patients included in the study had low risk thyroid cancer that may not warrant radioactive iodine ablation according to current guidelines. More data is needed to determine if patients with more aggressive thyroid cancer would respond in a similar fashion. In any event, for patients who have more worrisome features, administration of radioactive iodine within 3 months from surgery is most likely preferable.

— Maria Papaleontiou, MD

ATA THYROID BROCHURE LINKS

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

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

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THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

Differentiated thyroid cancers: Most thyroid cancers are differentiated cancers. The cells in these cancers look a lot like normal thyroid tissue when seen with a microscope. These cancers develop from thyroid follicular cells and include papillary and follicular thyroid cancers.

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

Thyroid Remnant Ablation: destruction of the small amount of thyroid tissue that remains after surgery (thyroidectomy) with the use of radioactive iodine.

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.

Excellent response: undetectable thyroglobulin (tumor marker) with negative imaging in thyroid cancer patients following treatment

Biochemical incomplete response: detectable thyroglobulin (tumor marker) with negative imaging in thyroid cancer patients following treatment

Structural incomplete response: evidence of persistent structural disease on imaging in thyroid cancer patients following treatment

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THYROID CANCER

Implications of residual cancer in lymph nodes after surgery for patients with intermediate to high risk thyroid cancer.

BACKGROUND

Thyroid cancer is the fastest rising cancer in women. While spread of the cancer to the lymph nodes in the neck is common at the time of surgery, the prognosis is usually excellent. Indeed, when talking about risk in patients with thyroid cancer, it is risk of cancer recurrence rather than risk of death that is discussed. There are 3 risk levels based on the risk of cancer recurrence: low, intermediate and high. Up to 50% of patients with intermediate-high risk thyroid cancer have clinically meaningful cancer that has spread to the lymph nodes at the time of surgery. Despite recommendations for patients with known lymph node involvement to have 'compartment-oriented' lymph node dissections (all of the lymph nodes in a given area removed, not 'berry-picking' of individual nodes), persistent or residual cancer in lymph nodes is the most common cause of recurrent thyroid cancer. This study's aim was to identify the most common location of persistent lymph node cancer as well as the primary reason why there remained cancer in patients with intermediate and high risk thyroid cancer.

THE FULL ARTICLE TITLE

Miller JE et al 2018 Location and causation of residual lymph node metastases after surgical treatment of regionally advanced differentiated thyroid cancer. Thyroid 28:593–600. Epub 2018 Apr 23. PMID: 29562827.

SUMMARY OF THE STUDY

A total of 352 patients with intermediate or high-risk thyroid cancer treated with total thyroidectomy, +/- some form of neck dissection, and radioactive iodine therapy at a single institution were reviewed. All patients had a specialized thyroid scan right before and after radioactive iodine therapy to look for persistent abnormal lymph nodes after surgery. Approximately 40% of patients had residual cancer in the lymph nodes after their surgery but before radioactive iodine therapy. Patients with persistent cancer in the lymph nodes were, on average, 10 years younger, more likely to have multifocal cancer, cancer <2cm, and not have known central lymph node involvement at the time of surgery. Of patients with persistent cancer in the lymph nodes, more than 50% had a surgery that removed other lymph nodes in that location and the most common location was in the central area near where the thyroid was.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Patients that have intermediate and high-risk thyroid cancer have a high rate of residual cancer in the lymph nodes after initial surgery. If a patient has known intermediate-high risk disease before surgery, consideration should be given to thoroughly removing lymph nodes in the central compartment (because it's the most common place for residual disease), and making sure to have good imaging looking at the entire neck before surgery. But importantly, there is not a 'one-size-fits-all' approach to either surgery or post-operative therapy.

— Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

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

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ABBREVIATIONS & DEFINITIONS

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

Thyroid scan: this imaging test uses a small amount of a radioactive substance, usually radioactive iodine, to obtain a picture of the thyroid gland. A "cold" nodule means that the nodule is not functioning normally. A patient with a "cold" nodule should have a fine needle aspiration biopsy of the nodule. A "functioning", or "hot", nodule means that the nodule is taking up radioactive iodine to a degree that is either similar to or greater than the uptake of normal cells. The likelihood of cancer in these nodules is very low and a biopsy is often not needed.

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).

Total thyroidectomy: surgery to remove the entire thyroid gland.

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*).

Central neck compartment: the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries.

Prophylactic central neck dissection: careful removal of all lymphoid tissue in the central compartment of the neck, even if no obvious cancer is apparent in these lymph nodes.

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ATA Alliance for Thyroid Patient Education

GOAL

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

We look forward to future collaborations and continuing to work together 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

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www.thyroidcanceralliance.org
www.thyroidcancerpatientinfo.org
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AMERICAN THYROID ASSOCIATION
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GRAVES' DISEASE & THYROID FOUNDATION

BITE ME CANCER!

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THYROID CANCER ALLIANCE

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Graves' Disease & Thyroid Foundation

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Light of Life Foundation
checkyourneck.com

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Thyroid Disease and You...

Do you have any concerns about your thyroid function? Have you or a family member been diagnosed with thyroid disease or have you noticed a lump in your neck?

The American Thyroid Association and our Alliance Partners Invite Thyroid Patients and their Families to join us for the:

2018 ATA Alliance for Thyroid Patient Education Health Forum

Saturday, October 6, 2018
2:00 pm – 4:00 pm
Marriott Marquis Washington, DC
901 Massachusetts Ave NW – Tulip Room, Mezzanine Level
Washington, DC 20001 | Phone: 844-203-5027

ATA Physician Members and our ATA Alliance Partners are available to meet with thyroid patients and their families during the forum. This program is free and open to the public, please register / confirm your participation here: **https://www.eventbrite.com/e/thyroid-disease-and-you-ata-thyroid-education-public-health-forum-tickets-48658607204**

Who should attend?

Please come if you have questions, symptoms, or concerns about a thyroid problem. We invite anyone who has had an overactive or underactive thyroid, thyroiditis, a thyroid nodule, thyroid cancer, or a family history of thyroid problems or related disorders, including rheumatoid arthritis, juvenile diabetes, or pernicious anemia. Free educational materials will be available for all.

Reservations requested. Walk-ins welcome.

E-mail **thyroid@thyroid.org** with any questions or requests for additional information.

American Thyroid Association | 6066 Leesburg Pike, Suite 550 | Falls Church, VA
www.thyroid.org | thyroid@thyroid.org

AMERICAN THYROID ASSOCIATION
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Friends of the ATA

FOUNDED 2005

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

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

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

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

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

www.thyroid.org

AMERICAN THYROID ASSOCIATION
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Donate Now!

JOIN US

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

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

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

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

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

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

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

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

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.

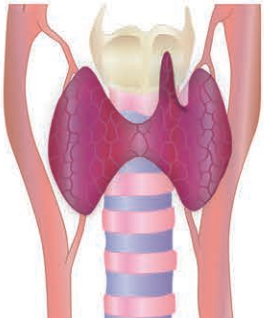
You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see *Nuclear Radiation and the Thyroid brochure*). This prevents the absorption of radioactive iodine and has been shown to reduce the risk of thyroid cancer. The American Thyroid Association 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

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

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

Thyroid Cancer
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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.

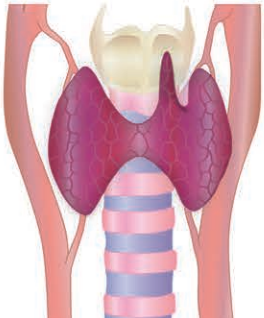
Alternatively, TSH can be increased sufficiently without stopping thyroid hormone medication by injecting TSH into your body. Recombinant human TSH (rhTSH, Thyrogen®) can be given as two injections in the days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on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

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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