Volume 13 | Issue 9 | September 2020

Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

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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, MCT8 – AHDS Foundation, ThyCa: Thyroid Cancer Survivors' Association, Thyroid Cancer Canada, Thyroid Cancer Alliance* and *Thyroid Federation International*.

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

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

September is Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Are new chemotherapy drugs effective against anaplastic thyroid cancer?
- If you had a low risk papillary thyroid cancer, would you choose to monitor closely or to have surgery?
- How common is salivary gland damage after radioactive iodine therapy for thyroid cancer?
- Due positive thyroglobulin antibodies indicate a recurrence of thyroid cancer?
- Are there effective non-surgical options for the treatment of benign thyroid nodules?
- Is a fixed dose of radioactive iodine effective treatment for toxic multinodular goiters?

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

Immune checkpoint inhibitor therapy using spartalizumab for anaplastic thyroid cancer

BACKGROUND

In contrast to the common types of thyroid cancer, anaplastic thyroid cancer is a rare, aggressive form of thyroid cancer which can be rapidly progressive and fatal. Depending on the extent of cancer and the goals of the cancer treatment (in considering the patient's overall health and preferences), treatment options for anaplastic thyroid cancer may include surgery, external beam radiation treatment, chemotherapy, or combinations of those. However, survival rates of patients with anaplastic thyroid cancer are generally very low, with survival often <6 months after diagnosis, and more research is needed for effective treatments that can improve survival.

Immune checkpoint inhibitor therapy is a type of cancer treatment that stimulates the body's immune system to fight the cancer, and it is used for a variety of cancers. Spartalizumab is an example of an immune checkpoint inhibitor and it is an antibody which blocks the programmed death-1 and 2 (PD-1 and PD-2) receptors on the surface of immune T cells, which then stimulates immune cells to attack cancer cells. Since anaplastic thyroid cancer cells often express the binding protein that attaches to the PD-1 receptor (programmed cell death-ligand 1 (PD-L1)), spartalizumab may be an effective treatment for this aggressive cancer. The investigators of the study performed a clinical trial to examine the clinical response of anaplastic thyroid cancer patients treated with spartalizumab. The investigators reported on the response of the tumors, survival of patients and side of the treatment.

THE FULL ARTICLE TITLE

Capdevila J et al PD-1 Blockade in Anaplastic Thyroid Carcinoma. J Clin Oncol. 2020 38:2620-2627. doi: 10.1200/JCO.19.02727.

SUMMARY OF THE STUDY

The investigators performed a phase II international multicenter study of Spartalizumab in 42 patients with locally advanced or metastatic anaplastic thyroid cancer. Of these patients, 60% had prior cancer drug treatment, 71% had prior radiation treatment, and 67% had prior thyroid cancer surgery (thyroidectomy with or without removal of lymph nodes). Both the patients and their doctors were aware of the treatment given. The study was funded by the manufacturer of the drug, Novartis. There was no comparison group, so all of the patients received the drug under study. The drug was given intravenously every 4 weeks, but could be held or stopped if there was toxicity (serious side effects). The primary outcome was the overall response rate according to Response Evaluation Criteria in Solid Tumors (RECIST). The average duration of study treatment was 8 weeks, but ranged from about 2 to 114 weeks.

The overall response rate was 19%, which included 3/42 patients (7% of the entire study population) who had a complete response (disappearance of cancer lesions that were measured at the beginning of the study) and 5/42 patients (12%) of patients who had a partial response (some reduction in the amount of cancer seen on imaging, but some visible cancer on scans). Of the 40 patients whose cancers could be evaluated for PD-L1 expression, 28/40 (70%) expressed this marker at baseline. Further, only the patients whose cancers expressed PD-L1 (8/28, 29%) responded to the drug as none of the patients whose cancers did not express PD-L1 (0/12) responded. The overall survival rate was 5.9 months, with 40% of patients alive at one year. Adverse events were reported in 41/42 (98%) of patients and more serious adverse events were reported in 29/42 patients (69%).

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that a subset of patients with anaplastic thyroid cancer had a significant response to spartalizumab, particularly those patients whose cancers expressed PD-L1. Further, the treatment was generally well-tolerated by patients and the side effects were similar to those seen in other clinical trials of drugs in this class. This is exciting news for patients newly diagnosed with anaplastic thyroid cancer. It will be important to confirm these findings in other studies.

— Anna M. Sawka, MD, PhD

THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Anaplastic Thyroid Cancer: https://www.thyroid.org/anaplastic-thyroid-cancer/

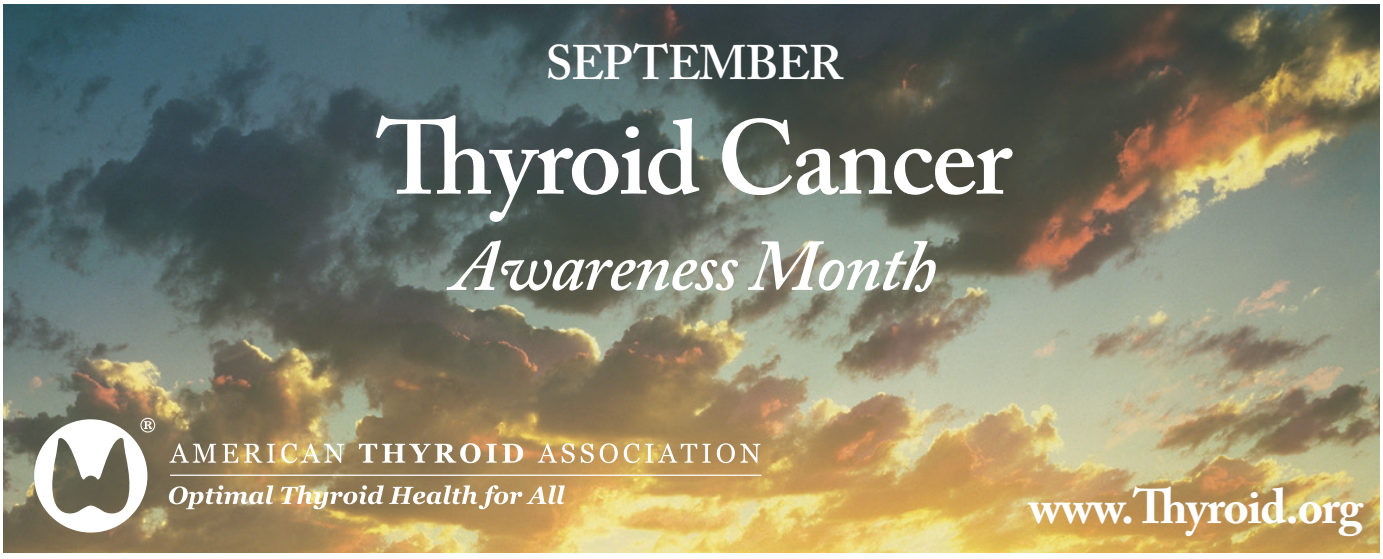
ABBREVIATIONS & DEFINITIONS

Anaplastic thyroid cancer: a very rare but very aggressive type of thyroid cancer. In contrast to all other types of thyroid cancer, most patients with anaplastic thyroid cancer die of their cancer.

Clinical trials: when a new drug is developed, it must undergo an extensive series of steps, called phases, to prove that it is more effective in patients than the drugs that are currently available to treat the condition. A Phase I trial tests a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range and identify side effects. A Phase II trial gives the drug to a larger group of people to see if it is effective and to further evaluate its safety. A Phase III trial gives the drug to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments and collect information that will allow the drug or treatment to be used safely.

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.

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



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THYROID CANCER

If you had a small, low risk papillary thyroid cancer, would you choose to monitor closely or to have surgery?

BACKGROUND

There has been an increase in thyroid cancer diagnosis in the last 30 years without an increase in thyroid cancer-related deaths. This is believed to be due to detection of very small papillary thyroid cancers that are unlikely to grow or cause harm. Traditional treatment for thyroid cancer is surgery to remove the thyroid gland completely or partially. Surgery is sometimes followed with radioactive iodine therapy. Side effects with these treatments are small but present.

On the other hand, there is new information that most of the small papillary thyroid cancers may be growing so slowly that patients may live out their life without having any symptoms due to the thyroid cancer. Active surveillance (close observation without surgery) may be a good alternative to surgery for these patients and there are multiple ongoing studies investigating the safety of this option. Since this is a relatively new approach, authors designed this study to answer 2 main questions: 1) if it is offered as an alternative, how often do patients choose active surveillance over surgery and 2) what are the reasons for their choices.

THE FULL ARTICLE TITLE

Sawka AM et al 2020 A prospective mixed-methods study of decision-making on surgery or active surveillance for low-risk papillary thyroid cancer. Thyroid. Epub 2020 Apr 8. PMID: 32126932.

SUMMARY OF THE STUDY

The patients were recruited from thyroid cancer specialty clinics at the University Health Network in Toronto. The study is still ongoing and the results from the first 100 patients were analyzed and reported. Patients were 18 years or older with low risk papillary thyroid cancers <2 cm. Only the patients without evidence of spread of the cancer outside of thyroid were included in the study. Patients were given detailed information about prognosis and options of surgery (standard of care) or active surveillance (alternative as part of the study). Clinical information was obtained from medical records review. Characteristics of patients (such as age, gender etc) and level of confidence in making an informed management decision were assessed by questionnaires. Level of satisfaction with the decision was determined using a scale. As the last step patients were asked "what is the main reason why you decided to have surgery or active surveillance (no surgery) for your thyroid cancer?"

The average age was 52 years, and ~75% of participants were female, married and had an undergraduate college degree or higher. Active surveillance was the choice of 71% of patients. These patients were older and more likely had very small (<1cm) papillary thyroid cancers. Patients were satisfied and confident in the ability to make the decision.

Opportunity to be involved in the treatment choice and to receive medical information were important in their decision for both groups. In the active surveillance group concerns were worry about surgical risk, possibility of taking thyroid medications, and potential impact on quality of life. Patients who chose surgery had concerns about anxiety from having cancer and not curing it.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this study, the majority of patients with small, low risk papillary thyroid cancers preferred active surveillance over surgery if given the option. They valued receiving medical information and participating in the final decision. Personal perceptions about cancer or surgery, family considerations and trust in their healthcare team were important in making the treatment decision.

As we find more than one good management option based on evidence, it is important for the patients to receive and understand the information about their condition and to share their values and preferences with their physician to make the best possible treatment decisions.

— Ebru Sulanc, MD

THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): https://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).

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

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

Active surveillance: this is close observation of a small low risk thyroid cancer without surgery

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THYROID CANCER

Salivary gland damage associated with dose of radioactive iodine received in papillary thyroid cancer treatment

BACKGROUND

Papillary thyroid cancer is the most common thyroid cancer. Overall, the prognosis of papillary thyroid cancer is very good because of the effective treatments available. Most patient are treated with surgery first, followed by thyroid hormone suppression. For patients at higher risk of thyroid cancer recurrence, radioactive iodine therapy following surgery is very effective in seeking out and destroying thyroid cancer cells. Radioactive iodine works by being taken up and concentrated in the thyroid cancer cells and killing them with the radiation. A few other cells in the body, such as those in the salivary and parotid glands, also take up radioactive iodine but do not concentrate it so the radiation usually does little or no damage. However, high doses of radioactive iodine therapy can cause salivary gland damage, known as chronic sialadenitis (inflammation of the salivary gland). While usually mild, it can be severe and is the most common adverse side effect of radioactive iodine therapy. Imaging of the neck with an ultrasound can detect salivary gland damage due to radioactive iodine therapy. The purpose of this study is to determine how often ultrasound-detected sialadenitis and parotid gland damage is noted due to radioactive iodine therapy and to identify risk factors associated with salivary gland damage.

THE FULL ARTICLE TITLE

Horvath E et al. 2020 Radioiodine-Induced Salivary Gland Damage Detected by Ultrasonography in Patients Treated for Papillary Thyroid Cancer: Radioactive Iodine Activity and Risk. Thyroid 2020 Jun 10. PMID: 32370663.

SUMMARY OF THE STUDY

Patients with papillary thyroid cancer who were treated with radioactive iodine therapy between 2007 and 2017 at a single institution were evaluated for this study. Patients included in the study had a preoperative (before removal of the thyroid) and post-radioactive iodine therapy neck ultrasound that included images of the salivary glands. Patients with salivary gland disease prior to their diagnosis of papillary thyroid cancer were excluded. Patients were placed into groups based on the increasing radioactive iodine therapy dose administered: Group A (30-35 mCi), Group B (48-58 mCi), Group C (99-110 mCi), Group D (150-160 mCi) and Group E (200-500 mCi). Some of the patients completed a survey about their salivary gland symptoms. Ultrasound features were used to determine salivary gland damage after radioactive iodine therapy.

Of the 667 patients with papillary thyroid cancer treated with radioactive iodine therapy, 570 patients were included in this study. The study group consisted of 435 females (76.3%) with an average age of 43 years. The average radioactive iodine therapy dose received was 100 mCi. There were 143 patients (25.1%) with salivary gland damage on ultrasound and 77 (53.8%) of them had bilateral parotid gland atrophy (loss of tissue). The median follow up was 49 months. The risk of sialadenitis was significantly correlated with both radioactive iodine activity and gender (14.1 % of males had salivary gland damage compared to 28.5% of females). The main risk factor for salivary gland damage was the radioactive iodine dose received. No salivary gland injury was noted in 156 patients who received radioactive iodine therapy doses between 30 mCi and 58 mCi (Group A and B). In patients receiving 100 mCi, 150 mCi, and ≥ 200 mCi (Group C, D and E), atrophy was noted in 21%, 46.9% and 77.8% of patients, respectively. There were 54 patients who completed the salivary gland survey, and 16 of the patients with parotid atrophy (70%) reported parotid gland discomfort.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Chronic sialadenitis is one of the more common side effect of radioactive iodine therapy. This study shows that 25% of patients who receive radioactive iodine doses ≥ 100 mCi are affected. The main risk factor for salivary

THYROID CANCER, continued

gland damage is the total radioactive iodine therapy dose received. Importantly, chronic sialadenitis was not observed at radioactive iodine doses <100 mCi. Using the lowest effective radioactive iodine therapy dose for papillary thyroid cancer treatment can minimize damage to the salivary gland. Ultrasound is useful to diagnose post-radioactive iodine therapy salivary gland atrophy or damage.

— Priya Mahajan, MD

ATA THYROID BROCHURE LINKS

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

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

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer: 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).

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.

Sialadenitis: inflammation of salivary gland.

Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland and neck. Ultrasound uses sound waves to create a picture of the structure of the thyroid gland and surrounding neck.

mCi: millicurie, the units used for I-131.

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THYROID CANCER

Serum thyroglobulin antibodies switching from negative to positive does not necessarily indicate structural thyroid cancer recurrence

BACKGROUND

Thyroglobulin is a protein only produced by thyroid cells and is used as a thyroid cancer marker in patient who have undergone thyroid surgery. Since normal thyroid tissue has been removed, thyroid cancer cells would be the only source of thyroglobulin. Serum thyroglobulin autoantibodies (TgAbs) may be found in ~25% of patients with thyroid cancer following initial surgery and are known to interfere with the measurement of serum thyroglobulin. Therefore, the two tests must be performed together. When TgAbs levels go down and become undetectable, it is also seen as a likely sign there is no more thyroid cancer present. Alternatively, when a patient has had a negative TgAb level that becomes positive, providers worry this may indicate thyroid cancer recurrence.

The true level of thyroid cancer recurrence and how concerning newly detected TgAb levels are has not been studied in detail. This study was designed to look at how significant it is for a patient with a history of thyroid cancer to develop TgAbs when they were previously undetectable.

THE FULL ARTICLE TITLE

Yin N et al 2020 The De novo detection of anti-thyroglobulin antibodies and differentiated thyroid cancer recurrence. Thyroid. Epub 2020 May 7. PMID: 32228151.

SUMMARY OF THE STUDY

This study looked at cases from several academic medical centers that are logged in a national database of thyroid cancer disease (The National Thyroid Cancer Treatment Cooperative Registry). Cases from 1996 and later that included patients without persistent cancer after initial treatment, TgAb data available and at least 3 years of follow up recorded with at least 3 visits were analyzed. A total of 812 patients were studied. The cases of interest were those whose TgAb status changed from negative to positive (40 patients total).

Structural recurrence of thyroid cancer (meaning ability to visualize thyroid cancer on imaging) occurred at a similar rate between patients who remained TgAb negative (74/772 or 9.6%) and those who developed new TgAbs (6/40 or 15%). Interestingly, the TgAbs became detectable on average 2 years after thyroid cancer was detected in that population by imaging.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Based on this group of patients studied, only about 5% of patients with a history of thyroid cancer will develop newly detectable TgAbs. The development of TgAbs does not necessarily indicate there will be new, visible thyroid cancer that needs surgery or other treatment. This study is important as both patients and clinicians fear any indicator of thyroid cancer recurrence. This study suggests that though patients should have a thorough evaluation with physical exam, lab testing and imaging after the development of new TgAbs, most patients will not have visible thyroid cancer that needs additional treatment.

— Joshua Klopper, MD

ATA THYROID BROCHURE LINKS

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

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

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

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

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THYROID NODULES

Radiofrequency and laser ablation of benign thyroid nodules are similarly effective at 6 months in a prospective, randomized trial

BACKGROUND

Thyroid nodules are common and occur in up to 50% of individuals. Most are benign (non-cancerous) and only require monitoring. However, sometimes even benign nodules become large enough to either cause pressure symptoms in the neck or be otherwise bothersome to the patient. Surgery is then an option, but leaves a scar, and, depending upon the extent of surgery needed, can result in hypothyroidism and rarely problems with the parathyroid glands that control calcium in the blood.

When nodules are cystic, ethanol infusion can be used to decrease the size. However, with solid nodules, other methods, such as radiofrequency ablation (RFA) and laser ablation (LA), have been used. Both have been shown to be effective in many studies including a recent meta-analysis with volume reduction rates at 6 months, 1 year, and 2 years were 68%, 75%, and 87% for RFA and 48%, 52%, and 45% for LA. However the two techniques have not been compared head to head.

This study was done to directly compare RFA and LA in their ability to decrease the size and symptoms of benign, solid thyroid nodules.

THE FULL ARTICLE TITLE

Cesareo R et al 2020 Laser ablation versus radiofrequency ablation for benign non-functioning thyroid nodules: Six-month results of a randomized, parallel, open-label, trial (LARA trial). Thyroid 2020 30: 847-856; PMID: 32056501.

SUMMARY OF THE STUDY

The authors selected adult patients who had a solid thyroid nodule with a volume >5 and either was symptomatic to the patient (compression symptoms or cosmetic concern) or had grown more than 20% in follow up over the previous year. Patients could only be included if all labs related to the thyroid were normal and the nodule had a benign core needle biopsy result. A total of 60 patients were then randomized to treatment with either RFA or LA. Patients were then followed for 6 mo with repeat ultrasound. Six months after the procedure, thyroid nodule volume was reduced by 64% after RFA and by 53% after LA. Greater than 50% volume reduction was achieved in 87% of patients after RFA and in 67% after LA. The procedure time was slightly longer for LA vs RFA (23 vs 16 minutes), but this was not significant. Compressive symptoms were improved by 2 points on a 10-point scale, and cosmetic concerns improved by 2 points on a 4-point scale in both groups. Side effects included 1 patient in each group who had voice changes during the procedure, bruising in 3 and 2 patients, local pain in 6 and 5 patients and a short episode of thyroid over-activity in 1 and 2 patients after RFA and LA respectively.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that either RFA or LA were effective and safe, leading to similar decrease in compressive symptoms and cosmetic concerns. Nodules treated with RFA showed a somewhat greater decrease in size. This study is important because it directly compares two non-surgical treatment options for larger, symptomatic thyroid nodules and offers patients a viable alternative to thyroid surgery. It is important to note that this study was performed in an institution with extensive experience using these two techniques and results may not be same in other locations.

— Marjorie Safran, MD

THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

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

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.

Radiofrequency ablation (RFA): is a minimally invasive procedure that uses electrical energy and heat to destroy cells. The radiologist uses imaging tests to guide a thin needle through the skin or through an incision and into the tissue. High-frequency energy passes through the needle and causes the surrounding tissue to heat up, killing the nearby cells.

Laser ablation (LA): surgery is a treatment useing light to heat and destroy unwanted cells.

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HYPERTHYROIDISM

Fixed-dose radioactive iodine therapy reduces goiter size and treats hyperthyroidism in most patients with toxic multinodular goiter

BACKGROUND

The 2 most common causes of hyperthyroidism are Graves' disease and toxic multinodular goiter. Graves' disease is an autoimmune disorder while toxic multinodular goiter (TMNG) results from thyroid enlargements forming lumps that make too much thyroid hormone and become overactive. Toxic multinodular goiter is common in the elderly and in areas of the world with low iodine in their diet. Definitive treatment for both causes of hyperthyroidism includes radioactive iodine therapy and surgery. Radioactive iodine is taken up into the thyroid gland and works by damaging the thyroid cells causing a decrease in the production of thyroid hormones and, eventually, a decrease in the size of the thyroid. Radioactive iodine therapy is better tolerated in older people who have additional medical problems that result in an increased surgical risk. Additionally, it is less expensive. However, it can take some months until the patients' thyroid levels normalize after the treatment. The size of the thyroid usually decreases after the treatment.

The best dose of radioactive iodine to treat Graves' disease can be calculated using the radioactive iodine uptake, since the entire thyroid is overactive. It is more challenging to determine the best dose of radioactive iodine to treat a toxic multinodular goiter since only parts of the thyroid are overactive. This study examines the effect of treating patients with toxic multinodular goiter with a fixed dose of radioactive iodine.

THE FULL ARTICLE

Roque C et al 2020 Long-term effects of radioiodine in toxic multinodular goitre: Thyroid volume, function and autoimmunity. J Clin Endocrinol Metab. Epub 2020 Apr 22. PMID: 32320467.

SUMMARY OF THE STUDY

This is a study performed on 153 adults with a toxic multinodular goiter in Siena, Italy. All patients were treated with a fixed dose of 15 mCi of radioactive iodine. The authors measured the size of thyroid with ultrasound before and after treatment and followed thyroid hormone levels and thyroid antibodies. They followed these patients for up to 12 years.

One year after the radioactive iodine therapy, the size of the thyroid was reduced by about 30%. Over time, there was further reduction of the thyroid size, with the maximal reduction in size observed after 3-6 years. Subsequently, a total of 22% had an increase in the size of the goiter, but the growth in all cases remained below the initial size of the thyroid. The baseline size of the goiter did not affect the eventual decrease in size obtained after treatment. A total of 61% of the patients had thyroid hormone levels in the normal range at 1 year after radioactive iodine therapy while 11 % remained hyperthyroid and 27% became hypothyroid. Of those that remained hyperthyroid, ~90% of the patients eventually became cured from their hyperthyroidism. There were minimal side effects from the treatment.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The treatment of toxic multinodular with a fixed dose of radioactive iodine (15 mCi) was effective in resolving hyperthyroidism in almost 90% of patients and significantly reducing the size of the goiter by more than half. About a quarter of the patients became hypothyroid. The treatment was well tolerated and safe. This suggests that fixed dose radioactive iodine therapy is effective in treating hyperthyroidism. In addition, the reduction in the size of the goiter seems to be higher in this study as compared to other studies in the literature, suggesting that it may be more effective at reducing the size of the goiter in a population from an iodine insufficient area.

— Susana Ebner MD

HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/

ABBREVIATIONS & DEFINITIONS

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.

Toxic multinodular goiter: characterized by one or more nodules or lumps in the thyroid that may gradually grow and increase their activity so that the total output of thyroid hormone in the blood is greater than normal.

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

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

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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.

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www.thyroid.org
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thyroid@thyroid.org

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

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

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

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

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

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

Thyroid Cancer Canada
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Thyroid Federation International
www.thyroid-fed.org
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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.

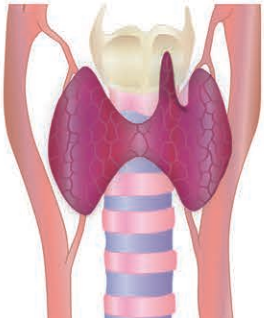
You can be protected from developing thyroid cancer in the event of a nuclear disaster by taking potassium iodide (see *Nuclear Radiation and the Thyroid brochure*). This prevents the absorption of radioactive iodine and has been shown to reduce the risk of thyroid cancer. The American Thyroid Association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

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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.

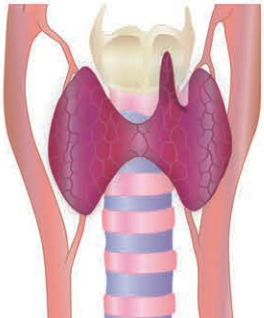
Alternatively, TSH can be increased sufficiently without stopping thyroid hormone medication by injecting TSH into your body. Recombinant human TSH (rhTSH, Thyrogen®) can be given as two injections in the days prior to radioactive iodine treatment. The benefit of this approach is that you can stay on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



FURTHER INFORMATION

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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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