Volume 14 | Issue 6 | June 2021

Clinical Thyroidology® for the Public



AMERICAN **THYROID** ASSOCIATION **Optimal Thyroid Health for All**

EDITOR'S COMMENTS2

Active surveillance for papillary thyroid microcarcinomas

The ATA guidelines recommend 2 possible options for management of papillary thyroid microcarcinomas, which are considered low risk cancers: 1) thyroid lobectomy as a definitive treatment or 2) active surveillance. However, a small minority of papillary thyroid microcarcinomas do have aggressive features on pathology and may not be low risk. The aim of this study was to determine how common these microcarcinomas are and how many have aggressive features using a large database of patient with papillary thyroid microcarcinomas who also had surgery.

Al-Qurayshi Z et al 2020 Wolf in sheep's clothing: Papillary thyroid microcarcinoma in the US. J Am Coll Surg **230**:484–491. PMID: 32220437.

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Who is eligible for active surveillance in a **population with a restrictive diagnostic protocol?** A worldwide increase in the incidence of small papillary thyroid cancers has been observed in the past couple of decades. This trend, however, shows clear regional differences. Active surveillance has been presented as an approach toward minimizing thyroid cancer overdiagnosis and overtreatment. This study describes characteristics of patients with small papillary thyroid cancers, as well as the proportion of patients who are potential candidates for active surveillance for low-risk thyroid cancers in the Netherlands.

Lončar I et al 2021 Active surveillance for papillary thyroid microcarcinoma in a population with restrictive diagnostic work-up strategies. Thyroid. Epub 2021 Jan 11. PMID: 33430696.

THYROID NODULES7

Risk of clinically significant thyroid cancer is low during long-term follow-up of thyroid nodules Thyroid biopsies are performed to identify those nodules that require surgery. Biopsy results are ranked according to the risk of cancer in a system known as the Bethesda System. This study was done to evaluate the risk of cancer in each Bethesda category by examining both surgical and long-term clinical outcomes in patients who did not undergo surgery.

Ng DL et al 2021 A large thyroid fine needle aspiration biopsy cohort with long-term population-based follow-up.Thyroid. Epub 2021 Jan 29. PMID: 33371796.

follicular thyroid cancer staging, and should the cutoffs be different?

Currently papillary and follicular thyroid cancer is staged using the same criteria. Age is included in the staging criteria as older age is a known risk factor for increasing risk of death in thyroid cancer and recently the age cutoffs were changed. This study examined if there should be a different age cutoff for the two different types of thyroid cancer.

van Velsen EFS et al 2021 Finding the optimal age cutoff for the UICC/AJCC TNM staging system in patients with papillary or follicular thyroid cancer. Thyroid. Epub 2021 Mar 4. PMID: 33487121

THYROID CANCER.....II

Combination pembrolizumab plus lenvatinib may be a treatment option for patients with anaplastic and poorly differentiated thyroid cancer Anaplastic thyroid cancer (ATC) and poorly differentiated thyroid cancer (PDTC) are rare but very aggressive type of thyroid cancer. Both have 10-year survival rates of 5-10%. Despite of the significant progress and the availability of numerous combination chemotherapies to treat cancer, treatment options for ATC and PDTC are still limited. The goal of this study was to evaluate the response of a combination of 2 new types of chemotherapy in patients with metastatic ATC and PDTC who failed standard chemotherapy.

Dierks C et al. 2021 The lenvatinib/pembrolizumab combination is an effective treatment option for anaplastic and poorly differentiated thyroid carcinoma. Thyroid. Epub 2021 Jan 28. PMID: 33509020.

THYROID NODULES**13** The role of radio-frequency ablation and laser therapy for benign thyroid nodules

Radio-frequency ablation and laser ablation are 2 non-surgical options to decrease the size of thyroid nodules. These procedures are currently being used more frequently in Europe, but are gaining popularity in the United States. This study reviewed the experience of multiple centers in Italy using these techniques and the rates of nodule regrowth and need for repeat treatment after the initial therapy.

Bernardi S et al 2020 Five-year results of radiofrequency and laser ablation of benign thyroid nodules: A multicenter study from the Italian Minimally Invasive Treatments of the Thyroid Group. Thyroid 30:1759–1770. PMID: 32578498.



www.thyroid.org

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Clinical Thyroidology for the Public

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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 <u>Twitter</u> at *@* thyroidfriends and on <u>Facebook</u>. 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. (<u>https://www.thyroid.org/covid-19/</u>)

June is Differentiated Thyroid Cancer Awareness Month.

In this issue, the studies ask the following questions:

- Is active surveillance appropriate in thyroid cancer?
- Are there regional differences in patients eligible for active surveillance?
- What is the risk of thyroid cancer in nodules during long-term follow-up?
- What is the ideal age cutoff in thyroid cancer staging?
- Are there new chemotherapy options for patients with aggressive thyroid cancer?
- Are there effective non-surgical options for benign thyroid nodules?

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,

You Tube

THYROID CANCER

Active surveillance for papillary thyroid microcarcinomas

BACKGROUND

Thyroid cancer is the fastest rising cancer in women. Indeed, autopsy studies have shown that up to 1/3rd of adults who die of other causes will have a small (<1 cm) papillary thyroid microcarcinoma within their thyroid gland that was not identified while the individual was alive. This is part of the reason that the American Thyroid Association guidelines for the management of thyroid nodules and cancer do not recommend biopsy of small thyroid nodules (<1-1.5 cm). Also, at the time of surgery for larger nodules that have been diagnosed as papillary thyroid cancers, up to 30% end up being diagnosed as papillary thyroid microcarcinomas.

The guidelines recommend 2 possible options for management of papillary thyroid microcarcinomas: 1) thyroid lobectomy as a definitive treatment, provided there is no evidence spread outside of the neck or the patient is at high risk or 2) active surveillance, which is monitoring them over time with ultrasound and physical exam and avoiding surgery. Active surveillance is an option due to the overall low risk of these cancers. However, a small minority of papillary thyroid microcarcinomas do have aggressive features on pathology and may not be low risk.

The aim of this study was to determine how common these microcarcinomas are and how many have aggressive features using a large database of patient with papillary thyroid microcarcinomas who also had surgery.

THE FULL ARTICLE TITLE

Al-Qurayshi Z et al 2020 Wolf in sheep's clothing: Papillary thyroid microcarcinoma in the US. J Am Coll Surg **230:**484–491. PMID: 32220437.

SUMMARY OF THE STUDY

This study used the National Cancer Database from 2010 to 2014 and analyzed adult patients with a primary diagnosis of papillary thyroid microcarcinoma who had undergone thyroid surgery. Independent factors assessed were age, sex, race, type of thyroid surgery, lymph

node involvement, whether they received radioactive iodine therapy and the total size of the papillary thyroid microcarcinoma. The association between each of these independent factors and the risk of aggressive features was tested and overall survival was determined.

The study group consisted of 30,180 patients, of whom 5628 (18.7%) had at least one aggressive feature (spread to lymph nodes, extension outside of the thyroid or into the blood vessels or spread of the cancer outside of the neck.) The average follow-up was ~39 months. The 5-year overall survival was 98.5%, which was similar to the overall survival of patients without aggressive features (98.4%). Most patients (82%) were otherwise healthy. The majority of patients (82.6%) underwent a total thyroidectomy, 52.2% underwent concomitant neck dissection and 25.4% received radioactive iodine therapy.

Patients with aggressive features were more likely to be young (<55 years old), male, white and treated in hospitals that see a lot of thyroid cancer patient. With regard overall survival, spread to either the central or lateral lymph nodes, as well as extension outside of the thyroid and spread outside of the neck were associated with decreased survival.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that ~19% of papillary thyroid microcarcinomas have aggressive features on pathology. Based on these results, the authors suggest a lobectomy is the best option to manage these patients. However, the presence of aggressive features did not significantly alter overall survival, which is excellent. Longer studies are needed to confirm the survival results. Since active surveillance requires ongoing regular monitoring with ultrasound and physical exam and leads to surgery with any changes, both lobectomy and active surveillance remain reasonable options for management of papillary thyroid microcarcinomas. Patients and doctors show discuss these options to determine the best option for any individual patient.

— Alan P. Farwell, MD

Clinical Thyroidology® for the Public (from recent articles in Clinical Thyroidology)



THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <u>https://www.thyroid.org/thyroid-nodules/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u> Thyroid Surgery: <u>https://www.thyroid.org/thyroid-surgery/</u> Radioactive Iodine Therapy: <u>https://www.thyroid.org/radioactive-iodine/</u>

ABBREVIATIONS & DEFINITIONS

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

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.

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 I 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.

Lobectomy: surgery to remove one lobe of the thyroid.

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.

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THYROID CANCER

Who is eligible for active surveillance in a population with a restrictive diagnostic protocol?

BACKGROUND

A worldwide increase in the incidence of small papillary thyroid cancers (microcarcinomas) has been observed in the past couple of decades. This trend, however, shows clear regional differences. While the rise in cases of papillary thyroid cancer has increased as much as 10-fold in South Korea, the increase in many northern European countries has been minimal or nonexistent. Further, in the United States, up to 30% of larger nodules that have been diagnosed as papillary thyroid cancers end up being diagnosed as papillary thyroid microcarcinomas at the time of surgery. One factor that explains regional differences in the number of patients with thyroid cancer is the different policies guiding the use of thyroid biopsy. For instance, in the United States, specialists involved in thyroid nodule assessment generally agree to biopsy thyroid nodules >1 cm with suspicious patterns on ultrasound, even if the nodule is not felt on exam. These recommendations contrast with the Dutch national guidelines published in 2007, which recommend biopsies only of palpable thyroid nodules.

These differences in the thresholds for performing thyroid biopsies create an opportunity to examine the role of active surveillance, which is monitoring of suspicious or confirmed low-risk thyroid cancers (usually <1 cm) over time with ultrasound and physical exam and avoiding surgery. Active surveillance has been presented as an approach toward minimizing thyroid cancer overdiagnosis and overtreatment. This study describes characteristics of patients with small papillary thyroid cancers, as well as the proportion of patients who are potential candidates for active surveillance for low-risk thyroid cancers in the Netherlands.

THE FULL ARTICLE TITLE

Lončar I et al 2021 Active surveillance for papillary thyroid microcarcinoma in a population with restrictive diagnostic work-up strategies. Thyroid. Epub 2021 Jan 11. PMID: 33430696.

SUMMARY OF THE STUDY

Data collection was performed using the Netherlands Cancer Registry to identify patients diagnosed and treated for micropapillary thyroid cancer (≤1 cm) in the Netherlands from January 2005 to December 2015. Patients were categorized into three groups according to the indication for surgery: (1) preoperative biopsy–proven spread into the lymph nodes, (2) micropapillary thyroid cancer identified after surgery for another indication (Graves' disease, multinodular goiter, etc.), and (3) thyroid nodules <1 cm that had been previously biopsied with cytology read as cancer or suspicious for cancer. Cancer recurrence was assessed in all three groups during follow-up.

A total of 6,477 patients were diagnosed with thyroid cancer during this 11-year period. From this group, 1,018 patients fit the criteria to be analyzed. Overall, micropapillary thyroid cancer accounted for 15.7% of the total number of cases of thyroid cancers in that country. The average cancer size was 6 mm. A total of 152 (14.9%) patients were in group 1, 667 (65.5%) patients in group 2 and 199 (19.5%) patients in group 3. As expected for the usual demographics for thyroid cancer, 75.8% of the group was female with an average age of 50 years. Overall, the rate of cancer recurrence was low (3.8%) over an average follow-up time of 68.7 months.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that papillary thyroid microcarcinomas account for substantially lower proportion of thyroid cancer in the Netherlands than that of many other countries, such as the United States. The authors suggest that this is likely due to the more restrictive use of thyroid biopsies in the Netherlands practiced since 2007, leading, therefore, to less frequent detection of thyroid cancers. Overall, an estimated 3% of all patients with papillary thyroid cancer, and about 20% of patients

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THYROID CANCER, continued

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Optimal Thyroid Health for All

with micropapillary thyroid cancer, would have been candidates for active surveillance in this population. Further study is needed to determine if the overall survival of patients in the Netherlands is affected by these practices.

-Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <u>https://www.thyroid.org/thyroid-nodules/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u>

ABBREVIATIONS & DEFINITIONS

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

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

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.

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THYROID NODULES

Risk of clinically significant thyroid cancer is low during longterm follow-up of thyroid nodules

BACKGROUND

Thyroid nodules are very common, but only a small percentage of them ever turn out to be cancers of significance. Thyroid biopsies are performed to identify those nodules that require surgery. Biopsy results are ranked according to the risk of cancer in a system known as the Bethesda System. This system is: category I: nondiagnostic; category II: benign; category III: atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS); category IV: follicular neoplasm or Hürthle-cell neoplasm; category V: suspicious for cancer; and cagtegory VI: cancer. The higher the category, the higher the cancer risk. If this risk is low (category II), patients are usually followed with physical exam and periodic thyroid ultrasounds. If the risk is higher, surgery is usually recommended.

However, most studies that evaluated the accuracy the Bethesda System in determining thyroid cancer risk used a comparison to patients who underwent surgery. This may have led to some inaccurate results. This study was done to evaluate the risk of cancer in each Bethesda category by examining both surgical and long-term clinical outcomes in patients who did not undergo surgery.

THE FULL ARTICLE TITLE

Ng DL et al 2021 A large thyroid fine needle aspiration biopsy cohort with long-term population-based follow-up. Thyroid. Epub 2021 Jan 29. PMID: 33371796.

SUMMARY OF THE STUDY

The study involved all thyroid biopsies from a single pathology database at the University of California, San Francisco for 8 years from January 1997 to December 2004. All biopsies were recoded according to the most recent Bethesda grading system. Patients were then matched through July 2015 (average follow up 13.9 yrs) to the UCSF cancer registry and the California Cancer Registry and considered to be without cancer if they were not in either registry. A total of 2233 patients with 2758 biopsy reports were available; 26 were excluded, for a final count of 2207. The average age was 48 years (range, 7–92) and 1880 patients (85.2%) were female. Of the 2207 test results, 236 (10.7%) were determined to be nondiagnostic, 1575 (71.4%) benign, 57 (2.58%) atypia of undetermined significance (AUS), 78 (3.53%) follicular lesion of undetermined significance (FLUS), 107 (4.85%) follicular neoplasm or Hürthle-cell neoplasm, 20 (0.9%) suspicious for malignancy, and 134 (6.07%) malignant. Average follow-up after the initial biopsy was 13.9 years (range, 10.5–18.4), and 279 (12.6%) patients were diagnosed with thyroid cancer during that period.

Thyroid cancer was ultimately identified in only a few patients with initially benign biopsies (cancer rate of 2.42 per 1000 person-years). Cancer was diagnosed only twice as often if the biopsy was non-diagnostic, 9 times as often for AUS/FLUS, 11 times as often for follicular neoplasm, and 49 times as often for suspicious for malignancy. Only 52 of the nodules with an initial benign biopsy (1575) ultimately were diagnosed with thyroid cancers and 29 of those were papillary thyroid microcarcinomas, which rarely spread beyond the thyroid. Only 15 patients died from their thyroid cancer and none of these patients had a benign biopsy initially.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that thyroid biopsy and the Bethesda grading system are accurate in detecting thyroid cancer. Long-term follow up showed low rates of cancer in nondiagnostic biopsies. There was an extremely low rate of death when biopsy was benign or non-diagnostic. This information supports our current recommendations regarding handling of thyroid nodules. Patients with benign biopsies are unlikely to eventually need surgery for thyroid cancer. Even patients with non-diagnostic biopsies have a relatively low risk for cancer. The up to date Bethesda system of categorizing thyroid biopsy rarely misses a cancer of significance and patients should be reassured.

— Marjorie Safran, MD

Clinical **Thyroidology®** for the **Public** (from recent articles in *Clinical Thyroidology*)



THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <u>https://www.thyroid.org/thyroid-nodules/</u> Fine Needle Aspiration Biopsy of Thyroid Nodules: <u>https://www.thyroid.org/fna-thyroid-nodules/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u>

ABBREVIATIONS & DEFINITIONS

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.

Bethesda System: a grading system of thyroid biopsy results that assigns a category I-VI depending on what the biopsy looks like under a microscope. The higher the category, the higher the cancer risk. 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 I cm in diameter.

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



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THYROID CANCER

What is the ideal age cutoff for papillary and follicular thyroid cancer staging, and should the cutoffs be different?

BACKGROUND

Thyroid cancer is the fastest rising cancer in the United States. There are 2 main types of thyroid cancer: papillary (most common) and follicular. Response to therapy for both types is usually excellent and >95% of patients with thyroid cancer do well and survive their thyroid cancer.

Currently papillary and follicular thyroid cancer is staged using the same criteria. This helps predicts survival from thyroid cancer. Age is included in the staging criteria as older age is a known risk factor for increasing risk of death in thyroid cancer. Recently the age cutoff for "old" was changed from 45 to 55 years of age, which has led to better risk predictors of death. However, papillary and follicular cancers have a somewhat different clinical course and the same age cutoff may not be appropriate for both disease. Therefore, this study examined if there should be a different age cutoff for the two different types of thyroid cancer.

THE FULL ARTICLE TITLE

van Velsen EFS et al 2021 Finding the optimal age cutoff for the UICC/AJCC TNM staging system in patients with papillary or follicular thyroid cancer. Thyroid. Epub 2021 Mar 4. PMID: 33487121

SUMMARY OF THE STUDY

All patients in two large databases in the Netherlands and Germany that had thyroid surgery for cancer and complete survival and pathology data were analyzed to find the best age cutoff for "old" for thyroid cancer staging. Age cutoffs were analyzed at 5-year increments from 20 up to 85 years and by 1-year increments between 35 and 55 years.

In over 3000 patients, 2355 (77%) had papillary thyroid cancer and 719 (23%) had follicular thyroid cancer, with an average follow-up of 84 months. The average age was 48.7 years, and 69.5% were female. When compared to patients with papillary thyroid cancer, patients with follicular thyroid cancer were older (54.2 years vs. 47.1 years), more likely to be male (37.1% vs. 28.5%), less likely to have spread of the cancer to the lymph nodes (9.2% vs. 27.3%) and more likely to have spread of the cancer outside of the neck (18.2% vs. 6.0%). Overall, this population showed that an age cutoff for "old" of 50 years seemed best for patients with papillary thyroid cancer, and 40 for patients with follicular thyroid cancer.

WHAT ARE THE IMPLICATIONS **OF THIS STUDY?**

This study suggests that there should be different staging cutoffs for papillary and follicular thyroid cancer and a younger age cutoff should be used over what is currently in the most updated staging system. This is important for patients in that the age cutoff may be fluid in that 40-55 year old range. Since a hard cutoff can drastically change staging, the physician should discuss this with patients. Moreover, a lower age cutoff should likely be used for patients with follicular cancer, which may upstage some previously staged I and II to a more advanced stage with an increased risk of death. These patient may benefit from more aggressive treatments.

- Melanie Goldfarb, MD

ATA THYROID BROCHURE LINKS

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

Clinical Thyroidology® for the Public (from recent articles in Clinical Thyroidology)

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THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

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

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

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

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.

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

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You Tube

THYROID CANCER

Combination pembrolizumab plus lenvatinib may be a treatment option for patients with anaplastic and poorly differentiated thyroid cancer

BACKGROUND

Most types of thyroid cancer have an excellent prognosis and patient do well. Two significant exceptions are anaplastic thyroid cancer (ATC) and poorly differentiated thyroid cancer (PDTC), both of which are rare but very aggressive type of thyroid cancer. Overall, ATC has an extremely high death rate and a 10-year survival of less than 5%. PDTC has a more favorable prognosis than ATC, however, the 10-year survival is still lower than 10%. One of the reasons for this poor prognosis is that neither of these thyroid cancers take up radioactive iodine, which serves as a magic bullet to kill thyroid cancer cells in the more common types of papillary and follicular thyroid cancer. Thus, treatment for ATC and PDTC is limited to surgery, with chemotherapy the only option if the cancer is persistent or recurrent after surgery.

Despite of the significant progress and the availability of numerous combination chemotherapies to treat cancer, treatment options for ATC and PDTC are still limited. The goal of this study was to evaluate the response of a combination of 2 new types of chemotherapy: a multikinase inhibitor (lenvatinib) and an immune checkpoint inhibitor (pembrolizumab) in patients with metastatic ATC and PDTC who failed standard chemotherapy.

THE FULL ARTICLE TITLE:

Dierks C et al. 2021 The lenvatinib/pembrolizumab combination is an effective treatment option for anaplastic and poorly differentiated thyroid carcinoma. Thyroid. Epub 2021 Jan 28. PMID: 33509020.

SUMMARY OF THE STUDY:

This is a study of patients with metastatic ATC (6 patients) and PDTC (2 patients), who failed other treatments and received a combination therapy of lenvatinib and pembrolizumab between March 2016 and December 2019 at a medical center in Germany. The

patients were started on lenvatinib 20 to 24 mg daily and then pembrolizumab was added at a fixed dose of 200 mg intravenously every 3 weeks. The lenvatinib dose was progressively decreased if side effects occurred. Lenvatinib was given for at least 1 year and then stopped in patients with complete response to treatment after a maximum of 24 months. Pembrolizumab was continued after reaching a complete response for a maximum of 40 months during the study. The individual treatment duration was 1, 4, 11, 15, 19, 25, 27, and 40 months.

Based on the RECIST criteria, within 16 months of treatment, 4 out of 6 (66%) ATC patients had a complete remission, 1 (16%) had stable disease, and 1 (16%) had progressive disease and died within the first month of treatment. Both patients with PDTC had partial remission. The average time without disease progression was 17.75 months for all patients and 16.5 months for the ATC patients. The average survival time was 18.5 months, with 3 ATC patients being still alive without relapse (at 40, 27, and 19 months) despite metastatic disease at the start of treatment.

Most side effects resolved after decreasing the lenvatinib dose. However, this medication had to be discontinued in two patients due to severe weight loss/loss of appetite, while a patient had a severe bleeding leading to death while being in complete remission.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study results suggest that the combination therapy with lenvatinib and pembrolizumab is well tolerated in general and it might be an effective treatment in patients with ATC or PDTC, resulting in complete and long-term remissions. At present, this combination treatment is being evaluated in patients with ATC and PDTC in a phase 2 clinical trial (Anaplastic Thyroid Carcinoma Lenvatinib Pembrolizumab – ATLEP).

— Alina Gavrila, MD, MMSc

Clinical Thyroidology® for the Public (from recent articles in Clinical Thyroidology)



THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Anaplastic Thyroid Cancer - <u>https://www.thyroid.org/anaplastic-thyroid-cancer/</u> Thyroid Cancer (Papillary and Follicular): <u>https://www.thyroid.org/thyroid-cancer/</u>

ABBREVIATIONS & DEFINITIONS

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

Cancer remission: disappearance or decrease in severity of the signs and symptoms of cancer.

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.

Multikinase inhibitors: cancer medications that decrease the tumor growth and spread by blocking multiple enzymes (kinases) located at the surface or inside the cancer cells. Kinases are overactive in many of the pathways that cause cells to be cancerous. Immune checkpoint inhibitors: cancer medications that block immune checkpoint proteins, thus allowing the immune cells in the body to kill cancer cells. As part of the immune system, checkpoint proteins prevent an immune response from being too strong and destroying healthy cells in the body;

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.

Clinical **Thyroidology**® for the **Public** (from recent articles in *Clinical Thyroidology*)



THYROID NODULES

The role of radio-frequency ablation and laser therapy for benign thyroid nodules

BACKGROUND

Thyroid nodules are quite common. The concern of any thyroid nodule is whether they are cancerous. Overall, only ~5% of nodules are cancerous, so the vast majority are benign. Even though most are benign, sometimes they cause problems, including neck discomfort from compression or patients do not like their appearance. At present, surgery is the main option for benign nodules causing these problems. However, patients may prefer a non-surgical treatment to get rid of or reduce the size of the nodule if this were available.

Two such non-surgical options are radio-frequency ablation (RFA – like localized microwave energy in a nodule via a needle) or laser ablation (LA – localized laser treatments in a nodule via a needle). These procedures are currently being used more frequently in Europe, but are gaining popularity in the United States.

One downside to these procedures is the possibility of nodule regrowth. This study reviewed the experience of multiple centers in Italy using these techniques and the rates of nodule regrowth and need for repeat treatment after the initial therapy.

THE FULL ARTICLE TITLE

Bernardi S et al 2020 Five-year results of radiofrequency and laser ablation of benign thyroid nodules: A multicenter study from the Italian Minimally Invasive Treatments of the Thyroid Group. Thyroid **30:**1759– 1770. PMID: 32578498.

SUMMARY OF THE STUDY

This study evaluated the outcomes of RFA or LA from 8 Italian medical centers for 5 years after initial treatment and tried to determine factors that predicted success in terms of no nodule regrowth or not needing retreatment over that time.

There was a total of 406 patients analyzed (average age 57 and 75% women). Of these, 53% received RFA and 47%

received LA. About 94% of the nodules were completely solid or mostly solid with only 5% mostly fluid filled and 1% completely fluid filled. At the end of 5 years after initial treatment, there was an overall 77% reduction in size of the nodules undergoing RFA while LA resulted in an average of 57% reduction in size after 5 years.

In all, 28% of patients (115 patients) had nodule regrowth and 32 of them (28%) required retreatment. The main predictor of regrowth was the amount of energy delivered to the nodule by either technique (the lower the energy, the greater chance of regrowth). Overall, more nodules undergoing LA had regrowth as compared to RFA. A total of 46 patients (11%) ultimately had surgery remove their thyroid. Of the patients that ultimately had surgery for these presumed benign thyroid nodules, 35% had a thyroid cancer discovered. If the initial RFA or LA treatment resulted in < 20% decreased nodule size in the first year, this was more likely to mean the nodule had thyroid cancer in it.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

RFA and LA are minimally invasive, non-surgical options for decreasing the size of bothersome thyroid nodules. Most nodules do not regrow, though RFA seems to be more effective overall. If the nodule does not shrink by > 20% a year after treatment, one should consider it may contain a thyroid cancer.

This study is important to patients as it shows an overall less invasive technique for shrinking bothersome thyroid nodules and suggests the treatment is likely to be successful with most nodules staying significantly smaller for at least 5 years. These techniques should not be used as primary treatment for known thyroid cancer, but if the nodules do not shrink as much as expected (<20% after the first year), the chance of thyroid cancer being present should be considered.

— Joshua Klopper, MD

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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. Radio-frequency ablation (RFA): the use of targeting localized microwave energy in a nodule via a needle to decrease the size of the nodule.

Laser ablation (LA): the use of targeting localized laser treatments in a nodule via a needle to decrease the size of the nodule.

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AMERICAN THYROID ASSOCIATION Optimal Thyroid Health for All

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Clinical Thyroidology[®] for the Public

ATA Alliance for Thyroid Patient Education

GOAL The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases. We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.





CANCER









Thyroid Cancer Canada Cancer de la thyroïde Canada



American Thyroid Association

Foundation

www.thyroid.org

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

Bite Me Cancer

www.bitemecancer.org info@bitemecancer.org

Graves' Disease and Thyroid Foundation

www.gdatf.org (Toll-free): 877-643-3123 info@ngdf.org

Light of Life Foundation

www.checkyourneck.com info@checkyourneck.com

MCT8 – AHDS Foundation

mct8.info Contact@mct8.info

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

(Toll-free): 877-588-7904 thyca@thyca.org

Thyroid Cancer Alliance

www.thyroidcanceralliance.org www.thyroidcancerpatientinfo.org Rotterdam. The Netherlands

Thyroid Cancer Canada

www.thyroidcancercanada.org 416-487-8267 info@thyroidcancercanada.org

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