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Clinical Thyroidology® for the Public

AMERICAN THYROID ASSOCIATION
Optimal Thyroid Health for All

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Clinical Thyroidology® for the Public

www.thyroid.org

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CHARITY NAVIGATOR
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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.

January is Thyroid Awareness Month.

In this issue, the studies ask the following questions:

- Does COVID-19 vaccination affect the thyroid?
- Is Graves' disease associated with COVID-19 vaccination?
- Is there in increased risk of cancer after radioactive iodine therapy?
- Is age 18 still be best cutoff separating adult and pediatric thyroid cancer patients?
- Does nerve monitoring help prevent nerve injury during thyroid surgery?
- Is there a link between fatty liver disease and the thyroid?

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

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THYROID AND COVID-19

COVID-19 vaccination may not increase the risk of thyroid problems

BACKGROUND

Since December 2020, 15 vaccine candidates against SARS-CoV-2 to prevent COVID-19 infection have been approved to reduce infection and related hospitalizations and deaths. The rapid progress and limited follow-up data have generated public concerns about the safety of COVID-19 vaccines. Recently, thyroiditis, Graves' disease, and hypothyroidism following COVID-19 vaccination have been described in a few case studies. Nevertheless, the effects of COVID-19 vaccines on thyroid function remain poorly understood. The current study aimed to characterize the association of mRNA and inactivated COVID-19 vaccines with the risk of thyroid dysfunction in the general population.

THE FULL ARTICLE TITLE

Wong CKH et al 2022 Risk of thyroid dysfunction associated with mRNA and inactivated COVID-19 vaccines: A population-based study of 2.3 million vaccine recipients. BMC Med **20:**339. PMID: 36229814.

SUMMARY OF THE STUDY

This large population-based study obtained vaccine safety data by cross-linking electronic medical records from 2018 through 2021 with vaccination records of active patients from the Hong Kong Hospital Authority. The vaccine group included participants who received at least one dose of the CoronaVac (inactivated whole-virus) or BNT162b2 (viral mRNA) vaccine. Participants who received mixed COVID-19 vaccines, tested positive for COVID-19, or had thyroid problems within 3 years prior to the study were excluded. The observation timeline consisted of a baseline period before vaccination, followed by a risk period (defined as the 56 days after vaccination), from February 2021 through September 2021. The number of events per 100,000 doses, and crude incidence rates per 100,000 person-years after each dose were calculated.

A total of 2,288,239 participants were included in the final analyses, consisting of 966,486 CoronaVac recipients and 1,321,753 BNT162b2 recipients. A total of 92.2% of CoronaVac recipients and 94.3% of BNT162b2 recipients received two vaccine doses. Overall, the risk of starting thyroid hormone therapy or developing either a decreased or increased TSH did not change significantly following either type of COVID-19 vaccination. Moreover, the risk of developing clinical thyroiditis or Graves' disease did not change significantly following either type of COVID-19 vaccination. These findings were consistent by sex or age.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this largest vaccinated group analysis to date, there was no significant increase in the incidence of thyroid problems in the 56 days after COVID-19 vaccination by either the inactivated virus or by mRNA.

— Alan P. Farwell, MD

ATA THYROID BROCHURE LINKS

COVID-19 and the Thyroid: https://www.thyroid.org/covid-19/

Thyroiditis: https://www.thyroid.org/thyroiditis/

Graves' Disease: https://www.thyroid.org/graves-disease/

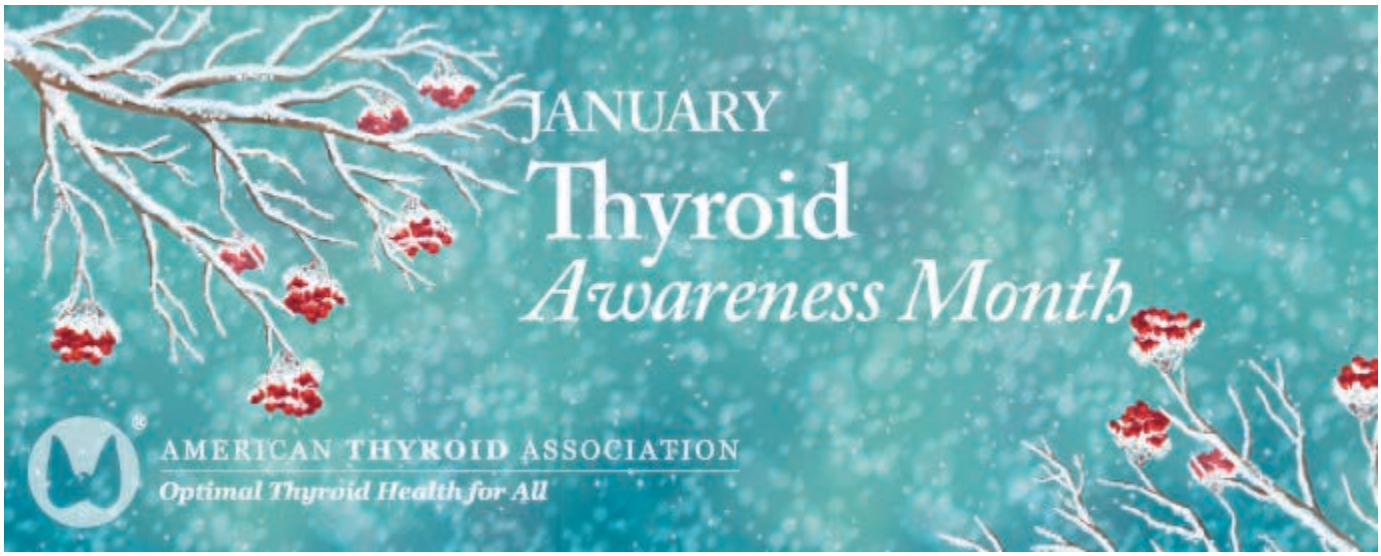
THYROID AND COVID-19, continued

ABBREVIATIONS & DEFINITIONS

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Thyroiditis: inflammation of the thyroid, most commonly cause by antibodies that attack the thyroid as seen in Hashimoto's thyroiditis and post-partum thyroiditis. It can also result from an infection in the thyroid.

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.



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COVID-19 AND THE THYROID

Early-onset Graves' disease after COVID-19 vaccination responds rapidly to low-dose methimazole

BACKGROUND

COVID-19 infection has been associated with the development of several endocrine problems including different forms of thyroiditis and Graves' disease. The likely reasons for this include the virus directly attaching thyroid cells and the increase in activation of the immune system and increasing antibodies during and after COVID-19 infection. This is because both hyperthyroidism and hypothyroidism are usually caused by antibodies attacking the thyroid.

Vaccination against COVID-19 has been a worldwide effort and has been closely monitored. There have been some case reports of the development of autoimmune thyroid problems following COVID-19 vaccination. This study examined the characterization of Graves' disease occurring after COVID-19 vaccination.

THE FULL ARTICLE TITLE

di Filippo L et al 2022 Distinct clinical features of post-COVID-19 vaccination early-onset Graves' disease (PoVEO GD). J Clin Endocrinol Metab. Epub 2022 Sep 21. PMID: 36130234.

SUMMARY OF THE STUDY

This study included adult patients who received vaccination against COVID-19 and were followed at an endocrine referral center for a new diagnosis of Graves' disease between January 1, 2021, and December 31, 2021. The study group was divided between the timing of presentation with hyperthyroidism—either early (within 4 weeks postvaccination), between weeks 4 and 8, or late (>8 weeks postvaccination).

Based on the analysis of 64 patients exposed to at least one immunization dose against COVID-19, either with the Pfizer (63.9%), Moderna (21.3%), or Astra Zeneca (14.8%) vaccine, the authors found that Graves' disease pre-existed in 35 patients (55%) and developed after the vaccination in 29 patients (45%). Among the latter group, 20 patients presented with Graves' disease within 4 weeks after vaccination, and their symptoms developed as early as 9 days after immunization, while in 9 patients Graves' disease occurred later—more than 8 weeks after exposure. Those with early-onset post-COVID vaccination Graves' disease were characterized by an older age at presentation (average 51 years vs. 35 years) and a higher occurrence in men (40% vs. 13.6%) than in those with preexisting and late-onset Graves' disease after vaccination. Moreover, patients with early-onset post-COVID vaccination Graves' disease were characterized by a quicker response to Methimazole after 3 months of follow-up than those with preexisting and late-onset Graves' disease after vaccination.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Early-onset post-COVID vaccination Graves' disease is characterized by unique clinical features, including an older age at presentation, a higher occurrence in men, and a faster recovery to normal thyroid levels, as compared with those with preexisting and late-onset Graves' disease after vaccination. The latter observation suggests a potentially self-limiting nature of the early-onset autoimmunity after exposure to COVID-19 vaccines.

— Alan P. Farwell, MD

COVID-19 AND THE THYROID, continued

ATA THYROID BROCHURE LINKS

COVID-19 and the Thyroid: https://www.thyroid.org/covid-19/

Graves' Disease: https://www.thyroid.org/graves-disease/

Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/

ABBREVIATIONS & DEFINITIONS

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

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.

Thyroiditis: inflammation of the thyroid, most commonly cause by antibodies that attack the thyroid as seen in Hashimoto's thyroiditis and post-partum thyroiditis. It can also result from an infection in the thyroid.

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HYPERTHYROIDISM

Cancer risk following radioiodine treatment of hyperthyroidism

BACKGROUND

Radioactive iodine plays a valuable role in diagnosing and treating thyroid problems as it is taken up only by thyroid cells. There are 2 forms of radioactive iodine: one does not damage the thyroid cells and is used to take pictures of the thyroid (I-123) and the other (radioactive iodine therapy) is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer or an overactive (hyperthyroid) thyroid (I-131). Radioactive iodine therapy is a mainstay in treating patients with thyroid cancer. While radioactive iodine therapy is an effective treatment for hyperthyroidism, additional therapies are available including antithyroid medications and surgery. Treatment decisions consider the risks and benefits associated with each option. In recent years, there has been an increased concern regarding the risk of radioactive iodine therapy in hyperthyroidism since there are alternative treatments.

Conflicting data has been published in the literature regarding whether radioactive iodine therapy for hyperthyroidism is associated with an increased risk of developing cancer. This study sought to determine the cancer risk following treatment with radioactive iodine therapy for hyperthyroidism. Specifically, the authors examined the risk of cancer development and death after radioactive iodine therapy exposure.

THE FULL ARTICLE TITLE:

Shim SR et al 2021 Cancer risk after radioactive iodine treatment for hyperthyroidism: A systematic review and meta-analysis. JAMA Netw Open **4:**e2125072. PMID: 34533571.

SUMMARY OF THE STUDY:

This study included results from 12 studies with a total of 479,452 study participants. Studies were included in the analysis if they met the following criteria: included patients treated for hyperthyroidism with radioactive iodine therapy and followed until cancer diagnosis or death and included at least one comparison patient group not treated with radioactive iodine therapy.

Results of this analysis indicated that no significant differences in overall cancer risk between patients treated with radioactive iodine therapy. There was no increased risk for any specific cancer except thyroid cancer, which showed a slight increased risk in patients treated with radioactive iodine therapy. They also observed a significant correlation between radioactive iodine therapy dose and increased risk of breast and solid cancer death in a small subset of studies. Overall, the data were reassuring and suggest that the potential increased risk of cancer following radioactive iodine therapy treatment is small and only associated with higher doses of radioactive iodine.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

This data shows that there overall no increased risk of cancer after treating patients with hyperthyroidism with radioactive iodine therapy. This study provides general reassurance to the patient and doctor. However, there may be some increased risk following high doses of radioactive iodine therapy and further research is needed in this area. Careful discussion of the risks and benefits of each treatment option are important to determine the best hyperthyroid treatment for the individual patient.

— Whitney Woodmansee MD

HYPERTHYROIDISM, continued

ATA THYROID BROCHURE AND WEBSITE LINKS

Radioactive Iodine Therapy: https://www.thyroid.org/radioactive-iodine/
Hyperthyroidism (Overactive): https://www.thyroid.org/hyperthyroidism/
Graves' Disease: https://www.thyroid.org/graves-disease/

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. **I-123** is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

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.

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

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THYROID CANCER

Age less than 18 is not a reliable cutoff age for the pediatric classification of thyroid cancer

BACKGROUND

The management of thyroid cancer is different for children as compared to adults. For example, children with thyroid cancer are recommended to undergo total thyroidectomy, even for low risk cancers. In adults, some low risk cancers can be managed with lobectomy instead (a surgery where only one lobe of the thyroid is resected). The reason for this more aggressive surgical approach in children had to do with the often more aggressive behavior of the cancer: recurrence and spread of the cancer outside of the thyroid are more common in children. For the purposes of thyroid cancer recommendations, the definition of the pediatric population is any child 18 years or younger. The authors of this study wanted to find out if 18 years is the appropriate cut off age for the pediatric guidelines.

THE FULL ARTICLE

Sugino K et al 2022. Cutoff age between pediatric and adult thyroid differentiated cancer: Is 18 years old appropriate? Thyroid 32:145–152. PMID: 34549602

SUMMARY OF THE STUDY

The authors studied 288 patients, all less than 21 years old, who were seen at Ito Hospital, Japan from 1979 to 2004. They followed these patients from 1.4-38 years. They looked at the thyroid pathology, type of surgery, thyroglobulin levels over time and radiology (ultrasound) imaging. The authors divided the patients in groups by age: younger than 15, 15 to 18 years, and over 18 years of age. They looked at the rate of the cancer coming back (recurrence, expressed as disease free survival, DFS) and rate of the cancer recurring in organs outside the neck area (expressed as distant metastasis free survival, DMFS).

The majority of patients had papillary thyroid cancer and over 80% were more than 14 years old. Only 29% of patient had a total thyroidectomy, but 83% had lymph node resection. Only 6% of the patients had radioactive iodine treatment. Overall 7% of the patients had distant metastasis (lung affected) at presentation. There were 3 deaths, all from this last group. After 30 years of follow-up, the DFS was 68% (percent of children that did not have evidence of disease) and the DMFS was 86% (percent of children without evidence of distal metastasis)

No significant difference was found in DFS between the two age cutoff groups. However, DMSF was significantly different between the group younger than 15 years old and over 15 years (less distant metastasis or higher DMSF). There was no difference in DMFS between the group 15-18 and over 18 years of age. Children younger than 15 years, presented with a more aggressive cancer.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Although more studies are needed, it appears that children younger than 15 years old had distinct clinical presentation and cancer behavior, including higher rates of distant metastasis. A cut off age of less than 15 rather than less than 19 may be more appropriate for children with DTC in terms of guiding interventions, perhaps less aggressive for children older than 15.

— Susana Ebner MD

ATA THYROID BROCHURE LINKS

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

THYROID CANCER, continued

ABBREVIATIONS & DEFINITIONS

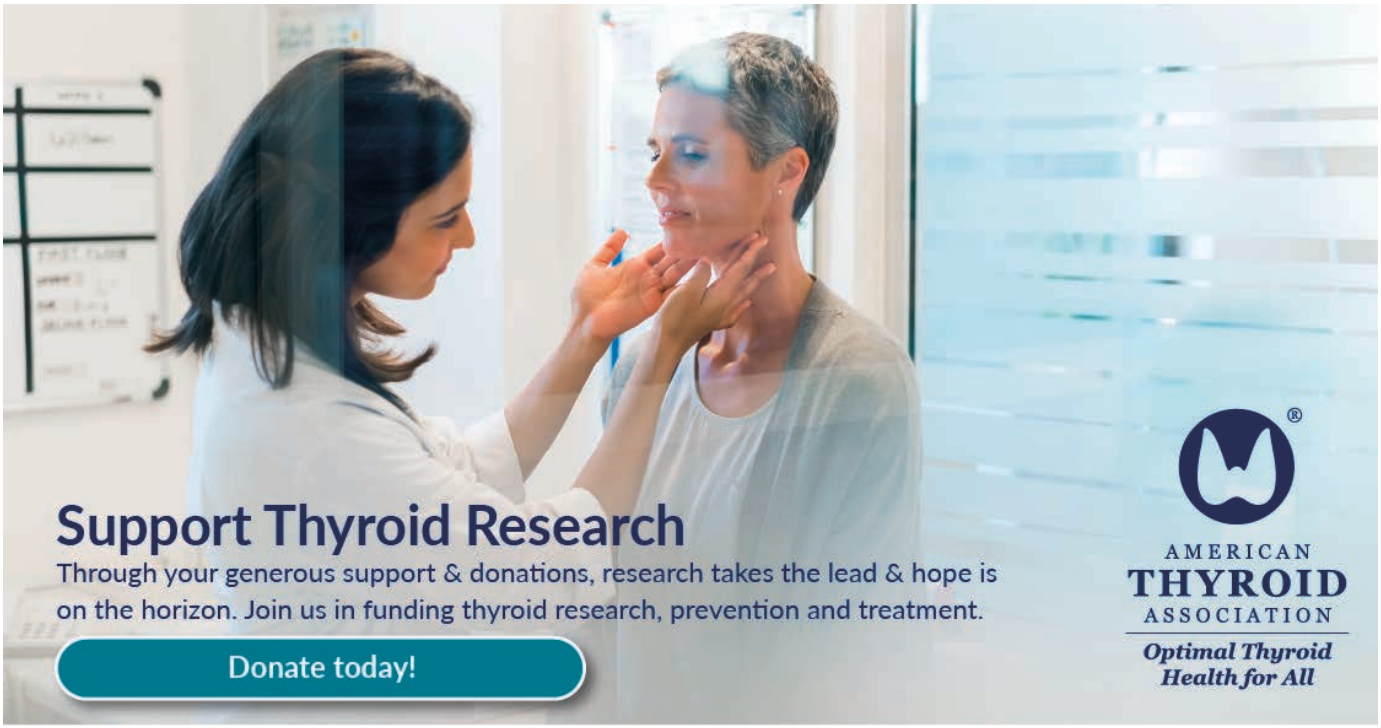
Total thyroidectomy: surgery to remove the entire thyroid gland.

Lobectomy: surgery to remove one lobe of the thyroid.

Papillary thyroid cancer: the most common type of thyroid cancer.

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

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.



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THYROID SURGERY

Does nerve monitoring help prevent nerve injury during thyroid surgery?

BACKGROUND

Surgery to remove all, or part, of the thyroid gland (thyroidectomy) is a common procedure for treating some types of benign and cancerous thyroid disease. As is true for every kind of surgery, complications (unexpected problems) can happen during thyroid surgery and these complications can result in unexpected problems after surgery. One of the most important complications that can happen during thyroid surgery is accidental injury to the recurrent laryngeal nerves. These 2 nerves come up from the chest, one on each side of the neck, and travel by the thyroid to insert into the voice box. They control the vocal cords and are very delicate. One of the surgeon's jobs during thyroid surgery is to gently move these nerves away from the thyroid while removing the gland. If one of these nerves is injured during while doing this, the voice may be hoarse following surgery and this may be permanent. This may also cause coughing or choking when swallowing liquids. If both nerves are injured while removing the thyroid, a person may have difficulty breathing after surgery and may need to undergo emergency tracheostomy (placement of a tube through the skin into the windpipe) to allow breathing.

One tool a surgeon may use to try and avoid injuring the recurrent laryngeal nerves (and so avoid voice, swallowing and breathing problems after surgery) is called nerve monitoring. This technology allows a surgeon to verify (monitor) that these nerves are working throughout the operation and may also help the surgeon identify exactly where the nerves are located, relative to a person's thyroid gland, while surgery is being performed. This information may help a surgeon avoid accidentally injuring one, or both, of these nerves. The research described here aims to determine if using nerve monitoring decreases the risk of recurrent laryngeal nerve injury during thyroid surgery.

FULL ARTICLE TITLE

Memeh K et al 2022 Effect of intraoperative neuromonitoring on the risks of recurrent laryngeal nerve injury during thyroidectomy: A doubly robust approach. Ann Surg. Epub 2022 Jul 15. PMID: 35837957.

SUMMARY OF THE STUDY

The authors of this study looked at a large database that includes information about people who undergo surgery in North America. The study identified 24,370 people who had undergone thyroid surgery between 2016 and 2019. In this group, 15,681 people had thyroid surgery that included use of nerve monitoring technology. The risk of injury to a recurrent laryngeal nerve during thyroid surgery was lower when nerve monitoring was used (5.9% risk of injury if monitoring was used compared to 6.8% without monitoring). This means that the risk of injury to a recurrent laryngeal nerve was lowered by 23% when nerve monitoring was used. One drawback of using nerve monitoring identified by the authors was that thyroid surgery took longer than if monitoring was not used. On the other hand, the authors found that the overall length of time a person was in the hospital after thyroid surgery was shorter when nerve monitoring was used.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Minimizing the risk of recurrent laryngeal nerve injury during thyroid surgery, and thus the risk of associated voice, swallowing and/or breathing problems after surgery, is a critically important part of a thyroid surgeon's job. Any technology that facilitates this risk reduction should be considered for use during thyroid surgery. This study indicates that using nerve monitoring technology during thyroid surgery helps thyroid surgeons avoid injuring the recurrent laryngeal nerves during surgery. Furthermore, the study authors did not identify any significant drawbacks associated with using nerve monitoring technology. Thyroid surgeons should thus strongly consider using nerve monitoring technology during thyroid surgery.

— Jason D. Prescott, MD PhD

THYROID SURGERY, continued

ATA THYROID BROCHURE LINKS

Thyroid Surgery: https://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS & DEFINITIONS

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.

Recurrent laryngeal nerves: 2 nerves that come up from the chest, one on each side of the neck, and travel by the thyroid to insert into the voice box. They control the vocal cords and are very delicate.

Nerve monitoring: This technology allows a surgeon to monitor that these nerves are working throughout the operation and may also help the surgeon identify exactly where the nerves are located, relative to a person's thyroid gland, while surgery is being performed. This information may help a surgeon avoid accidentally injuring one, or both, of these nerves.

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HYPOTHYROIDISM

Fatty liver disease and the thyroid: Is there a link?

BACKGROUND

Fatty liver disease is now recognized as a significant cause of liver problems, including cirrhosis and liver failure. In this condition, fat deposits in the liver may form over time. Fatty liver disease is linked with a variety of conditions such as obesity, diabetes and high cholesterol levels. There are 2 types of fatty liver disease: once caused by alcohol (alcoholic liver disease) and one not related to alcohol (nonalcoholic fatty liver disease, or NAFLD).

The potential association between NAFLD and thyroid function has remained controversial. A possible link between this condition and thyroid disease has been an area of study. Recent studies have emerged suggesting that individuals with NAFLD have an increased incidence of hypothyroidism, which leads to a wide range of metabolic complications. This study was performed to assess the relationships between TSH levels and NAFLD and whether having thyroid disease increases the risk of developing NAFLD.

THE FULL ARTICLE TITLE

Fan H et al 2022 Thyroid stimulating hormone levels are associated with genetically predicted nonalcoholic fatty liver disease, J Clin Endocrinol Metab. Epub 2022 Jun 28. PMID: 35763044.

SUMMARY OF THE STUDY

This study reviewed medical charts of over 14,000 patients. The age of the participants ranged from 20 to 74 years. Those included in the study had an ultrasound of their abdomen as well as thyroid blood work tested (TSH, T4). The authors used genetic data from a large database to look for possible connections. In addition, statistical methods were utilized to look at a possible association. This analysis included 1801 patients with NAFLD and 6185 healthy patients without liver disease.

It was found that TSH levels were related to NAFLD to a certain extent. Patients who did not have NAFLD typically had lower TSH and higher T4 levels. The data suggested that NAFLD caused an increase in TSH levels while TSH levels did not significantly change the risk of NAFLD.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study is one of the few that have looked at the link of NAFLD with thyroid diseases. It suggests that there may be a link of increased TSH levels and NAFLD. However, further studies will be needed to investigate this link further to determine whether thyroid disease is in fact a risk factor for fatty liver disease.

—Vibhavasu Sharma, MD, FACE

ATA THYROID BROCHURE LINKS

Thyroid Function Tests: https://www.thyroid.org/thyroid-function-tests/

ABBREVIATIONS & DEFINITIONS

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

Fatty liver disease: liver diseases including cirrhosis caused by deposits of fat in the liver. This can be caused by alcohol (alcoholic fatty liver disease) or not related to alcohol (nonalcoholic fatty liver disease, NAFLD). NAFLD can be seen in patients with diabetes and/or obesity.

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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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(Toll-free): 1-800-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
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