



ESES Review of Recently Published Literature

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SR: systematic review, **MA:** meta-analysis, **RCT:** randomized controlled trial,
CG: consensus statement/guidelines

Pubmed-ID: PubMed-Identifier (unique number for each Pubmed entry)

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Preliminary

Finally, the last ESES collection of 2023 is complete. Sorry, for the delay.

For 2024, which also is already more than half over, there will be some changes in the ESES collection. Starting on a personal note, I will go into retirement this year. Thus, it was decided to hand over the task of putting the ESES collection together, to someone younger. Along with this transfer, a detailed handbook was drafted to describe the process in great detail to help future generations to prepare the collection (so far I did it a little bit like an “artist“, using some sketchy notes and making changes of the process on the run. It was a continuous development.) Starting with this edition of the ESES collection, Paola Sartori from the Department of Surgery at the Desio Hospital in Desio, Italy will compile the collection. For this edition we did the job together, the next editions she will do it on her own, perhaps with some supervision from my side.

Furthermore, the list of journals that will be covered, will be revised and made more comprehensive. So I think there will be a promising future for the ESES collection.

Unfortunately I did not attend the ESES congress in Rome, however I was told, that my work for ESES was well received, and I would like to thank everyone this way for the great appreciation.

So, this was my last ESES collection. I look back on a great time doing the collection, while facing a lot of tasks to be solved and putting the papers together in a decent and appealing way (when I started we even had the collection in Endnote and in ReferenceManager. Whoever tried to transfer a library between these two programs knows what a daunting task this is.) And I would like to thank Thomas for his great collaboration, for his ongoing support and his endless patience, when I was -like so often - far too late with finishing the collection.

I will miss you
yours
Ulrich Beutner

Journals covered

Journal	IF2022	Journal	IF2022
Acta Cytol	1.8	J Bone Miner Res	6.2
Am J Kidney Dis	13.2	J Clin Endocrinol Metab	5.8
Am J Nephrol	4.2	J Clin Oncol	45.3
Am J Surg	3.0	J Endocrinol	4.0
Am Surgeon	1.0	J Endocrinol Invest	5.4
Ann Surg	9.0	J Nephrol	3.4
Ann Surg Oncol	3.7	J Nucl Med	9.3
ANZ J Surg	1.7	J Surg Oncol	2.5
Br J Surg	9.6	Lancet	168.9
Cancer	6.2	Langenbecks Arch Surg	2.3
Chirurgie (formerly: Chirurg)	0.9	Laryngoscope	2.6
Clin Endocrinol Oxf	3.2	N Engl J Med	158.5
Clin Nucl Med	10.6	Nat Rev Endocrinol	40.5
Curr Opin Oncol	3.4	Nat Rev Clin Oncol	78.8
Endocr Relat Cancer	3.9	Nephrol Dial Transplant	6.1
Endocr Rev	20.3	Neuroendocrinology	4.1
Eur Arch Otorhinolaryngol	2.6	Oncologist	5.8
Eur J Endocrinol	5.8	Otolaryngol Head Neck Surg	3.4
Eur J Surg Oncol	3.8	Surg Clin North Am	3.1
Gland Surg	1.8	Surg Endosc	3.1
Head Neck	2.9	Surg Laparosc Endosc Percutan Tech	1.0
Horm Metab Res	2.2	Surg Oncol	2.3
JAMA Otolaryngol Head Neck Surg	7.8	Surg Oncol Clin N Am	1.9
JAMA Surg	16.9	Surgery	3.8
Int J Cancer	6.4	Thyroid	6.6
J Am Coll Surg	5.2	Updates In Surgery	2.6
J Am Soc Nephrol	13.6	World J Surg	2.6
J Bone Miner Metab	3.3		

Journal names are links to the journal's homepage!, IF2022: [Impact factor](#)

Thyroid

Meta-Analyses

A combination of computed tomography scan and ultrasound provides optimal detection of cervical lymph node metastasis in papillary thyroid carcinomas: A systematic review and meta-analysis.

Head Neck, 45(9):2173-84.

A. L. Albuck, P. P. Issa, M. Hussein, M. Aboueisha, A. S. Attia, M. Omar, R. Munshi, M. Shama, E. Toraih, G. W. Randolph and E. Kandil. 2023.

BACKGROUND: Lymph node metastasis (LNM) in patients with papillary thyroid carcinoma (PTC) is common. This meta-analysis assesses the diagnostic accuracy of computed tomography (CT), ultrasound (US), and CT + US in detecting central and lateral LNM. **METHODS:** A systematic review and meta-analysis was performed by searching PubMed, Embase, and Cochrane for studies published up to April 2022. The pooled sensitivity, specificity, and diagnostic odds ratio (DOR) were calculated. The area under the curve (AUC) for summary receiver operating curves (sROC) were compared. **RESULTS:** The study population included 7902 patients with a total of 15 014 lymph nodes. Twenty-four studies analyzed the sensitivity of the overall neck region in which dual CT + US imaging (55.9%) had greater sensitivities ($p < 0.001$) than either US (48.4%) or CT (50.4%) alone. The specificity of US alone (89.0%) was greater ($p < 0.001$) than CT alone (88.5%) or dual imaging (86.8%). The DOR for dual CT + US imaging was greatest ($p < 0.001$) at 11.134, while the AUCs of the three imaging modalities were similar ($p > 0.05$). Twenty-one studies analyzed the sensitivity of the central neck region in which both CT (45.8%) and CT + US imaging (43.4%) had greater sensitivities ($p < 0.001$) than US alone (35.3%). The specificity of all three modalities was higher than 85%. The DOR for CT (7.985) was greater than US alone (4.723, $p < 0.001$) or dual CT + US imaging (4.907, $p = 0.015$). The AUC of both CT + US (0.785) and CT alone (0.785) were significantly greater ($p < 0.001$) than US alone (0.685). Of the 19 studies that reported lateral LNM, CT + US imaging sensitivity (84.5%) was higher than CT alone (69.2%, $p < 0.001$) and US alone (79.7%, $p = 0.038$). The specificity of all imaging techniques was all greater than 80.0%. CT + US imaging DOR (35.573) was greater than CT (20.959, $p = 0.024$) and US (15.181, $p < 0.001$) individually. The AUC of independent imaging was high (CT: 0.863, US: 0.858) and improved significantly when combined (CT + US: 0.919, $p = 0.024$ and $p < 0.001$, respectively). **CONCLUSIONS:** We report an up-to-date analysis elucidating the diagnostic accuracy of LNM detection by either CT, US, or in combination. Our work suggests dual CT + US to be the best for overall detection of LNM and CT to be preferable in detecting central LNM. The use of either CT or US alone may detect lateral LNM with acceptable accuracy, yet dual imaging (CT + US) significantly improved detection rates.

PubMed-ID: [37417426](#)

DOI: [10.1002/hed.27451](#)

The Diagnostic Value of (18)F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Differentiated Thyroid Cancer Patients with Elevated Thyroglobulin/Thyroglobulin Antibody Levels and Negative Iodine Scintigraphy: A Systematic Review and Meta-Analysis.

Thyroid, 33(10):1224-36.

J. I. Bang, S. Park, K. Kim, Y. Seo, A. Chong, C. M. Hong, M. Choi, S. W. Lee and S. W. Oh. 2023.

Background: The objective of this study is to evaluate the diagnostic accuracy of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) in detecting recurrence in patients with differentiated thyroid cancer (DTC) who have negative whole-body scans (WBSs) but elevated serum thyroglobulin (Tg) or thyroglobulin antibody (TgAb) levels. **Methods:** This systematic review/meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Diagnostic Test Accuracy criteria (International Prospective Register of Systematic Reviews registration number: CRD42022340924). A comprehensive search of the MEDLINE, EMBASE, and Cochrane databases identified articles reporting the diagnostic accuracy of FDG PET/CT for the detection of recurrence in patients with DTC with negative WBS and elevated serum Tg or TgAb levels published between January 2012 and June 2023. Meta-analyses were performed to determine the diagnostic accuracy of FDG PET/CT on the total target population as well as on subgroups stratified by serum Tg or TgAb, and thyrotropin (TSH) stimulation status at the time of FDG PET/CT. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework was applied to evaluate the quality of evidence and the strength of recommendations to facilitate translation of the meta-analysis results into practical recommendations for clinical guidelines. **Results:** A total of 24 studies involving 1988 patients were included for analysis. The overall pooled sensitivity and specificity values were 0.87 (95% confidence interval [CI] = 0.83-0.92; $I(2) = 75%$) and 0.84 (CI = 0.80-0.89; $I(2) = 44%$), respectively. Subgroup analyses revealed no significant

differences in the diagnostic accuracy of FDG PET/CT in patients stratified by serum Tg or TgAb levels, and TSH stimulation status at the time of PET/CT. Treatment plans were changed following FDG PET/CT imaging in 40% (CI = 34-47%; I(2) = 39%) of cases. The quality level of evidence for using FDG PET/CT was moderate in both sensitivity and specificity according to the GRADE system. Conclusion: There is moderate quality evidence demonstrating the high diagnostic accuracy of FDG PET/CT in detecting recurrence in patients with DTC with negative WBS and elevated serum Tg or TgAb levels. This evidence corroborates the current guidelines' endorsement of FDG PET/CT as a diagnostic tool in such patients.

PubMed-ID: [37597200](#)

DOI: [10.1089/thy.2023.0264](#)

Implementation strategies to support ultrasound thyroid nodule risk stratification: A systematic review.

Clin Endocrinol (Oxf), 99(4):417-27.

M. Edwards, J. P. Brito, R. G. Salloum, J. Hoang and N. Singh Ospina. 2023.

BACKGROUND: Ultrasound risk stratification can improve the care of patients with thyroid nodules by providing a structured and systematic approach for the evaluation of thyroid nodule features and thyroid cancer risk. The optimal strategies to support implementation of high quality thyroid nodule risk stratification are unknown. This study seeks to summarise strategies used to support implementation of thyroid nodule ultrasound risk stratification in practice and their effects on implementation and service outcomes. METHODS: This is a systematic review of studies evaluating implementation strategies published between January 2000 and June 2022 that were identified on Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane, Scopus, or Web of Science. Screening of eligible studies, data collection and assessment for risk of bias was completed independently and in duplicate. Implementation strategies and their effects on implementation and service outcomes were evaluated and summarised. RESULTS: We identified 2666 potentially eligible studies of which 8 were included. Most implementation strategies were directed towards radiologists. Common strategies to support the implementation of thyroid nodule risk stratification included: tools to standardise thyroid ultrasound reports, education on thyroid nodule risk stratification and use of templates/forms for reporting, and reminders at the point of care. System based strategies, local consensus or audit were less commonly described. Overall, the use of these strategies supported the implementation process of thyroid nodule risk stratification with variable effects on service outcomes. CONCLUSIONS: Implementation of thyroid nodule risk stratification can be supported by development of standardised reporting templates, education of users on risk stratification and reminders of use at the point of care. Additional studies evaluating the value of implementation strategies in different contexts are urgently needed.

PubMed-ID: [37393196](#)

DOI: [10.1111/cen.14942](#)

PMCID: PMC10529907

Transoral endoscopic thyroidectomy vestibular approach vs. transoral robotic thyroidectomy: systematic review and meta-analysis.

Updates Surg, 75(7):1773-81.

M. Y. Oh, Y. J. Chai, H. W. Yu, S. J. Kim, J. Y. Choi and K. E. Lee. 2023.

This study aimed to conduct a systematic review and meta-analysis to compare the surgical outcomes of the transoral endoscopic thyroidectomy vestibular approach (TOETVA) and transoral robotic thyroidectomy (TORT). We carried out a systematic literature search of PubMed, Web of Science, Cochrane Library, and Google Scholar on studies comparing TOETVA and TORT until January 2023. A total of five articles published between 2018 and 2023 that matched the inclusion criteria were included in the systematic review and meta-analysis. The studies included 641 patients (394 TOETVA patients and 247 TORT patients). TOETVA group was associated with a significantly shorter operative time with a mean difference of 60.08 min [95% confidence interval (CI) - 83.95 to - 36.20; $P < 0.001$]. Transient recurrent laryngeal nerve palsy was more common in the TOETVA group than the TORT group (OR 3.00; 95% CI 1.14-7.88; $P = 0.03$). There were no significant differences in the other outcomes, including the length of hospital stay, postoperative pain scores, number of central lymph nodes retrieved, permanent recurrent laryngeal nerve injuries, and transient and permanent hypoparathyroidism. The TOETVA group was associated with shorter operative time and more transient recurrent laryngeal nerve palsy than the TORT group. Each procedure has its benefits and limitations. The surgical approach should be determined by considering the patient's characteristics and preferences, as well as the surgeon's preference and area of expertise.

PubMed-ID: [37556081](#)

DOI: [10.1007/s13304-023-01623-3](#)

Randomized controlled trials

Impact of autofluorescence for detection of parathyroid glands during thyroidectomy on postoperative parathyroid hormone levels: parallel multicentre randomized clinical trial.

Br J Surg, 110(12):1824-33.

A. Bergenfelz, M. Barczynski, A. Heie, A. Muth, C. Passler, M. Schneider, P. Wierzbicka, A. Konturek, K. Brauckhoff, A. K. Elf, J. Dahlberg and M. Hermann. 2023.

BACKGROUND: Techniques for autofluorescence have been introduced to visualize the parathyroid glands during surgery and to reduce hypoparathyroidism after thyroidectomy. **METHODS:** This parallel multicentre RCT investigated the use of Fluobeam(R) LX to visualize the parathyroid glands by autofluorescence during total thyroidectomy compared with no use. There was no restriction on the indication for surgery. Patients were randomized 1 : 1 and were blinded to the group allocation. The hypothesis was that autofluorescence enables identification and protection of the parathyroid glands during thyroidectomy. The primary endpoint was the rate of low parathyroid hormone (PTH) levels the day after surgery. **RESULTS:** Some 535 patients were randomized, and 486 patients received an intervention according to the study protocol, 246 in the Fluobeam(R) LX group and 240 in the control group. Some 64 patients (26.0 per cent) in the Fluobeam(R) LX group and 77 (32.1 per cent) in the control group had low levels of PTH after thyroidectomy ($P = 0.141$; relative risk (RR) 0.81, 95 per cent c.i. 0.61 to 1.07). Subanalysis of 174 patients undergoing central lymph node clearance showed that 15 of 82 (18 per cent) in the Fluobeam(R) LX group and 31 of 92 (33 per cent) in the control group had low levels of PTH on postoperative day 1 ($P = 0.021$; RR 0.54, 0.31 to 0.93). More parathyroid glands were identified during operation in patients who had surgery with Fluobeam(R) LX, and fewer parathyroid glands in the surgical specimen on definitive histopathology. No specific harm related to the use of Fluobeam(R) LX was reported. **CONCLUSION:** The use of autofluorescence during thyroidectomy did not reduce the rate of low PTH levels on postoperative day 1 in the whole group of patients. It did, however, reduce the rate in a subgroup of patients. Registration number: NCT04509011 (<http://www.clinicaltrials.gov>).

PubMed-ID: [37758507](https://pubmed.ncbi.nlm.nih.gov/37758507/)

DOI: [10.1093/bjs/znad278](https://doi.org/10.1093/bjs/znad278)

PMCID: PMC10638529

Preliminary Results of a Double-Blind Randomized Controlled Trial Evaluating the Cardiometabolic Effects of Levothyroxine and Liothyronine Compared to Levothyroxine with Placebo in Athyreotic Low-Risk Thyroid Cancer Patients.

Thyroid, 33(12):1402-13.

B. Biondi, M. Pucci, G. Pontieri, P. Formisano and R. Esposito. 2023.

Background: Evidence is needed on the risks and benefits of combination therapy with levothyroxine (LT4)+liothyronine (LT3) for the treatment of hypothyroidism. **Objective and Methods:** We performed a randomized, double-blind placebo-controlled study to assess the effects of LT4+LT3 therapy versus LT4+placebo in a homogeneous group of athyreotic patients, without cardiovascular risk factors during long-term replacement monotherapy with LT4. The primary objective of the study was to assess the effects of combination LT4+LT3 therapy on heart rate, cardiac rhythm, and sensitive cardiovascular parameters of cardiac morphology and function by means of electrocardiography and Doppler echocardiography. The secondary objective of the study was to evaluate patient compliance, tolerability, and potential adverse events. **Results:** Thirty-eight patients with postsurgical hypothyroidism satisfying the inclusion criteria were selected from a group of 300 patients with low-risk thyroid cancer followed for a routine follow-up; they were randomized to receive LT4+LT3 or LT4+placebo. Twenty-four patients were evaluated after 1 year of treatment. All clinical and laboratory parameters were compared with the results obtained from 50 healthy euthyroid volunteers without comorbidities, matched for gender, age, physical activity, and lifestyle. Participants and clinicians remained blinded to the treatment allocation. After 1 year of combination therapy, a significant improvement in the diastolic function, evidenced by a significant reduction in the E/e' ratio ($p = 0.046$) and its positive trend over time, was observed in the LT4+LT3 group versus the LT4+placebo group. In addition, the univariate analyses showed a significant relationship between free triiodothyronine (fT3) levels (in pg/mL) with Delta of variation of the E/e' ratio in the LT4+LT3 group (standardized beta coefficient = 0.603 [confidence interval: 0.001-1.248], $p = 0.050$) after combination therapy. No adverse events including tachycardia, arrhythmias, atrial fibrillation, or other important events occurred between the first administration and the end of the study. **Conclusions:** In this preliminary report, combination treatment with LT4+LT3 induced favorable changes in cardiovascular parameters of diastolic function without any adverse cardiovascular events. Trial Registration: EUDRACT number: 2017-001261-25.

PubMed-ID: [37725587](#)
DOI: [10.1089/thy.2023.0135](#)

The Effect of Vitamin D Supplementation on Hypothyroidism in the Randomized Controlled D-Health Trial.

Thyroid, 33(11):1302-10.

M. Waterhouse, H. Pham, S. T. Rahman, C. Baxter, B. Duarte Romero, B. K. Armstrong, P. R. Ebeling, D. R. English, G. Hartel, J. C. van der Pols, A. J. Venn, P. M. Webb, D. C. Whiteman, D. S. A. McLeod and R. E. Neale. 2023.

Background: Hypothyroidism is common, and in iodine-sufficient areas, it is primarily caused by autoimmune destruction of the thyroid gland. Observational studies have consistently shown an inverse association between serum 25-hydroxyvitamin D concentration and autoimmune diseases; however, there is a lack of evidence from randomized controlled trials to support a benefit of vitamin D supplementation, particularly for autoimmune thyroid diseases. We, therefore, aimed to assess the effect of vitamin D supplementation on the incidence of hypothyroidism. Methods: We analyzed data from the D-Health Trial (n = 21,315), a randomized double-blind placebo-controlled trial of 60,000 international units per month of supplemental vitamin D(3) among Australians aged 60 years and over. Hypothyroidism, a tertiary outcome of the D-Health Trial, was defined by treatment with levothyroxine, ascertained through linkage with the Australian Pharmaceutical Benefits Scheme. The outcome was time to first prescription of levothyroxine. We began follow-up at 12 months after randomization; people who had died or who had been dispensed levothyroxine during the first year were excluded. Flexible parametric survival models were used to assess the effect of vitamin D supplementation on hypothyroidism, overall and within strata defined by age, sex, body mass index, and predicted baseline vitamin D status. Results: We included 17,851 participants in the main analysis (vitamin D = 8939; placebo = 8912). During a median follow-up of 4.1 years (interquartile range 4.1-4.1), 293 participants developed hypothyroidism (vitamin D = 138 [1.5%]; placebo = 155 [1.7%]). Vitamin D supplementation did not significantly reduce the incidence of hypothyroidism (overall hazard ratio [HR] 0.89; 95% confidence interval [CI] 0.71-1.12). There was some suggestion of an effect in females (overall HR 0.78; CI 0.58-1.06) but not in males (overall HR 1.06; CI 0.74-1.50; p interaction 0.20). Conclusions: Vitamin D supplementation did not reduce the incidence of hypothyroidism overall; however, the possible beneficial effect observed in females warrants further investigation. Clinical Trial Registration: Australian New Zealand Clinical Trials Registry: ACTRN12613000743763.

PubMed-ID: [37698908](#)
DOI: [10.1089/thy.2023.0317](#)

Consensus Statements/Guidelines

2023 European Thyroid Association Clinical Practice Guidelines for thyroid nodule management.

Eur Thyroid J, 12(5)

C. Durante, L. Hegedus, A. Czarniecka, R. Paschke, G. Russ, F. Schmitt, P. Soares, T. Solymosi and E. Papini. 2023.

With the widespread use of sensitive imaging techniques, which include neck visualization, a conspicuous number of thyroid nodules emerge and demand attention. Most lesions are benign, asymptomatic, and do not warrant treatment. In the case of cancer diagnosis, most are small, intrathyroidal and indolent neoplasms that can safely be managed conservatively. There is a pronounced need for more cost-effective, risk-adapted approaches to the management of this highly prevalent condition, taking the wishes of the patient into consideration. Thus, the present guidelines aim at providing a clinical practice guide for the initial workup and the subsequent management of adult individuals harboring thyroid nodules. Importantly, these guidelines are not intended to cover the management of thyroid malignancy. The manuscript and the specific recommendations were developed by reconciling the best available research evidence with the knowledge and clinical experience of the panelists and updating aspects of a number of previous European Thyroid Association guidelines.

PubMed-ID: [37358008](#)
DOI: [10.1530/ETJ-23-0067](#)
PMCID: PMC10448590

Other Articles

The Optimal Age Threshold for Stratifying the Risks of Disease Progression in Patients with Highly Suspicious Sub-centimeter Thyroid Nodules.

Ann Surg Oncol, 30(9):5463-9.

L. Zhuge, Z. Huang, H. Cai, S. Wang, L. Niu and Z. Li. 2023.

PURPOSE: The study aimed to identify the value and optimal age cutoff to predict the progression of highly suspicious thyroid nodules ≤ 10 mm during active surveillance (AS), and to reveal distinct risk factors in patients of different ages. **METHODS:** A total of 779 patients with highly suspicious thyroid nodules were enrolled and followed up by ultrasonography. Locally weighted scatterplot smoothing (LOWESS) and the package 'changepoint' were used to identify the optimal age cutoffs using R. Multivariate Cox regression was performed to identify independent prognostic factors in each patient group divided according to age. **RESULTS:** Age was an independent predictor of nodule progression ($P = 0.038$). The optimal age cutoff to stratify the risk of nodule progression was 30 years. Younger patients were more likely to have progression of nodules during AS ($P < 0.001$), including enlargement of nodule size ($P = 0.011$) and new lesion occurrence ($P < 0.001$). Nodule size was identified as a risk factor for disease progression in patients younger than 30 years old ($P = 0.008$, OR 7.946, 95% CI 1.715-36.820), while multifocality ($P = 0.018$, OR 2.315, 95% CI 1.155-4.639) and thyroiditis ($P = 0.028$, OR 2.265, 95% CI 1.092-4.699) were independent predictors in patients over 30 years old. **CONCLUSIONS:** Highly suspicious thyroid nodules ≤ 10 mm in young patients tended to be more progressive. The predictors of disease progression were distinct in patients of different ages.

PubMed-ID: [37061650](#)

DOI: [10.1245/s10434-023-13497-1](#)

Is There an Age Threshold for Active Surveillance in Highly Suspicious Subcentimeter Thyroid Nodules?

Ann Surg Oncol, 30(9):5318-9.

S. Young and M. Goldfarb. 2023.

PubMed-ID: [37233953](#)

DOI: [10.1245/s10434-023-13682-2](#)

Five-year Outcome Between Radiofrequency Ablation vs Surgery for Unilateral Multifocal Papillary Thyroid Microcarcinoma.

J Clin Endocrinol Metab, 108(12):3230-8.

L. Yan, Z. Yang, Y. Li, X. Li, J. Xiao, H. Jing and Y. Luo. 2023.

CONTEXT: Ultrasound (US)-guided radiofrequency ablation (RFA) has been considered as an alternative to surgery or active surveillance for papillary thyroid microcarcinoma (PTMC). However, little is known about the long-term outcomes of RFA in comparison with surgery for unilateral multifocal PTMC. **OBJECTIVE:** This work aims to report the comparison between RFA vs surgery for unilateral multifocal PTMC over a more than 5-year follow-up period. **METHODS:** This was a retrospective study at a primary care center with a median follow-up period of 72.9 months. A total of 97 patients with unilateral multifocal PTMC were treated with RFA (RFA group, $n = 44$) or surgery (surgery group, $n = 53$). In the RFA group, patients were treated by a bipolar RFA generator and an 18-gauge bipolar RF electrode with a 0.9-cm active tip. In the surgery group, patients underwent thyroid lobectomy with prophylactic central neck dissection. **RESULTS:** During the follow-up, no statistically significant differences were found in disease progression (4.5% vs 3.8%; $P = \geq .999$), lymph node metastasis (2.3% vs 3.8%; $P = \geq .999$), persistent lesion (2.3% vs 0%; $P = .272$), and RFS rates (97.7% vs 96.2%; $P = .673$) in the RFA and surgery groups. Patients undergoing RFA had a shorter hospitalization (0 vs 8.0 [3.0] d; $P < .001$), shorter procedure time (3.5 [2.4] vs 80.0 [35.0] min; $P < .001$), lower estimated blood loss (0 vs 20.0 [15.0] mL; $P < .001$), and lower costs (\$1768.3 [0.1] vs \$2084.4 [1173.8]; $P = .001$) than those in the surgery group. The complication rate in the surgery group was 7.5%, whereas none of the RFA-treated patients experienced any complications ($P = .111$). **CONCLUSION:** This study revealed 6-year comparable outcomes between RFA and surgery for unilateral multifocal PTMC. RFA may be a safe and effective alternative to surgery in selected patients with unilateral multifocal PTMC.

PubMed-ID: [37318878](#)

DOI: [10.1210/clinem/dgad360](#)

New Insights on the Importance of the Extent of Vascular Invasion in Widely Invasive Follicular Thyroid Carcinoma.

World J Surg, 47(11):2767-75.

H. Yamazaki, K. Sugino, R. Katoh, K. Matsuzu, W. Kitagawa, M. Nagahama, Y. Rino and K. Ito. 2023.

BACKGROUND: This study aimed to investigate the association between the extent of vascular invasion (VI) and the outcome of widely invasive follicular thyroid carcinoma (WI-FTC). **METHODS:** The records of 107 patients with WI-FTC confirmed by surgical specimens from January 2005 to December 2016 were retrospectively reviewed. **RESULTS:** Among the 107 patients with WI-FTC, those with a VI of < 4 (n = 62) and \geq 4 (n = 45) had a 10 year cause-specific survival (CSS) rate of 97.7% and 89.4% (p = 0.008), respectively. Univariate analysis identified M1 (p = 0.001), and the number of VI of \geq 4 as significant negative prognostic factors for CSS. Multivariate analysis identified M1 (hazard ratio [HR] = 9.366) as independent negative prognostic factor for CSS. Among the 72 patients with M0 WI-FTC, those with a VI of < 2 (n = 33) and \geq 2 (n = 39) had a 10-year distant metastasis-free survival (DMFS) rate of 96.8% and 56.8% (p = 0.001), respectively. Univariate analysis identified age \geq 55 years (p = 0.011), presence of VI, the number of VI of \geq 2, and resection margin status (p < 0.001) as significant negative prognostic factors for DMFS. Multivariate analysis identified the number of VI \geq 2 (HR = 9.137), and resection margin status (HR = 5.853) as independent negative prognostic factors for DMFS. **CONCLUSIONS:** It may be unnecessary that WI-FTC with curative resection margin status and a VI of < 2, especially in capsular invasion only, routinely undergo completion thyroidectomy and postoperative ablation.

PubMed-ID: [37516689](https://pubmed.ncbi.nlm.nih.gov/37516689/)

DOI: [10.1007/s00268-023-07127-w](https://doi.org/10.1007/s00268-023-07127-w)

Prognostic Value of Tumor Multifocality in Pediatric Papillary Thyroid Carcinoma: A Real-Life Multicentric Study.

Otolaryngol Head Neck Surg, 169(6):1606-14.

Y. Xu, L. Shi, J. Wu, H. Li, Y. Wang and B. Liu. 2023.

OBJECTIVE: To investigate the association of multifocality with clinical outcomes in pediatric papillary thyroid cancer. **STUDY DESIGN:** Multicenter retrospective study of prospectively collected data. **SETTING:** Tertiary referral center. **METHODS:** This study included patients 18 years or younger who underwent total thyroidectomy and radioiodine ablation for papillary thyroid carcinoma (PTC) between 2005 and 2020 at 3 tertiary adult and pediatric hospitals in China. For disease-free survival (DFS), events were defined as persistent and/or recurrent diseases. The primary outcome was the association of tumor multifocality and DFS, assessed using Cox proportional hazards regression models. **RESULTS:** One hundred and seventy-three patients (median age 16 years [range, 5-18 years]) were recruited. Multifocal diseases were seen in 59 patients (34.1%). After a median follow-up of 57 (range, 12-193 months) months, 63 (36.4%) patients had persistent diseases. There was a significant association between tumor multifocality and decreased DFS on univariable analysis (hazard ratio [HR] = 1.90, p = .01), yet it was nonsignificant after multivariate adjustment (HR = 1.20, p = .55). In a subgroup analysis of 132 pediatric patients with clinically M0 PTC, neither unadjusted HR (2.21, p = .06) nor adjusted HR (1.70, p = .27) of multifocal PTC was significantly higher in comparison to unifocal PTC. **CONCLUSION:** In this highly selective surgical pediatric patient cohort with PTC, tumor multifocality was not an independent risk factor for decreased DFS.

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DOI: [10.1002/ohn.373](https://doi.org/10.1002/ohn.373)

Determining the Power Required for Comparing Lobectomy vs Total Thyroidectomy for Papillary Thyroid Carcinoma-Reply.

JAMA Surg, 158(9):984.

S. Xu, S. Liu and J. Liu. 2023.

PubMed-ID: [37195671](https://pubmed.ncbi.nlm.nih.gov/37195671/)

DOI: [10.1001/jamasurg.2023.1063](https://doi.org/10.1001/jamasurg.2023.1063)

The Feasibility Study of Intraoperative RLN Monitoring Using Cricothyroid Membrane-Inserted Needle Electrodes During Thyroid Surgery.

Otolaryngol Head Neck Surg, 169(3):589-97.

C. Xu, X. Wang, J. Liu, J. Yan, S. Zhang, Z. Zheng, Q. Zhao, Y. Feng, Y. Bai, R. Zhao, H. Li and X. Yao. 2023.

OBJECTIVE: This study evaluated the feasibility, stability, safety, and economy of cricothyroid membrane (CM)-inserted needle electrodes for recurrent laryngeal nerve monitoring. **STUDY DESIGN:** Parallel and controlled study. **SETTING:** Clinical research center for thyroid diseases of Shaanxi province. **METHODS:** A total of 64 patients in the needle electrodes group (104 recurrent laryngeal nerves [RLNs]) and 44 patients in the endotracheal tube (ETT)-based electrodes group (80 RLNs) underwent monitored thyroidectomy. The evoked electromyography (EMG) signals detected by the 2 electrodes

were recorded and analyzed. The changes in EMG during Berry's ligament traction and tracheal displacement were compared. All patients underwent preoperative and postoperative laryngoscopy within 1 week. RESULTS: Both electrodes successfully recorded typical evoked laryngeal EMG waveforms from RLNs. The needle electrodes recorded relatively higher amplitudes and similar latencies compared to ETT-based electrodes. The evoked EMG signals attributed to needle electrodes could accurately predict the function of RLNs with 100% sensitivity and specificity. The reduction in the recorded amplitudes attributed to needle electrodes was higher than that observed with ETT-based electrodes during Berry's ligament traction or trachea displacement, whereas a similar increase in the latencies was recorded in the 2 groups. Particularly, Berry's ligament traction was more likely to lead to EMG amplitude reduction and latency prolongation. The needle electrodes group recorded 2 cases of minor bleeding on the CM. The needle electrodes were more cost-effective than ETT-based electrodes. CONCLUSION: The CM-inserted needle electrodes are feasible, stable, safe, and economical for RLN monitoring, and they provide an alternative novel intraoperative neural monitoring format for thyroid surgeons.

PubMed-ID: [37051891](#)

DOI: [10.1002/ohn.338](#)

Thyroid surgery in children and adolescents: results from a multi-institutional German and Austrian database.

Br J Surg, 110(12):1808-14.

T. Weber, R. Hummel, C. Vorlander, A. Zielke, M. Hermann, A. Krappitz, T. Negele, C. Dotzenrath, A. Trupka, J. Schabram, I. Schmidtman, C. Klinger and K. Lorenz. 2023.

BACKGROUND: Outcomes of paediatric thyroid surgery have only been reported in smaller series or over long intervals. The aim of this multicentre study was to describe the recent outcomes of paediatric thyroid surgery in Germany and Austria. METHODS: Patients aged less than or equal to 18 years who underwent thyroid surgery and were prospectively documented in the StuDoQ|Thyroid registry between March 2017 and August 2022 were studied. RESULTS: In total, 604 patients from 90 institutions were included. The mean age was 15.4 years and 75 per cent of patients were female. The most frequent benign pathologies were nodular goitre (35.6 per cent), follicular adenoma (30.1 per cent), and Graves' disease (28.5 per cent). Among 126 thyroid malignancies, papillary thyroid carcinoma was diagnosed in 77.8 per cent of patients, follicular thyroid carcinoma was diagnosed in 10.3 per cent of patients, and medullary thyroid carcinoma was diagnosed in 8.7 per cent of patients. Lymph node metastases were found in 45.9 per cent of patients with papillary thyroid carcinoma and in 36.4 per cent of patients with medullary thyroid carcinoma. Vascular invasion was found in 62.9 per cent of patients with follicular thyroid carcinoma. The mean tumour diameters were 18, 42, and 13 mm in patients with papillary thyroid carcinoma, follicular thyroid carcinoma, and medullary thyroid carcinoma respectively. Early postoperative recurrent laryngeal nerve injury was seen in 27 of 556 patients (4.9 per cent) (22 of 617 (3.6 per cent) nerves at risk with intermittent intraoperative nerve monitoring and 5 of 237 (2.1 per cent) nerves at risk with continuous intraoperative nerve monitoring). Persistent recurrent laryngeal nerve injury was documented in 4 of 556 patients (0.7 per cent). Early postoperative hypoparathyroidism correlated with Graves' disease, thyroid carcinoma, and lymph node dissection. CONCLUSION: Papillary thyroid carcinoma and follicular thyroid carcinoma in children were often advanced at presentation. Persistent or recurrent lymph node metastases were mainly seen in papillary thyroid carcinoma. Overall survival was excellent, but longer follow-up is needed.

PubMed-ID: [37758484](#)

DOI: [10.1093/bjs/znad255](#)

Adjuvant Radioiodine for Intermediate-Risk Papillary Thyroid Cancer-To Treat or Not to Treat.

J Clin Endocrinol Metab, 108(10):e1149-e50.

E. F. S. van Velsen and F. A. Verburg. 2023.

PubMed-ID: [36964916](#)

DOI: [10.1210/clinem/dgad171](#)

PMCID: PMC10505540

Clinical classification of recurrent laryngeal nerve palsy.

Gland Surg, 12(9):1203-8.

C. Tomoda, K. Yoshioka, Y. Saito, C. Masaki, J. Akaishi, K. Y. Hames, R. Okamura, A. Suzuki, K. Matsuzu, W. Kitagawa, K. Sugino and K. Ito. 2023.

BACKGROUND: The application of intraoperative neurophysiological monitoring (IONM) has been accepted to avoid injury of a recurrent laryngeal nerve (RLN). Loss of the neuromonitoring signal indicates nerve injury and is subdivided into segmental type and global type nerve paralysis. This study aimed to determine the course of vocal cord function recovery

after definitive loss of signal (LOS) types. METHODS: This retrospective study included 1,442 patients (with 2,752 nerves at risk) who had thyroidectomies between January 2018 and December 2021. Preoperative and postoperative vocal cord functions were evaluated by laryngoscopic examination. RESULTS: LOS occurred in 168 of 1,442 (11.7%) patients and 171 of 2,748 (6.2%) nerves at risk during surgery. Of LOS nerves of benign tumors, 74.2% showed global type. In cancer cases, segmental paralysis was more common, accounting for 51.3% of LOS nerves. Of nerves with segmental LOS in cancer patients, 55.3% needed partial layer resection for RLN invasion. Intraoperative recovery was seen in 9 of 62 nerves (14.5%) with segmental LOS and 32 of 109 (29.4%) nerves with global type LOS. The vocal cord palsy rate on postoperative days (PODs) 2-3 was lower after global type nerve paralysis (63.6%) than after segmental loss (84.9%). At 6 months postoperatively, the rate of vocal cord paralysis in benign tumors was not significantly different between segmental type and global type (P=0.586). However, cancer patients with segmental LOS significantly more often had vocal cord dysfunction than those with global LOS at 6 months postoperatively (rate of nerve palsy: segmental 40.0% vs. global 3.4%) (P<0.001). CONCLUSIONS: The intraoperative recovery rate and early nerve recovery rate are significantly higher for patients with global LOS than for patients with segmental LOS. Cancer patients with segmental LOS significantly more often had vocal cord dysfunction than those with global LOS at 6 months postoperatively.

PubMed-ID: [37842531](#)

DOI: [10.21037/gs-23-149](#)

PMCID: PMC10570980

Reassessing surgical guidelines for papillary thyroid cancer impact on survival: Expanding indications for lobectomy.
Surgery, 174(3):542-8.

A. Stevens, J. Meier, A. Bhat, S. J. Knight, D. J. Vanness and C. Balentine. 2023.

BACKGROUND: Comparisons of lobectomy versus total thyroidectomy for papillary thyroid cancer have not addressed significant threats to valid inference from observational data. The purpose of this study was to compare survival after lobectomy versus total thyroidectomy for papillary thyroid cancer while addressing bias from unmeasured confounding. METHODS: This retrospective cohort study included 84,300 patients treated with lobectomy or total thyroidectomy for papillary thyroid cancer in the National Cancer Database from 2004 to 2017. The primary outcome was overall survival evaluated by flexible parametric survival models and inverse probability weighting on the propensity score. Bias from unobserved confounding was assessed using two-way deterministic sensitivity analysis and 2-stage least squares regression. RESULTS: The median age of treated patients was 48 years (interquartile range, 37-59), 78% were women, and 76% were white. We found no statistically significant differences in overall survival or 5- and 10-year survival between patients treated with lobectomy or total thyroidectomy. Additionally, we found no statistically significant difference in survival by subgroups, including tumor size (<4 cm or ≥4 cm), age (<65 or ≥65), or estimated risk of mortality. Sensitivity analyses suggested that an unmeasured confounder would need to have an extremely large effect to change the primary finding. CONCLUSION: This is the first study to compare lobectomy and total thyroidectomy outcomes while adjusting for and quantifying the potential effects of unmeasured confounding variables on observational data. The findings suggest that total thyroidectomy is unlikely to offer a survival advantage over lobectomy regardless of tumor size, patient age, or overall risk of death.

PubMed-ID: [37393154](#)

DOI: [10.1016/j.surg.2023.05.033](#)

PMCID: PMC10526679

Incidence and prognosis of contralateral vocal fold paralysis after hemithyroidectomy in previously unoperated patients.

BJS Open, 7(6)

S. Sinz, F. Grafen, W. Kolb, J. Rosenfeld and T. Clerici. 2023.

PubMed-ID: [37955871](#)

DOI: [10.1093/bjsopen/zrad126](#)

PMCID: PMC10642612

Cytological and Ultrasound Features of Thyroid Nodules Correlate With Histotypes and Variants of Thyroid Carcinoma.

J Clin Endocrinol Metab, 108(11):e1186-e92.

D. Sgro, A. Brancatella, G. Greco, L. Torregrossa, P. Piaggi, N. Viola, T. Rago, F. Basolo, R. Giannini, G. Materazzi, R. Elisei, F. Santini and F. Latrofa. 2023.

CONTEXT: Prognosis is excellent for papillary thyroid carcinoma (PTC), noninvasive follicular thyroid neoplasia with papillary-like nuclear features (NIFT-P), and follicular thyroid carcinoma (FTC) but is poor for poorly differentiated thyroid

carcinoma (PDTc) and anaplastic thyroid carcinoma (ATC). Among PTCs, the prognosis is more favorable for follicular (FV-PTC) and classic (CV-PTC) than for tall cell (TCV-PTC), and solid (SV-PTC) variants. OBJECTIVE: To associate histotypes and variants of thyroid carcinoma with ultrasound and cytological features. METHODS: Histology of 1018 benign tumors and 514 PTC (249 CV, 167 FV, 49 TC, 34 SV, and 15 other variants), 52 NIFT-P, 50 FTC, 11 PDTc, and 3 ATC was correlated with fine-needle aspiration biopsy categories (Italian classification: TIR1, TIR2, TIR3A, TIR3B, TIR4, and TIR5) and ultrasound features at the Endocrinology Unit, University Hospital of Pisa. In total, 1117 patients with thyroid nodule(s) who underwent thyroidectomy were included. RESULTS: Of PTC, 36.3% had indeterminate cytology (TIR3A or TIR3B), 56.6% were suspicious for malignancy or malignant (TIR4 or TIR5); 84.0% FTC and 69.3% NIFT-P were TIR3A or TIR3B; 72.5% FV-PTC and 73.6% SV-PTC were TIR3A or TIR3B; 79.9% CV-PTC and 95.9% TCV-PTC were TIR4 or TIR5. The association of a hypoechoic pattern, irregular margins, and no microcalcifications was more frequent in TCV-PTC than in CV-PTC ($P = .02$, positive predictive value = 38.9%; negative predictive value = 85.5%). CONCLUSION: At cytology, most FTC, NIFT-P, FV-PTC, and SV-PTC were indeterminate, most CV-PTC and TCV-PTC were suspicious for malignancy or malignant. Ultrasound can be helpful in ruling out TCV-PTC.

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DOI: [10.1210/clinem/dgad313](https://doi.org/10.1210/clinem/dgad313)

Is Multifocality a Predictor of Poor Outcome in Childhood and Adolescent Papillary Thyroid Carcinoma?

J Clin Endocrinol Metab, 108(12):3135-44.

D. W. Scholfield, J. Lopez, A. Eagan, Z. Antal, R. M. Tuttle, R. Ghossein, M. LaQuaglia, A. R. Shaha, J. P. Shah, R. J. Wong, S. G. Patel and I. Ganly. 2023.

CONTEXT: Total thyroidectomy in pediatric papillary thyroid carcinoma (PTC) is recommended in national guidelines because of the high incidence of multifocal disease (MFD). OBJECTIVE: To determine the incidence of MFD in childhood and adolescent vs adult PTC and whether MFD is a predictor for poorer outcomes in childhood and adolescent PTC. METHODS: We conducted an institutional review board-approved review of patients with PTC undergoing surgery (1986-2021) at Memorial Sloan Kettering Cancer Center. Clinical and pathological characteristics in patients with unifocal disease (UFD) and MFD were compared using Pearson's chi2 test. Survival outcomes were analyzed using the Kaplan-Meier method and log-rank test. Multivariate analysis assessed the impact of MFD on outcome. RESULTS: MFD was less common in childhood and adolescent patients with PTC (45%; 127/283) than in adults (54%; 3023/5564; $P = .002$). Childhood and adolescent patients with UFD and MFD had similar tumor stage and PTC subtype at presentation, with no significant difference in histopathologic features. Median follow-up was 68 months. There was no significant difference in 5-year recurrence-free probability and overall survival was 100% in both groups. There was no significant difference in 5-year contralateral lobe PTC-free probability between patients with UFD and MFD treated with lobectomy. Multivariate analysis showed MFD was not a predictor for recurrence. CONCLUSION: MFD was less common in childhood and adolescent patients with PTC than adults and was not a predictor of poor outcome on multivariate analysis, with excellent long-term outcomes in all patients with PTC. MFD does not appear to warrant completion thyroidectomy in childhood and adolescent patients selected for lobectomy.

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DOI: [10.1210/clinem/dgad369](https://doi.org/10.1210/clinem/dgad369)

PMCID: PMC10655537

Complications of Thyroid Cancer Surgery in Pediatric Patients at a Tertiary Cancer Center.

Ann Surg Oncol, 30(12):7781-8.

D. W. Scholfield, J. Lopez, N. D. Badillo, A. Eagan, H. Levyn, M. LaQuaglia, A. R. Shaha, J. P. Shah, R. J. Wong, S. G. Patel and I. Ganly. 2023.

BACKGROUND: The incidence of complications and risk factors for hypocalcemia after pediatric thyroid cancer surgery has not been clearly defined in the literature because most reports fail to distinguish between benign and malignant disease. The trend away from total thyroidectomy (TT) to thyroid lobectomy in low-risk disease means there is a need to clearly define the complication profile of malignant disease. METHODS: After institutional review board (IRB) approval, a retrospective chart review was undertaken at Memorial Sloan Kettering Cancer Center for pediatric patients undergoing surgery for well-differentiated thyroid cancer from 1986 to 2021. Clinicopathologic characteristics and complications were evaluated. Multivariable analysis was performed to identify factors independently associated with postoperative hypocalcemia. RESULTS: The study identified 307 pediatric patients with well-differentiated thyroid carcinoma (median follow-up period, 61 months). Of these patients, 69% underwent TT and 31% received a partial thyroidectomy. Among them, 40% had N0 disease, 28% had N1a disease, and 33% had N1b disease. Postoperatively, no patients experienced a neck hematoma, 1.6% had temporary unilateral vocal cord palsy (VCP), and 0.7% had permanent VCP due to recurrent

laryngeal nerve (RLN) invasion. Temporary and permanent hypocalcemia occurred in respectively 32.6 % and 5.2 % of the patients. Multivariable analysis identified central neck dissection (CND) (odds ratio [OR] 3.30; $p < 0.001$) and N1 disease (OR 2.51; $p = 0.036$) as independent risk factors for temporary hypocalcemia and N stage (OR 3.64; $p = 0.018$) as a risk factor for permanent hypocalcemia. CONCLUSION: Pediatric thyroid cancer surgery results in low complication rates despite nodal metastases. Vocal cord paralysis is rare unless disease is found to be invading the RLN intraoperatively. Both N stage and CND are independent risk factors for hypocalcemia, helping to identify high-risk patients.

PubMed-ID: [37574514](#)

DOI: [10.1245/s10434-023-14079-x](#)

PMCID: PMC11001250

Resection of Papillary Thyroid Carcinoma Involving a Functioning Recurrent Laryngeal Nerve: Pushing Boundaries to Preserve Nerve Function.

Ann Surg Oncol, 30(12):6960-2.

A. T. Saxton and R. P. Scheri. 2023.

PubMed-ID: [37713120](#)

DOI: [10.1245/s10434-023-14287-5](#)

Radioiodine versus no radioiodine outcomes in low-risk differentiated thyroid cancers: A propensity-score matched analysis.

Clin Endocrinol (Oxf), 99(5):483-91.

S. Satapathy, A. Tupalli, K. R. Chandekar, S. Ballal and C. Bal. 2023.

OBJECTIVE: The 2015 American Thyroid Association guidelines recommend against radioiodine (RAI) ablation for patients with low-risk papillary microcarcinoma. However, its role in other low-risk differentiated thyroid cancer (DTC) patients remains controversial. Here, we compare long-term outcomes with RAI versus no-RAI in a large cohort comprising all low-risk DTCs. METHODS: Patients with low-risk, histologically-proven DTC post-thyroidectomy, treated with RAI or kept on follow-up without RAI, between 1990 and 2019 were included. The main outcomes included recurrence rate and recurrence-free survival (RFS), and were validated by propensity-score matching analysis. RESULTS: Of the 2074 low-risk DTC patients (median age: 35 years), 1686 patients underwent RAI-ablation (RAI group), while 388 patients underwent no-RAI follow-up (NOI group). Over a median follow-up of 8 years (range: 3-29), the recurrence rates were similar between the RAI and NOI groups (2.0% vs. 3.3%, $p = .161$). The 5- and 10-year RFS probabilities were 99.2% and 97.4%, respectively in RAI group versus 98.4% and 96.2%, respectively, in NOI group ($p = .055$). Subgroup regression analyses showed that patients with age < 55 years ($p = .044$), male sex ($p = .015$), papillary histology ($p = .043$), pT3a tumours ($p = .049$) and postoperative thyroglobulin $> / = 5$ ng/mL ($p = .002$) had significantly better RFS with RAI compared to NOI follow-up. Propensity-score matching generated 776 matched pairs with no significantly different outcomes between the two groups. CONCLUSIONS: In low-risk DTC patients post-thyroidectomy, RAI ablation does not confer significant survival advantage over no-RAI follow-up. Further studies are required to demonstrate any long-term benefit with RAI, specifically in patients with tumour size > 4 cm and elevated postoperative thyroglobulin.

PubMed-ID: [37491776](#)

DOI: [10.1111/cen.14950](#)

Body Mass Index (BMI) Related Morbidity with Thyroid Surgery.

Laryngoscope, 133(10):2823-30.

F. Rind, S. Zhao, C. Haring, S. Y. Kang, A. Agrawal, E. Ozer, M. O. Old, R. L. Carrau and N. B. Seim. 2023.

OBJECTIVES: The increase in incidence of thyroid cancer correlates with strict increases in body mass index (BMI) and obesity in the United States. Thyroid hormone dysregulation has been shown to precipitate circulatory volume, peripheral resistance, cardiac rhythm, and even cardiac muscle health. Theoretically, thyroid surgery could precipitate injury to the cardiopulmonary system. METHODS: The American College of Surgery National Quality Improvement Program database was queried for thyroidectomy cases in the 2007-2020 Participant User files. Continuous and categorical associations between BMI and cardiopulmonary complications were investigated as reported in the database. RESULTS: The query resulted 186,095 cases of thyroidectomy procedures in which the mean age was 51.3 years and sample was 79.3% female. No correlation was evident in univariate and multivariate analyses between BMI and the incidence of postoperative stroke or myocardial infarction. The incidence of complications was extremely low. However, risk of deep venous thrombosis correlated with BMI in the categorical, univariate, and multivariate (OR 1.036, CI 1.014-1.057, $p < 0.01$) regression analysis. Additionally, increased BMI was associated with increased risk of pulmonary embolism (PE) (OR 1.050 (1.030, 1.069), $p < 0.01$), re-intubation (OR 1.012 (1.002, 1.023), $p = 0.02$), and prolonged intubation (OR 1.031 (1.017, 1.045), $p < 0.01$).

CONCLUSION: Despite the rarity of cardiopulmonary complications during thyroid surgery, patients with very high BMI carry a significant risk of deep venous thrombosis, PE, and prolonged intubation. LEVEL OF EVIDENCE: 3 Laryngoscope, 133:2823-2830, 2023.

PubMed-ID: [37265205](#)

DOI: [10.1002/lary.30789](#)

Biological variation in thyroid function tests in older adults and clinical implications.

Clin Endocrinol (Oxf), 99(6):598-605.

J. Riis, L. Westergaard, J. Karmisholt, S. L. Andersen and S. Andersen. 2023.

OBJECTIVE: Interpreting thyroid function tests can be challenging due to inherent variation, and the need for tests rises with age. While age-related changes in thyrotropin (TSH) levels are known, the biological variation in older adults remains unclear. DESIGN: We recruited nineteen 65-99-year-old (older adults) without thyroid disease for monthly blood sampling for 1 year. PATIENTS AND MEASUREMENTS: Serum was stored at -20C degrees, and TSH, total thyroxine (TT4) and total triiodothyronine (TT3) were analysed in random order in a single batch for each participant. Results were compared to test results from 15 euthyroid men aged 24-53 years (younger adults) collected previously using a similar methodology. RESULTS: Interindividual coefficients of variation in older/younger adults were 46.7%/44.0% for TSH, 12.7%/19.5% for TT4 and 14.6%/22.4% for TT3. Intraindividual coefficients of variation (CV(I)) were 19.0%/25.4% for TSH, 5.5%/10.8% for TT4 and 6.9%/13.2% for TT3. The index of individuality was below 0.6 for all hormones in all age groups. The number of samples required to determine the homeostatic set-point at 10% precision in older adults was 14-21 for TSH and 2 for TT4 and TT3. TT4 in older adults was the only parameter in any group with comparable CV(I) between individuals ($p = .22$). CONCLUSIONS: CV(I) for TT4 and TT3 was halved in older compared to younger adults with two tests of TT4 needed to describe the individual set-point. Similar CV(I) between older adults caused TT4 to provide a reliable estimate of thyroid function, and the added value of measuring thyroxine could improve clinical practice.

PubMed-ID: [37723656](#)

DOI: [10.1111/cen.14973](#)

The Impact of Diabetes on Morbidity and Mortality Following Thyroidectomy.

Laryngoscope, 133(12):3628-32.

R. V. Patel, A. Randhawa, K. S. Randhawa, O. M. Aftab, I. M. Khawaja, M. Hegazin, J. A. Eloy and C. H. Fang. 2023.

OBJECTIVES: To explore the association between diabetes and outcomes in thyroidectomy patients. METHODS: This retrospective cohort analysis used the 2015-2017 American College of Surgeons National Surgery Quality Improvement Program database. Current Procedural Terminology (CPT) codes were used to identify thyroidectomy cases (60210, 60212, 60220, 60225, 60240, 60252, 60254, 60260, 60270, and 60271). Demographics, comorbidities, and complication incidences were compared between diabetic and nondiabetic patients using Pearson's chi-square test/Fisher's exact test as appropriate. The independent effect of diabetes on outcomes was analyzed using binary logistic regression. RESULTS: A total of 47,776 (95.4%) nondiabetic and 2307 (4.6%) diabetic patients undergoing thyroidectomy were identified from 2015 to 2017. Chi-square analysis demonstrated that diabetic patients had higher incidences of obesity (55.2% vs. 33.2%; $p < 0.001$), dyspnea (12.7% vs. 4.8%; $p < 0.001$), poor functional status (1.9% vs. 0.4%; $p < 0.001$), ventilator dependence (0.6% vs. 0.1%; $p < 0.001$), chronic obstructive pulmonary disease (COPD; 6.8% vs. 2.2%; $p < 0.001$), congestive heart failure (1.1% vs. 0.3%; $p < 0.001$), acute renal failure (0.3% vs. 0.0%; $p < 0.001$), hypertension (79.2% vs. 32.4%; $p < 0.001$), dialysis (2.0% vs. 0.4%; $p < 0.001$), open wound (1.1% vs. 0.1%; $p < 0.001$), steroid use (5.3% vs. 2.3%; $p < 0.001$), bleeding disorders (3.6% vs. 0.9%; $p < 0.001$), preoperative blood transfusions (0.2% vs. 0.0%; $p = 0.001$), and systemic sepsis (1.0% vs. 0.3%; $p < 0.001$). Demographic characteristics were significantly different between the cohorts including gender ($p < 0.001$), age ($p < 0.001$), race ($p < 0.001$), and Hispanic ethnicity ($p = 0.033$). After adjusting for these factors, logistic regression analyses showed that diabetes was associated with acute renal failure (OR: 5.836; 95% CI: 1.060-32.134; $p = 0.043$), wound disruption (OR: 6.194; 95% CI: 1.752-21.900; $p = 0.005$), prolonged length of stay (OR: 1.430; 95% CI: 1.261-1.622; $p < 0.001$), unplanned readmission (OR: 1.380; 95% CI: 1.096-1.737; $p = 0.006$), superficial incisional surgical site infections (OR: 0.240; 95% CI: 0.058-0.995; $p = 0.049$), urinary tract infection occurrences (OR: 2.173; 95% CI: 1.186-3.980; $p = 0.012$), organ space surgical site infection occurrences (OR: 3.322; 95% CI: 1.016-10.864; $p = 0.047$), pneumonia occurrences (OR: 2.091; 95% CI: 1.125-3.884; $p = 0.020$), any medical complication (OR: 1.697; 95% CI: 1.246-2.313; $p = 0.001$), and any complication (OR: 1.495; 95% CI: 1.136-1.968; $p = 0.004$). CONCLUSION: Diabetes mellitus is a significant factor associated with increased odds of complications following thyroidectomy. LEVEL OF EVIDENCE: 3 Laryngoscope, 133:3628-3632, 2023.

PubMed-ID: [37470297](#)

DOI: [10.1002/lary.30902](#)

Surgical and Biochemical Outcomes in Nerve Monitored Reoperation Surgery for Recurrent Papillary Thyroid Carcinoma.

Otolaryngol Head Neck Surg, 169(5):1234-40.

K. R. Patel, B. Wang, A. H. Abdelhamid Ahmed, O. C. Okose, H. Ma, I. J. Behr, A. Y. Cheung, Y. Saito, D. Kamani, A. Silver Karcioglu, W. Liddy, H. Takami, M. Cunnane and G. W. Randolph. 2023.

OBJECTIVE: To study the surgical and biochemical outcomes in nerve-monitored reoperation or revision surgery for recurrent thyroid cancers. STUDY DESIGN: A single-center retrospective study. SETTING: Tertiary center. METHODS: We identified patients with recurrent papillary thyroid carcinoma (PTC) who underwent reoperation/revision surgery. Study outcomes were surgical complications frequency, recurrence, distant metastasis, and biological complete response (BCR) by comparing preoperative and postoperative thyroglobulin (Tg) levels. RESULTS: Out of 227 patients, 33.9% presented for ≥ 2 reoperation surgeries. Nineteen (8.4%) had permanent preoperative hypoparathyroidism while 22 patients (9.7%) had preoperative vocal cord paralysis (VCP). Following reoperation surgery, there were 12 cases (5.3%) of permanent hypocalcemia and no cases of unexpected postoperative VCP. BCR was achieved in 31 patients (35.2%) with complete Tg data. Mean preoperative Tg was 47.7 ng/mL and was 19.7 ng/mL postoperatively ($p = .003$). The cervical nodal recurrence rate after final surgery was 7.0% ($n = 16$). CONCLUSION: Reoperation surgery for recurrent PTC may help achieve biochemical remission regardless of age or the number of prior surgeries.

PubMed-ID: [37245079](#)

DOI: [10.1002/ohn.389](#)

Letter to Editor in Response to Article Entitled "Selection Criteria for Completion Thyroidectomy in Follicular Thyroid Carcinoma Using Primary Tumor Size and TERT Promotor Mutational Status".

Ann Surg Oncol, 30(13):8546-7.

H. Park, T. Y. Kim, T. H. Kim and J. H. Kim. 2023.

PubMed-ID: [37789109](#)

DOI: [10.1245/s10434-023-14357-8](#)

Contralateral Low-to-Intermediate Suspicion Nodule Is Not a Contraindication for Lobectomy in Patients with Papillary Thyroid Carcinoma.

Thyroid, 33(11):1339-48.

S. J. Pak, D. Kwon, B. C. Kim, J. W. Cho, W. W. Kim, Y. M. Lee, T. Y. Sung, J. H. Baek, W. G. Kim, W. B. Kim and K. W. Chung. 2023.

Background: The optimal extent of surgery for unilateral papillary thyroid carcinoma (PTC) with contralateral nodules remains unclear. This study evaluated the long-term outcomes in a large cohort of patients with unilateral PTC and contralateral low-to-intermediate suspicious nodules who underwent lobectomy. Methods: This retrospective cohort study included patients with unilateral PTC who underwent lobectomy between January 2016 and December 2017 at Asan Medical Center in Korea. Patients were divided into two groups, those with and without contralateral nodules at the time of lobectomy: the Present group and the Absent group. All contralateral nodules observed at the time of surgery and during follow-up were evaluated. Results: The study cohort consisted of 1761 patients (1879 nodules), including 700 (39.8%) with and 1061 (60.2%) without contralateral nodules. The median size of the contralateral nodules was 0.5 cm. After a median follow-up of 59 months, the median growth of the contralateral nodules in the Present group was 0.1 cm (range, -3.4 to 4.7 cm). Of the contralateral nodules present at the time of lobectomy, 54.7% remained unchanged, decreased in size, or disappeared; whereas 14.8% increased ≥ 0.3 cm. Of the 700 patients with contralateral nodules, 20 (2.9%) were diagnosed with contralateral PTC. The 5-year contralateral PTC disease-free survival rates in patients with and without contralateral nodules were 98.2% and 99.3% ($p = 0.003$), respectively, whereas the 5-year recurrence-free survival rates did not differ significantly in these two groups. Of the 39 patients who underwent completion thyroidectomy, 2 (5.1%) experienced permanent hypocalcemia. Conclusions: Lobectomy may be a safe and feasible initial treatment option for patients with unilateral low-risk PTC and contralateral low-to-intermediate suspicious nodules.

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DOI: [10.1089/thy.2023.0270](#)

The utility of parathyroid autofluorescence as an adjunct in thyroid and parathyroid surgery 2023.

Head Neck, 45(12):3157-67.

P. Pace-Asciak, J. Russell, C. Solorzano, E. Berber, M. Singer, A. R. Shaha, A. Khafif, P. Angelos, I. Nixon and R. P. Tufano. 2023.

Thyroid and parathyroid surgery requires careful dissection around the vascular pedicle of the parathyroid glands to avoid excessive manipulation of the tissues. If the blood supply to the parathyroid glands is disrupted, or the glands are inadvertently removed, temporary and/or permanent hypocalcemia can occur, requiring post-operative exogenous calcium and vitamin D analogues to maintain stable levels. This can have a significant impact on the quality of life of patients, particularly if it results in permanent hypocalcemia. For over a decade, parathyroid tissue has been noted to have unique intrinsic properties known as "fluorophores," which fluoresce when excited by an external light source. As a result, parathyroid autofluorescence has emerged as an intra-operative technique to help with identification of parathyroid glands and to supplement direct visualization during thyroidectomy and parathyroidectomy. Due to the growing body of literature surrounding Near Infrared Autofluorescence (NIRAF), we sought to review the value of using autofluorescence technology for parathyroid detection during thyroid and parathyroid surgery. A literature review of parathyroid autofluorescence was performed using PubMed. Based on the reviewed literature and expert surgeons' opinions who have used this technology, recommendations were made. We discuss the current available technologies (image vs. probe approach) as well as their limitations. We also capture the opinions and recommendations of international high-volume endocrine surgeons and whether this technology is of value as an intraoperative adjunct. The utility and value of this technology seems promising and needs to be further defined in different scenarios involving surgeon experience and different patient populations and conditions.

PubMed-ID: [37807364](#)

DOI: [10.1002/hed.27538](#)

Magic Pen?-An Innovative Adjunct for Intraoperative Identification of Parathyroid Glands.

JAMA Surg, 158(10):1059-60.

M. B. Mulder and Q. Y. Duh. 2023.

PubMed-ID: [37531121](#)

DOI: [10.1001/jamasurg.2023.3257](#)

Evolving variation in the extent of surgery for low-risk papillary thyroid cancer in the United States.

Surgery, 174(4):828-35.

K. B. Montgomery, J. M. Fazendin and K. K. Broman. 2023.

BACKGROUND: The continued debate over total thyroidectomy versus lobectomy and declining favor for prophylactic central neck dissection for patients with clinically node-negative papillary thyroid cancer ≤ 4 cm is ongoing after the 2015 guideline updates from the American Thyroid Association. This study aimed to evaluate contemporary trends in the extent of surgery in this low-risk cohort. **METHODS:** Retrospective data from the National Cancer Database were used to identify adult patients with clinically node-negative papillary thyroid cancer ≤ 4 cm who underwent resection from 2012 to 2020. The primary outcome was the extent of surgery (lobectomy or total thyroidectomy, with or without prophylactic central neck dissection). Multivariable regression was performed to identify characteristics associated with variation in the extent of surgery. **RESULTS:** Of 83,464 included patients, 79.3% were female patients with a median age of 51 years. The majority underwent total thyroidectomy either with prophylactic central neck dissection (39.1%) or without (37.5%) versus lobectomy with prophylactic central neck dissection (7.2%) or without (16.2%). Lobectomy rates increased from 18.3% in 2012 to 29.9% in 2020. Prophylactic central neck dissection rates also increased (42.9% to 52.1%). Patients who were male sex, Asian American, had smaller tumors or were treated at community cancer programs had a decreased likelihood of total thyroidectomy. Patients who were older, male sex, Black race, with smaller tumors, or were treated at community cancer programs or mid- or low-volume facilities had decreased likelihood of prophylactic central neck dissection. **CONCLUSION:** Proportional use rates of operative approaches for low-risk, clinically node-negative papillary thyroid cancer have changed in recent years after the American Thyroid Association guideline changes, including increasing overall rates of lobectomy as well as prophylactic central neck dissection, with differences noted based on patient- and facility-level factors.

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DOI: [10.1016/j.surg.2023.07.001](#)

PMCID: PMC10529036

Improved Adherence to ATA Medullary Thyroid Cancer Treatment Guidelines.

Ann Surg Oncol, 30(12):7165-71.

J. L. McMullin, J. Sharma, T. Gillespie, S. G. Patel, C. J. Weber and N. D. Saunders. 2023.

BACKGROUND: The 2009 American Thyroid Association (ATA) guidelines for medullary thyroid cancer (MTC) were created to unify national practice patterns. Our aims were to (1) evaluate national adherence to ATA guidelines before and after 2009, (2) identify factors that are associated with concordance with guidelines, and (3) evaluate whether there is an association between survival and concordant treatment. **PATIENTS AND METHODS:** Patients with MTC were identified from the 2009 to 2015 National Cancer Database. Adherence to ATA recommendations regarding extent of surgery (R61-R66) was analyzed. Logistic regression was used to determine predictors of discordance and propensity score matching was used to compare concordant treatment rates between time periods. Kaplan-Meier survival analysis was used to determine association between survival and concordant treatment. **RESULTS:** There were 3421 patients with MTC, and of these 3087 had M0 disease and 334 had M1 disease. We found that 72% of M0 cases adhered to R61-66, and 68% of M0 cases without advanced local disease were adherent to R61-63. Following propensity score matching, the adherence rate was 67% before 2009 and 74% after. Patient factors associated with discordant treatment were female gender, older age, treatment at a nonacademic facility, and living within 50 miles of the treatment facility. Adherence to guidelines was associated with improved overall survival (OS) ($p < 0.01$). **CONCLUSIONS:** Treatment of MTC was discordant from guidelines in 26% of cases from 2009 to 2015 compared with 33% prior to 2009 in a propensity matched analysis, and was most often in cases with localized, noninvasive disease. Improved adherence to guidelines may improve overall survival.

PubMed-ID: [36367629](#)

DOI: [10.1245/s10434-022-12734-3](#)

The Changing Face of Multiple Endocrine Neoplasia 2A: From Symptom-Based to Preventative Medicine.

J Clin Endocrinol Metab, 108(9):e734-e42.

A. Machens, K. Lorenz, T. Brandenburg, D. Fuhrer-Sakel, F. Weber and H. Dralle. 2023.

CONTEXT: Early genetic association studies yielded too high risk estimates for multiple endocrine neoplasia (MEN2A), suggesting a need for extended surgery. **OBJECTIVE:** The objective was to delineate temporal changes in MEN2A presentation by birth cohort analyses. **METHODS:** Birth cohort analyses (10-year increments; ≤ 1950 to 2011-2020) of carriers of rearranged during transfection (RET) mutations who underwent surgery for MEN2A. **RESULTS:** Included in this study were 604 carriers (155 index, 445 nonindex, 4 additional patients), with 237 carriers harboring high-risk mutations, 165 carriers moderate-high risk mutations, and 202 carriers low-moderate risk mutations. With increasing recency of birth cohorts, there was a continual decline in index patients from 41-74% to 0% ($P < .001$) and of medullary thyroid cancer (MTC) from 96-100% to 0-33% ($P < .001$). Node metastases diminished from 62-70% to 0% ($P \leq .001$; high and low-moderate risk mutations), whereas biochemical cure after thyroidectomy surged from 17-33% to 100% ($P \leq .019$; high and low-moderate mutations). Surgical interventions for MEN2A-related tumors were performed increasingly earlier, causing median carrier age to fall: from 51-63 to 3-5 years at thyroidectomy ($P < .001$); from 46-51 to 24-25 years at first adrenalectomy ($P \leq .013$; high and moderate-high risk mutations); and from 43.5-66 to 16.5-32 years at parathyroidectomy. MTC diameters were more effectively decreased from 14-32 to 1-4 mm ($P \leq .002$) than pheochromocytoma diameters (nonsignificant). **CONCLUSION:** These insights into MEN2A presentation, adjusted by birth year, illustrate the shift from reactive to preventative medicine, enabling less extensive risk-reducing surgery.

PubMed-ID: [36930525](#)

DOI: [10.1210/clinem/dgad156](#)

Lymph node ratio as a tool to stratify patients with N1b papillary thyroid cancer.

Langenbecks Arch Surg, 408(1):315.

Z. Luo, H. Hei, J. Qin, C. Zheng, W. Gong and B. Zhou. 2023.

BACKGROUND: The prognostic significance of lymph node ratio (LNR) in N1b papillary thyroid cancer is unclear. Therefore, the impact of LNR on disease-specific mortality (DSM) and overall survival (OS) in patients with N1b papillary thyroid cancer (PTC) needs to be defined. **METHODS:** We used the Surveillance, Epidemiology, and End Results (SEER) database of patients who had undergone thyroidectomy and lymph node dissection. Factors associated with DSM and OS were analyzed and identified using univariate and multivariate Cox proportional risk models. X-tile software was used to find the best cutoff value of LNR. Kaplan-Meier estimates for DSM were plotted for LNR and were compared with the log-rank test. The ROC curve evaluated the validity of the model. **RESULTS:** A total of 3223 patients with N1b PTC were identified in the SEER database between 1975 and 2019. The best cutoff value for LNR was 0.6. The multivariate Cox proportional risk model showed that age, race, T3/T4 classification, distant metastasis, extent of surgery, number of metastatic lymph nodes, and $LNR > 0.6$ were independent risk factors for DSM (all $p < 0.05$). Age, sex, T4 classification, distant metastasis,

extent of surgery, and LNR > 0.6 were independent risk factors for OS (all $p < 0.05$). The Kaplan-Meier method plotted a cumulative risk curve and showed that patients with LNR > 0.6 had a significantly higher risk of DSM than patients with LNR ≤ 0.6 ($p = 0.002$). CONCLUSION: LNR was a powerful predictor of DSM and OS in N1b PTC patients. LNR could be a useful tool for the stratification of PTC patients with lateral neck metastases.

PubMed-ID: [37584830](#)

DOI: [10.1007/s00423-023-03033-w](#)

The Relationship Between Perineural Invasion and Extranodal Extension in Papillary Thyroid Cancer.

Ann Surg Oncol, 30(12):7187-8.

X. Luo, K. Wu, X. Geng, T. Yang and X. Meng. 2023.

PubMed-ID: [37552346](#)

DOI: [10.1245/s10434-023-14035-9](#)

European experience with the Afirma Gene Expression Classifier for indeterminate thyroid nodules: A clinical utility study in the Netherlands.

Head Neck, 45(9):2227-36.

I. Loncar, E. F. S. van Velsen, E. T. Massolt, F. J. van Kemenade, A. C. H. van Engen-van Grunsven, B. M. van Hemel, F. H. van Nederveen, R. Netea-Maier, T. P. Links, R. P. Peeters and T. M. van Ginhoven. 2023.

BACKGROUND: The Gene Expression Classifier (GEC) and Genomic Sequencing Classifier (GSC) were developed to improve risk stratification of indeterminate nodules. Our aim was to assess the clinical utility in a European population with restrictive diagnostic workup. METHODS: Clinical utility of the GEC was assessed in a prospective multicenter cohort of 68 indeterminate nodules. Diagnostic surgical rates for Bethesda III and IV nodules were compared to a historical cohort of 171 indeterminate nodules. Samples were post hoc tested with the GSC. RESULTS: The GEC classified 26% as benign. Surgical rates between the prospective and historical cohort did not differ (72.1% vs. 76.6%). The GSC classified 59% as benign, but misclassified six malignant lesions as benign. CONCLUSION: Implementation of GEC in management of indeterminate nodules in a European country with restrictive diagnostic workup is currently not supported, especially in oncocytic nodules. Prospective studies with the GSC in European countries are needed to determine the clinical utility.

PubMed-ID: [37490544](#)

DOI: [10.1002/hed.27472](#)

A Neural Integrity Monitor Electromyography Endotracheal Tube Causes More Severe Postoperative Sore Throat Than a Standard Endotracheal Tube in Adults: A Prospective Cohort Study.

World J Surg, 47(10):2409-15.

X. Liu, Z. Cheng, X. Chen, Z. Rao and A. Wang. 2023.

BACKGROUND: This study aimed at figuring out the different effects of a neural integrity monitor electromyography endotracheal tube (NIM-EMG-ETT) and a standard endotracheal tube (ETT) on postoperative sore throat (POST). METHODS: This prospective cohort study enrolled 143 patients scheduled to undergo general anesthesia with endotracheal intubation. Patients were allocated into three groups: Group A, non-thyroid surgery with a standard ETT; Group B, thyroid surgery with a standard ETT; Group C, thyroid surgery with a NIM-EMG-ETT. The incidence, the severity and visual analog scale (VAS) of POST were recorded. The incidence and the severity of POST were tested by chi(2) test or Fisher's exact test. And VAS of POST was tested by Kruskal-Wallis test. RESULTS: The incidences of POST in Group B and Group C were significantly higher than that of Group A at all the time points after extubation ($P < 0.001$). The incidences of POST in Group C was significantly higher than that in Group B at 8 h, 24 h and 48 h after extubation (89.4% vs. 68.8%, $P = 0.014$, relative risk (RR) 1.30, 95% confidence interval (CI) 1.05-1.61; 89.4% vs. 58.3%, $P = 0.001$, RR 1.53, 95% CI 1.18-1.98; 76.6% vs. 45.8%, $P = 0.002$, RR 1.67, 95% CI 1.18-2.36). Moreover, there was a significant higher VAS of POST and more serious POST with Group C than with Group B. CONCLUSIONS: A NIM-EMG-ETT may induce higher incidence of POST and more serious POST than a standard ETT. TRAIL REGISTRATION: Chinese Clinical Trail Registry (<http://www.chictr.org.cn/index.aspx>, ChiCTR2200058896, 2022-4-18).

PubMed-ID: [37555971](#)

DOI: [10.1007/s00268-023-07092-4](#)

Age-dependent changes in the prognostic advantage of papillary thyroid cancer in women: A SEER-based study.

Clin Endocrinol (Oxf), 99(3):342-9.

Q. Liu, B. Ma, M. Song, W. Sun and H. Zhang. 2023.

BACKGROUND: Papillary thyroid cancer (PTC) is more prevalent in women, and women show a better prognosis than men;

however, the factors contributing to this prognostic difference are confounding. Therefore, we aimed to investigate the effect of the interaction between sex and age on the prognosis of PTC. METHODS: A total of 108,459 patients with PTC were retrospectively analysed, and Cox-regression models were used to assess differences in disease specific survival (DSS) by sex, with inverse probability of treatment weighting (IPTW) to control for between-group differences in prognosis by sex due to age change. Restricted cubic splines were used to analyse prognostic differences between sexes for papillary thyroid microcarcinoma (PTMC) and PTC. Multiple mediation analyses were used to assess the direct or indirect effect of sex on DSS. RESULTS: The DSS was higher for women than men (98.6% vs. 95.4%, $\chi^2(2) = 458.57$, $p < .001$). After IPTW adjustment, the DSS of women was better than that of men (HR = 0.67, 0.60-0.76). In the subgroup analysis, women had an advantage in DSS across most age intervals (crude HR = 0.166 [0.082-0.337], $p < .001$, IPTW-adjusted HR = 0.331 [0.161-0.681], $p < .001$). The difference between the two gradually narrowed with increasing age, and the prognosis of women was better than that of men in PTMC, while this advantage was not obvious in PTC. CONCLUSIONS: The overall PTC prognosis of women is better than that of men, but the prognostic advantage of women diminishes with age and tumour growth. These differences in prognosis may be due to some indirect factors caused by different sexes.

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DOI: [10.1111/cen.14896](#)

Active surveillance versus immediate surgery: A comparison of clinical and quality of life outcomes among patients with highly suspicious thyroid nodules 1 cm or smaller in China.

Eur J Surg Oncol, 49(9):106917.

C. Liu, H. Zhao, Y. Xia, Y. Cao, L. Zhang, Y. Zhao, L. Gao, R. Liu, Y. Liu, H. Liu, Z. Meng, S. Liu, Y. Lu and X. Li. 2023.

INTRODUCTION: Active surveillance (AS) is considered an alternative to immediate surgery (IS) for low-risk papillary thyroid microcarcinoma (PTMC) patients. However, it is difficult to decide between AS and IS due to limited evidence regarding risks and benefits for patients in China. METHODS: This study prospectively enrolled 485 patients with highly suspicious thyroid nodules ≤ 1 cm who chose AS and 331 patients who underwent IS during the same period. The oncological outcomes, adverse events and quality of life, were compared between the two groups. RESULTS: The oncological outcomes of the IS and AS groups were similarly excellent. The IS group had significantly higher rates of temporary vocal cord paralysis (VCP) and temporary hypoparathyroidism than the AS group (2.7% vs. 0.2%, $p = 0.002$; 13.6% vs. 1.9%, $p < 0.001$, respectively). The IS group had significantly more patients on hormone replacement therapy (98.4% vs. 10.9%, $p < 0.001$) and a significantly higher incidence of neck scarring (94.3% vs. 9.1%, $p < 0.001$) compared to the AS group. In the early stages, the quality of life questionnaire showed significant differences with respect to three items: voice, throat/mouth, and surgical scarring, with more complaints in the IS group. However, one year or more after surgery, the main complaint was surgical scarring. CONCLUSION: In China, AS can achieve similar short-term therapeutic effects as IS. As this approach can reduce the occurrence of unfavorable events, achieve better quality of life, it is a feasible option for patients with highly suspicious thyroid nodules.

PubMed-ID: [37137793](#)

DOI: [10.1016/j.ejso.2023.04.016](#)

Criteria to Evaluate Tumor Enlargement During the Active Surveillance of High-Risk Thyroid Nodules: Which is Better, Diameter or Volume?

World J Surg, 47(12):3214-21.

C. Liu, H. Zhao, Y. Lu, Y. Xia, Y. Cao, L. Zhang, Y. Zhao, L. Gao, R. Liu, Y. Liu, H. Liu, Z. Meng and X. Li. 2023.

INTRODUCTION: Tumor enlargement is the most common parameter identifying disease progression during active surveillance, but the value and significance of the changes in tumor diameter and volume in the evaluation of tumor growth have not been compared. METHODS: This cohort study included 468 patients with high-risk thyroid nodule, in whom nodule size change was monitored using ultrasound, to compare the changes in tumor diameter and volume in assessing tumor growth. RESULTS: A total of 569 high-risk thyroid nodules were found in the 468 patients. A total of 14 nodules (2.5%) showed a diameter increase ≥ 3 mm. The number of nodules with a peak volume change exceeding 50% and 100% was 185 (32.5%) and 86 (15.1%), respectively. Among the 555 stable nodules, the number of nodules with volume fluctuations exceeding 50% and 100% was 171 (30.8%) and 72 (13.0%), respectively. Among 212 stable nodules at the baseline and in the first three follow-up, the percentage of peak volume fluctuations exceeding 50% (48.5% vs. 28.5%, $p = 0.004$) and 100% (26.5% vs. 8.3%, $p < 0.001$) in the nodules with the sum of three diameters (SOTDs) ≤ 1 cm was significantly higher than that of nodules with SOTDs > 1 cm. A statistically significant difference was also found in the range distribution of SOTDs ≤ 1 cm and SOTDs > 1 cm ($p = 0.007$). CONCLUSIONS: Volume is not an appropriate method for determining tumor growth. Tumor diameter measurement alone serves as a better surrogate for disease progression in sonographically high-risk thyroid nodules than volume.

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DOI: [10.1007/s00268-023-07185-0](#)

Radiofrequency Ablation of Unifocal Papillary Thyroid Microcarcinoma With BRAF V600E Mutation.

J Clin Endocrinol Metab, 108(11):e1298-e305.

Y. Lin, Z. R. Wu, Y. P. Shi, M. Ding, X. Y. Tang, Y. He, B. Zhai and P. Li. 2023.

CONTEXT: To date there is no study on the feasibility of radiofrequency ablation (RFA) for papillary thyroid microcarcinomas (PTMCs) with BRAF V600E mutation. OBJECTIVE: This study was designed to evaluate the efficiency, safety, and prognosis of ultrasound (US)-guided percutaneous RFA for unifocal PTMCs with BRAF V600E mutation. MATERIALS AND METHODS: Sixty patients with 60 unifocal BRAF V600E mutation-positive PTMCs who received US-guided RFA between January 2020 and December 2021 were retrospectively analyzed. The mean maximum PTMC tumor diameter was 5.8 +/- 1.7 mm (range, 2.5-10.0 mm). All PTMCs were pathologically confirmed by fine needle aspiration or core needle biopsy, and BRAF V600E mutation was confirmed to be positive by real-time fluorescent quantitative polymerase chain reaction. Contrast-enhanced ultrasound (CEUS) was performed immediately after RFA to evaluate whether PTMCs were extendedly ablated. Ultrasound was performed 1, 3, 6, and 12 months after RFA and every 6 months thereafter to evaluate the changes in the ablation zone, local recurrence, and cervical lymph node metastasis (LNM). The complications were recorded and evaluated. RESULTS: Extended ablation was achieved in all enrolled patients. The ablation zone sizes increased immediately after RFA compared with those of tumors before treatment. One month later, the ablation zone sizes were smaller than immediately after RFA. At the last follow-up assessment, 42 nodules (70.0%) completely disappeared and the ablation zones of 18 nodules (30.0%) showed fissure-like changes. No local recurrence or cervical LNM was detected. Voice change (1.7%) was the only major complication. CONCLUSION: RFA is effective and safe in treating unifocal PTMCs with BRAF V600E mutation, especially when surgery is not feasible or refused by patients who are unwilling to continue active surveillance.

PubMed-ID: [37220176](#)

DOI: [10.1210/clinem/dgad269](#)

Shaving Papillary Thyroid Carcinoma Involving Functioning Recurrent Laryngeal Nerve: Safety of Incomplete Tumor Resection and Nerve Sparing.

Ann Surg Oncol, 30(12):7157-64.

H. S. Lee, Y. Kim, S. B. Kim, D. G. Choi, H. K. Cha, J. S. Park, S. Jun and K. D. Lee. 2023.

BACKGROUND: Whether to sacrifice or spare the recurrent laryngeal nerve (RLN) when papillary thyroid carcinoma (PTC) involves a functioning RLN remains controversial. Oncological outcomes after shaving PTC with gross remnant on the RLN have been rarely reported. The objective of this study was to evaluate the oncological outcomes of patients who underwent shaving of a PTC from the RLN, leaving a gross residual tumor with the intent of vocal function preservation. METHODS: A retrospective, cohort study was conducted in 47 patients who were determined to have PTC invasion of the RLN via intraoperative inspection and underwent tumor shaving with macroscopic remnant (R2 resection) less than 1 cm in length and 4 mm in thickness. Median follow-up period was 93 (range, 60-215) months. The primary endpoint was the recurrence-free survival and the progression-free survival. Secondary endpoints were biochemical outcomes (serum thyroglobulin) and vocal cord function. RESULTS: Of the 47 patients, five (10.6%) patients showed recurrence (central neck, 3; lateral neck, 2) without death or distant metastasis. The RLN was resected along with the tumor in one (2.1%) patient who presented with progression of the residual tumor. Postoperative temporary vocal cord paralysis occurred in six (12.8%) patients without permanent cases. The final nonstimulated serum thyroglobulin was 0.7 +/- 1.8 ng/ml. CONCLUSIONS: Shaving a tumor from a RLN with gross residual disease may be considered an alternative strategy to preserve vocal function when complete tumor resection with nerve preservation is impossible in patients with PTC invading a functioning RLN.

PubMed-ID: [37605083](#)

DOI: [10.1245/s10434-023-14142-7](#)

ASO Author Reflections: Is it Safe to Shave Papillary Thyroid Carcinoma Involving a Functioning Recurrent Laryngeal Nerve with Incomplete Tumor Resection?

Ann Surg Oncol, 30(12):7181-2.

H. S. Lee, Y. Kim, S. Jun and K. D. Lee. 2023.

PubMed-ID: [37587358](#)

DOI: [10.1245/s10434-023-14149-0](#)

MERAIODE: A Phase II Redifferentiation Trial with Trametinib and (131)I in Metastatic Radioactive Iodine Refractory RAS Mutated Differentiated Thyroid Cancer.

Thyroid, 33(9):1124-9.

S. Leboulleux, D. Benisvy, D. Taieb, M. Attard, C. Bournaud, M. Terroir-Cassou-Mounat, L. Lacroix, N. Anizan, A. Schiazza, M. E. Garcia, A. A. Ghuzlan, L. Lamartina, M. Schlumberger, Y. Godbert and I. Borget. 2023.

PubMed-ID: [37350119](#)

DOI: [10.1089/thy.2023.0240](#)

Low serum iPTH at the end of surgery is the earliest predictor of postoperative hypocalcemia after total thyroidectomy.

Langenbecks Arch Surg, 408(1):450.

A. Lalos, A. Wilhelm, K. Linke, S. Taha-Mehlitz, B. Muller, A. Posabella and B. Kern. 2023.

BACKGROUND: The most frequent complication of total thyroidectomy remains hypocalcemia due to low postoperative levels of serum intact parathyroid hormone (iPTH). The purpose of this study was to investigate the role of decreased iPTH at the end of surgery in predicting hypocalcemia. In addition, we examined the percentage decrease of iPTH as potential indicator of hypocalcemia. METHODS: We retrospectively collected the data of patients who underwent total thyroidectomy for benign and malignant diseases at our institution between 2010 and 2022. The iPTH level was measured before and at the end of surgery, and serum calcium levels on the first postoperative day. Demographic, clinical, and biochemical characteristics of patients with low iPTH were compared with patients with normal iPTH levels using ANOVA for continuous variables and chi2-tests for categorical variables. Multivariable logistic regression analysis evaluated the association of iPTH at the end of surgery and the relative reduction of iPTH with postoperative hypocalcemia. RESULTS: The mean age of the 607 patients in this study was 55.6 years, and the female-to-male ratio was 5:1. Goiter was the most common indication for surgery (N = 382, 62.9%), followed by Graves' disease (N = 135, 22.2%). The mean preoperative iPTH was 49.0 pg/ml, while the mean postoperative iPTH was 29.3 pg/ml. A total of 197 patients (32.5%) had an iPTH level below normal, 77 patients (39%), had iPTH levels of 10-15.0 pg/ml and 120 patients (61%) of < 10.0 pg/ml at the end of surgery. Among all patients, 124 (20.4%) developed hypocalcemia on the first postoperative day. The mean percentage of decrease of iPTH was highest among patients with iPTH < 10 pg/ml (76.9%, p < 0.01); this group of patients had also the highest rate of postoperative hypocalcemia on day one (45.0% vs. 26.0% vs 12.2%, p < 0.01). CONCLUSIONS: Measurement of iPTH at the end of total thyroidectomy predicts patients who are at risk for postoperative hypocalcemia. The combination of low serum iPTH with a decrease in iPTH level of >= 50% may improve prediction of hypocalcemia compared to iPTH levels alone allowing for early calcium substitution in these patients at high risk of developing postoperative hypocalcemia.

PubMed-ID: [38030913](#)

DOI: [10.1007/s00423-023-03194-8](#)

PMCID: PMC10687095

Bethesda III and IV Thyroid Nodules Managed Nonoperatively After Molecular Testing With Afirma GSC or Thyroseq v3.

J Clin Endocrinol Metab, 108(9):e698-e703.

N. E. Kim, R. S. Raghunathan, E. G. Hughes, X. R. Longstaff, C. H. Tseng, S. Li, D. S. Cheung, Y. A. Gofnung, P. Famini, J. X. Wu, M. W. Yeh and M. J. Livhits. 2023.

CONTEXT: Molecular testing has improved risk stratification and increased nonoperative management for patients with indeterminate thyroid nodules, but data on the long-term outcomes of current molecular tests Afirma Gene Sequencing Classifier (GSC) and Thyroseq v3 are limited. OBJECTIVE: To determine the rate of delayed operation and the false negative rate of the Afirma GSC and Thyroseq v3 in Bethesda III and IV thyroid nodules. METHODS: Prospective follow-up of a single center, randomized, clinical trial comparing the performance of Afirma GSC and Thyroseq v3 in the diagnosis of indeterminate thyroid nodules at the University of California, Los Angeles (UCLA). Consecutive participants who underwent thyroid biopsy in the UCLA health system with Bethesda III and IV cytology from August 2017 to November 2019. The main outcome measure was false negative rate of molecular testing. RESULTS: Of 176 indeterminate nodules with negative or benign molecular test results, 14 (8%) nodules underwent immediate resection, with no malignancies found on surgical pathology. Nonoperative management with active surveillance was pursued for 162 (92%) nodules with benign or negative test results. The median surveillance was 34 months (range 12-60 months), and 44 patients were lost to follow-up. Of 15 nodules resected during surveillance, 1 malignancy was found (overall false negative rate of 0.6%). This was a 2.7 cm minimally invasive Hurthle cell carcinoma that initially tested negative with Thyroseq v3 and underwent delayed resection due to sonographic growth during surveillance. CONCLUSIONS: The majority of Bethesda III/IV thyroid nodules with negative or benign molecular test results are stable over 3 years of follow-up. These findings support the high sensitivity of current molecular tests and their role in ruling out malignancy in indeterminate thyroid nodules.

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DOI: [10.1210/clinem/dgad181](#)
PMCID: PMC10438873

Natural History and Predictive Factors of Outcome in Medullary Thyroid Microcarcinoma.

J Clin Endocrinol Metab, 108(10):2626-34.

N. Kesby, R. Mechera, T. Fuchs, A. Papachristos, M. Gild, V. Tsang, R. Clifton-Bligh, B. Robinson, M. Sywak, S. Sidhu, A. Chou, A. J. Gill and A. Glover. 2023.

CONTEXT: Management of sporadic medullary thyroid microcarcinoma smaller than 1 cm (micro-MTC) is controversial because of conflicting reports of prognosis. As these cancers are often diagnosed incidentally, they pose a management challenge when deciding on further treatment and follow-up. OBJECTIVE: We report the outcomes of surgically managed sporadic micro-MTC in a specialist endocrine surgery and endocrinology unit and identify associations for recurrence and disease-specific survival in this population. METHODS: Micro-MTCs were identified from a prospectively maintained surgery database, and slides were reviewed to determine pathological grade. The primary end points were recurrence, time to recurrence and disease-specific survival. Prognostic factors assessed included size, grade, lymph node metastasis (LNM), and postoperative calcitonin. RESULTS: From 1995 to 2022, 64 patients were diagnosed with micro-MTC with 22 excluded because of hereditary disease. The included patients had a median age of 60 years, tumor size of 4 mm, and 28 (67%) were female. The diagnosis was incidental in 36 (86%) with 4 (10%) being high grade, 5 (12%) having LNM and 9 (21%) having elevated postoperative calcitonin. Over a 6.6-year median follow-up, 5 (12%) developed recurrence and 3 (7%) died of MTC. High grade and LNM were associated with 10-year survival estimates of 75% vs 100% for low grade and no LNM (hazard ratio = 831; $P < .01$). High grade, LNM, and increased calcitonin were associated with recurrence ($P < .01$). Tumor size and type of surgery were not statistically significantly associated with recurrence or survival. No patients with low grade micro-MTC and normal postoperative calcitonin developed recurrence. CONCLUSION: Most sporadic micro-MTCs are detected incidentally and are generally associated with good outcomes. Size is not significantly associated with outcomes. Using grade, LNM, and postoperative calcitonin allows for the identification of patients at risk of recurrence to personalize management.

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PMCID: PMC10505538

Surgical strategy for patients with papillary thyroid carcinoma invading the trachea: a comparison of tracheal sleeve resection with end-to-end anastomosis and window resection with tracheocutaneous fistula.

Gland Surg, 12(9):1167-78.

Y. Inoue, A. Ebina, K. Toda, W. Shimbashi, K. Yamada, H. Mitani, Y. Tanaka and I. Sugitani. 2023.

BACKGROUND: Sleeve resection with end-to-end anastomosis (Procedure A) and window resection with a tracheocutaneous fistula (Procedure B) are the major surgical procedures for patients with papillary thyroid carcinoma (PTC) exhibiting transluminal tracheal invasion. For each procedure, the indications, postoperative course, and treatment results were examined retrospectively. METHODS: Of 1,456 patients with PTC (maximum tumor diameter >1 cm) who received initial treatment between 1993 and 2013, we reviewed 51 patients. Of these 51 cases, 45 showed full-layer tracheal invasion, and 6 did not reach the tracheal mucosa, but required full-layer tracheal resection. Twenty-four patients underwent Procedure A, and 27 patients underwent Procedure B. RESULTS: Regarding surgical procedure selection, Procedure B was selected significantly more frequently than Procedure A for cases with preoperative recurrent laryngeal nerve (RLN) palsy, tumor invasion of the esophagus, clinical lymph node metastasis, or a large number of resected tracheal rings. Postoperative airway-related complications were not significantly different between the procedures, but decreased with the use of intraoperative neuromonitoring (IONM). The postoperative hospital stay was significantly longer for Procedure B than for Procedure A. In addition, the rate of a permanent postoperative tracheostoma was higher with Procedure B than with Procedure A. Local recurrence-free survival (LRFS) and cause-specific survival (CSS) did not differ significantly between the two procedures. CONCLUSIONS: Certain patients may benefit from Procedure A with IONM in terms of a shorter hospital stay and avoiding the need for a permanent tracheostoma. Although Procedure B was indicated for patients with more advanced disease than Procedure A, treatment outcomes were similar.

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DOI: [10.21037/gs-23-171](#)
PMCID: PMC10570975

Surgical Outcomes in Patients With Low-risk Papillary Thyroid Microcarcinoma From MAeSTro Study: Immediate Operation Versus Delayed Operation After Active Surveillance A Multicenter Prospective Cohort Study.

Ann Surg, 278(5):e1087-e95.

H. Hwang, J. Y. Choi, H. W. Yu, J. H. Moon, J. H. Kim, E. K. Lee, Y. K. Kim, C. Y. Lee, S. W. Cho, E. J. Chung, C. H. Ryu, J. Ryu, K. H. Yi, D. J. Park, K. E. Lee, Y. J. Park, S. J. Kim and Y. S. Jung. 2023.

OBJECTIVE: To investigate surgical, and clinical outcomes in patients with low-risk papillary thyroid microcarcinoma (PTMC) according to treatment options [immediate operation (IOP) vs delayed operation after active surveillance (AS) (DOP)]. **BACKGROUND:** AS has been adopted as an alternative to immediate surgery in patients with low-risk PTMC. Although some patients undergo surgery during AS, there is little information on surgical, and clinical outcomes after delayed operation after AS. **METHODS:** A multicenter prospective cohort study including 1177 patients was conducted at 3 tertiary hospitals in Korea from June 2016 to January 2020. Patients with low-risk PTMC were enrolled. The participants were self-assigned into AS or IOP, and during AS, the patients underwent surgery if there were signs of disease progression or if the patient's choice changed. **RESULTS:** A total of 516 patients underwent operation; 384 (74.4%) in the IOP group and 132 (25.6%) in the DOP group. Compared with the IOP group, the DOP group was significantly associated with a larger tumor size ($P = 0.002$), higher rates of lymphatic invasion ($P = 0.002$), and multifocality ($P = 0.008$). However, the rates of total thyroidectomy, postoperative hypoparathyroidism and vocal cord palsy did not differ significantly between the groups ($P = 0.283$, $P = 0.184$, and $P = 0.284$, respectively). Of the 132 patients in the DOP group, disease progression was present in 39 (29.5%) patients. The DOP group with disease progression had a significantly higher rate of lymph node metastasis ($P = 0.021$) and radioiodine therapy ($P = 0.025$) than the DOP group without disease progression. **CONCLUSIONS:** These results suggest that AS might be considered an alternative treatment option for patients with low-risk PTMC regarding the extent of thyroidectomy and postoperative complications in the DOP group. To assess oncologic outcomes, long-term follow-up will be needed. **TRIAL REGISTRATION:** ClinicalTrials.gov Identifier: NCT02938702.

PubMed-ID: [36912439](#)

DOI: [10.1097/SLA.0000000000005841](#)

Outcomes of Patients with an Intermediate-Risk Group According to the Japanese Risk Classification of Papillary Thyroid Carcinoma.

World J Surg, 47(10):2464-73.

K. Horiuchi, M. Fujimoto, K. Hidenori, Y. Yoshida, E. Noguchi, Y. Omi and T. Okamoto. 2023.

BACKGROUND: The management of intermediate-risk group of papillary thyroid cancer (PTC) is still vague, particularly regarding whether or not total thyroidectomy, postoperative radioactive iodine ablation (RAI-a), and postoperative TSH suppression are mandatory. **METHODS:** This retrospective study evaluated 680 PTC patients from 2010 to 2017, who were classified into the three risk groups as low, intermediate, and high-risk groups according to the criteria of the Japanese Association of Endocrine Surgeons (JAES) 2010 and underwent surgery according to the JAES guidelines. We retrospectively collected patient data for analyses of disease-free survivals in the intermediate-risk group patients. **RESULTS:** We performed surgery on 680 PTC patients from 2010 to 2017. Of them, 297 were classified as the intermediate-risk group. DFS was not statistically significantly different in patients with/without total thyroidectomy and postoperative TSH suppression therapy. For RAI-a, DFS (95% confidence interval) at 3, 5, and 8 years were 93.2% (84.6 ~ 97.2), 81.6% (68.3 ~ 90.2), and 70.7% (51.4 ~ 84.6) in patients with postoperative RAI-a and 100%, 100%, and 100% in patients without postoperative RAI-a after total thyroidectomy, respectively. DFS of patients without RAI-a was superior to those with RAI-a ($P < 0.0004$). Multivariable analysis by stepwise selection method revealed that postoperative RAI-a was a risk factor with a hazard ratio of 5.69. (95% CI 1.998-16.21) ($P = 0.001131$). **CONCLUSIONS:** Our study did not show the efficacy of RAI-a in patients with intermediate-risk PTC. This study implies that judging the efficacy of adjuvant therapy such as RAI or Tsh suppression in intermediate-risk patients is difficult.

PubMed-ID: [37266697](#)

DOI: [10.1007/s00268-023-07073-7](#)

PMCID: PMC10474173

Liothyronine prescribing in England: costs versus need.

Lancet, 402(10417):2074-5.

A. Heald, M. Stedman, B. Okosieme, L. Premawardhana, P. Taylor and C. Dayan. 2023.

PubMed-ID: [37979592](#)

DOI: [10.1016/S0140-6736\(23\)01792-0](#)

Intraoperative indocyanine green angiography for predicting postoperative hypoparathyroidism.

Surg Endosc, 37(12):9540-5.

V. V. Grubnik, R. S. Parfentiev, Y. V. Grubnik and V. V. Grubnyk. 2023.

BACKGROUND: Postoperative hypocalcemia is a common complication of thyroidectomy. This problem is most often associated with accidental devascularization or excision of the parathyroid glands (PG). **AIM:** Aim was to study near-infrared (NIR) fluorescent imaging with intraoperative PG indocyanine green (ICG) angiography to help identify and preserve PG during total thyroidectomy in order to avoid postoperative hypocalcemia. **MATERIAL AND METHODS:** From 2017 to 2022, a total of 92 patients underwent total thyroidectomy at Odessa Regional Hospital. Indications for surgery were multinodular goiter (n = 42), thyroid cancer (n = 43), and Graves' disease (n = 7). By randomization all patients were divided into two groups: in the control group, 48 patients underwent standard total thyroidectomy, and in the main group, 44 patients underwent NIR-assisted total thyroidectomy with ICG angiography. Serum calcium and parathyroid hormone levels were compared between the two groups of patients in 1, 7-15 days after surgery and then 3, 6 months later. **RESULTS:** In the control group, based on a visual assessment of the PG, autotransplantation of the PG was conducted in only five cases. In the second group, autotransplantation was performed in 16 patients. The transient postoperative hypocalcemia was observed in 8 patients of the control group (16, 70%) and in the 2 patients of ICG group (4, 50%) on 5-10 postoperative days. In the first group, 2 patients at 3 months after surgery had permanent hypocalcaemia. **CONCLUSION:** NIR fluorescent imaging with intraoperative PG ICG angiography is a safe and an easily repeatable method. This technique provides improved detecting and assessment of the perfusion of the PG. The need for autotransplantation of the PG can be determined more objectively using ICG imaging than simple visualization.

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DOI: [10.1007/s00464-023-10466-3](#)

A Reappraisal of Suspicious Sonographic Features of Thyroid Nodules: Shape Is Not an Independent Predictor of Malignancy.

J Clin Endocrinol Metab, 108(9):e816-e22.

G. Grani, V. Del Gatto, V. Cantisani, S. J. Mandel and C. Durante. 2023.

CONTEXT: For the correct clinical application of the sonographic risk-stratification systems, the definition of independent risk features that are foundational to each system is crucial. **OBJECTIVE:** The aim of this study was to identify the gray-scale sonographic features independently associated with malignancy, and to compare different definitions. **METHODS:** This prospective, diagnostic accuracy study took place in a single thyroid nodule referral center. All patients consecutively referred to our center for fine-needle aspiration cytology of a thyroid nodule between November 1, 2015 and March 30, 2020, were enrolled before cytology. Each nodule was examined by 2 experienced clinicians to record the sonographic features on a rating form. Histologic (when available) or cytologic diagnosis was used as the reference standard. For each single sonographic feature and definition, the sensitivity, specificity, positive and negative predictive values, and diagnostic odds ratios (DOR) were calculated. The significant predictors were then included in a multivariable regression model. **RESULTS:** The final study cohort consisted of 903 nodules in 852 patients. A total of 76 nodules (8.4%) were malignant. Six features were independent predictors of malignancy: suspicious lymph node (DOR 16.23), extrathyroidal extension (DOR 6.60), irregular or infiltrative margins (DOR 7.13), marked hypoechoogenicity (DOR 3.16), solid composition (DOR 3.61), and punctate hyperechoic foci (including microcalcifications and indeterminate foci; DOI 2.69). Taller-than-wide shape was not confirmed as an independent predictor. **CONCLUSION:** We identified the key suspicious features of thyroid nodules and provided a simplified definition of some debated ones. Malignancy rate increases with number of features.

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DOI: [10.1210/clinem/dgad092](#)

ASO Author Reflections: Applying the Lens of Equity to Anaplastic Thyroid Cancer Care.

Ann Surg Oncol, 30(11):6799-800.

S. P. Ginzberg, J. A. Gasior and H. Wachtel. 2023.

PubMed-ID: [37523118](#)

DOI: [10.1245/s10434-023-14024-y](#)

Disparities in Presentation, Treatment, and Survival in Anaplastic Thyroid Cancer.

Ann Surg Oncol, 30(11):6788-98.

S. P. Ginzberg, J. A. Gasior, J. E. Passman, J. M. S. Ballester, C. B. Finn, G. C. Karakousis, R. R. Kelz and H. Wachtel. 2023.

BACKGROUND: Disparities have been previously described in the presentation, management, and outcomes of other

thyroid cancer subtypes; however, it is unclear whether such disparities exist in anaplastic thyroid cancer (ATC). METHODS: We identified patients with ATC from the National Cancer Database (2004-2020). The primary outcomes were receipt of surgery, chemotherapy, and radiation. The secondary outcome was 1-year survival. Multivariable logistic and Cox proportional hazards regressions were used to assess the associations between sex, race/ethnicity, and the outcomes. RESULTS: Among 5359 patients included, 58% were female, and 80% were non-Hispanic white. Median tumor size was larger in males than females (6.5 vs. 6.0 cm; $p < 0.001$) and in patients with minority race/ethnicity than in white patients (6.5 vs. 6.0 cm; $p < 0.001$). After controlling for tumor size and metastatic disease, female patients were more likely to undergo surgical resection (odds ratio [OR]: 1.20; $p = 0.016$) but less likely to undergo chemotherapy (OR: 0.72; $p < 0.001$) and radiation (OR: 0.76; $p < 0.001$) compared with males. Additionally, patients from minority racial/ethnic backgrounds were less likely to undergo chemotherapy (OR: 0.69; $p < 0.001$) and radiation (OR: 0.71; $p < 0.001$) than white patients. Overall, unadjusted, 1-year survival was 23%, with differences in treatment receipt accounting for small but significant differences in survival between groups. CONCLUSIONS: There are disparities in the presentation and treatment of ATC by sex and race/ethnicity that likely reflect differences in access to care as well as patient and provider preferences. While survival is similarly poor across groups, the changing landscape of treatments for ATC warrants efforts to address the potential for exacerbation of disparities.

PubMed-ID: [37474696](#)

DOI: [10.1245/s10434-023-13945-y](#)

Mortality After Total Thyroidectomy for Amiodarone-Induced Thyrotoxicosis According to Left Ventricular Ejection Fraction.

Otolaryngol Head Neck Surg, 169(6):1542-9.

S. Frey, C. Caillard, P. Mahot, S. Pattier, C. Volteau, G. Knipping, G. Lande, D. Druil and E. Mirallie. 2023.

OBJECTIVE: To report cardiac outcomes after total thyroidectomy for amiodarone-induced thyrotoxicosis according to the baseline left ventricular ejection fraction in a tertiary referral center. STUDY DESIGN: Retrospective, monocentric. SETTING: The tertiary health care system. METHODS: Patients who underwent total thyroidectomy for amiodarone-induced thyrotoxicosis between 2010 and 2020 with age >18 and available preoperative left ventricular ejection fraction were included in this study. Patients were dichotomized into: group 1 with left ventricular ejection fraction $\geq 40\%$ (mildly reduced/normal ejection fraction), and group 2 with left ventricular ejection fraction $<40\%$ (reduced ejection fraction). RESULTS: There were 34 patients in group 1 and 17 to group 2. The latter were younger (median 58.4 [Q1-Q3 48.0-64.9] vs. 69.8 years in group 1 [59.8-78.3], $p = .0035$) and they presented more cardiomyopathy (58.8 vs. 26.5%, $p = .030$). Overall, the median time until surgery referral was 3.1 [1.9-7.1] months and 47.1% underwent surgery after restoration of euthyroidism. Surgical complications accounted for 7.8%. In group 2, the median left ventricular ejection fraction was significantly improved after surgery (22.5 [20.0-25.0] vs. 29.0% [25.3-45.5], $p = .0078$). Five-year cardiac mortality was significantly higher in group 2 ($p < .0001$): 47.0% died of cardiac causes versus 2.9% in group 1. A baseline left ventricular ejection fraction $<40\%$ and a longer time until surgery referral were significantly associated with cardiac mortality (multivariable Cox regression analysis, $p = .015$ and $.020$, respectively). CONCLUSION: These results reinforce the idea that surgery, if chosen, should be performed quickly in patients with left ventricular ejection fraction $<40\%$.

PubMed-ID: [37317630](#)

DOI: [10.1002/ohn.405](#)

Effect of Thyroidectomy on Tracheal Remodeling and Airway Physiology in Apparently Asymptomatic Patients with Goiter: A Prospective Study.

World J Surg, 47(12):3222-8.

L. Enny, S. Garg, S. Mouli, S. Manjunath, K. R. Singh, P. Ramakant and A. K. Mishra. 2023.

BACKGROUND: Tracheal airflow limitation is frequently reported in patients with goiter but is severely underestimated, and studies on how goiter and its treatment affect trachea are scarce. Moreover, the choice of the optimal treatment for individual patient with asymptomatic goiter is not straightforward. Therefore, in this study we aim to investigate the effect of goiter and subsequent thyroidectomy on tracheal anatomy and change in airflow in asymptomatic patient with goiter. METHODS: Seventy patients undergoing total/hemithyroidectomy (TT/HT) from Feb 2020 to Feb 2021 satisfying inclusion criteria were enrolled in the study. Neck radiograph (NR) and forced spirometry (FS) were performed preoperatively and on postoperative day 10 and 6 weeks and 3 months. RESULTS: Out of 70 patients, 84.3% patients were female, and mean duration and weight of goiter were 54.7 months and 72.21 gm, respectively. Of 70 patients, 57 were of benign pathology. Significant improvement in tracheal compression with moderate improvement in deviation was observed after surgery. Preoperative spirometry showed significant reduction in almost all parameters. After surgery, a weak improvement was observed at postoperative day 10 and 6 weeks; however, significant improvement in FEV1, PEFR, FEV1/FEV0.5, and

FEF50%/FIF50% was observed at postoperative 3 months. Patient with right sided and those with ≥ 8 mm deviation were associated with poorer pulmonary function. Weak correlation was observed between neck NR and spirometry parameters. Weight of the thyroid gland significantly correlated with ratio of MVV/FEV1. CONCLUSION: Patients with asymptomatic goiter can have significant abnormal changes in airflow as evidenced by FS and NR. Thyroidectomy is followed by gradual restoration of tracheal deviation and compression with significant improvement in pulmonary airflow.

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DOI: [10.1007/s00268-023-07192-1](#)

Re-operative surgery for differentiated thyroid cancer: A single institutional experience of 182 cases.

Eur J Surg Oncol, 49(10):107042.

S. Deo, B. Bansal, S. Bhorawal, C. S. Bal, A. Mishra, J. Sharma, S. Singh, P. Jayakumar, S. Agarwal, S. Bhatnagar, S. Mishra, S. J. Bharati, V. Kumar and S. Thulkar. 2023.

INTRODUCTION: Re-operative thyroid surgery (RTS) is performed in patients of differentiated thyroid cancer (DTC) with residual or recurrent disease. However, there is a paucity of literature discussing experience and technique of RTS. This study aims to address this gap by providing a comprehensive review of RTS for DTC, utilizing experiences from a dedicated complex thyroid surgical oncology program at the apex hospital in a developing country. METHODS: A retrospective analysis was conducted using data from the Department of Surgical Oncology's thyroid cancer database. The study period spanned from 2006 to 2022. Clinical presentation, prior surgical history, operative details of RTS, and post-operative outcomes were assessed. Descriptive analysis was performed. RESULTS: During the study period, a total of 182 patients underwent re-operative thyroid surgery (RTS). The primary surgeries performed prior to RTS included near-total or total thyroidectomy in most cases (69.2%), and approximately half of the patients (48.4%) had prior neck node interventions. The RTS procedures consisted of completion total thyroidectomy in 30.8% of cases and surgery for thyroid bed recurrence in 9.9% of cases, while central node dissection was performed in 46.2% of patients and unilateral or bilateral template neck dissection was performed in 41.8% of cases. Extended resections were required in 9.3% of patients. Post-operative complications included permanent hypoparathyroidism (2.7%) and unilateral recurrent laryngeal nerve palsy (1.6%). CONCLUSIONS: RTS is a complex procedure with high rates of post-operative morbidity reported in literature. Optimal outcomes require a multidisciplinary approach, thorough assessment, and skilled surgeons.

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DOI: [10.1016/j.ejso.2023.107042](#)

Investigation of pre-operative demographic, biochemical, sonographic and cytopathological findings in low-risk thyroid neoplasms.

Clin Endocrinol (Oxf), 99(5):502-10.

M. S. Deniz, D. Ozdemir, N. N. Imga, H. Baser, F. N. Cuhaci Seyrek, A. A. Altinboga, O. Topaloglu, R. Ersoy and B. Cakir. 2023.

OBJECTIVE: The present article analyses pre-operative demographic, biochemical, sonographic and histopathological characteristics of low-risk thyroid neoplasms (LRTNs), with a focus on four subgroups, "well-differentiated carcinoma-not otherwise specified" (WDC-NOS), "non-invasive follicular thyroid neoplasm with papillary like nuclear features" (NIFTP), "well-differentiated tumours of uncertain malignant potential" (WDT-UMP) and "follicular tumour of uncertain malignant potential" (FT-UMP). METHODS: The study retrospectively analyzed the histopathology of 2453 malignant thyroids and the final analyses included 99 cases diagnosed with LRTNs. The demographic and clinical features, pre-operative thyroid function, ultrasonography results, cytopathology results, histopathology results and prognostic classifications were assessed. RESULTS: The groups were similar demographic characteristics and the majority of clinical data, including comorbidities, thyroid function tests, thyroid cancer/neck radiotherapy history. NIFTPs represented 69.7% of all LRTNs. All (100%) WDT-UMPs had solitary nodules. Index nodule volume differed among the groups ($p = .036$), it was the lowest in WDC-NOS [0.68 (0.63-0.72 cc)] and highest in FT-UMP [12.6 (0.5-64 cc)]. Echogenicity findings were similar. Index nodule TIRADS demonstrated a significant difference ($p = .021$) but index nodule halo sign and BETHESDA scores were similar in all groups. The diameter, localisation and multicentric structure of LRTNs were again similar for all groups. Finally, prognostic scores suggested similar outcomes in all groups. CONCLUSION: The majority of LRTNs were NIFTPs in our population and all WDT-UMPs were solitary lesions. Index nodule volume was the most essential discriminating sonographic finding but further research must be performed before discriminatory potential can be described.

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DOI: [10.1111/cen.14965](#)

Intraoperative Identification of Thyroid and Parathyroid Tissues During Human Endocrine Surgery Using the MasSpec Pen.

JAMA Surg, 158(10):1050-9.

R. J. DeHoog, M. E. King, M. F. Keating, J. Zhang, M. Sans, C. L. Feider, K. Y. Garza, A. Bensussan, A. Krieger, J. Q. Lin, S. Badal, E. Alore, C. Pirko, K. Brahmhatt, W. Yu, R. Grogan, L. S. Eberlin and J. Suliburk. 2023.

IMPORTANCE: Intraoperative identification of tissues through gross inspection during thyroid and parathyroid surgery is challenging yet essential for preserving healthy tissue and improving outcomes for patients. **OBJECTIVE:** To evaluate the performance and clinical applicability of the MasSpec Pen (MSPen) technology for discriminating thyroid, parathyroid, and lymph node tissues intraoperatively. **DESIGN, SETTING, AND PARTICIPANTS:** In this diagnostic/prognostic study, the MSPen was used to analyze 184 fresh-frozen thyroid, parathyroid, and lymph node tissues in the laboratory and translated to the operating room to enable in vivo and ex vivo tissue analysis by endocrine surgeons in 102 patients undergoing thyroidectomy and parathyroidectomy procedures. This diagnostic study was conducted between August 2017 and March 2020. Fresh-frozen tissues were analyzed in a laboratory. Clinical analyses occurred in an operating room at an academic medical center. Of the analyses performed on 184 fresh-frozen tissues, 131 were included based on sufficient signal and postanalysis pathologic diagnosis. From clinical tests, 102 patients undergoing surgery were included. A total of 1015 intraoperative analyses were performed, with 269 analyses subject to statistical classification. Statistical classifiers for discriminating thyroid, parathyroid, and lymph node tissues were generated using training sets comprising both laboratory and intraoperative data and evaluated on an independent test set of intraoperative data. Data were analyzed from July to December 2022. **MAIN OUTCOMES AND MEASURES:** Accuracy for each tissue type was measured for classification models discriminating thyroid, parathyroid, and lymph node tissues using MSPen data compared to gross analysis and final pathology results. **RESULTS:** Of the 102 patients in the intraoperative study, 80 were female (78%) and the median (IQR) age was 52 (42-66) years. For discriminating thyroid and parathyroid tissues, an overall accuracy, defined as agreement with pathology, of 92.4% (95% CI, 87.7-95.4) was achieved using MSPen data, with 82.6% (95% CI, 76.5-87.4) accuracy achieved for the independent test set. For distinguishing thyroid from lymph node and parathyroid from lymph node, overall training set accuracies of 97.5% (95% CI, 92.8-99.1) and 96.1% (95% CI, 91.2-98.3), respectively, were achieved. **CONCLUSIONS AND RELEVANCE:** In this study, the MSPen showed high performance for discriminating thyroid, parathyroid, and lymph node tissues intraoperatively, suggesting this technology may be useful for providing near real-time feedback on tissue type to aid in surgical decision-making.

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DOI: [10.1001/jamasurg.2023.3229](#)

PMCID: PMC10398548

Molecular Profiling of 50 734 Bethesda III-VI Thyroid Nodules by ThyroSeq v3: Implications for Personalized Management.

J Clin Endocrinol Metab, 108(11):2999-3008.

S. Chiosea, S. P. Hodak, L. Yip, D. Abraham, C. Baldwin, Z. Baloch, S. A. Gulec, Z. C. Hannoush, B. R. Haugen, L. Joseph, A. Y. Kargi, E. Khanafshar, M. J. Livhits, B. Mclver, K. Patel, S. G. Patel, G. W. Randolph, A. R. Shaha, J. Sharma, N. Stathatos, A. van Zante, S. E. Carty, Y. E. Nikiforov and M. N. Nikiforova. 2023.

CONTEXT: Comprehensive genomic analysis of thyroid nodules for multiple classes of molecular alterations detected in a large series of fine needle aspiration (FNA) samples has not been reported. **OBJECTIVE:** To determine the prevalence of clinically relevant molecular alterations in Bethesda categories III-VI (BCIII-VI) thyroid nodules. **METHODS:** This retrospective analysis of FNA samples, tested by ThyroSeq v3 using Genomic Classifier and Cancer Risk Classifier at UPMC Molecular and Genomic Pathology laboratory, analyzed the prevalence of diagnostic, prognostic, and targetable genetic alterations in a total of 50 734 BCIII-VI nodules from 48 225 patients. **RESULTS:** Among 50 734 informative FNA samples, 65.3% were test-negative, 33.9% positive, 0.2% positive for medullary carcinoma, and 0.6% positive for parathyroid. The benign call rate in BCIII-IV nodules was 68%. Among test-positive samples, 73.3% had mutations, 11.3% gene fusions, and 10.8% isolated copy number alterations. Comparing BCIII-IV nodules with BCV-VI nodules revealed a shift from predominantly RAS-like alterations to BRAF V600E-like alterations and fusions involving receptor tyrosine kinases (RTK). Using ThyroSeq Cancer Risk Classifier, a high-risk profile, which typically included TERT or TP53 mutations, was found in 6% of samples, more frequently BCV-VI. RNA-Seq confirmed ThyroSeq detection of novel RTK fusions in 98.9% of cases. **CONCLUSION:** In this series, 68% of BCIII-IV nodules were classified as negative by ThyroSeq, potentially preventing diagnostic surgery in this subset of patients. Specific genetic alterations were detected in most BCV-VI nodules, with a higher prevalence of BRAF and TERT mutations and targetable gene fusions compared to BCIII-IV nodules, offering prognostic and therapeutic information for patient management.

PubMed-ID: [37071871](#)

DOI: [10.1210/clinem/dgad220](https://doi.org/10.1210/clinem/dgad220)

PMCID: PMC10583990

Transoral endoscopic and robotic thyroidectomy for thyroid cancer: the mid-term oncological outcome.

Surg Endosc, 37(10):7829-38.

Y. H. Chen, W. P. Chao, S. H. Wang, Y. T. Huang and S. C. Ng. 2023.

BACKGROUND: Traditional open thyroidectomy is the surgical standard for thyroid cancer; however, it inevitably leaves a visible scar on the neck and affects the patient's quality of life. Therefore, to avoid making a neck incision, the transoral endoscopic thyroidectomy vestibular approach (TOETVA) and transoral robotic thyroidectomy (TORT) have been developed recently, and the surgical outcomes of these techniques are as favorable as open surgery for benign disease. Additionally, positive short-term surgical outcomes have also been achieved in a few patients with thyroid cancer. However, no data on the mid-to-long-term recurrence and survival rates of transoral thyroidectomy in thyroid cancer are available. Therefore, in this study, we analyzed the surgical outcomes and mid-term oncological results of the TOETVA and TORT in patients with thyroid cancer. **METHODS:** We reviewed patients who had received TOETVA or TORT between July 2017 and November 2021 and followed up on their oncological outcomes until December 2022. Perioperative surgical and mid-term oncological outcomes were analyzed. **RESULTS:** The 115 patients underwent 122 operations (57 TOETVAs and 65 TORTs), including seven complete thyroidectomies for differentiated thyroid cancer (DTC), Stage I-II, including T1-T3, N0-N1a, and initial low- to high-risk groups. There was no conversion from transoral to open surgery. TORT required a longer operating time (median [interquartile range]) than TOETVA (lobectomy: 279 [250, 318] vs. 196 [173, 253] min, $p < 0.001$; bilateral total thyroidectomy: 375 [309, 433] vs. 279 [238, 312] min, $p < 0.001$); however, no difference was found between the two groups regarding perioperative complications. Complete thyroidectomy with a second transoral approach was safe. TOETVA and TORT achieved favorable oncological outcomes with 100% survival and 98.2% acceptable response (excellent and indeterminate response) during a mean 37.88 +/- 12.42 months mid-term follow-up. **CONCLUSIONS:** Transoral endoscopic and robotic thyroidectomy was safe and achieved favorable mid-term oncological outcomes in a selected cohort of patients with early-stage DTC.

PubMed-ID: [37605012](https://pubmed.ncbi.nlm.nih.gov/37605012/)

DOI: [10.1007/s00464-023-10339-9](https://doi.org/10.1007/s00464-023-10339-9)

ASO Author Reflections: Targeted Therapy Combined with Immunotherapy as Neoadjuvant Treatment for Locally Advanced Differentiated Thyroid Cancer.

Ann Surg Oncol, 30(12):7183-4.

J. Y. Chen, Y. L. Wang, Y. Wang and Q. H. Ji. 2023.

PubMed-ID: [37612548](https://pubmed.ncbi.nlm.nih.gov/37612548/)

DOI: [10.1245/s10434-023-14063-5](https://doi.org/10.1245/s10434-023-14063-5)

The Efficacy and Safety of Surufatinib Combined with Anti PD-1 Antibody Toripalimab in Neoadjuvant Treatment of Locally Advanced Differentiated Thyroid Cancer: A Phase II Study.

Ann Surg Oncol, 30(12):7172-80.

J. Y. Chen, N. S. Huang, W. J. Wei, J. Q. Hu, Y. M. Cao, Q. Shen, Z. W. Lu, Y. L. Wang, Y. Wang and Q. H. Ji. 2023.

BACKGROUND: Surgery is the primary treatment for locally advanced differentiated thyroid cancer (DTC). However, some locally advanced patients are not candidates for R0/1 resection. There is limited evidence of neoadjuvant treatment in locally advanced DTC. Surufatinib targets multiple kinases, which is efficient, tolerable, and safe in patients with radioiodine-refractory DTC. In addition, surufatinib plus toripalimab (an anti-PD-1 antibody) showed encouraging antitumor activity in advanced solid tumors. This study was designed to evaluate the efficacy and safety of surufatinib plus toripalimab in locally advanced DTC in the neoadjuvant setting. **METHODS:** In this single-arm, phase II study, patients with pathologically confirmed unresectable or borderline resectable DTC were eligible and received a combination of 250 mg of surufatinib (orally daily) with 240 mg of toripalimab (intravenous, every 3 weeks). Treatment continued until satisfied for curative surgery, disease progression, withdrawal of consent, unacceptable toxicity, or investigator decision. Primary endpoint was objective response rate (ORR). Secondary endpoints included R0/1 resection rate, adverse events (AEs), etc. **RESULTS:** Ten patients were enrolled and received at least 4 cycles of treatment. The ORR was 60%. Nine patients received R0/1 resections after neoadjuvant treatment. The median best percentage change in the sum of the target lesion diameter was 32%. Most adverse events (AEs) were grade 1 or 2. **CONCLUSIONS:** Surufatinib in combination with toripalimab as neoadjuvant therapy for locally advanced DTC was feasible, and the majority of patients achieved R0/1 resection. It represents a new option for locally advanced DTC and needs further investigation.

PubMed-ID: [37543550](#)

DOI: [10.1245/s10434-023-14031-z](#)

Outcomes of ATA Low-Risk Pediatric Thyroid Cancer Patients Not Treated With Radioactive Iodine Therapy.

J Clin Endocrinol Metab, 108(12):3338-44.

M. Bojarsky, J. A. Baran, S. Halada, A. Isaza, H. Zhuang, L. States, F. D. Grant, S. Robbins, L. Sisko, J. C. Ricarte-Filho, K. Kazahaya, N. S. Adzick, S. Mostoufi-Moab and A. J. Bauer. 2023.

CONTEXT: The American Thyroid Association (ATA) Pediatric Guidelines recommend patients not receive radioactive iodine therapy (RAIT) for differentiated thyroid cancer (DTC) confined to the thyroid. Since publication, there is ongoing concern whether withholding RAIT will result in a lower rate of remission. OBJECTIVE: This study explores whether ATA low-risk patients treated with and without RAIT achieved similar remission rates. METHODS: Medical records of patients <19 years old diagnosed with DTC and treated with total thyroidectomy between 2010 and 2020 were reviewed. Multivariate logistic regression was performed to evaluate factors influencing RAIT administration and remission rate. RESULTS: Ninety-five patients with ATA low-risk DTC were analyzed: 53% (50/95) and 47% (45/95) were treated with and without RAIT, respectively. RAIT was used to treat 82% of patients before 2015 compared with 33% of patients after 2015 ($P < .01$). No significant difference in 1-year remission rate was found between patients treated with and without RAIT, 70% (35/50) vs 69% (31/45), respectively. With longer surveillance, remission rates increased to 82% and 76% for patients treated with and without RAIT, respectively. Median follow-up was 5.8 years (IQR 4.3-7.9, range 0.9-10.9) and 3.6 years (IQR 2.7-6.6; range 0.9-9.3) for both cohorts. No risk factors for persistent or indeterminate disease status were found, including RAIT administration, N1a disease, and surgery after 2015. CONCLUSION: Withholding RAIT for pediatric patients with ATA low-risk DTC avoids exposure to radiation and does not have a negative impact on remission rates. Dynamic risk stratification at 1-year after initial treatment is a suitable time point to assess the impact of withholding RAIT for these patients.

PubMed-ID: [37265226](#)

DOI: [10.1210/clinem/dgad322](#)

PMCID: PMC10655549

Letter to the Editor in Response to the Article Entitled "Selection Criteria for Completion Thyroidectomy in Follicular Thyroid Carcinoma Using Primary Tumor Size and TERT Promotor Mutational Status".

Ann Surg Oncol, 30(13):8545.

D. P. Behra and A. Mishra. 2023.

PubMed-ID: [37751118](#)

DOI: [10.1245/s10434-023-14354-x](#)

Impact of Sternothyroid Muscle Division on Patient-Reported Voice Outcomes After Thyroid Surgery: A Prospective Study.

Otolaryngol Head Neck Surg, 169(6):1550-5.

C. Barron, A. Hamberis, B. Gold, J. Yun and R. L. Chai. 2023.

OBJECTIVE: Division of the sternothyroid muscle during thyroidectomy is a widely accepted surgical technique to provide improved exposure of the thyroid gland, thus facilitating the ligation of superior pole vessels and identification of the laryngeal nerves. However, few have examined the impact on voice outcomes. We evaluate the impact of sternothyroid muscle division on patient-perceived voice outcomes after thyroidectomy. STUDY DESIGN: Prospective cohort study. SETTING: Tertiary academic institution. METHODS: A prospective cohort study was conducted comparing pre- and postoperative voice outcome data after thyroidectomy, measured using Voice Handicap Index-10. The cohort of 109 patients underwent lobectomy or total thyroidectomy by a single surgeon at 1 institution. The sternothyroid muscle was fully divided in all surgeries. The integrity of the recurrent laryngeal and external branches of the superior laryngeal nerve was assessed using intraoperative nerve monitoring and postoperative laryngoscopy. Pre- and postoperative Voice Handicap Index-10 scores were compared. RESULTS: No statistically significant difference was found between total pre- and postoperative Voice Handicap Index-10 scores ($\mu(\text{preop}) = 1.92$, $\mu(\text{postop}) = 1.83$, $p = .87$). There were no questions yielding statistically significant responses between pre- and postoperative groups. This was consistent regardless of whether the sternothyroid muscle was cut unilaterally or bilaterally. Men showed a statistically significant improvement in score after surgery. CONCLUSION: These findings support no difference in postoperative voice outcomes after the intraoperative division of the sternothyroid muscle. This supports the usage of this technique as a safe means to facilitate exposure during thyroid surgery and will serve as important information to guide intraoperative surgical decision-making.

PubMed-ID: [37313972](#)

DOI: [10.1002/ohn.401](#)

Determining the Power Required for Comparing Lobectomy vs Total Thyroidectomy for Papillary Thyroid Carcinoma.

JAMA Surg, 158(9):983-4.

C. Balentine. 2023.

PubMed-ID: [37195700](#)

DOI: [10.1001/jamasurg.2023.1060](#)

Time-Driven Activity-Based Cost Comparison of Thyroid Lobectomy and Radiofrequency Ablation.

Otolaryngol Head Neck Surg, 169(4):830-6.

N. F. Ayoub, K. Balakrishnan, L. A. Orloff and J. E. Noel. 2023.

OBJECTIVE: Radiofrequency ablation (RFA) of benign thyroid nodules has gained traction for its therapeutic effectiveness, thyroid function preservation, and minimally invasive nature. While a growing body of evidence reports positive outcomes from thyroid RFA, financial comparisons between both procedures remain limited. This analysis aims to more accurately measure the direct cost of thyroid RFA in comparison to thyroid lobectomy. STUDY DESIGN: Bottom-up financial cost analysis. SETTING: Tertiary endocrine head and neck surgery center. METHODS: Time-driven activity-based costing was utilized to obtain unit-based cost estimates. The care cycles for thyroid lobectomy and RFA were defined, and process maps were developed comprising all personnel and work in the care cycle. Time estimates were calculated for all personnel involved, and public government data were used to obtain capacity cost rates for each component of the care cycle. Consumable supply and overhead costs were obtained for both procedures, and overall costs were compared. RESULTS: For thyroid lobectomy, total personnel costs were \$1087.97, consumable supplies were \$942.68, and overhead costs \$17,199.10. For thyroid nodule RFA performed in an office setting, the total personnel cost calculated was \$379.90, consumable supplies \$1315.28, and overhead \$7031.20. Overall, the total cost for thyroid lobectomy was \$19,229.75 compared to \$8726.38 for RFA. CONCLUSION: In-office thyroid nodule RFA is associated with lower direct costs than thyroid lobectomy, and overhead is the greatest cost driver for both procedures. If clinical and patient-centered outcomes are comparable, then RFA may provide higher value for appropriately selected patients.

PubMed-ID: [37157972](#)

DOI: [10.1002/ohn.360](#)

Clinical use of Molecular Data in Thyroid Nodules and Cancer.

J Clin Endocrinol Metab, 108(11):2759-71.

A. S. Alzahrani. 2023.

Over the past 3 decades, advances in the molecular genetics of thyroid cancer (TC) have been translated into diagnostic tests, prognostic markers, and therapeutic agents. The main drivers in differentiated TC pathogenesis are single-point mutations and gene fusions in components of the Mitogen-activated protein kinase (MAPK) and phosphoinositide-3-kinase-protein kinase B/Akt (PI3K/Akt) pathways. Other important genetic alterations in the more advanced types of TC include TERT promoter, TP53, EIF1AX, and epigenetic alterations. Using this knowledge, several molecular tests have been developed for cytologically indeterminate thyroid nodules. Currently, 3 commercially available tests are in use including a DNA/RNA-based test (ThyroSeq v.3), an RNA-based test (Afirma Gene Sequencing Classifier), and a hybrid DNA/miRNA test, ThyGeNEXT/ThyraMIR. These tests are mostly used to rule out malignancy in Bethesda III and IV thyroid nodules because they all have high sensitivities and negative predictive values. Their common use, predominantly in the United States, has resulted in a significant reduction in unnecessary thyroid surgeries for benign nodules. Some of these tests also provide information on the underlying molecular drivers of TC; this may support decision making in initial TC management planning, although this practice has not yet been widely adopted. More importantly, molecular testing is essential in patients with advanced disease before using specific mono-kinase inhibitors (eg, selipercatinib for RET-altered TC) because these drugs are ineffective in the absence of a specific molecular target. This mini-review discusses the utilization of molecular data in the clinical management of patients with thyroid nodules and TC in these different clinical situations.

PubMed-ID: [37200449](#)

DOI: [10.1210/clinem/dgad282](#)

The 2023 Bethesda System for Reporting Thyroid Cytopathology.

Thyroid, 33(9):1039-44.

S. Z. Ali, Z. W. Baloch, B. Cochand-Priollet, F. C. Schmitt, P. Vielh and P. A. VanderLaan. 2023.

Since the publication of the first edition in 2010, The Bethesda System for Reporting Thyroid Cytopathology has allowed

cytopathologists to use a standardized, category-based reporting system for thyroid fine needle aspirations. The third edition builds on the success of the 2 earlier editions and offers several key updates. The most important is the assignment of a single name for each of the 6 diagnostic categories: (i) nondiagnostic; (ii) benign; (iii) atypia of undetermined significance; (iv) follicular neoplasm; (v) suspicious for malignancy; and (vi) malignant. Each of the categories has an implied risk of malignancy (ROM), which has been updated and refined based on data reported after the second edition. The third edition offers an average ROM for each category, in addition to the expected range of cancer risk. The atypia of undetermined significance subcategorization is simplified into 2 subgroups based on the implied ROM and molecular profiling. A discussion of pediatric thyroid disease has been added, and pediatric ROMs and management algorithms are discussed in the relevant sections. Nomenclature has been updated to align with the 2022 World Health Organization Classification of Thyroid Neoplasms. Two new chapters have been added: one that addresses the significant and expanded use of molecular and ancillary testing in thyroid cytopathology, and another that summarizes clinical perspectives and imaging findings in thyroid disease.

PubMed-ID: [37427847](#)

DOI: [10.1089/thy.2023.0141](https://doi.org/10.1089/thy.2023.0141)

Parathyroids

Meta-Analyses

Comparison of 4D computed tomography and F-18 fluorocholine PET for localisation of parathyroid lesions in primary hyperparathyroidism: A systematic review and meta-analysis.

Clin Endocrinol (Oxf), 99(3):262-71.

D. D. Patel, S. Bhattacharjee, A. K. Pandey, C. R. Kopp, A. G. Ashwathanarayana, H. V. Patel, R. Barnabas, S. K. Bhadada and M. H. Dodamani. 2023.

Minimally invasive parathyroidectomy (MIP) is the standard of care for primary hyperparathyroidism (PHPT). Four dimensional computed tomography(4DCT) and F-18 Fluorocholine positron emission tomography/computed tomography (FCH PET/CT) localize adenomas accurately to perform MIP. We aimed to conduct a systematic review and metanalysis to evaluate the diagnostic performance of 4DCT and FCH PET/CT scan for quadrant wise localisation in PHPT patients and to do head-to-head comparison between these two modalities. DESIGN, PATIENTS AND MEASUREMENT : After searching through PubMed and EMBASE databases, 46 studies (using histology as a gold standard) of 4DCT and FCH PET/CT were included. RESULTS: Total number of patients included were 1651 and 952 for 4DCT scan (studies n = 26) and FCH PET/CT scan (studies n = 24) respectively. In per patient analysis, FCH PET/CT and 4DCT had pooled sensitivities of 92% (88-94) and 85% (73-92) respectively and in per lesion analysis, 90% (86-93) and 79% (71-84), respectively. In the subgroup with negative conventional imaging/persistent PHPT, FCH PET/CT had comparable sensitivity to 4DCT (84% [74-90] vs. 72% [46-88]). As per patient wise analysis, FCH PET/CT had better detection rates than 4DCT ([92.4 vs. 76.85], odds ratio -3.89 [1.6-9.36] p = .0024) in the subpopulation where both FCH PET/CT and 4DCT were reported. CONCLUSION: Both 4DCT and FCH PET/CT scan performed well in newly diagnosed patients, patients with persistent disease and in those with inconclusive conventional imaging results. FCH PET/CT scan had a higher pooled sensitivity than 4DCT in detecting patients with PHPT in head to head comparison.

PubMed-ID: [36593125](https://pubmed.ncbi.nlm.nih.gov/36593125/)

DOI: [10.1111/cen.14875](https://doi.org/10.1111/cen.14875)

Long-term Recurrence Rates After Surgery in Primary Hyperparathyroidism.

J Clin Endocrinol Metab, 108(11):3022-30.

M. Zaman, L. Raveendran, A. Senay, H. Sayles, R. Acharya and M. Dhir. 2023.

CONTEXT: Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia, yet long-term (5- and 10-year) recurrence rates after curative surgery have been unclear. OBJECTIVE: To perform the first systematic review and meta-analysis investigating the long-term recurrence rates of sporadic PHPT after successful parathyroidectomy.

METHODS: A comprehensive search of multiple databases (including PubMed, EMBASE, Cochrane, EBSCO-CINHAL, EMBASE, Ovid, Scopus, and Google Scholar) was performed from each database's inception to January 18, 2023.

Observational studies reporting at least 5 years of follow-up data after surgical resection were included. Two reviewers independently screened articles for relevance. Of 5769 articles initially identified, 242 were examined in full-text review and 34 were deemed eligible for inclusion. Two authors independently performed data extraction and study appraisal, using the National Institutes of Health study quality assessment tools. RESULTS: Of 30 658 participants, 350 patients (1.1%) experienced recurrence after resection. A meta-analysis of proportions was performed to obtain the pooled recurrence rates. The pooled estimate for overall recurrence rate was 1.56% (95% CI 0.96-2.28%; I² = 91%). The pooled estimates for 5- and 10-year recurrence rate after resection were 0.23% (0.04-0.53%, 19 studies; I² = 66%) and 1.03% (0.45-1.80%, 14 studies; I² = 89%), respectively. Sensitivity analyses did not find a statistically significant difference when adjusting for study size, diagnosis, or surgical approach. CONCLUSION: Approximately 1.56% of sporadic PHPT patients eventually develop recurrence following parathyroidectomy. The initial diagnosis and procedure type does not influence recurrence rates. Consistent long-term follow-up is warranted to help identify recurrent disease.

PubMed-ID: [37279502](https://pubmed.ncbi.nlm.nih.gov/37279502/)

DOI: [10.1210/clinem/dgad316](https://doi.org/10.1210/clinem/dgad316)

Randomized controlled trials

Does the Use of Probe-based Near-infrared Autofluorescence Parathyroid Detection Benefit Parathyroidectomy?: A Randomized Single-center Clinical Trial.

Ann Surg, 278(4):549-58.

C. M. Kiernan, G. Thomas, A. Patel, R. Fan, F. Ye, P. A. Willmon and C. C. Solorzano. 2023.

OBJECTIVE: To evaluate the benefits of probe-based near-infrared autofluorescence (NIRAF) parathyroid identification during parathyroidectomy. **BACKGROUND:** Intraoperative parathyroid gland identification during parathyroidectomy can be challenging, while additionally requiring costly frozen sections. Earlier studies have established NIRAF detection as a reliable intraoperative adjunct for parathyroid identification. **METHODS:** Patients undergoing parathyroidectomy for primary hyperparathyroidism were prospectively enrolled by a senior surgeon (>20 years experience) and a junior surgeon (<5 years experience), while being randomly allocated to the probe-based NIRAF or control group. Data collected included procedure type, number of parathyroids identified with high confidence by the surgeon and the resident, number of frozen sections performed, parathyroidectomy duration, and number of patients with persistent disease at the first postoperative visit. **RESULTS:** One hundred sixty patients were randomly enrolled under both surgeons to the probe group (n=80) versus control (n=80). In the probe group, parathyroid identification rate of the senior surgeon improved significantly from 3.2 to 3.6 parathyroids per patient ($P < 0.001$), while that of the junior surgeon also rose significantly from 2.2 to 2.5 parathyroids per patient ($P = 0.001$). Parathyroid identification was even more prominent for residents increasing significantly from 0.9 to 2.9 parathyroids per patient ($P < 0.001$). Furthermore, there was a significant reduction in frozen sections utilized in the probe group versus control (17 vs 47, $P = 0.005$). **CONCLUSION:** Probe-based NIRAF detection can be a valuable intraoperative adjunct and educational tool for improving confidence in parathyroid gland identification, while potentially reducing the number of frozen sections required.

PubMed-ID: [37389537](https://pubmed.ncbi.nlm.nih.gov/37389537/)

DOI: [10.1097/SLA.0000000000005985](https://doi.org/10.1097/SLA.0000000000005985)

PMCID: PMC10836830

Consensus Statements/Guidelines

- None -

Other Articles

Incidence of Primary Hyperparathyroidism in the Current Era: Have We Finally Reached a Steady State?

J Clin Endocrinol Metab, 108(12):e1749-e50.

R. A. Wermers. 2023.

PubMed-ID: [37170854](https://pubmed.ncbi.nlm.nih.gov/37170854/)

DOI: [10.1210/clinem/dgad267](https://doi.org/10.1210/clinem/dgad267)

PMCID: PMC10655524

Phenotypic Profiling and Molecular Mechanisms in Hyperparathyroidism-jaw Tumor Syndrome.

J Clin Endocrinol Metab, 108(12):3165-77.

R. Tora, J. Welch, J. Sun, S. K. Agarwal, D. A. Bell, M. Merino, L. S. Weinstein, W. F. Simonds and S. Jha. 2023.

CONTEXT: Hyperparathyroidism-jaw tumor (HPT-JT) syndrome is a heritable form of primary hyperparathyroidism caused by germline inactivating mutations in CDC73 encoding parafibromin and is associated with an increased risk of parathyroid cancer. There is little evidence to guide the management of patients with the disease. **OBJECTIVE:** (1) Characterize the natural history of HPT-JT, (2) correlate genotype and histology of parathyroid tumors with parafibromin immunostaining, (3) understand molecular changes downstream to CDC73 loss. **DESIGN:** Retrospective study of patients with HPT-JT syndrome (genetically confirmed or affected first-degree relatives). Independent review of uterine tumor from 2 patients and staining for parafibromin on parathyroid tumors from 19 patients (13 adenomas, 6 carcinomas) was performed. RNA-sequencing was performed in 21 parathyroid samples (8 HPT-JT-related adenomas, 6 HPT-JT-related carcinomas, and 7 sporadic carcinomas with wild-type CDC73). **RESULTS:** We identified 68 patients from 29 kindreds with HPT-JT with median

age at last follow-up of 39 [interquartile range, 29-53] years. A total of 55/68 (81%) developed primary hyperparathyroidism; 17/55 (31%) had parathyroid carcinoma. Twelve of 32 (38%) females developed uterine tumors. Of the 11 patients who had surgical resection for uterine tumors, 12/24 (50%) tumors were rare mixed epithelial mesenchymal polypoid lesions. Four of 68 patients (6%) developed solid kidney tumors; 3/4 had a CDC73 variant at p.M1 residue. Parafibromin staining of parathyroid tumors did not correlate with tumor histology or genotype. RNA-sequencing showed a significant association of HPT-JT-related parathyroid tumors with transmembrane receptor protein tyrosine kinase signaling pathway, mesodermal commitment pathway, and cell-cell adhesion. CONCLUSIONS: Multiple, recurrent atypical adenomyomatous uterine polyps appear to be enriched in women with HPT-JT and appear characteristic of the disease. Patients with CDC73 variants at p.M1 residue appear predisposed to kidney tumors. CLINICAL TRIAL NUMBER: NCT04969926.

PubMed-ID: [37339334](#)

DOI: [10.1210/clinem/dgad368](#)

PMCID: PMC10655532

Stable Incidence and Increasing Prevalence of Primary Hyperparathyroidism in a Population-based Study in Scotland.

J Clin Endocrinol Metab, 108(10):e1117-e24.

E. Soto-Pedre, P. J. Newey and G. P. Leese. 2023.

CONTEXT: Previous studies, including our own, have demonstrated a highly variable incidence of primary hyperparathyroidism (PHPT) from year to year. OBJECTIVE: We planned to provide a current estimate of the incidence and prevalence of PHPT in a community-based study. METHODS: A population-based retrospective follow-up study was conducted in Tayside (Scotland) from 2007 to 2018. Record-linkage technology (demography, biochemistry, prescribing, hospital admissions, radiology, and mortality data) was used to identify all patients. Cases of PHPT were defined as those with at least 2 raised serum corrected calcium concentration CCA (> 2.55 mmol/L) and/or hospital admissions with PHPT diagnoses and/or surgery records with parathyroidectomy during the follow-up period. The number of prevalent and incident cases of PHPT per calendar year by age and sex were estimated. RESULTS: A total of 2118 people (72.3% female, mean age 65 years) were identified with an incident case of PHPT. The overall prevalence of PHPT over the 12 years of the study was 0.84% (95% CI, 0.68%-1.02%), steadily increasing from 0.71% in 2007 to 1.02% in 2018. From 2008, the incidence of PHPT was relatively stable from 4 to 6 cases per 10 000 person-years, declining from 11.5 per 10 000 person-years in 2007. The incidence varied from 0.59 per 10 000 person-years (95% CI, 0.40%-0.77%) for those aged 20 to 29 years, to 12.4 per 10 000 person-years (95% CI, 11.2%-13.3%) in those aged 70 to 79 years. Incidence of PHPT was 2.5 times higher in women than in men. CONCLUSION: This study is the first showing a relatively steady annual incidence of PHPT at 4 to 6 per 10 000 person-years. This population-based study reports a PHPT prevalence of 0.84%.

PubMed-ID: [37022975](#)

DOI: [10.1210/clinem/dgad201](#)

PMCID: PMC10505547

Morbidity Associated With Primary Hyperparathyroidism—A Population-based Study With a Subanalysis on Vitamin D.

J Clin Endocrinol Metab, 108(9):e842-e9.

E. Soto-Pedre, Y. Y. Lin, J. Soto-Hernaez, P. J. Newey and G. P. Leese. 2023.

CONTEXT: Primary hyperparathyroidism (PHPT) is associated with increased risk of morbidity and death, and vitamin D levels are a potentially confounding variable. OBJECTIVE: The aim of this study was to assess morbidity and mortality associated with primary hyperparathyroidism (PHPT). METHODS: In this population-based retrospective matched cohort study, data linkage of biochemistry, hospital admissions, prescribing, imaging, pathology, and deaths was used to identify patients across the region of Tayside, Scotland, who had PHPT from 1997 to 2019. Cox proportional hazards models and hazards ratios (HR) were used to explore the relationship between exposure to PHPT and several clinical outcomes. Comparisons were made with an age- and gender-matched cohort. RESULTS: In 11 616 people with PHPT (66.8% female), with a mean follow-up period of 8.8 years, there was an adjusted HR of death of 2.05 (95% CI, 1.97-2.13) for those exposed to PHPT. There was also an increased risk of cardiovascular disease (HR = 1.34; 95% CI, 1.24-1.45), cerebrovascular disease (HR = 1.29; 95% CI, 1.15-1.45), diabetes (HR = 1.39; 95% CI, 1.26-1.54), renal stones (HR = 3.02; 95% CI, 2.19-4.17) and osteoporosis (HR = 1.31; 95% CI, 1.16-1.49). Following adjustment for serum vitamin D concentrations (n = 2748), increased risks for death, diabetes, renal stones, and osteoporosis persisted, but not for cardiovascular or cerebrovascular disease. CONCLUSION: In a large population-based study, PHPT was associated with death, diabetes, renal stones, and osteoporosis, independent of serum vitamin D concentration.

PubMed-ID: [36810667](#)

DOI: [10.1210/clinem/dgad103](https://doi.org/10.1210/clinem/dgad103)

PMCID: PMC10438903

The role of (18)F-fluoromethylcholine-positron emission tomography-computed tomography for preoperative localization of hyperfunctioning parathyroid glands with special emphasis on multiglandular disease: a retrospective cohort study.

Gland Surg, 12(11):1567-78.

H. Murad, C. Ciacoi-Dutu, G. Lindblom and M. Almquist. 2023.

BACKGROUND: Primary hyperparathyroidism (PHPT) is a common endocrine disorder. Definitive treatment is surgical. Preoperative localization of diseased glands increases the chance of successful treatment. The aim of this study is to investigate the diagnostic performance of (18)F-fluoromethylcholine-positron emission tomography-computed tomography ((18)F-FCh-PET-CT) in preoperative localization of diseased parathyroid glands, when first-line examinations were inconclusive. METHODS: This is a retrospective study. All patients with PHPT who underwent (18)F-FCh-PET-CT, after inconclusive ultrasound examination and (99m)Tc-methoxyisobutylisonitrile/single-photon emission CT-CT, were included in cohort I. Patients who were subsequently operated for their parathyroid disease, were included in cohort II. The performance of (18)F-FCh-PET-CT was analyzed in two sets: per-lesion, and per-gland analysis. RESULTS: Out of 52 patients in cohort I, (18)F-FCh-PET-CT identified single or multiple parathyroid lesions in 43 patients (83%). Nine patients had multiglandular disease. Thirty-four (65%) patients were subsequently operated and included in cohort II. Forty-four lesions were removed from these patients and 33 patients (97%) were cured. (18)F-FCh-PET-CT localized 40 out of 44 lesions, with per-lesion and per-gland sensitivities of 97% and 95%, and positive predictive values (PPVs) of 93% and 87%, respectively, in addition to a specificity of 97% and a negative predictive value (NPV) of 94% in the per-gland analysis. Comparable excellent results were detected in multiglandular disease with sensitivity of 94.1%, specificity of 89%, PPV of 84%, and NPV of 94%. CONCLUSIONS: Our study demonstrates the high diagnostic performance of (18)F-FCh-PET-CT in the preoperative localization of diseased parathyroid gland in patients with PHPT, especially in multiglandular PHPT.

PubMed-ID: [38107488](https://pubmed.ncbi.nlm.nih.gov/38107488/)

DOI: [10.21037/gs-23-232](https://doi.org/10.21037/gs-23-232)

PMCID: PMC10721563

Magic Pen?-An Innovative Adjunct for Intraoperative Identification of Parathyroid Glands.

JAMA Surg, 158(10):1059-60.

M. B. Mulder and Q. Y. Duh. 2023.

PubMed-ID: [37531121](https://pubmed.ncbi.nlm.nih.gov/37531121/)

DOI: [10.1001/jamasurg.2023.3257](https://doi.org/10.1001/jamasurg.2023.3257)

A contemporary analysis of the pre- and intraoperative recognition of multigland parathyroid disease.

Langenbecks Arch Surg, 408(1):389.

E. Lawrence, G. Johri, R. Dave, R. Li and A. Gandhi. 2023.

BACKGROUND: Despite advances in biochemical and radiological identification of parathyroid gland enlargement, primary hyperparathyroidism (PHPT) due to sporadic multigland parathyroid disease (MGPD) remains a perioperative diagnostic dilemma. Failure to recognise MGPD pre- or intraoperatively may negatively impact surgical cure rates and result in persistent PHPT and ongoing patient morbidity. METHODS: We have conducted a comprehensive review of published literature in attempt to determine factors that could aid in reliably diagnosing sporadic MGPD pre- or intraoperatively. We discuss preoperative clinical features and examine pre- and intraoperative biochemical and imaging findings concentrating on those areas that give practicing surgeons and the wider multi-disciplinary endocrine team indications that a patient has MGPD. This could alter surgical strategy. CONCLUSION: Biochemistry can provide diagnosis of PHPT but cannot reliably discriminate parathyroid pathology. Histopathology can aid diagnosis between MGPD and adenoma, but histological appearance can overlap. Multiple negative imaging modalities indicate that MGPD may be more likely than a single parathyroid adenoma, but the gold standard for diagnosis is still intraoperative identification during BNE. MGPD remains a difficult disease to both diagnose and treat.

PubMed-ID: [37806985](https://pubmed.ncbi.nlm.nih.gov/37806985/)

DOI: [10.1007/s00423-023-03087-w](https://doi.org/10.1007/s00423-023-03087-w)

PMCID: PMC10560634

Diagnostic utility of (11) C-methionine PET/CT in primary hyperparathyroidism in a UK cohort: A single-centre experience and literature review.

Clin Endocrinol (Oxf), 99(3):233-45.

K. A. Huynh, J. MacFarlane, C. Newman, D. Gillett, T. Das, D. Scoffings, H. K. Chew, P. Moyle, O. Koulouri, I. Harper, L. Aloj, I. A. Mendichovszky, D. Inchiappa, H. N. Buch, T. T. Chung, H. L. Simpson, A. S. Powlson, B. G. Challis, W. A. Bashari, V. J. Stokes, L. Masterson, P. Jani, B. Fish, M. Gurnell and R. T. Casey. 2023.

OBJECTIVE: Primary hyperparathyroidism is a common endocrine disorder, with 80% of all cases usually caused by one single hyperfunctioning parathyroid adenoma. Conventional imaging modalities for the diagnostic work-up of primary hyperparathyroidism (PHPT) include ultrasound of the neck, 99mTc-sestamibi scintigraphy, and four-dimensional computed tomography (4D-CT). However, the role of other imaging modalities, such as 11C-methionine PET/CT, in the care pathway for PHPT is currently unclear. Here, we report our experience of the diagnostic utility of 11C-methionine PET/CT in a single-center patient cohort (n = 45). **DESIGN:** Retrospective single-center cohort study. **PATIENTS AND MEASUREMENTS:** The data of eligible patients that underwent 11C-methionine PET/CT between 2014 and 2022 at Addenbrooke's Hospital (Cambridge, UK) were collected and analyzed. The clinical utility of imaging modalities was determined by comparing the imaging result with histopathological and biochemical outcomes following surgery. **RESULTS:** In patients with persistent primary hyperparathyroidism following previous surgery, 11C-methionine PET/CT identified a candidate lesion in 6 of 10 patients (60.0%), and histologically confirmed in 5 (50.0%). 11C-methionine PET/CT also correctly identified a parathyroid adenoma in 9 out of 12 patients (75.0%) that failed to be localized on other imaging modalities. 11C-methionine PET/CT had a sensitivity of 70.0% (95% CI 55.8 - 84.2%) for the detection of parathyroid adenomas. **CONCLUSIONS:** This study highlights a diagnostic role for 11C-methionine PET/CT in patients that have undergone unsuccessful prior surgery or have equivocal or negative prior imaging results, aiding localization and a targeted surgical approach.

PubMed-ID: [37272391](#)

DOI: [10.1111/cen.14933](#)

Parathyroidectomy and the Risk of Major Cerebrovascular and Cardiovascular Events in the Elderly.

Ann Surg, 278(6):1032-7.

R. R. C. Grant, B. E. Moroz, C. Nilubol, E. K. Cahoon, R. M. Pfeiffer and N. Nilubol. 2023.

OBJECTIVE: We aimed to determine the incidence of major cardiovascular and cerebrovascular events in elderly patients with primary hyperparathyroidism (pHPT) and the impact of parathyroidectomy. **SUMMARY BACKGROUND DATA:** pHPT is underdiagnosed and undertreated in the United States. It is associated with increased cardiovascular disease risk, but its association with cerebrovascular disease risk is not well-established. It is also unknown if parathyroidectomy reduces these risks. **METHODS:** The incidence of major cerebrovascular and cardiovascular events in 108,869 patients with pHPT diagnosed in the Medicare database between 2008 and 2018 and a matched comparison group of 1,088,690 Medicare subjects was prospectively evaluated. We estimated hazard ratios (HR) for the association of pHPT and parathyroidectomy for the risk of these outcomes from Cox proportional hazards models. Survival curves were calculated to obtain 5-year disease-free survival estimates. **RESULTS:** For patients with pHPT, five-year disease-free survival was lower, and HRs were higher than the comparison group for any outcome (75.9% vs. 78.4%; HR 1.11, 95% confidence interval [CI] 1.09-1.13), major cerebrovascular events (84.5% vs. 86.3%; HR 1.14, 95% CI 1.12-1.17), and major cardiovascular events (87.7% vs. 88.8%; HR 1.06, 95% CI 1.03-1.08). However, in patients who had parathyroidectomy, the risks of major cerebrovascular and cardiovascular events did not differ from the comparison cohort. The lower risk in patients who had parathyroidectomy was maintained in subgroup analyses. **CONCLUSIONS:** Older patients with pHPT have an increased risk of major cerebrovascular and cardiovascular events compared with patients without the disease. Physicians treating older patients with primary hyperparathyroidism should consider parathyroidectomy. R.M.P. and N.N. contributed equally to the preparation of this manuscript.

PubMed-ID: [37450696](#)

DOI: [10.1097/SLA.0000000000005999](#)

PMCID: PMC10792119

Prevalence and risk factors for secondary hyperparathyroidism (SHPT) in patients undergoing bariatric surgery.

Surg Endosc, 37(10):8019-28.

L. E. Fischer, F. Moreno-Garcia, R. Tran, A. Harmon, C. Little, G. Domingue, K. Stewart, F. Mier Giraud and R. Thakral. 2023.

INTRODUCTION: Secondary hyperparathyroidism (SHPT) after bariatric surgery has significant adverse implications for bone metabolism, increasing the risk for osteoporosis and fracture. Our aim was to characterize prevalence and identify risk factors for SHPT in bariatric surgery patients. **METHODS:** We performed a single-institution, retrospective chart review

of patients who underwent bariatric surgery from June 2017 through December 2021. Demographic and clinical data were collected, including serum parathyroid hormone, calcium, and vitamin D3 at enrollment and 3, 6, and 12-months postoperatively. Chi-square or Fisher's exact tests were used to analyze categorical data and Mann-Whitney U test for continuous data. Multivariable analysis using binomial logistic regression assessed risk factors for SHPT. P-values ≤ 0.05 were considered significant. RESULTS: 350 patients were analyzed. SHPT prevalence at any time point was 72.9%. 65.8% had SHPT at enrollment; 45.9% resolved with intensive vitamin supplementation; and 19.7% had recurrent SHPT. New-onset SHPT occurred in 8.6%. Persistent SHPT was present in 42.4% at 1-year. Baseline SHPT correlated with black race and T2DM. SHPT at any time point correlated with T2DM and higher baseline BMI. 1-year SHPT correlated with RYGB, depression, and longer time in program. SHPT was not correlated with %TBWL at any time point. In patients with SHPT, vitamin D3 deficiency prevalence was significantly higher at baseline (77.0%) compared to all post-bariatric time points (16.7%, 17.3%, and 23.1%; $P < 0.0001$). CONCLUSIONS: SHPT is highly prevalent in patients with obesity seeking weight loss surgery. 42% had persistent SHPT at 1-year despite appropriate vitamin supplementation. Current vitamin D3 and calcium supplementation protocols may not effectively prevent SHPT in many post-bariatric patients. Low prevalence of concomitant vitamin D3 deficiency with SHPT after bariatric surgery suggests that there may be alternative mechanisms in this population. Further studies are needed to develop effective treatment strategies to mitigate the adverse effects of bariatric surgery on bone metabolism.

PubMed-ID: [37464065](#)

DOI: [10.1007/s00464-023-10218-3](#)

The Influence of Hyperparathyroidism Patient Profile on Quality of Life After Parathyroidectomy.

World J Surg, 47(9):2197-205.

B. Febrero, J. J. Ruiz-Manzanera, I. Ros-Madrid, A. M. Hernandez-Martinez and J. M. Rodriguez. 2023.

BACKGROUND: Improvements in quality of life (QoL) after parathyroidectomy in patients with primary hyperparathyroidism (PHPT) is discussed. It has not been analyzed whether these improvements can be influenced by a specific socio-personal or clinical patient profile. OBJECTIVES: to analyze QoL differences after parathyroidectomy and to determine a socio-personal and clinical profile that influences improvement after parathyroidectomy. METHODS: A longitudinal prospective cohort study in patients with PHPT. SF-36 and PHPQOL questionnaires were completed by the patients. A comparative preoperative analysis was carried out, at three and twelve months after surgery. Student's t test was used for the correlations. The size of the effect was assessed using G*Power software. A multivariate analysis was performed to evaluate the socio-personal and clinical variables affecting the improvement in QoL after surgery. RESULTS: Forty-eight patients were analyzed. Three months after surgery an improvement was found in physical function, general health, vitality, social function, emotional role, mental health and in the patient's declared health assessment. One year after the intervention a general improvement was observed, with a greater effect on mental health and declared health evolution. Patients with bone pain presented with a higher probability of improvement after surgery. Patients with prior psychological disease had a lower associated probability of an improvement and high levels of PTH related to a greater probability of improvement after surgery. CONCLUSIONS: There is an improvement in the QoL of PHPT patients after parathyroidectomy. Patients with bone pain and high PTH levels prior to the parathyroidectomy present with a greater probability of having a greater improvement in QoL after surgery.

PubMed-ID: [37210692](#)

DOI: [10.1007/s00268-023-07066-6](#)

New Perspective on the Genetic Dissection Underlying the Development of Parathyroid Cancer.

J Clin Endocrinol Metab, 108(12):e1751-e2.

A. Falchetti. 2023.

PubMed-ID: [37149780](#)

DOI: [10.1210/clinem/dgad253](#)

PMCID: PMC10655506

The importance of hypophosphatemia in the clinical management of primary hyperparathyroidism.

J Endocrinol Invest, 46(9):1935-40.

H. Duger, H. Bostan, U. Gul, B. Ucan, S. Hepsen, D. Sakiz, P. Akhanli, E. Cakal and M. Kizilgul. 2023.

AIM: The levels of serum phosphorus (P) are low or low-normal in primary hyperparathyroidism (PHPT), and there is an inverse relationship between the levels of parathormone (PTH) and P. However, when considering the diagnostic and surgical indication criteria of PHPT, serum P levels are generally ignored. The aim of this study was to retrospectively evaluate the association of serum P levels with the clinical outcomes of PHPT. MATERIALS AND METHODS: A retrospective

evaluation was made of the data of 424 consecutive patients (370 females, 54 males) with PHPT who presented at our centre. RESULTS: The mean age of the study population was 57 +/- 11.68 years. The mean P was 2.57 +/- 0.53 mg/dl. Asymptomatic disease was determined in 199 (47%) patients. Male patients had significantly lower levels of P. Symptomatic patients and patients with renal stones, vitamin D < 20 microg/l, calcium level >= 11.2 mg/dl, 24 h urinary calcium > 400 mg/day, or hypomagnesemia, were seen to have significantly lower levels of P (p < 0.05). Hypophosphatemia (hypoP) was found in 202 of 424 patients (47%), and these patients had a higher rate of symptomatic disease (63% to 44%, p < .0001). Of the 61 (88%) patients with moderate hypoP, 54 (88%) had at least one of the surgical criteria. A statistically significant increase in the incidence of hypoP was determined in symptomatic and male patients. In the patients with hypoP, serum PTH and urine calcium levels were found to be higher, and lumbar T-scores and serum vitamin D levels were lower. The patients with hypoP had higher rates of renal stones and osteoporosis (p < 0.05). CONCLUSIONS: The current study results show that hypoP is associated with a higher risk of osteoporosis and renal stones in PHPT patients. Even if patients are asymptomatic, moderate hypoP may be associated with poor outcomes of PHPT. Therefore, moderate hypoP may be a new criterion for parathyroidectomy, regardless of hypercalcemia level.

PubMed-ID: [36929458](#)

DOI: [10.1007/s40618-023-02064-w](#)

Intraoperative Identification of Thyroid and Parathyroid Tissues During Human Endocrine Surgery Using the MasSpec Pen.

JAMA Surg, 158(10):1050-9.

R. J. DeHoog, M. E. King, M. F. Keating, J. Zhang, M. Sans, C. L. Feider, K. Y. Garza, A. Bensussan, A. Krieger, J. Q. Lin, S. Badal, E. Alore, C. Pirko, K. Brahmhatt, W. Yu, R. Grogan, L. S. Eberlin and J. Suliburk. 2023.

IMPORTANCE: Intraoperative identification of tissues through gross inspection during thyroid and parathyroid surgery is challenging yet essential for preserving healthy tissue and improving outcomes for patients. OBJECTIVE: To evaluate the performance and clinical applicability of the MasSpec Pen (MSPen) technology for discriminating thyroid, parathyroid, and lymph node tissues intraoperatively. DESIGN, SETTING, AND PARTICIPANTS: In this diagnostic/prognostic study, the MSPen was used to analyze 184 fresh-frozen thyroid, parathyroid, and lymph node tissues in the laboratory and translated to the operating room to enable in vivo and ex vivo tissue analysis by endocrine surgeons in 102 patients undergoing thyroidectomy and parathyroidectomy procedures. This diagnostic study was conducted between August 2017 and March 2020. Fresh-frozen tissues were analyzed in a laboratory. Clinical analyses occurred in an operating room at an academic medical center. Of the analyses performed on 184 fresh-frozen tissues, 131 were included based on sufficient signal and postanalysis pathologic diagnosis. From clinical tests, 102 patients undergoing surgery were included. A total of 1015 intraoperative analyses were performed, with 269 analyses subject to statistical classification. Statistical classifiers for discriminating thyroid, parathyroid, and lymph node tissues were generated using training sets comprising both laboratory and intraoperative data and evaluated on an independent test set of intraoperative data. Data were analyzed from July to December 2022. MAIN OUTCOMES AND MEASURES: Accuracy for each tissue type was measured for classification models discriminating thyroid, parathyroid, and lymph node tissues using MSPen data compared to gross analysis and final pathology results. RESULTS: Of the 102 patients in the intraoperative study, 80 were female (78%) and the median (IQR) age was 52 (42-66) years. For discriminating thyroid and parathyroid tissues, an overall accuracy, defined as agreement with pathology, of 92.4% (95% CI, 87.7-95.4) was achieved using MSPen data, with 82.6% (95% CI, 76.5-87.4) accuracy achieved for the independent test set. For distinguishing thyroid from lymph node and parathyroid from lymph node, overall training set accuracies of 97.5% (95% CI, 92.8-99.1) and 96.1% (95% CI, 91.2-98.3), respectively, were achieved. CONCLUSIONS AND RELEVANCE: In this study, the MSPen showed high performance for discriminating thyroid, parathyroid, and lymph node tissues intraoperatively, suggesting this technology may be useful for providing near real-time feedback on tissue type to aid in surgical decision-making.

PubMed-ID: [37531134](#)

DOI: [10.1001/jamasurg.2023.3229](#)

PMCID: PMC10398548

Neck Reoperation for Recurrent or Persistent Renal Hyperparathyroidism.

World J Surg, 47(11):2784-91.

L. C. Chang, S. I. Liu and T. J. Liang. 2023.

BACKGROUND: Patients with renal hyperparathyroidism undergoing parathyroidectomy may experience relapse. Reoperation for persistent or recurrent disease, particularly in the neck region, is challenging and has a high complication rate because of difficult exploration. We aimed to evaluate the effectiveness of neck reoperation in renal hyperparathyroidism. METHODS: Patients with recurrent or persistent renal hyperparathyroidism who underwent neck

reoperation between January 2015 and August 2022 were investigated, focusing on operative findings, perioperative biochemical changes, and significance of intraoperative parathyroid hormone (PTH) measurements. RESULTS: During reoperation, 35 parathyroid glands were identified and removed from the 26 enrolled patients, with one, two, and three glands retrieved from 19 (73.2%), five (19.2%), and two (7.6%) patients, respectively. Most removed glands (68.6%) were located in the lower neck, followed by the mediastinum, carotid sheath, and upper neck. Successful resection, defined as a postoperative PTH level of <300 pg/mL, was achieved in 21 patients (80.8%). The remaining four (15.4%) and one (3.9%) patients were classified as having persistent and recurrent disease, respectively. The extent of PTH reduction was correlated with specimen weight, specimen volume, and preoperative alkaline phosphatase (ALP) level. The mean intraoperative PTH ratio (10 min after excision/pre-excision) was 0.23, and all patients with persistent or recurrent disease had a PTH ratio >0.3. Severe hypocalcemia (<7.5 mg/dL) occurred in 19 (73.0%) patients after reoperation. CONCLUSIONS: Neck reoperation is an effective therapeutic option in patients with recurrent or persistent renal hyperparathyroidism. A decrease in PTH level by >70% during reoperation (PTH ratio <0.3) predicts successful resection.

PubMed-ID: [37714965](#)

DOI: [10.1007/s00268-023-07172-5](#)

Identifying Parathyroids in Pediatric Thyroid/Parathyroid Surgery by Near Infrared Autofluorescence.

Laryngoscope, 133(11):3208-15.

R. H. Belcher, G. Thomas, P. A. Willmon, J. N. Gallant, N. Baregamian, M. E. Lopez, C. C. Solomicronrzano and A. Mahadevan-Jansen. 2023.

OBJECTIVES: Compared to adult patients undergoing thyroid surgery, pediatric patients have higher rates of hypoparathyroidism often related to parathyroid gland (PG) inadvertent injury or devascularization. Previous studies have shown that near-infrared-autofluorescence (NIRAF) can be reliably used intraoperatively for label-free parathyroid identification, but all prior studies have been performed in adult patients. In this study, we assess the utility and accuracy of NIRAF with a fiber-optic probe-based system to identify PGs in pediatric patients undergoing thyroidectomy or parathyroidectomy. METHODS: All pediatric patients (under 18 years of age) undergoing thyroidectomy or parathyroidectomy were enrolled in this IRB-approved study. The surgeon's visual assessment of tissues was first noted and the surgeon's confidence level in the tissue identified was recorded. A fiber-optic probe was then used to illuminate tissues-of-interest with a wavelength of 785 nm and resulting NIRAF intensities from these tissues were measured while the surgeon was blinded to results. RESULTS: NIRAF intensities were measured intraoperatively in 19 pediatric patients. Normalized NIRAF intensities for PGs (3.63 +/- 2.47) were significantly higher than that of thyroid (0.99 +/- 0.36, $p < 0.001$) and other surrounding soft tissues (0.86 +/- 0.40, $p < 0.001$). Based on the PG identification ratio threshold of 1.2, NIRAF yielded a detection rate of 95.8% (46/48 pediatric PGs). CONCLUSION: Our findings indicate that NIRAF detection can potentially be a valuable and non-invasive technique to identify PGs during neck operations in the pediatric population. To our knowledge, this is the first study in children to assess the accuracy of probe-based NIRAF detection for intraoperative parathyroid identification. LEVEL OF EVIDENCE: Level 4 *Laryngoscope*, 133:3208-3215, 2023.

PubMed-ID: [36866696](#)

DOI: [10.1002/lary.30633](#)

PMCID: PMC10475145

Adrenals

Meta-Analyses

Adrenal Medullary Hyperplasia: A Systematic Review and Meta-analysis.

J Clin Endocrinol Metab, 108(9):e885-e92.

R. Ganni, D. J. Torpy, H. Falhammar and R. Louise Rushworth. 2023.

CONTEXT: Adrenal medullary hyperplasia (AMH) is a rare, incompletely described disorder of the adrenal medulla that is associated with catecholamine excess. OBJECTIVE: To increase knowledge about AMH by reviewing the reported cases of this disorder. DESIGN: Systematic review and meta-analysis of the genotype/phenotype relationship in all reported cases of AMH. SETTING: Literature review and analysis. PATIENTS OR OTHER PARTICIPANTS: All cases of AMH published to date. MAIN OUTCOME MEASURE(S): Characteristics of AMH cases and genotype-phenotype relationships. RESULTS: A total of 66 patients, median age of 48 years, were identified from 29 reports. More than one-half were male (n = 39, 59%). The majority had unilateral (73%, n = 48) disease; 71% (n = 47) were sporadic and 23% (n = 15) were associated with the MEN2. Most (91%, n = 60) displayed signs and symptoms of excess catecholamine secretion, particularly hypertension. Elevated catecholamine concentrations (86%, n = 57) and adrenal abnormalities on imaging were common (80%, n = 53). More than one-half (58%, n = 38) had concurrent tumors: pheochromocytoma (42%, n = 16/38); medullary thyroid cancer (24%, n = 9/38); and adrenocortical adenoma (29%, n = 11/38). Most (88%, n = 58) underwent adrenalectomy with 45/58 achieving symptom resolution. Adrenalectomy was less common in patients under 40 years and those with bilateral disease (both $P < .05$). CONCLUSION: AMH may be sporadic or associated with MEN2, most have catecholamine excess and imaging abnormalities. Unilateral involvement is more common. Most reported patients have been treated with adrenalectomy, which is usually curative with regard to catecholamine hypersecretion.

PubMed-ID: [36896586](#)

DOI: [10.1210/clinem/dgad121](#)

PMCID: PMC10438876

The Diagnostic Value of 18F-FDG PET/CT Scan in Characterizing Adrenal Tumors.

J Clin Endocrinol Metab, 108(9):2435-45.

M. Schaafsma, A. M. A. Berends, T. P. Links, A. H. Brouwers and M. N. Kerstens. 2023.

CONTEXT: Imaging plays an important role in the characterization of adrenal tumors, but findings might be inconclusive. The clinical question is whether 18F fluodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) is of diagnostic value in this setting. OBJECTIVE: This meta-analysis was aimed at the diagnostic value of 18F-FDG PET/CT in differentiating benign from malignant adrenal tumors discovered either as adrenal incidentaloma or during staging or follow-up of oncologic patients. DATA SOURCES: PubMed, EMBASE, Web of Science, and Cochrane Library were searched to select articles between 2000 and 2021. STUDY SELECTION: We included studies describing the diagnostic value of 18F-FDG PET/CT in adult patients with an adrenal tumor. Exclusion criteria were 10 or fewer participants, insufficient data on histopathology, clinical follow-up, or PET results. After screening of title and abstract by 2 independent reviewers, 79 studies were retrieved, of which 17 studies met the selection criteria. DATA EXTRACTION: Data extraction using a protocol and quality assessment according to QUADAS-2 was performed independently by at least 2 authors. DATA SYNTHESIS: A bivariate random-effects model was applied using R (version 3.6.2.). Pooled sensitivity and specificity of 18F-FDG PET/CT for identifying malignant adrenal tumors was 87.3% (95% CI, 82.5%-90.9%) and 84.7% (95% CI, 79.3%-88.9%), respectively. The pooled diagnostic odds ratio was 9.20 (95% CI, 5.27-16.08; $P < .01$). Major sources of heterogeneity (I², 57.1% [95% CI, 27.5%-74.6%]) were in population characteristics, reference standard, and interpretation criteria of imaging results. CONCLUSIONS: 18F-FDG PET/CT had good diagnostic accuracy for characterization of adrenal tumors. The literature, however, is limited, in particular regarding adrenal incidentalomas. Large prospective studies in well-defined patient populations with application of validated cutoff values are needed.

PubMed-ID: [36948598](#)

DOI: [10.1210/clinem/dgad138](#)

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Corticotropin-releasing hormone test predicts the outcome of unilateral adrenalectomy in primary bilateral macronodular adrenal hyperplasia.

J Endocrinol Invest, 47(3):749-56.

I. Tizianel, M. Detomas, T. Deutschbein, M. Fassnacht, N. Albiger, M. Iacobone, C. Scaroni and F. Ceccato. 2024.
PURPOSE: Primary bilateral adrenal hyperplasia (PBMAH) is associated with hypercortisolism and a heterogeneous clinical expression in terms of cortisol secretion and related comorbidities. Historically, treatment of choice was bilateral adrenalectomy (B-Adx); however, recent data suggest that unilateral adrenalectomy (U-Adx) may be an effective alternative. For the latter, factors predicting the postsurgical outcome (e.g., biochemical control) have not been identified yet. METHODS: PBMAH patients undergoing U-Adx for overt Cushing's syndrome (CS) in two tertiary care centers were retrospectively analysed. Remission was defined as a normalization of urinary free cortisol (UFC) without the need for medical treatment. The potential of hCRH test as a predictor of U-Adx outcome was evaluated in a subgroup. RESULTS: 23 patients were evaluated (69% females, mean age 55 years). Remission rate after U-Adx was 74% at last follow up (median 115 months from UAdx). Before U-Adx, a positive ACTH response to hCRH (Delta%ACTH increase > 50% from baseline) was associated with higher remission rates. CONCLUSIONS: Three of four patients with PBMAH are surgically cured with U-Adx. Pre-operative hCRH testing can be useful to predict long-term remission rates.

PubMed-ID: [37796369](#)

DOI: [10.1007/s40618-023-02204-2](#)

PMCID: PMC10904413

New Findings on Presentation and Outcome of Patients With Adrenocortical Cancer: Results From a National Cohort Study.

J Clin Endocrinol Metab, 108(10):2517-25.

S. Puglisi, A. Calabrese, F. Ferrau, M. A. Violi, M. Lagana, S. Grisanti, F. Ceccato, C. Scaroni, G. Di Dalmazi, A. Stigliano, B. Altieri, L. Canu, P. Loli, R. Pivonello, E. Arvat, V. Morelli, P. Perotti, V. Basile, P. Berchialla, S. Urru, C. Fiori, F. Porpiglia, A. Berruti, A. Pia, G. Reimondo, S. Cannavo and M. Terzolo. 2023.

CONTEXT: Because of the rarity of adrenocortical cancer (ACC), only a few population-based studies are available, and they reported limited details in the characterization of patients and their treatment. OBJECTIVE: To describe in a nationwide cohort the presentation of patients with ACC, treatment strategies, and potential prognostic factors. METHODS: Retrospective analysis of 512 patients with ACC, diagnosed in 12 referral centers in Italy from January 1990 to June 2018. RESULTS: ACC diagnosed as incidentalomas accounted for overall 38.1% of cases, with a frequency that increases with age and with less aggressive pathological features than symptomatic tumors. Women (60.2%) were younger than men and had smaller tumors, which more frequently secreted hormones. Surgery was mainly done with an open approach (72%), and after surgical resection, 62.7% of patients started adjuvant mitotane therapy. Recurrence after tumor resection occurred in 56.2% of patients. In patients with localized disease, cortisol secretion, ENSAT stage III, Ki67%, and Weiss score were associated with an increased risk of recurrence, whereas margin-free resection, open surgery, and adjuvant mitotane treatment were associated with reduced risk. Death occurred in 38.1% of patients and recurrence-free survival (RFS) predicted overall survival (OS). In localized disease, age, cortisol secretion, Ki67%, ENSAT stage III, and recurrence were associated with increased risk of mortality. ACCs presenting as adrenal incidentalomas showed prolonged RFS and OS. CONCLUSION: Our study shows that ACC is a sex-related disease and demonstrates that an incidental presentation is associated with a better outcome. Given the correlation between RFS and OS, RFS may be used as a surrogate endpoint in clinical studies.

PubMed-ID: [37022947](#)

DOI: [10.1210/clinem/dgad199](#)

The Utility of Salivary Cortisone in the Overnight Dexamethasone Suppression Test in Adrenal Incidentalomas.

J Clin Endocrinol Metab, 108(10):e937-e43.

B. G. Issa, F. W. F. Hanna, A. A. Fryer, G. Ensah, I. Ebere, D. Marshall and B. Keevil. 2023.

CONTEXT: Guidelines recommend the assessment of cortisol secretion in patients with adrenal incidentalomas (AI) using the overnight dexamethasone suppression test (ONDST). This requires attendance at a health care facility and venepuncture. Alternatively, the ONDST can be done by measuring salivary cortisol and cortisone, which can be collected at home. OBJECTIVE: We aimed to assess the utility of these measurements in patients with AI. METHODS: A retrospective analysis of data from 173 patients with AI who underwent an ONDST and salivary cortisol/cortisone diurnal studies. Serum and salivary cortisol and salivary cortisone were collected at 09:00, late night, and at 09:00 the following morning after dexamethasone. Dexamethasone levels were measured in the postdexamethasone samples. Serum and salivary samples were analyzed with liquid chromatography-tandem mass spectrometry. RESULTS: We identified a strong correlation between salivary cortisone and serum cortisol after 1 mg of dexamethasone ($r = 0.95$). Stepwise multivariate regression showed that postdexamethasone salivary cortisone, baseline serum cortisol, salivary cortisone suppression (predexamethasone/postdexamethasone ratio), and sex were the only significant or near-significant independent variables. Performance of predictive indices using these 4 parameters (sensitivity = 88.5%, specificity = 91.2%; kappa 0.80) and postdexamethasone salivary cortisone alone (sensitivity = 85.3%, specificity = 91.7%; kappa 0.77) were comparable when used to predict an ONDST serum cortisol of ≤ 50 nmol/L. No correlation was observed with any of the other measured parameters. CONCLUSION: In AI patients, after dexamethasone, salivary cortisone correlates very strongly with serum cortisol in the ONDST and could therefore be used as an alternative sampling method which does not require venepuncture or attendance at hospital.

PubMed-ID: [37155577](#)

DOI: [10.1210/clinem/dgad242](#)

Same day discharge after minimally invasive adrenalectomy: a national study.

Surg Endosc, 37(11):8316-25.

L. E. Hendrick, A. M. Fleming, P. V. Dickson and O. M. DeLozier. 2023.

BACKGROUND: Same day discharge (SDD) may be considered in some patients undergoing minimally invasive adrenalectomy (MIA). Recent studies have demonstrated similar outcomes between SDD and admitted patients; however, most excluded pheochromocytoma and adrenal metastases. This study evaluates 30-day complications and hospital readmission in a large cohort of patients undergoing MIA. METHODS: Adult patients undergoing MIA (2010-2020) for benign adrenal disorders, pheochromocytoma, and adrenal metastases were identified within the ACS-NSQIP database. Comparisons between patients having SDD versus admission were performed. Factors associated with 30-day complications and unplanned readmission were evaluated by multivariable regression modeling. RESULTS: Of 7316 patients who underwent MIA, 254 had SDD. Baseline characteristics were similar between groups, although SDD patients had lower ASA class ($p < 0.001$) and were more likely to undergo MIA for nonfunctioning adenoma or primary aldosteronism ($p = 0.001$). After adjusting for covariates, higher ASA class and presence of medical comorbidities were associated with increased complications ($p < 0.001$; $p < 0.05$) and unplanned readmission ($p < 0.001$; $p < 0.05$). Additionally, prolonged operative time was associated with 30-day complications ($p < 0.001$). Notably, SDD was not associated with increased complications (OR 0.78, 95% CI 0.38-1.61, $p = 0.502$) or unplanned readmission (OR 0.76, 95% CI 0.35-1.64, $p = 0.490$). The rate of SDD for MIA increased from 1.48% in 2017 to 10.81% in 2020. CONCLUSIONS: Not all patients undergoing MIA should have SDD; however, the current analysis demonstrates a trend toward SDD and supports its safety in select patients with adrenal metastases and benign adrenal disorders including pheochromocytoma.

PubMed-ID: [37679582](#)

DOI: [10.1007/s00464-023-10355-9](#)

Adrenal Venous Sampling and Primary Aldosteronism: in Search of the Perfect Denominator.

J Clin Endocrinol Metab, 108(12):e1745-e6.

M. A. Grytaas and K. Lovas. 2023.

PubMed-ID: [37235779](#)

DOI: [10.1210/clinem/dgad296](#)

Thirty day postoperative outcomes following laparoscopic adrenalectomy for functional adrenal tumors.

Surg Endosc, 37(10):7893-900.

R. R. Gao, N. Chilukuri, P. Rokhlin and S. Shebrain. 2023.

BACKGROUND: Functional adrenal tumors (FATs) are rare and if left untreated, there is a substantial risk of morbidity and mortality due to uncontrolled excess hormone secretion. The three most common FATs are cortisone-producing tumors (hypercortisolism), aldosterone-producing tumors (hyperaldosteronism), and catecholamines-producing tumors (pheochromocytomas). The study aims to evaluate demographic characteristics and 30-day outcomes after laparoscopic adrenalectomy of FATs. **METHODS:** Patients who underwent laparoscopic adrenalectomy for FATs were selected from the ACS-NSQIP database (2015-2017), and divided into three groups (hyperaldosteronism, hypercortisolism, and pheochromocytoma). Preoperative demographics, medical comorbidities, and 30-day postoperative outcomes among the three groups were analyzed using the chi-squared test, analysis of variance (ANOVA) and Kruskal-Wallis one-way analysis of variance. Multivariable logistic regression was performed to assess the effects independent variables on the likelihood of increased overall morbidity. **RESULTS:** Of a total of 2410 patients who underwent laparoscopic adrenalectomy, 345 (14.3%) patients with FATs were included. Patients in the hypercortisolism group were younger, had higher proportion of females, had higher BMI, had a higher proportion of White ethnicity and had a higher proportion of diabetes. The hyperaldosteronism group had a higher proportion of Black ethnicity and a higher proportion of hypertension (HTN) requiring medication. Thirty day postoperative outcomes showed that the pheochromocytoma group had a higher rate of serious morbidity, overall morbidity, and highest readmission rates. There were three deaths, 1 in the pheochromocytoma and 2 in the hypercortisolism groups. Operative time (in minutes) was longer in the hypercortisolism group. Median length of stay was higher in hypercortisolism (2 days) and pheochromocytoma (1.5 day) groups. **CONCLUSION:** Functional adrenal tumors show distinct variations in patient demographics and postoperative outcomes. It is essential to use this information during the preoperative period to optimize patients prior to intervention and counsel patients about potential postoperative outcomes.

PubMed-ID: [37415017](https://pubmed.ncbi.nlm.nih.gov/37415017/)

DOI: [10.1007/s00464-023-10255-y](https://doi.org/10.1007/s00464-023-10255-y)

Risk factors for intraoperative complications, postoperative complications, and prolonged length of stay after laparoscopic adrenalectomy by transperitoneal lateral approach: a retrospective cohort study of 547 procedures.

Surg Endosc, 37(10):7573-81.

D. Fouche, G. Chenais, M. Haissaguerre, D. Bouriez, C. Gronnier, D. Collet, A. Tabarin and H. Najah. 2023.

BACKGROUND: Laparoscopic adrenalectomy (LA) is the gold standard for the resection of most adrenal lesions. A precise delineation of factors influencing its outcomes is lacking. The aim of this study was to assess factors associated with intraoperative complications, postoperative complications, and prolonged length of stay (LOS) after LA. **METHODS:** Patients who underwent LA from 1999 to 2021 in a single-academic-institution were included. Patient and disease-specific data, intraoperative complications, postoperative complications according to Dindo-Clavien (DC) scale, and LOS were recorded. Predictive factors of complications and prolonged LOS were determined by logistic regression. **RESULTS:** We identified 530 patients who underwent 547 LA. Intraoperative complications occurred in 33 patients (6.0%). Postoperative complications \geq DC grade 2 occurred in 73 patients (13.35%); severe postoperative complications \geq DC grade 3 in 14 patients (2.56%). Postoperative complications were positively associated with age \geq 72 (OR 1.14 [95% CI 1.02-1.29]), intraoperative complications (OR 1.36 [95% CI 1.14-1.63]), and negatively associated with non functional adenomas (OR 0.88 [95% CI 0.7-0.99]), and right adrenalectomy (OR 0.91 [95% CI 0.86-0.97]). Severe postoperative complications were positively associated with chronic obstructive pulmonary disease (COPD, OR 1.08 [95% CI 1.00-1.17]), and negatively associated with right adrenalectomy (OR 0.97 [95% CI 0.92-0.99]). Prolonged LOS was associated with age \geq 72 (OR 1.21 [95% CI 1.05-1.41]), and COPD (OR 1.20 [95% CI 1.01-1.44]). **CONCLUSIONS:** LA remains safe when performed by surgeons with expertise. Right adrenalectomy resulted in less postoperative overall and severe complications. The risk-benefit equation should be carefully assessed before left LA in older patients with COPD.

PubMed-ID: [37442834](https://pubmed.ncbi.nlm.nih.gov/37442834/)

DOI: [10.1007/s00464-023-10148-0](https://doi.org/10.1007/s00464-023-10148-0)

Retroperitoneoscopic adrenalectomy may be superior to laparoscopic transperitoneal adrenalectomy in terms of costs and profit: a retrospective pair-matched cohort analysis.

Surg Endosc, 37(10):8104-15.

A. Fischer, O. Schoffski, A. Niessen, A. Hamm, E. A. Langan, M. W. Buchler and F. Billmann. 2023.

BACKGROUND: A direct comparison of the cost-benefit analysis of retroperitoneoscopic adrenalectomy (RPA) versus the minimally invasive transperitoneal access (LTA) approach is currently lacking. We hypothesized that RPA is more cost

effective than LTA; promising significant savings for the healthcare system in an era of ever more limited resources. METHODS: We performed a monocentric retrospective observational cohort study based on data from our Endocrine Surgery Registry. Patients who were operated upon between 2019 and 2022 were included. After pair-matching, both cohorts (RPA vs. LTA) were compared for perioperative variables and treatment costs (process cost calculation), revenue and profit. RESULTS: Two homogenous cohorts of 43 patients each (RPA vs. LTA) were identified following matching. Patient characteristics between the cohorts were comparable. In terms of both treatment-associated costs and profit, the RPA procedure was superior to LTA (costs: US\$5789.99 for RPA vs. US\$6617.75 for LTA, $P = 0.043$; profit: US\$1235.59 for RPA vs. US\$653.33 for LTA, $P = 0.027$). The duration of inpatient treatment and comorbidities significantly influenced the cost of treatment and the overall profit. CONCLUSIONS: RPA appears not only to offer benefits over LTA in terms of perioperative morbidity and length of hospital stay, but also has a superior financial cost/benefit profile.

PubMed-ID: [37658201](#)

DOI: [10.1007/s00464-023-10395-1](#)

PMCID: PMC10519868

Metastatic Pheochromocytoma and Paraganglioma: Somatostatin Receptor 2 Expression, Genetics, and Therapeutic Responses.

J Clin Endocrinol Metab, 108(10):2676-85.

A. Fischer, S. Kloos, U. Maccio, J. Friemel, H. Remde, M. Fassnacht, C. Pamporaki, G. Eisenhofer, H. Timmers, M. Robledo, S. M. J. Fliedner, K. Wang, J. Maurer, A. Reul, K. Zitzmann, N. Bechmann, G. Zygiene, S. Richter, C. Hantel, D. Vetter, K. Lehmann, H. Mohr, N. S. Pellegata, M. Ullrich, J. Pietzsch, C. G. Ziegler, S. R. Bornstein, M. Kroiss, M. Reincke, K. Pacak, A. B. Grossman, F. Beuschlein and S. Nolting. 2023.

CONTEXT: Pheochromocytomas and paragangliomas (PPGLs) with pathogenic mutations in the succinate dehydrogenase subunit B (SDHB) are associated with a high metastatic risk. Somatostatin receptor 2 (SSTR2)-dependent imaging is the most sensitive imaging modality for SDHB-related PPGLs, suggesting that SSTR2 expression is a significant cell surface therapeutic biomarker of such tumors. OBJECTIVE: Exploration of the relationship between SSTR2 immunoreactivity and SDHB immunoreactivity, mutational status, and clinical behavior of PPGLs. Evaluation of SSTR-based therapies in metastatic PPGLs. METHODS: Retrospective analysis of a multicenter cohort of PPGLs at 6 specialized Endocrine Tumor Centers in Germany, The Netherlands, and Switzerland. Patients with PPGLs participating in the ENSAT registry were included. Clinical data were extracted from medical records, and immunohistochemistry (IHC) for SDHB and SSTR2 was performed in patients with available tumor tissue. Immunoreactivity of SSTR2 was investigated using Volante scores. The main outcome measure was the association of SSTR2 IHC positivity with genetic and clinical-pathological features of PPGLs. RESULTS: Of 202 patients with PPGLs, 50% were SSTR2 positive. SSTR2 positivity was significantly associated with SDHB- and SDHx-related PPGLs, with the strongest SSTR2 staining intensity in SDHB-related PPGLs ($P = .01$). Moreover, SSTR2 expression was significantly associated with metastatic disease independent of SDHB/SDHx mutation status ($P < .001$). In metastatic PPGLs, the disease control rate with first-line SSTR-based radionuclide therapy was 67% ($n = 22$, $n = 11$ SDHx), and with first-line "cold" somatostatin analogs 100% ($n = 6$, $n = 3$ SDHx). CONCLUSION: SSTR2 expression was independently associated with SDHB/SDHx mutations and metastatic disease. We confirm a high disease control rate of somatostatin receptor-based therapies in metastatic PPGLs.

PubMed-ID: [36946182](#)

DOI: [10.1210/clinem/dgad166](#)

PMCID: PMC10505550

Prevalence of Cortisol Cosecretion in Patients With Primary Aldosteronism: Role of Metanephrine in Adrenal Vein Sampling.

J Clin Endocrinol Metab, 108(9):e720-e5.

F. Buffolo, J. Pieroni, F. Ponzetto, V. Forestiero, D. Rossato, P. Fonio, A. Nonnato, F. Settanni, P. Mulatero, G. Mengozzi and S. Monticone. 2023.

CONTEXT: Adrenal venous sampling (AVS) is the gold standard procedure for subtype diagnosis in patients with primary aldosteronism (PA). Cortisol is usually adopted for the normalization of aldosterone levels in peripheral and adrenal samples. However, asymmetrical cortisol secretion can potentially affect the lateralization index, leading to subtype misdiagnosis. OBJECTIVE: We aimed to assess the prevalence of asymmetrical cortisol secretion in patients undergoing AVS and whether variations in adrenal vein cortisol might influence AVS interpretations. We then evaluated the use of metanephrines for the normalization of aldosterone levels for lateralization index. METHODS: We retrospectively included 101 patients with PA who underwent AVS: 49 patients underwent unstimulated AVS, while 52 patients underwent both unstimulated and cosyntropin-stimulated AVS. Eighty-eight patients had bilateral successful AVS according to

metanephrine ratio. We assessed the prevalence of asymmetrical cortisol secretion through the cortisol to metanephrine (C/M) lateralization index (LI). We then evaluated whether the use of aldosterone to metanephrine (A/M) LI can improve the diagnostic accuracy of AVS compared with aldosterone to cortisol (A/C) LI. RESULTS: Asymmetrical cortisol secretion is present in 18% of patients with PA. Diagnosis with A/M LI and A/C LI is discordant in 14% of patients: 9% had a diagnosis of unilateral PA with A/M LI instead of bilateral PA with A/C LI and 5% had a diagnosis of bilateral PA with A/M LI instead of unilateral PA. CONCLUSION: The assessment of metanephrine levels in AVS is useful for the determination of selectivity and lateralization, allowing an accurate diagnosis, especially in patients with asymmetrical cortisol secretion.

PubMed-ID: [36974473](#)

DOI: [10.1210/clinem/dgad179](#)

Characterization of indocyanine green fluorescence imaging patterns of pheochromocytomas.

Surg Endosc, 37(11):8357-61.

B. Berber, G. Isiktas and V. D. Krishnamurthy. 2023.

BACKGROUND: Indocyanine green (ICG) fluorescence is a new intraoperative imaging modality for adrenal tumors. Previous work suggested that pheochromocytomas did not show fluorescence, but experience is limited. The objective of this study is to analyze fluorescence imaging patterns of pheochromocytomas. METHODS: This was an IRB-approved retrospective study. Patients who underwent adrenalectomy with ICG imaging were identified from a departmental database. Intraoperative fluorescence patterns were analyzed by reviewing surgical videos. Descriptive and comparative statistical analyses were performed to determine factors associated with different fluorescence patterns of pheochromocytomas. RESULTS: Of the 46 pheochromocytomas included, 50% (n = 23) exhibited fluorescence. Parameters predicting fluorescence on univariate analysis were age, tumor size and hereditary. On multivariate analysis, tumor size was the only predictive parameter of ICG fluorescence, with loss of fluorescence at a threshold of > 3.2 cm (p = 0.004). CONCLUSIONS: This is the largest cohort to date assessing fluorescence properties of pheochromocytomas. In contrast to previous studies, we demonstrated that smaller pheochromocytomas do exhibit fluorescence. This may support the application of intraoperative ICG imaging for smaller or bilateral pheochromocytomas, which may assist in identification and/or cortical-sparing during adrenalectomy.

PubMed-ID: [37700011](#)

DOI: [10.1007/s00464-023-10344-y](#)

NET

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for digestive neuroendocrine carcinoma.

J Neuroendocrinol, 35(3):e13249.

H. Sorbye, E. Grande, M. Pavel, M. Tesselaar, N. Fazio, N. S. Reed, U. Knigge, E. Christ, V. Ambrosini, A. Couvelard and E. Tiensuu Janson. 2023.

This ENETS guidance paper, developed by a multidisciplinary working group, provides up-to-date and practical advice on the diagnosis and management of digestive neuroendocrine carcinoma, based on recent developments and study results. These recommendations aim to pave the road for more standardized care for our patients resulting in improved outcomes. Prognosis is generally poor for digestive NEC, most are advanced at diagnosis and median survival in metastatic disease is 11-12 months. Surgery can be of benefit for localized disease after extensive preoperative imaging. Carboplatin in combination with etoposide is recommended as first-line treatment for metastatic disease. Irinotecan with fluoropyrimidines has the best evidence as second-line treatment. Immunotherapy plays a minor role in biomarker-unselected patients. Molecular profiling if available is encouraged to identify new targets. More prospective clinical trials are highly needed to fulfil the unmet needs in this field, especially on new predictive and prognostic biomarkers and to improve survival of patients with advanced disease.

PubMed-ID: [36924180](#)

DOI: [10.1111/jne.13249](#)

European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for colorectal neuroendocrine tumours.

J Neuroendocrinol, 35(6):e13309.

A. Rinke, V. Ambrosini, C. Dromain, R. Garcia-Carbonero, A. Haji, A. Koumariou, E. N. van Dijkum, D. O'Toole, G. Rindi, J. Y. Scoazec and J. Ramage. 2023.

This ENETS guidance paper, developed by a multidisciplinary working group, provides an update on the previous colorectal guidance paper in a different format. Guided by key clinical questions practical advice on the diagnosis and management of neuroendocrine tumours (NET) of the caecum, colon, and rectum is provided. Although covered in one guidance paper colorectal NET comprises a heterogeneous group of neoplasms. The most common rectal NET are often small G1 tumours that can be treated by adequate endoscopic resection techniques. Evidence from prospective clinical trials on the treatment of metastatic colorectal NET is limited and discussion of patients in experienced multidisciplinary tumour boards strongly recommended. Neuroendocrine carcinomas (NEC) and mixed neuroendocrine non-neuroendocrine neoplasms (MiNEN) are discussed in a separate guidance paper.

PubMed-ID: [37345509](#)

DOI: [10.1111/jne.13309](#)

European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for gastroduodenal neuroendocrine tumours (NETs) G1-G3.

J Neuroendocrinol, 35(8):e13306.

F. Panzuto, J. Ramage, D. M. Pritchard, M. F. van Velthuysen, J. Schrader, N. Begum, A. Sundin, M. Falconi and D. O'Toole. 2023.

The aim of the present guidance paper was to update the previous ENETS guidelines on well-differentiated gastric and duodenal neuroendocrine tumours (NETs), providing practical guidance for specialists in the diagnosis and management of

gastroduodenal NETs. Type II gastric NETs, neuroendocrine carcinomas (NECs), and functioning duodenal NETs are not covered, since they will be discussed in other ENETS guidance papers.

PubMed-ID: [37401795](#)

DOI: [10.1111/jne.13306](#)

European Neuroendocrine Tumor Society (ENETS) 2022 Guidance Paper for Carcinoid Syndrome and Carcinoid Heart Disease.

J Neuroendocrinol, 34(7):e13146.

S. Grozinsky-Glasberg, J. Davar, J. Hofland, R. Dobson, V. Prasad, A. Pascher, T. Denecke, M. E. T. Tesselaar, F. Panzuto, A. Albage, H. M. Connolly, J. F. Obadia, R. Riechelmann and C. Toumpanakis. 2022.

PubMed-ID: [35613326](#)

DOI: [10.1111/jne.13146](#)

PMCID: PMC9539661

Other Articles

Metastatic small-bowel neuroendocrine tumours: medical management of the primary.

Br J Surg, 110(10):1296-7.

P. Stalberg. 2023.

PubMed-ID: [37527436](#)

DOI: [10.1093/bjs/znad248](#)

Appendiceal neuroendocrine neoplasms and resection of the mesoappendix: a retrospective comparative study.

Langenbecks Arch Surg, 408(1):294.

A. Sarfarazi, M. Russell, G. Janssen and A. Taneja. 2023.

PURPOSE: Incidental appendiceal neoplasms are identified in approximately 1% of the specimens of suspected appendicitis. The current institutional policy is to perform en bloc mesoappendix resection during routine laparoscopic appendectomy allowing for staging, reducing the need for oncological right hemicolectomy (ORH). Herein, we review en bloc mesoappendectomy in clinical practice and its effects on the rate of ORH. **METHODS:** We reviewed all cases of appendectomy performed at the Auckland City Hospital between 1 May 2014 and 31 May 2019. Clinical notes and histopathological reports were reviewed. All neoplasms, surgical techniques and the need for further surgery were analysed. **RESULTS:** A total of 2455 appendectomies were performed with an approximately similar number of procedures between the sexes and an overall median age of 31 years. Overall, 86% (n = 2098) of the specimens included resection of the mesoappendix, and 58 (2.4%) appendiceal neoplasms were identified. Of them, 33 (1.3%) specimens included neuroendocrine appendiceal neoplasms. Eleven (33%) patients with appendiceal neuroendocrine neoplasms were recommended ORH. One of these patients may have avoided additional surgery, whereas 3 (9.1%) patients with tumours of 10-20 mm avoided ORH because their mesoappendix was resected. **CONCLUSION:** At our centre, there has been a significant change in the practice of mesoappendix resection, and we support resection of the mesoappendix during appendectomy. The procedure is technically straightforward and safe, incurs no increases in costs or time, allows for accurate tumour staging and guides decisions regarding further surgical interventions.

PubMed-ID: [37535180](#)

DOI: [10.1007/s00423-023-03019-8](#)

Metastatic small bowel neuroendocrine tumours: surgical management of the primary.

Br J Surg, 110(10):1293-5.

J. R. Howe. 2023.

PubMed-ID: [37566464](#)

DOI: [10.1093/bjs/znad247](#)

Detecting Somatic Mutations for Well-Differentiated Pancreatic Neuroendocrine Tumors in Endoscopic Ultrasound-Guided Fine Needle Aspiration with Next-Generation Sequencing.

Ann Surg Oncol, 30(12):7720-30.

E. M. Ghabi, J. R. Habib, S. Shoucair, A. A. Javed, J. Sham, W. R. Burns, J. L. Cameron, S. Z. Ali, E. J. Shin, P. G. Arcidiacono, C. Doglioni, M. Falconi, J. Yu, S. Partelli and J. He. 2023.

BACKGROUND: Pancreatic neuroendocrine tumors (PanNETs) exhibit heterogenous behavior, whereby some small tumors are aggressive with a propensity for metastasis. Detection of somatic mutations associated with aggressive biology may help with patient stratification and surgical decision-making in patients with well-differentiated PanNETs. Using next-generation sequencing (NGS), we investigated the feasibility of detecting somatic mutations in endoscopic ultrasound-guided, fine-needle aspiration (EUS-FNA) specimens and determining the mutational concordance between the EUS-FNA specimens and the primary tumors. **METHODS:** Thirty-eight patients with well-differentiated, nonfunctioning PanNETs were obtained from two tertiary referral centers. Patient demographic characteristics and tumor, clinicopathologic features were collected. Tissue from both the EUS-FNA specimen and the primary tumor was extracted from archival tissue blocks. NGS using a panel of ten genes was performed on both samples. **RESULTS:** In our series, the median age was 61.1 years. Tumors were predominantly left-sided (60.5%) and unifocal (94.7%). The median tumor size was 2.2 cm. NGS detected somatic mutations in 29% of primary tumors and 36.8% of EUS-FNA specimens. In primary tumors, DAXX/ATRX mutations were predominantly detected (63.6%). In EUS-FNA specimens, MEN1 mutations were predominantly detected (64.3%). Among non-wild-type specimens, mutational concordance was achieved in 31.6% of cases. In 11 patients with a detectable mutation in the primary tumor, a mutation was detected in the EUS-FNA specimen in 45.5% of cases, with a mutational concordance of 54.5%. **CONCLUSIONS:** NGS can detect somatic mutations in EUS-FNA specimens of well-differentiated PanNETs. Efforts to improve detection sensitivity and mutational concordance are required to overcome current technical limitations.

PubMed-ID: [37488390](#)

DOI: [10.1245/s10434-023-13965-8](#)

Blood-based Proteomic Signatures Associated With MEN1-related Duodenopancreatic Neuroendocrine Tumor Progression.

J Clin Endocrinol Metab, 108(12):3260-71.

J. F. Fahrman, A. R. Wasylshen, C. R. C. Pieterman, E. Irajizad, J. Vykoukal, R. Wu, J. B. Dennison, C. B. Peterson, H. Zhao, K. A. Do, D. M. Halperin, S. K. Agarwal, J. E. Blau, S. Jha, J. D. Rivero, N. Nilubol, M. F. Walter, J. M. Welch, L. S. Weinstein, M. R. Vriens, R. S. van Leeuwen, M. J. C. van Treijen, G. D. Valk, N. D. Perrier, S. M. Hanash and H. Katayama. 2023.

PURPOSE: Patients with multiple endocrine neoplasia type 1 (MEN1) are predisposed to develop duodenopancreatic neuroendocrine tumors (dpNETs), and metastatic dpNET is the primary cause of disease-related mortality. Presently, there is a paucity of prognostic factors that can reliably identify patients with MEN1-related dpNETs who are at high risk of distant metastasis. In the current study, we aimed to establish novel circulating molecular protein signatures associated with disease progression. **EXPERIMENTAL DESIGN:** Mass spectrometry-based proteomic profiling was conducted on plasmas procured through an international collaboration between MD Anderson Cancer Center, the National Institutes of Health, and the University Medical Center Utrecht from a cohort of 56 patients with MEN1 [14 with distant metastasis dpNETs (cases) and 42 with either indolent dpNETs or no dpNETs (controls)]. Findings were compared to proteomic profiles generated from serially collected plasmas from a mouse model of Men1-pancreatic neuroendocrine tumors (Men1fl/fIPdx1-CreTg) and control mice (Men1fl/fl). **RESULTS:** A total of 187 proteins were found to be elevated in MEN1 patients with distant metastasis compared to controls, including 9 proteins previously associated with pancreatic cancer and other neuronal proteins. Analyses of mouse plasmas revealed 196 proteins enriched for transcriptional targets of oncogenic MYCN, YAP1, POU5F1, and SMAD that were associated with disease progression in Men1fl/fIPdx1-CreTg mice. Cross-species intersection revealed 19 proteins positively associated with disease progression in both human patients and in Men1fl/fIPdx1-CreTg mice. **CONCLUSIONS:** Our integrated analyses identified novel circulating protein markers associated with disease progression in MEN1-related dpNET.

PubMed-ID: [37307230](#)

DOI: [10.1210/clinem/dgad315](#)

General

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Optimization of Subglottic View During Flexible Laryngoscopy With Patient Positioning.

Otolaryngol Head Neck Surg, 169(6):1556-63.

J. Highland, V. Torrecillas, T. Redding, B. Bixby, A. Iravani, T. Haller, M. Firpo, R. Nouraei and M. Smith. 2023.

OBJECTIVE: Determine the ideal head position to optimize visualization of the subglottis using flexible laryngoscopy.

STUDY DESIGN: Prospective cohort study. SETTING: Outpatient multidisciplinary airway clinic at a tertiary care center.

METHODS: Patients presenting to a multidisciplinary airway clinic undergoing nasoendoscopic airway examination were enrolled. Three head positions were utilized to examine the subglottis during laryngoscopy: "sniffing," chin tuck, and stooping positions. In-office reviewers and blinded clinician participants evaluated views of the airway based on Cormack-Lehane (CL) scale, airway grade (AG), and visual analog scale (VAS). Demographic data were obtained. Statistical analysis compared head positions and demographic data using Student's t test, analysis of variance, and Tukey's post hoc analysis. RESULTS: One hundred patients participated. No statistical differences existed among in-clinic or blinded reviewers for the CL score in any head position ($p = .35, .5$, respectively). For both AG and VAS, flexed and stooping positions were rated higher than the sniffing positions by both in-clinic and blinded reviewers ($p < .01$ for all analyses), but there was no statistical difference between these two positions ($p = .28, .18$, respectively). There was an inverse correlation between age and scores for AG and VAS in the flexed position for both sets of reviewers ($p = .02, <.01$ respectively), and a higher body mass index was significantly associated with the need to perform tracheoscopy for full airway evaluation ($p < .01$). CONCLUSION: Both flexion and stoop postures can be implemented by an experienced endoscopist in awake, transnasal flexible laryngoscopy to enhance visualization of the subglottic airway.

PubMed-ID: [37522249](#)

DOI: [10.1002/ohn.419](#)