



## ESES Review of Recently Published Literature

Collection: Sara Andreani, Guzmán Franch-Arcas, Irem Karatas,  
Rossella Melcarne, Michele Minuto, Barbara Mullineris, Ushanthan Uthayanan,  
Nikolaos Voloudakis, Leire Zarain Obrador

Compilation and design: Paola Sartori, [srtpvn@gmail.com](mailto:srtpvn@gmail.com)

*Affiliations see next page*

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

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## Collectors

### **Sara Andreani MD**

Oncological and Mininvasive Surgery, GOM Niguarda, Milan, Italy

### **Guzmán Franch-Arcas, MD**

F.E.B.S. in General Surgery & Neck Endocrine

Head of the Endocrine Surgical Unit

University Hospital of Salamanca, Spain

### **Irem Karatas MD**

Department of General Surgery, Mardin Training and Research Hospital, Mardin, Türkiye

### **Rossella Melcarne MD**

Department of Traslational and Precision Medicine, Sapienza University Rome, Italy

### **Michele Minuto MD PhD**

F.E.B.S.- Neck Endocrine and Adrenal Surgery

Associate Professor of Surgery

Endocrine Surgery Unit, Polyclinic Hospital San Martino,

Department of Surgical Sciences (DISC), University of Genoa, Italy

### **Barbara Mullineris MD**

Department of General Surgery, Emergency and New Technology, Azienda Ospedaliero-Universitaria of Modena, Baggiovara, Modena, Italy

### **Ushanthan Uthayanan MD**

Department of General, Visceral, Endocrine and Transplantation Surgery, HOCH Health Ostschweiz, Cantonal Hospital St. Gallen, Switzerland

### **Nikolaos Voloudakis MD**

F.E.B.S. Endocrine

Second Surgical Department, Aristotle University of Thessaloniki, G. Gennimatas General Hospital of Thessaloniki, Thessaloniki, Greece

„ MD PhD.

F.E.B.S - Neck Endocrine and Adrenal Surgery.

Endocrine Surgery Department. Hospital General Universitario Gregorio Marañon. Madrid. Spain.

## Compilation and Coordination

### **Paola Vincenza Sartori MD**

General and emergency Surgery Department, ASST Brianza- Pio XI Hospital, Desio, Italy

[srtpvn@gmail.com](mailto:srtpvn@gmail.com)

## Journals covered

| Journal                                  | Journal                                    |
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| <a href="#">Am J Surg</a>                | <a href="#">J Am Coll Surg</a>             |
| <a href="#">Ann Surg</a>                 | <a href="#">J Clin Endocrinol Metab</a>    |
| <a href="#">Ann Surg Oncol</a>           | <a href="#">J Endocrinol Invest</a>        |
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# Thyroid

## Randomized controlled trials

### **Calcium and vitamin D reduce hypoparathyroidism and hospital stay after thyroidectomy: A randomized controlled trial.**

*Surgery*, 192:110071.

V. Gkanis, K. Nastos, K. Ntalaperas, E. Agianni, S. Lainas, P. Raikou, N. Dafnios, I. Papakonstantinou and S. Lanitis. 2026. BACKGROUND: Transient hypoparathyroidism is a common complication after total thyroidectomy, prolonging hospitalization and necessitating calcium and/or vitamin D replacement. Evidence from prospective randomized trials on preventive supplementation remains limited. This study aimed to evaluate whether prophylactic calcium and vitamin D supplementation reduces transient hypoparathyroidism and shortens hospital stay after total thyroidectomy. METHODS: In this single-center, prospective, randomized, controlled, open-label trial, 600 patients undergoing total thyroidectomy without central neck dissection were randomized to receive prophylactic oral calcium carbonate/gluconate and alfacalcidol (group A, n = 300) or standard postoperative care (group B, n = 300). Primary outcomes were biochemical and symptomatic hypocalcemia and the need for intravenous calcium. Secondary outcomes included postoperative serum calcium levels and length of hospital stay. Statistical analyses used chi(2), Student's t test, Mann-Whitney U test, and odds ratio and 95% confidence interval. RESULTS: Laboratory hypocalcemia (serum calcium <8.5 mg/dL) occurred significantly less often in group A (16.9% vs 39.9%; odds ratio 0.305, 95% confidence interval 0.207-0.451, P < .001). Symptomatic hypocalcemia was also reduced (5.6% vs 12.3%; odds ratio 0.427, 95% confidence interval 0.232-0.785, P < .005), as was the need for intravenous calcium (1.8% vs 9.3%; odds ratio 0.175, 95% confidence interval 0.070-0.441, P < .001). Group A demonstrated higher mean serum calcium levels on postoperative days 1 and 2 (P < .001) and a shorter hospital stay (1.25 days vs 1.7 days, P < .001). Supplementation benefits were consistent across subgroups stratified by malignancy status and preoperative vitamin D levels. CONCLUSION: Routine calcium and vitamin D supplementation after total thyroidectomy significantly reduces transient hypoparathyroidism and shortens hospitalization. These findings support its use as a standard postoperative strategy to enhance recovery and reduce health care resource utilization.

PubMed-ID: [41604835](#)

DOI: [10.1016/j.surg.2025.110071](#)

### **The Effect of Standardized Postoperative Neck and Orofacial Rehabilitation Exercise on Quality of Life in Post-Thyroidectomy Patients: A Randomized Controlled Trial.**

*Thyroid*, 36(4):397-407.

J. Huang, W. Chen, J. Zhang, H. Xu, Y. Li, Y. Liu, B. Lin, R. Li, M. Liang, X. Xu and W. Lv. 2026.

BACKGROUND: Approximately 80% of post-thyroidectomy patients suffer from swallowing disorders even in the absence of definite laryngeal nerve injury. This study aimed to evaluate the efficacy of a standardized postoperative neck and orofacial rehabilitation exercise in enhancing quality of life (QoL), particular swallowing-related QoL, among post-thyroidectomy patients without definite laryngeal nerve injury during surgery. METHODS: This was a single-center, open-label randomized controlled trial. The trial was registered at the Chinese Clinical Trial Registry (ChiCTR2500097960). Participants were randomized 1:1 to rehabilitation exercise group (RE group) and control group. The RE group performed a standardized postoperative neck and orofacial rehabilitation exercise, which included neck extension, swallowing, and voice training, while the control group received only general advice to move their necks freely. The rehabilitation exercise program duration is 3 months. The QoL of participants was evaluated at 1 week, 1 month, 3 months, and 6 months postoperatively. The primary outcome was swallowing-related QoL evaluated by the MD Anderson Dysphagia Inventory (MDADI) at 1 month after surgery. Secondary outcomes included swallowing-related QoL at other follow-up time points, the thyroid cancer-specific QoL, scar assessment, and safety endpoints defined by postoperative drainage, pain scores, and adverse events. RESULTS: A total of 374 patients were recruited, and 356 participants were included in final analysis, including 176 in RE group and 180 in control group. The swallowing-related QoL in the RE group was significantly better than that in the control group at 1 month (MDADI total score 97.4 [80.3, 100] vs. 88.9 [75.8, 99.7], p = 0.004) and 6 months (MDADI total score 100 [96.8, 100] vs. 98.9 [85.5, 100], p = 0.020) postoperatively. The RE group reported higher pain levels at 1 week after surgery (p = 0.013) but no significant differences at subsequent time points. No statistically significant differences between groups were observed in other outcomes. No severe adverse event occurred during rehabilitation exercise. CONCLUSIONS: The standardized postoperative neck and orofacial rehabilitation exercise was an effective and safe approach for accelerating the recovery of the swallowing-related QoL in post-thyroidectomy patients

without definite laryngeal nerve injury during surgery.

PubMed-ID: [41778443](#)

DOI: [10.1177/10507256261427761](#)

### **Tracheal intubation in the thyroid surgical position improves recurrent laryngeal nerve monitoring: a dual-center randomized trial.**

*Int J Surg*, 112(1):1007-13.

E. Liu, J. Qin, X. Li, Y. Qi, L. Wang, X. Wu, Z. Yi, J. Chen and B. Lu. 2026.

**BACKGROUND:** Intraoperative neuromonitoring (IONM) is a critical adjunct in thyroid surgery to preserve recurrent laryngeal nerve function. This study aims to evaluate whether tracheal intubation in the thyroid surgical position enhances IONM signal quality compared with the standard supine position. **METHODS:** In this dual-center, parallel-group, randomized trial, 184 adults scheduled for elective thyroidectomy requiring IONM were allocated 1:1 to intubation in either the thyroid surgical position or the conventional supine position. The modified intention-to-treat cohort comprised 167 participants (85 vs 82) with an assessable baseline vagus response (V1). The primary outcome was the incidence of satisfactory electromyography (EMG) signals, defined as an initial vagus nerve EMG amplitude exceeding 500  $\mu$ V when stimulated at 1.0 mA. Secondary outcomes included EMG signal amplitude, intubation-related metrics (e.g., Cormack-Lehane grades, intubation difficulty scale scores, intubation time, and depth of intubation), postoperative complications (e.g., lip lesions, dental injury, postoperative nausea and vomiting, dizziness, and headache), and clinician satisfaction with patient positioning and mask ventilation. **RESULTS:** Satisfactory V1 signals occurred in 82/85 patients (96.47%) in the thyroid surgical position group versus 70/82 (85.37%) in the supine group (relative risk 1.13; 95% CI 1.03-1.24;  $P = 0.0145$ ). Intubation time and Cormack-Lehane grades did not differ significantly, but the thyroid surgical position group required deeper EMG tube insertion (22 cm [21-23] vs 22 cm [21-22]; median differences 1, 95% CI 0-1;  $P = 0.046$ ). Postoperative complications did not differ significantly between groups (all  $P > 0.05$ ). Clinician satisfaction scores were significantly higher in the thyroid surgical position group (median 9 vs 5; median differences 4, 95% CI 3-4;  $P < 0.0001$ ). Mask ventilation satisfaction was also rated higher in the thyroid surgical position group (median 9 vs 8; median differences 1, 95% CI 0-1  $P < 0.0001$ ). **CONCLUSIONS:** Tracheal intubation in the thyroid surgical position significantly improves IONM signal quality and clinician satisfaction without increasing intubation difficulty or postoperative complications. Adopting this simple positioning strategy can optimize EMG tube placement and enhance the reliability of IONM during thyroid surgery.

PubMed-ID: [40956172](#)

DOI: [10.1097/JS9.00000000000003481](#)

PMCID: PMC12825681

### **A Randomized Controlled Trial of Intraoperative Nerve Monitoring in Resident-Performed Thyroidectomy.**

*Laryngoscope*, 136(1):505-13.

P. Maneeprasopchoke, T. Chayasitthangkul, C. Chongkolwatana, S. Chumpathong, G. W. Randolph, M. D. Russell, A. H. Abdelhamid-Ahmed and P. Pithuksurachai. 2026.

**OBJECTIVE:** Intraoperative nerve monitoring (IONM) is widely used in thyroidectomy to aid recurrent laryngeal nerve (RLN) identification and preservation. This study assessed whether IONM improves RLN identification time and overall operative time in less experienced otorhinolaryngology residents performing thyroidectomies. **METHODS:** This randomized controlled trial was conducted at Siriraj Hospital, Bangkok, from January 2020 to February 2021. A total of 80 patients were randomly assigned to an IONM or non-IONM group. A total of 10 residents performed eight thyroidectomies each, using IONM in four procedures and non-IONM methods in the other four. **RESULTS:** RLN identification was significantly quicker in the IONM group (6.7 vs. 19.7 min for primary identification, 11.0 vs. 19.7 min for visual identification). IONM increased setup and nerve dissection time but without significant differences in overall operative time or RLN injury rates. **CONCLUSIONS:** IONM improves RLN identification efficiency in surgical training but does not significantly impact overall operative time or RLN injury rates. **TRIAL REGISTRATION:** Clinical Trials Registry (TCTR20191224001).

PubMed-ID: [41178695](#)

DOI: [10.1002/lary.70248](#)

### **Impact of Multimedia on Patient Comprehension in Thyroid Surgery: A Randomized Trial.**

*Otolaryngol Head Neck Surg*, 174(2):375-85.

H. Samarah, A. E. Moroco, K. Liu, K. Nunes, A. G. Thal, J. M. Curry and E. E. Cottrill. 2026.

**OBJECTIVE:** To assess whether the Thyroid Informed Surgical Consent Augmenting Video (TISCAV) improves knowledge retention, reduces decisional conflict, alleviates anxiety, and enhances satisfaction in thyroidectomy decision-making

compared to standard verbal consent. **STUDY DESIGN:** Randomized controlled trial. **SETTING:** Academic tertiary care center with urban outpatient and community-based clinics. **METHODS:** Forty-nine English-speaking adults scheduled for thyroid surgery were randomized to receive either standard verbal consent alone (control) or TISCAV followed by standard consent (intervention). Forty-three completed preoperative assessments and were included in the analysis. Knowledge was assessed before and after consent. Visual Analog Scale for Anxiety (VAS-A), Decisional Conflict Scale (DCS), and Satisfaction with Decision Scale (SDS) were measured preoperatively; SDS, Decision Regret Scale (DRS), and anxiety were reassessed at 22 and 100 days postoperatively. **RESULTS:** Both groups demonstrated significant knowledge gains post-consent ( $P < .0001$ ), with no significant difference between groups ( $P = .1812$ ). Patients with malignant/suspicious cytopathology had lower decisional conflict than those with benign findings ( $P = .03$ ); scores in indeterminate cases trended similarly ( $P = .11$ ). Among patients with indeterminate cytopathology, decisional conflict did not differ significantly ( $P = .06$ ), while preoperative satisfaction was lower in the video group ( $P = .02$ ); group differences resolved postoperatively ( $P \geq .55$ ). **CONCLUSION:** TISCAV and standard consent both improved knowledge acquisition. While video-based consent may transiently increase decisional conflict and reduce satisfaction among patients with indeterminate pathology, these effects did not persist postoperatively. Video tools may serve as a safe and accessible adjunct to verbal consent.

PubMed-ID: [41503824](#)

DOI: [10.1002/ohn.70111](#)

### **Intraoperative neuromonitoring reduces vocal cord injury in open thyroid cancer surgery: results from a randomized controlled trial.**

*Surg Endosc*, 40(2):1620-8.

Y. Xin, Y. Liu, Y. Liu, Q. Xie, C. Liu, G. Xu and X. Shang. 2026.

**BACKGROUND:** Intraoperative neuromonitoring (IONM) has been increasingly used in thyroid surgery, yet its clinical value remains controversial. **OBJECTIVES:** This randomized controlled trial aimed to evaluate the efficacy and safety of IONM in thyroid cancer surgery. **METHODS:** The standardized four-step monitoring protocol was used in the IONM group. Primary endpoints included RLN injury rates and postoperative voice function recovery. Secondary endpoints included surgical parameters (operation time, blood loss), complication rates, and oncological outcomes. Voice function was assessed using VHI-10 scoring and maximum phonation time (MPT). Patients were followed up for a median of 6 months. **RESULTS:** The IONM group demonstrated significantly lower rates of temporary vocal cord paralysis (2.0% vs 10.0%,  $P = 0.038$ ) and higher nerve identification rates (100% vs 96.0%) compared to the control group. Voice function recovery was notably faster in the IONM group, with smaller changes in VHI-10 scores ( $\Delta = 4.2 \pm 1.5$  vs  $7.6 \pm 2.1$ ,  $P < 0.001$ ) and shorter MPT recovery time ( $14.2 \pm 3.5$  vs  $25.6 \pm 5.2$  days,  $P < 0.001$ ). Although operation time was longer in the IONM group ( $125.6 \pm 18.3$  vs  $108.4 \pm 15.7$  min,  $P < 0.001$ ), no significant differences were found in blood loss ( $45.3 \pm 12.6$  ml vs  $48.7 \pm 13.2$  ml,  $P = 0.183$ ), complication rates, or oncological outcomes between the groups. **CONCLUSION:** IONM technology greatly lowers the risk of temporary recurrent laryngeal nerve injury and speeds up voice function recovery in thyroid cancer surgery. Although operation times are slightly extended, the technique is safe and preserves oncological integrity.

PubMed-ID: [41340008](#)

DOI: [10.1007/s00464-025-12411-y](#)

PMCID: PMC12881059

### **A Randomized Controlled Trial to Evaluate the Effects of Topical Intraoperative Corticosteroid Application on Voice Quality in Thyroid Surgery With Preserved Recurrent Laryngeal Nerves.**

*World J Surg*, 50(2):432-40.

D. Zhang, F. Brucchi, D. Barbieri, P. Indelicato, C. Colombo, G. Dionigi and H. Sun. 2026.

**BACKGROUND:** The effect of topical intraoperative corticosteroid application on voice quality in thyroid surgery with preserved RLN remains unclear. This randomized controlled trial aimed to evaluate the efficacy and safety of this intervention. **METHODS:** Between January 2023 and June 2024, 134 patients scheduled for thyroid surgery were screened for eligibility. Patients who developed loss of signal (LOS) during surgery or who had postoperative impaired vocal cord motility on laryngoscopy were not included in the final analysis. Fourteen patients were excluded (six for previous thyroid/parathyroid surgery, four for preoperative vocal cord paralysis, and four for corticosteroid allergy), leaving 120 patients who were randomized equally to receive either topical intraoperative corticosteroids ( $n = 60$ ) or standard treatment ( $n = 60$ ). Baseline demographic and clinical data were comparable between the groups. Dynamic function of the larynx was monitored intraoperatively using electromyography (EMG), and vocal outcomes were assessed 1 week postoperatively using the Voice Handicap Index (VHI) and voice-related quality of life (V-RQOL). Laryngeal findings and

adverse events were also recorded. RESULTS: No EMG signal was recognized in any patient. The EMG amplitudes and latencies of the vagus nerve (V1 and V2) did not differ significantly between the groups. EMG signal changes between V1 and V2 were observed in 16% of RLNs in the control group and in 18% in the corticosteroid group, but these were not associated with clinically significant decreases in amplitude or increases in latency. Postoperatively, the corticosteroid group had significantly lower (better) mean VHI scores (12.4 +/- 3.2 vs. 19.6 +/- 4.7;  $p < 0.01$ ) and higher V-RQOL scores (88.3 +/- 6.1 vs. 77.5 +/- 8.8;  $p = 0.02$ ) than the control group. The subgroup analysis of patients with EMG changes showed similar trends. Vocal fold edema occurred in 2 patients in the corticosteroid group and 5 in the control group, with complete resolution of stroboscopic abnormalities in all patients after 4 weeks. No local or systemic complications related to the use of corticosteroids were observed, and the postoperative courses were uneventful in both groups. CONCLUSIONS: Topical intraoperative use of corticosteroids in thyroid surgery with preserved RLN is safe and associated with improved early postoperative voice outcomes. No significant adverse events were observed, and RLN function was preserved in all cases. Further studies are needed to assess the long-term clinical relevance of these results.

PubMed-ID: [41273037](#)  
DOI: [10.1002/wjs.70157](#)

## Meta-Analyses

### **Prognostic Role of Histopathological Features in Pediatric Papillary Thyroid Carcinoma: Systematic Review and Meta-Analysis.**

*Head Neck*, 48(4):1130-40.

L. Canali, G. M. Pace, C. Zimello, L. Cerri, A. Costantino, F. Gaino, L. Malvezzi, G. Spriano, A. Paderno, F. Ferreli, G. Cristalli and G. Mercante. 2026.

OBJECTIVE: The aim of this study is to evaluate the impact of extrathyroidal extension (ETE), multifocality, and lateral neck lymph node metastasis on survival outcomes for pediatric patients with differentiated papillary thyroid carcinoma (PTC). METHODS: This study was conducted in conformity with the PRISMA statement. The pooled hazard ratios (HRs) and the 95% confidence interval (CI) were calculated to define the impact of different pathological factors on disease-free survival (DFS). RESULTS: A total of 13 studies, enrolling 2641 patients (males: 29.5%,  $n = 780$ ) with a median age of 16 years (95% CI: 15.4-19.0) years ( $n = 1370/2641$ ), were included. The incidence of multifocality and ETE was 30.7% ( $n = 806/2625$ ), and 45.4% ( $n = 1148/2528$ ), respectively. The incidence of lateral neck lymph node metastasis (LNM) was 51.6% ( $n = 1224/2372$ ). Overall, 61.5% of patients underwent postoperative radioactive iodine therapy (RAI) ( $n = 1381/2247$ ). The median follow-up time was 85 months (95% CI: 57.0-176.4) ( $n = 2534/2641$ ). The estimated pooled HRs for DFS were 1.86 (95% CI: 1.33-2.59;  $p = 0.002$ ) for multifocality, 1.78 (95% CI: 1.20-2.63;  $p = 0.010$ ) for ETE and 1.77 (95% CI: 0.76-4.11;  $p = 0.161$ ) for lateral neck LNM. CONCLUSIONS: Multifocality and ETE are significant predictors of recurrence in pediatric PTC, while lateral neck LNM does not seem to be a reliable prognostic factor. These results may warrant consideration in pediatric-specific risk stratification and help guide treatment and follow-up.

PubMed-ID: [41574652](#)

DOI: [10.1002/hed.70180](#)

### **Fluorescent Imaging in Thyroid Surgery to Preserve Parathyroid Function: A Systematic Review and Meta-Analysis.**

*Otolaryngol Head Neck Surg*, 174(1):30-44.

M. H. Cheung, M. T. Nguyen, S. A. Nguyen, S. I. Nassar, J. Murdaugh, J. G. Newman, E. M. Graboyes, W. G. Albergotti, A. Kejner, M. Bobian and D. Adilbay. 2026.

OBJECTIVE: Hypoparathyroidism and postoperative hypocalcemia are rare but dreaded complications of thyroid surgery, often requiring increased follow-up and contributing to financial and quality-of-life burdens. This systematic review evaluates the effectiveness of intraoperative fluorescent imaging of parathyroid glands (PGs) in improving PG identification and reducing iatrogenic complications during thyroid surgery. DATA SOURCE: Pubmed, Scopus, CINAHL. REVIEW METHODS: A systematic search of PubMed, Scopus, CINAHL, and Cochrane databases was conducted per PRISMA guidelines. Studies using intraoperative fluorescent imaging for PG identification and reporting postoperative calcium and parathyroid hormone (PTH) levels were included. Data on patient demographics, surgical technique, imaging modality, PG identification rates, incidental parathyroidectomy, autotransplantation, and postoperative calcium/PTH outcomes were extracted. Meta-analyses of proportions, odds ratios, and mean differences were performed using MedCalc and Cochrane Review Manager. RESULTS: Twenty-eight studies ( $n = 3876$ ) were included. Fluorescent imaging significantly improved PG identification rates (86.4% vs 70.6%,  $P < .0001$ ) and reduced incidental parathyroidectomy (5.3% vs 9.5%,  $P = .0017$ ).

Short-term hypoparathyroidism (16.7% vs 27.0%,  $P = .0004$ ) and postoperative hypocalcemia rates on Day 1 (10.6% vs 18.1%,  $P = .0016$ ) and in the short term (5.7% vs 11.5%,  $P = .0001$ ) were significantly lower in the fluorescent imaging group. Odds of transient hypocalcemia were also reduced (OR 0.37,  $P < .00001$ ). **CONCLUSION:** Fluorescent imaging in thyroid surgery significantly improves PG identification rates and reduces the incidence of postoperative hypocalcemia and hypoparathyroidism. Integrating intraoperative fluorescent imaging into the intraoperative thyroid surgery paradigm may enhance patient outcomes by minimizing the frequency of PG-associated complications.

PubMed-ID: [41126675](#)

DOI: [10.1002/ohn.70055](#)

PMCID: PMC12794782

### **Surgical Management of Substernal Goiters: A Systematic Review and Meta-Analysis.**

*Laryngoscope*, 136(2):575-85.

M. H. Cheung, A. M. Walker, S. A. Nguyen, H. Butehorn and W. G. Albergotti. 2026.

**OBJECTIVE:** Defining indication for intervention in substernal goiter, and secondarily define when thoracic intervention may be required. **DATA SOURCES:** PubMed, Scopus, CINAHL. **METHODS:** A systematic review and meta-analysis were performed on studies employing thyroidectomy for substernal goiters. Meta-analysis of continuous measures, proportions, and comparison of weighted proportions was performed for patient characteristics, symptoms, and outcomes. **RESULTS:** Data from 102 studies were included, with a total study population of 15,719 patients undergoing substernal thyroidectomies. Criteria for classifying substernal goiter were heterogeneous across studies, with a plurality (21/102) defining diagnosis by  $> 50\%$  of the goiter mass located below the thoracic inlet. There was a female predominance at 67% (CI 64.2-69.9) with a mean age of 58 years old (10-94). Most common preoperative symptoms were a described "neck mass" (71.1%, CI 57.6-82.9) and overall compressive symptoms (64.8%, CI 52.4-76.2). 27.6% (CI 22.4-33.1) of the population remained asymptomatic. On radiologic imaging, tracheal deviation and compression were identified in 60.6% (CI 52.5-68.5) and 48.6% (CI 37.6-59.6) of the population, respectively. Cervical approach alone was performed in 88.7% (CI 86.0-91.1) of the population, while 10.4% (CI 8.2-12.8) required additional thoracic intervention. Malignancy was moderate and seen in 12.4% (CI 10.4-14.6) of cases. **CONCLUSION:** Results highlight the indication for substernal surgery is largely due to the presence of clinical symptoms or compressive findings on imaging; however, over a quarter of the population is asymptomatic and over 50% are without compressive findings on imaging. When surgery is undertaken, a cervical approach is often adequate, suggesting that only a minority of the population may require thoracic intervention.

PubMed-ID: [40856014](#)

DOI: [10.1002/lary.70087](#)

PMCID: PMC12793967

### **Comparative efficacy and safety of thermal ablation versus surgery in thyroid cancer: umbrella review of meta-analyses of observational cohort studies.**

*Int J Surg*,

Y. Feng, L. Sang, J. Guo, Z. Shan, W. Teng, Y. Li and Y. Li. 2025.

**BACKGROUND:** Thermal ablation (TA) is gaining popularity for its minimally invasive nature, especially in specific thyroid cancer subtypes, but its efficacy remains inconclusive and it isn't recommended for thyroid cancer treatment. This umbrella review aimed to evaluate the efficacy and safety of TA compared to surgery, focusing on recurrence, complications, and quality of life. **METHODS:** A systematic search of PubMed, Embase, Web of Science, and Cochrane Library (up to November 2024) was conducted to identify observational cohort studies comparing perioperative and long-term outcomes between TA and surgical resection. Data were extracted for effect estimates, heterogeneity, and quality assessed using A Measurement Tool to Assess Systematic Reviews (AMSTAR-2) and evidence grading criteria. **RESULTS:** Eight meta-analyses ( $n = 7025$  patients) were included, with median follow-up durations of 25 months. Across overlapping datasets, TA, including radiofrequency (RFA), microwave (MWA), and laser ablation (LA) demonstrated consistent perioperative advantages compared with surgery in low-risk papillary thyroid carcinoma (PTC), predominantly papillary thyroid microcarcinoma (PTMC, T1aN0M0). Summary estimates from high-quality meta-analyses showed that TA was associated with a significantly lower overall complication rate (OR [Odds Ratio], 0.43; 95%CI, 0.23-0.80), shorter operation time (MD [Mean Difference], - 64.33; 95%CI, - 71.12--55.53), and lower hospital costs (MD, - 0.84; 95%CI, - 1.06--0.62). These trends were consistently observed across RFA and MWA subgroups, whereas LA data remained limited. In contrast, long-term oncologic outcomes, including recurrence (OR, 1.17; 95%CI, 0.67-2.02) and lymph node metastasis (RR [Risk Ratio], 0.77; 95%CI, 0.44-1.36) showed no statistically significant differences between TA and surgery, with wide confidence intervals indicating substantial uncertainty. Across the included meta-analyses, 38.9% of

associations showed high heterogeneity ( $I^2 > 50.0\%$ ), and the evidence quality was rated as moderate to low due to limited follow-up durations and the predominance of observational cohort data. **CONCLUSION:** TA offers short-term benefits such as fewer complications, shorter procedures, and lower hospital burden compared with surgery in low-risk PTMC. Yet, due to the predominance of observational data, limited follow-up, and significant heterogeneity, the current evidence remains insufficient to determine its long-term oncologic safety. TA should therefore be viewed as a selective treatment option for carefully chosen low-risk patients, pending confirmation from large, randomized studies with standardized endpoints and extended follow-up.

PubMed-ID: [41376351](#)

DOI: [10.1097/JS9.0000000000004411](#)

### **Comparative safety of completion thyroidectomy following lobectomy versus total thyroidectomy in differentiated thyroid cancer: A systematic review and meta-analysis.**

*Am J Surg*, 257:116977.

A. Ghani, L. M. Al Darwashi, M. Y. Hajeir, N. K. Hunter, M. Alogakos, S. Y. Ahmed, K. Hage, C. A. Than, H. Nakanishi, J. Shin and G. Romero-Velez. 2026.

**BACKGROUND:** This meta-analysis aimed to evaluate the operative safety of completion thyroidectomy (CT) following lobectomy compared with total thyroidectomy (TT) for differentiated thyroid cancer (DTC). **METHODS:** PubMed, Ovid Embase, Cochrane Library, CINAHL, and Web of Science were searched from their respective inception dates to October 2025 (PROSPERO ID: CRD420251178003). **RESULTS:** A total of 43,362 patients from twelve studies were included, of whom 6810 (15.7%) underwent CT. CT was associated with lower odds of transient hypocalcemia (OR = 0.46; 95% CI: 0.34 - 0.63;  $I(2) = 68\%$ ) compared with TT, while rates of permanent hypocalcemia (OR = 0.78; 95% CI: 0.61 - 1.01;  $I(2) = 16\%$ ), transient recurrent laryngeal nerve injury (OR = 0.99; 95% CI: 0.78 - 1.26;  $I(2) = 30\%$ ), permanent recurrent laryngeal nerve injury (OR = 1.12; 95% CI: 0.94 - 1.34;  $I(2) = 0\%$ ), and hematoma (OR = 1.34; 95% CI: 0.56 - 3.21;  $I(2) = 0\%$ ) were similar. **CONCLUSIONS:** Our analysis demonstrated that CT appears to have a similar safety profile when compared with upfront TT in selected DTC patients.

PubMed-ID: [41980321](#)

DOI: [10.1016/j.amjsurg.2026.116977](#)

### **The effect of iodine solution in total thyroidectomy for patients with Graves disease: A meta-analysis.**

*Surgery*, 190:109926.

A. M. Haroon, A. Ghani, A. R. Ayeshe, M. M. Witkowiak, M. Alogakos, J. Burns, C. A. Than, B. Wahba, H. Nakanishi and T. McKenzie. 2026.

**BACKGROUND:** Iodine solution has been used preoperatively in patients with Graves disease undergoing a total thyroidectomy to reduce the vascularization and its associated risk of complications. This meta-analysis aimed to investigate the safety and efficacy of preoperative administration of iodine solution in patients with Graves disease undergoing a total thyroidectomy. **METHODS:** Ovid MEDLINE, CINAHL, Ovid Embase, and the Cochrane Library were searched for articles since its inception to August 2024. The review was registered prospectively on the PROSPERO database (CRD42024585797). **RESULTS:** From the 2,243 studies screened, 11 studies met the eligibility criteria, with a total of 2,257 patients with Graves disease undergoing a total thyroidectomy either with iodine solution ( $n = 760$ ) or control ( $n = 1,497$ ) groups. Our study demonstrated that the iodine solution group had similar outcomes compared with the control group with regard to intraoperative estimated blood loss (mean difference = -24.6 mL, 95% confidence interval: -56.2, 7.0;  $I(2) = 82\%$ ), operative time (mean difference = -2.3 minutes, 95% confidence interval: -10.6, 6.0;  $I(2) = 68\%$ ), endocrine-related complications (odds ratio = 0.85, 95% confidence interval: 0.42, 1.74;  $I(2) = 76\%$ ), hypocalcemia (odds ratio = 1.11, 95% confidence interval: 0.65, 1.91;  $I(2) = 61\%$ ), hematoma (odds ratio = 1.44, 95% confidence interval: 0.39, 5.29;  $I(2) = 58\%$ ) or recurrent laryngeal nerve injury (odds ratio = 0.70, 95% confidence interval: 0.26, 1.93;  $I(2) = 53\%$ ). **CONCLUSION:** This meta-analysis demonstrates that preoperative iodine solution and control groups had similar clinical outcomes when undergoing total thyroidectomy for Graves disease. Further randomized control trials with larger samples and robust selection criteria are necessary to ascertain the perioperative effects of iodine solution in total thyroidectomy for patients with Graves disease.

PubMed-ID: [41351925](#)

DOI: [10.1016/j.surg.2025.109926](#)

### **Outcomes of Surgery Versus Radioactive Iodine as Definitive Therapy in Pediatric Graves' Disease: A Systematic Review and Meta-Analysis of Cohort Studies.**

*World J Surg*, 50(3):636-49.

G. S. He, J. L. Ling Chia, T. T. Hao, D. Pinto, M. C. De Jong, C. Ho, M. Samuel and R. Parameswaran. 2026.

**INTRODUCTION:** Definitive second-line treatment for pediatric Graves' disease (GD) includes radioiodine ablation (RAI) or thyroidectomy. The current treatment practice in pediatric GD patients is a contentious issue as the decision to consider either of the treatment options depends on preferences of patients, physicians, and access to surgical care and radioactive iodine treatment. This systematic review and meta-analysis were performed to compare the cure and relapse rates of RAI versus surgery as definitive therapy in children with Graves' Disease. **METHODS:** A comprehensive search on Cochrane library, Embase, PUBMED, MEDLINE (via Pubmed), and ClinicalTrials.gov for English articles published on definitive treatment of GD in children since 1985 to 2023 was performed. The data were extracted and meta-analyzed for efficacy and safety outcomes, risk of bias (ROB), and certainty of evidence summated using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) instrument. **RESULTS:** Twenty-nine (26 retrospective and 3 prospective) studies with a total of 1861 children and a mean age of 13.15 years with a mean follow up of 8 years were evaluated in the systematic review. Among these, 1061 children received RAI therapy, whereas 800 underwent thyroidectomy and were evaluated in the pooled analysis. 755 were excluded as details pertaining to definite treatment was not available. Studies were of low to moderate risk of bias. The pooled analysis suggests that RAI had significantly lower cure rate in children compared to children who underwent thyroidectomy (RR 0.89; 95% CI 0.81-0.99;  $p = 0.03$ ). In subgroup analysis of patients from 19 studies who underwent surgery, total thyroidectomy (2%) was more effective than subtotal thyroidectomy (13%) in preventing recurrent hyperthyroidism ( $p = 0.001$ ; moderate quality evidence). Hypothyroidism rates after RAI and surgery were similar (RR 0.97; 95% CI 0.67-1.40;  $p = 0.88$ ). There were no significant adverse outcomes reported such as secondary malignancy or quality of life after RAI. Following TT, adverse effects seen were permanent hypoparathyroidism (0.6%) and temporary recurrent laryngeal nerve palsy (5.1%). **CONCLUSION:** Thyroidectomy appears to be more effective than RAI in effecting cure in Graves' disease in children following failed remission with antithyroid medication therapy. However, access to thyroidectomy may not be universally available and RAI is an option in these children.

PubMed-ID: [41665506](#)

DOI: [10.1002/wjs.70247](#)

#### **The Role of Thyroidectomy in the Management of Thyroglossal Duct Carcinoma: A Systematic Review.**

*Otolaryngol Head Neck Surg*, 175(2):271-80.

I. J. HH, S. P. J. van Dijk, C. E. Cunningham, F. J. van Kemenade, R. P. Peeters, S. Keereweer and T. M. van Ginhoven. 2026.

**OBJECTIVE:** The extent of surgical management of thyroglossal duct-associated differentiated thyroid carcinoma remains controversial. This study aims to evaluate the role of total thyroidectomy in patients with thyroglossal duct-associated differentiated thyroid carcinoma and provide insights to support individualized, evidence-based care. **DATA SOURCES:** A systematic literature search was conducted in MEDLINE, Embase, Web of Science, Cochrane CENTRAL, and Google Scholar from inception to January 2025. **REVIEW METHODS:** Screening was performed independently by two reviewers. Studies were included if they reported treatment details for patients with thyroglossal duct carcinoma, and excluded if they were letters, abstracts, reviews, or meta-analyses. The primary outcome consisted of recurrent disease. Secondary outcomes were presence of synchronous thyroid cancer, surgical treatments, and mortality. The study protocol was registered in PROSPERO (CRD-42023489730). **RESULTS:** Three hundred thirteen studies (243 case reports, 70 case series; range 1-26 patients per study) were included compromising 645 patients with differentiated thyroid carcinoma. Notably, no cohort studies were found. Recurrent disease occurred in 24/436 (5.5%) patients with reported follow-up (median, 35.5 months [12.0-80.0]). Among patients without preoperative suspicion for synchronous cancer in the thyroid, recurrence rates did not differ significantly between the Sistrunk-only group ( $n = 3/92$  (3.3%), median follow-up 24 months [IQR, 12-48]) and the Sistrunk plus thyroidectomy group ( $n = 6/101$  (5.9%), median follow-up 24 months [IQR, 12-69];  $P = .502$ ). **CONCLUSIONS:** The Sistrunk procedure alone may be sufficient in appropriately selected patients with thyroglossal duct carcinoma. The decision to perform total thyroidectomy should be individualized based on tumor characteristics and thorough thyroid assessment.

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DOI: [10.1002/ohn.70270](#)

PMCID: PMC13418079

#### **Active Surveillance for Locoregional Recurrent Differentiated Thyroid Cancer: A Systematic Review and Meta-Analysis.**

*Thyroid*, 36(2):121-32.

H. Lim, S. J. Cho and J. H. Baek. 2026.

**BACKGROUND:** Active surveillance (AS) has been proposed as a management option for recurrence of thyroid cancer. However, the current evidence for AS remains limited because of retrospective study designs, small sample sizes, and

follow-up loss. We therefore performed a systematic review and meta-analysis to provide a more reliable estimate of disease progression during AS for recurrent thyroid cancers. **METHODS:** This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. We searched MEDLINE, EMBASE, and COCHRANE databases through July 2025. Eligible studies included patients with recurrent thyroid cancer (thyroid bed nodules or lymph node metastases) managed with AS after complete resection of the primary tumor. Pooled progression rates were calculated using a random-effects model, with subgroup, sensitivity, and meta-regression analyses also being performed. Progression rates were also adjusted using modeling for follow-up loss. **RESULTS:** Ten retrospective studies (n = 841) were included. All included lesions were locoregional metastases from differentiated thyroid cancer (DTC). The pooled mean follow-up duration was 51.6 months (95% confidence interval [CI], 36.0-67.2). Across 10 studies, the overall pooled progression rate was 23% [95% CI, 12-34%] and was higher in biopsy-confirmed cases (32%; 95% CI, 15-55%). Progression was higher in studies with <40 months of mean follow-up than in studies with ≥40 months of mean follow-up (36% vs. 17%, p < 0.05). Log-transformed baseline serum thyroglobulin levels were significantly higher in the progression group compared with the stable group (1.02 vs. -0.07, p < 0.05). Subgroup analyses revealed higher progression rates in studies with <75% Stage I patients (30% vs. 11%, p < 0.05) and with ≥5% Stage IV patients (28% vs. 14%, p < 0.05). Adjustment for follow-up loss increased the estimated pooled progression rate up to 35-70%. **CONCLUSIONS:** Reported progression rates of AS for locoregional recurrent DTC may be underestimated due to heterogeneity and follow-up loss. Consequently, AS should be considered with caution. Higher progression rates were observed in patients with elevated baseline serum thyroglobulin levels and advanced tumor stage, suggesting that these factors may help identify patients who require closer monitoring or earlier intervention.

PubMed-ID: [41791888](#)

DOI: [10.1177/10507256251412323](#)

#### **Remote robotic surgery: a systematic review.**

*Surg Endosc*, 40(4):2782-806.

Y. Liu, Z. Ma, P. Liu, X. Zhu, L. Zhao, Z. Xu, Y. Ma and J. Yang. 2026.

**AIM:** To assess the clinical effectiveness, safety, technical feasibility, and challenges of remote robotic surgery in general surgery, gynecology, orthopedics, and urology, focusing on issues like communication technology, ethics, and cost.

**METHODS:** Relevant reports on remote robotic surgery were retrieved from databases such as PubMed, EMBASE, Web of Science, Cochrane Library, VIP, CNKI, and Wanfang (2001-2025). Literature quality was evaluated using tools from the Joanna Briggs Institute (JBI). **RESULTS:** A total of 26 articles were included (13 in Chinese, 13 in English) covering general surgery, gynecology, orthopedics, urology, and thyroid surgery. The results showed that the average operation time was slightly longer than that of traditional methods (about 10-30 min), but the safety was good. Most studies had communications backup plans, such as backup networks or local physician take-overs, to deal with the risk of disruption. Tele-robotic surgery has a high success rate and accuracy with controllable network latency, showing the potential to expand access to medical resources, especially in remote areas. However, it still faces challenges such as network stability, equipment cost, operation accuracy, data privacy, and ethical issues. Most of the included studies reported successful cases, and there was a lack of in-depth analysis of failure cases or adverse outcomes of patients, which may have publication bias. **CONCLUSION:** Despite challenges, remote robotic surgery shows promise in overcoming geographical and resource limitations. The quality of current evidence is low, with serious methodological limitations and reporting bias. The establishment of international mandatory registration systems, standardized safety protocols, and transnational collaboration networks are urgent to promote this field from "proof of concept" to "clinical practice". But, with continuous technological advancements, it is expected to play an increasingly significant role in global healthcare.

PubMed-ID: [41813998](#)

DOI: [10.1007/s00464-026-12616-9](#)

#### **Comparative Efficacy of Radioiodine Therapy With Adjunctive Thionamides vs Either Treatment Alone in the Management of Graves Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.**

*J Clin Endocrinol Metab*, 111(3):892-903.

S. R. Mirjalili, E. Razmpoosh, R. Eshraghi, M. Ashoori and S. Soltani. 2026.

**CONTEXT:** Antithyroid drugs (ATDs) and radioactive iodine (RAI) are the main nonsurgical modalities for Graves disease, but there is no agreement on the optimal approach for utilizing these 2 alternatives, either individually or in combination.

**OBJECTIVE:** This systematic review and meta-analysis of randomized controlled trials (RCTs) aimed to evaluate the success (hypothyroidism/euthyroid) and failure (hyperthyroidism/relapse) of adjunctive (pre-RAI/post-RAI/both) and monotherapy with ATDs in Graves disease. **METHODS:** PubMed, CENTRAL, Scopus, and Web of Science were searched to December 2023 for RCTs on adjunctive ATDs with RAI or ATDs monotherapy in adults. Pooled relative risks were estimated

using a random-effects model. Certainty of findings was assessed with GRADE. RESULTS: We included 21 RCTs (1914 participants). Adjunctive ATDs showed no significant effect on success (RR: 0.96, 95% CI: 0.91-1.01) or failure (RR: 1.17, 95% CI: 0.97-1.42) rate (moderate GRADE) but increased the chance of euthyroid state and reduced hypothyroidism (RR: 0.67, 95% CI: 0.50-0.90) compared to RAI. ATDs monotherapy vs RAI with adjunctive ATDs showed no significant difference in resolving hyperthyroidism (RR: 0.93, 95% CI: 0.84-1.02). Propylthiouracil with RAI was associated with reduced likelihood of success (RR: 0.81, 95% CI: 0.69-0.96). CONCLUSION: ATDs do not significantly affect the success or failure rates of RAI therapy, particularly in long-term follow-up, but they may improve euthyroid outcomes and reduce hypothyroidism. Long-term ATD monotherapy showed no significant difference compared with RAI in resolving hyperthyroidism; however, additional long-term trials are needed to confirm these findings. Management of Graves disease requires individualized physician-patient decisions.

PubMed-ID: [41324316](#)

DOI: [10.1210/clinem/dgaf580](#)

### **Efficacy and safety of immunotherapy in anaplastic thyroid carcinoma: a systematic review and meta-analysis.**

*Int J Surg*, 112(1):1708-21.

K. Ning, Q. Chen, Y. Guo, H. Li, B. Zou, T. Cai, L. Wang, Y. Yu, Z. Luo, J. Bu, H. Hong, Z. Li, X. Wen, M. Jiang, T. Wu, T. Liu, W. Chen, Z. Jiao and A. Yang. 2026.

BACKGROUND: Anaplastic thyroid carcinoma (ATC) is a rare, aggressive solid tumor with poor prognosis. Traditional treatment such as surgery, radiotherapy, and chemotherapy has limited therapeutic effects. In recent years, immunotherapy is changing the treatment pattern of them. We systematically summarize the research status and application of immunotherapy in ATC to provide clinicians and relevant researchers with a comprehensive perspective. METHOD: A comprehensive search of the PubMed and Embase databases identified 18 studies investigating the application of immunotherapy in ATC. These included ten cohort studies and eight case reports. The quality of the included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS) and Joanna Briggs Institute checklist (JBI). Subsequently, a single-proportion meta-analysis and meta-regression were performed to evaluate the efficacy of immunotherapy in ATC. RESULTS: The favorable response rate to immunotherapy in ATC patients (33-100%) varies across cohorts, indicating substantial heterogeneity. The combination of immunotherapy with targeted therapy, as well as the use of neoadjuvant treatment, has led to improved outcomes for ATC. Single-proportion meta-analysis suggests that immunotherapy may provide clinical benefits for a subset of ATC patients (approximately one-third to one-half), but its effectiveness in controlling disease progression remains limited. Meta-regression further indicates that ATC patients with PD-L1 expression or BRAF V600E mutations tend to have better treatment responses. Among the 8 case reports, two patients achieved complete remission after immunotherapy, and four patients died of disease progression after immunotherapy. Mild adverse effects are common, but interstitial pneumonia is associated with poor prognosis in immunotherapy. CONCLUSION: Immunotherapy for ATC has demonstrated safety and efficacy in several studies, especially in patients with PD-L1 expression or BRAF V600E mutations. However, immune-related side effects should be carefully managed, particularly to prevent interstitial pneumonia.

PubMed-ID: [40865971](#)

DOI: [10.1097/JS9.0000000000003301](#)

PMCID: PMC12825863

### **Total thyroidectomy versus lobectomy for unilateral papillary thyroid cancer and lateral lymph node metastasis: A systematic review and meta-analysis.**

*Surgery*, 190:109937.

S. Wu, Y. Zhao, H. Li, G. Zhang, H. Yang, X. Fu, P. Li, P. He, Z. An, X. Wang and H. Luo. 2026.

BACKGROUND: The optimal surgical approach for unilateral papillary thyroid cancer with lateral lymph node metastasis remains a subject of ongoing debate. This systematic review and meta-analysis aims to provide available evidence to facilitate clinical decision-making. METHODS: This study was registered in PROSPERO (CRD420251049050). Indexed databases (PubMed, The Cochrane Library, Embase, and Web of Science) were searched from 2010 to 2025 comparing lobectomy and total thyroidectomy in patients with unilateral papillary thyroid cancer and lateral lymph node metastasis. The primary outcomes include recurrence-free survival, recurrence rate, and postoperative complications. The risk of bias was assessed using the Newcastle-Ottawa Scale. Data were pooled by using the fixed-effects model. Heterogeneity was assessed using the I(2) statistic and sensitivity analysis. RESULTS: Six studies with 1,894 participants were included. The mean duration of follow-up was 76.9 months. The results indicated that lobectomy has a lower risk of complications (risk ratio: 0.21, 95% confidence interval: 0.06-0.70, P = .01) compared with total thyroidectomy, especially for transient hypoparathyroidism (risk ratio: 0.01, 95% confidence interval: 0.00-0.05, P < .00001), permanent hypoparathyroidism (risk

ratio: 0.06, 95% confidence interval: 0.01-0.26,  $P = .0002$ ), and transient recurrent laryngeal nerve injury (risk ratio: 0.49, 95% confidence interval: 0.26-0.91,  $P = .02$ ). Furthermore, lobectomy and total thyroidectomy showed similar effects on 5-year recurrence-free survival (hazard ratio: 1.03, 95% confidence interval: 0.68-1.56,  $P = .91$ ) and recurrence rate (risk ratio = 1.10, 95% confidence interval: 0.77-1.58,  $P = .61$ ). **CONCLUSION:** After excluding gross extrathyroidal extension and aggressive subtypes, this meta-analysis suggests that lobectomy is a preferred surgical approach for unilateral papillary thyroid cancer with lateral lymph node metastasis, providing comparable oncologic outcomes with significantly lower complication rates versus total thyroidectomy. Further validation through prospective cohorts is recommended.

PubMed-ID: [41337976](#)

DOI: [10.1016/j.surg.2025.109937](#)

### **Risk factors for recurrent laryngeal nerve injury following thyroid surgery: a systematic review and meta-analysis.**

*Front Surg*, 12:1731701.

X. Yang, W. Ouyang and P. Ma. 2025.

**BACKGROUND:** Recurrent laryngeal nerve injury is one of the most common and severe complications in thyroid surgery, potentially leading to postoperative hoarseness, dysphagia, or even airway obstruction. Although numerous studies have investigated its risk factors, findings remain inconsistent. This systematic review and meta-analysis aim to synthesize existing evidence and explore risk factors for recurrent laryngeal nerve injury following thyroid surgery. **METHODS:** A systematic search was conducted in PubMed, Embase, Web of Science, and the Cochrane Library databases from their inception to October 1, 2025, to identify observational studies and randomized controlled trials investigating risk factors for recurrent laryngeal nerve injury following thyroid surgery. Two researchers independently performed literature screening, data extraction, and quality assessment using the Newcastle-Ottawa Scale (NOS). Stata 15 software was used to calculate pooled odds ratios (OR) and 95% confidence intervals (CI). **RESULTS:** A total of 20 articles ( $N = 108,343$ ) included, meta-analysis results suggest that older age [OR = 1.45, 95% CI (1.26, 1.66)], Female [OR = 1.15, 95% CI (1.03, 1.28)], extended thyroidectomy [OR = 1.65, 95% CI (1.20, 2.27)], node dissection [OR = 2.28, 95% CI (1.67, 3.09)], reoperation [OR = 2.16, 95% CI (1.86, 2.50)], retrosternal goitre [OR = 2.85, 95% CI (1.87, 4.35)], lack of neuromonitoring [OR = 1.64, 95% CI (1.31, 2.06)] may be associated with RLNI following thyroid surgery. **CONCLUSION:** This study indicates that older age, female gender, extended thyroidectomy, lymph node dissection, reoperation, retrosternal goiter, and absence of nerve monitoring may be independent risk factors for recurrent laryngeal nerve injury following thyroid surgery. **SYSTEMATIC REVIEW REGISTRATION:** <https://www.crd.york.ac.uk/PROSPERO/view/CRD420251106124>, identifier CRD420251106124.

PubMed-ID: [41573254](#)

DOI: [10.3389/fsurg.2025.1731701](#)

PMCID: PMC12819817

### **Simulation unlocked: transforming thyroid surgery training through high-fidelity and curriculum-based innovation-a systematic review.**

*Langenbecks Arch Surg*, 411(1)

D. Zhang, F. Brucchi, D. Barbieri, H. Y. Kim, C. Colombo, G. Donatini, P. Miccoli, W. Che-Wei, G. Dionigi and L. Wan. 2026.

**BACKGROUND:** Simulation-based and structured training have transformed surgical education, providing safe environments for skill acquisition and performance assessment. However, evidence in thyroid surgery remains fragmented across modalities such as simulation, video-based learning, intraoperative neuromonitoring (IONM), and fellowship programs. This systematic review aimed to synthesize primary evidence on educational interventions in thyroid surgery and their impact on technical performance and patient outcomes. **METHODS:** A systematic search of PubMed, Embase, Scopus, and Web of Science was conducted up to April 2025. Eligible studies included randomized trials, prospective or retrospective cohorts, and validation studies assessing simulation-based, structured, or supervised training. Two reviewers independently screened and extracted data, assessing quality using RoB 2, ROBINS-I, or CASP. Due to heterogeneity, results were summarized through a structured narrative synthesis by training modality. **RESULTS:** Ten primary studies (2011-2025) were included. Simulation and virtual-reality training improved technical performance, task completion time, and perceived realism. Supervised resident training reduced operative time after 30-50 cases, approximating senior benchmarks. Video-assisted learning decreased error rates by 49% and staff takeovers by 52%. IONM-based education lowered recurrent laryngeal nerve injury rates and enhanced procedural standardization. Fellowship-trained surgeons showed shorter operative times and fewer complications compared with non-fellowship peers. Across all modalities, training interventions improved either performance or safety outcomes. **CONCLUSIONS:** Structured educational programs-including simulation, supervised learning, and IONM or fellowship curricula-enhance surgical performance and safety in thyroid surgery. Despite limited quantitative evidence, findings support integrating multimodal, competency-based education into surgical training. Standardized outcome measures and multicenter validation are needed to define optimal

learning pathways.

PubMed-ID: [41814046](#)

DOI: [10.1007/s00423-026-04013-6](#)

PMCID: PMC13056755

### **Risk factors of perioperative hypoparathyroidism after thyroidectomy: a systematic review and meta-analysis.**

*Int J Surg*, 112(2):5061-74.

B. Zou, X. Zheng, Z. Li, B. Jiang, K. Ning, H. Li, T. Cai, Y. Yu, Y. Guo, Z. Luo, Q. Chen, Z. Zhang, J. Bu, H. Hong, M. Jiang, T. Wu, Z. Jiao, A. Yang, Z. Yang and W. Chen. 2026.

**BACKGROUND:** Perioperative hypoparathyroidism (hypoPT) represents a prevalent complication of thyroid surgery.

Reported risk factors remain inconsistent, and identical factors may exert different effects depending on whether hypoPT is defined by serum calcium concentration or parathyroid hormone (PTH) levels. A comprehensive synthesis was

undertaken to clarify risk factors for hypoPT under these distinct biochemical definitions. **MATERIALS AND METHODS:**

Three databases (PubMed, Embase, and Scopus) were searched from inception to 2025. Study quality was assessed using the Newcastle-Ottawa scale. Pooled odds ratios (ORs) were calculated to examine associations between risk factors and perioperative hypoPT defined by calcium or PTH. Subgroup analyses were performed according to biochemical definitions, and publication bias was assessed with Begg and Egger tests. **RESULTS:** Sixty-four studies reporting 19 risk factors were

included. Sex was the most frequently analyzed variable. For hypoPT defined by calcium, significant associations were observed with female sex, parathyroid glands remaining in situ, central neck dissection, lateral neck dissection, malignant

pathology, parathyroid autotransplantation, incidental parathyroidectomy, parathyroid tissue in the specimen, and type of surgery (total thyroidectomy vs partial thyroidectomy). Higher postoperative PTH levels acted as a protective factor for calcium-defined hypoPT. For PTH-defined hypoPT, only malignant pathology showed a statistically significant association.

**CONCLUSION:** Patients with thyroid cancer undergoing total thyroidectomy with lateral neck dissection are at greatest risk

of perioperative hypoparathyroidism. Risk reduction relies on precise intraoperative identification of the parathyroid glands, improved surgical proficiency and awareness, and prompt correction of inadvertent excision.

PubMed-ID: [41217744](#)

DOI: [10.1097/JS9.00000000000003871](#)

## Consensus Statements/Guidelines

### **Evaluation and Management of Thyroid Nodules: A Joint Consensus Statement From the British Thyroid Association (BTA), British Association of Endocrine and Thyroid Surgeons (BAETS) and Collaborating Bodies.**

*Clin Endocrinol (Oxf)*, 104(6):682-92.

R. Moorthy, S. P. Balasubramanian, K. Farnell, M. Kelly, G. Madani, M. Moonim, C. Moran, J. Priestley, M. Stechman, E. Watts and K. Boelaert. 2026.

PubMed-ID: [41784119](#)

DOI: [10.1111/cen.70116](#)

PMCID: PMC13124684

## Other Articles

### **Learning curve in autofluorescence-guided thyroid surgery.**

*Front Endocrinol (Lausanne)*, 17:1780244.

A. Abood, T. Ovesen, J. Bach and L. Rolighed. 2026.

**BACKGROUND:** Near-infrared autofluorescence (NIRAF) has been introduced as an adjunct to improve parathyroid gland (PG) identification during thyroid surgery. The extent to which its intraoperative application is influenced by a learning

curve remains unclear. This study aimed to evaluate and quantify a potential learning curve in NIRAF-guided thyroid surgery. **MATERIALS AND METHODS:** We conducted a retrospective cohort study including all consecutive patients undergoing image-based NIRAF-guided thyroid surgery between 2021 and 2023 at two Danish ENT departments. After each procedure, all surgeons completed a standardized form detailing the manner in which NIRAF was applied. The primary outcome was the minimum number of procedures per surgeon needed to achieve consistent surgical behavior, defined as systematic use of NIRAF or a stable pattern of PG autotransplantation. **RESULTS:** A total of 130 patients underwent NIRAF-guided thyroid surgery, performed by two surgeons. Near-infrared autofluorescence was most often utilized on the removed specimen (94.6%), before dissection of the lower thyroid pole (93.1%) and before latero-posterior dissection (88.5%). It was less likely to be utilized before upper thyroid pole dissection (62.3%). For both surgeons, NIRAF application was not systematic in the early phase but became increasingly consistent over time ( $\alpha = 11,0$  (95% CI: 3,5-18,6),  $p=0,013$  and  $\alpha = 5,6$  (95% CI: 0,03-11,2),  $p=0.049$ , respectively). Initially, both surgeons demonstrated remarkably high PG autotransplantation rates, which declined over time ( $\alpha = -3,9$  (95% CI: -7,9 - 0,07),  $p=0,053$  and  $\alpha = -4,8$  (95% CI: -8,1 - (-1,6)),  $p=0.01$ , respectively). Surgeon no. 1 adopted systematic NIRAF use after a minimum of 30 procedures, while surgeon no. 2 displayed consistent behavior with regard to PG autotransplantation after a minimum of 30 procedures. **CONCLUSIONS:** This study demonstrates a clear learning curve in NIRAF-guided thyroid surgery. A minimum of 30 procedures per surgeon was required to establish consistent surgical practice, either in terms of systematic NIRAF application or a stable pattern of PG autotransplantation. These findings underscore the importance of structured implementation strategies and targeted training when integrating the NIRAF technology into routine surgical practice.

PubMed-ID: [41948550](#)

DOI: [10.3389/fendo.2026.1780244](#)

PMCID: PMC13050706

#### **Pushing the Envelope: Expanding the use of thermal ablation techniques for small papillary thyroid carcinomas.**

*Am J Surg*, 253:116780.

P. Abraham and S. Dream. 2026.

PubMed-ID: [41419429](#)

DOI: [10.1016/j.amjsurg.2025.116780](#)

#### **Thyroid Function After Hemithyroidectomy in Children.**

*Thyroid*, 36(2):195-202.

Y. Adusumelli, C. R. Petty, C. E. Cherella, J. R. Smith, B. P. Modi and A. J. Wassner. 2026.

**BACKGROUND:** The risk of hypothyroidism after hemithyroidectomy is not well defined in the pediatric population. We sought to determine the incidence of hypothyroidism after hemithyroidectomy in children and the clinical factors associated with this risk. **METHODS:** This is a retrospective cohort study of consecutive pediatric patients (<19 years of age) who underwent hemithyroidectomy in a pediatric thyroid center between 1998 and 2023, with data available on postoperative thyroid function and/or levothyroxine (LT4) treatment. The primary outcome was the composite of persistent hypothyroidism (thyrotropin [TSH]  $\geq 5$  mIU/L) or LT4 treatment (PersHypo/LT4). Secondary outcomes were persistent hypothyroidism and transient hypothyroidism. Univariable and multivariable survival analysis and logistic regression were used to evaluate associations of these outcomes with clinical characteristics. **RESULTS:** A total of 136 eligible patients (85% female) underwent hemithyroidectomy at a median (range) age of 15.4 (0.14-19.0) years. The median (interquartile range) postsurgical follow-up was 1.10 (0.15-3.2) years for thyroid function and 1.76 (0.38-4.3) years for LT4 treatment status. PersHypo/LT4 occurred in 27/136 patients (20%), with an estimated risk of 18.1% [CI: 12.1-26.6%] at 1 year and 27.5% [CI: 18.7-39.2%] at 5 years. PersHypo/LT4 occurred within 12 months in 21/27 cases (78%) and after 12 months in 6/27 (22%). PersHypo/LT4 was associated with preoperative TSH (hazard ratio 1.89, [CI: 1.31-2.74],  $p = 0.001$ ), and preoperative TSH  $\geq 2$  mIU/L optimally distinguished patients with high (58.8%) versus low (12.8%) 5-year risk of PersHypo/LT4 (receiver operator characteristic AUC 0.73, [CI: 0.60-0.85]). The presence of thyroperoxidase (TPO) antibodies was independently associated with increased risk of PersHypo/LT4 (OR: 7.37, [CI: 1.09-49.9],  $p = 0.041$ ). Persistent hypothyroidism occurred in 14/128 patients (11%), with an estimated 5-year risk of 12.9% [CI: 7.7-21.1%]. Severe hypothyroidism occurred in 5/136 patients (3.7%), and transient hypothyroidism occurred in 22/136 patients (16%). **CONCLUSIONS:** Persistent hypothyroidism or LT4 treatment occurs in 27.5% of children within 5 years after hemithyroidectomy, usually in the first postoperative year. Preoperative TSH < 2 mIU/L may identify children at low risk, whereas preoperative TSH  $\geq 2$  mIU/L, particularly in conjunction with TPO antibodies, may identify children at high risk. Transient hypothyroidism also occurs commonly but may not require treatment. These data should inform preoperative counseling and postoperative monitoring around hemithyroidectomy in children.

PubMed-ID: [41468168](#)

DOI: [10.1177/10507256251412322](#)

**Long-Term Morbidity after Postoperative Hypoparathyroidism in Thyroid Cancer Patients: A Nationwide Population-Based Cohort Study.**

*Thyroid*, 36(3):320-9.

S. H. Ahn, S. H. Seo, C. Y. Jung, D. H. Yu, K. P. Kim, Y. Kim, Y. Cho, D. H. Seo, S. H. Kim, J. I. Yoo and S. Hong. 2026.

**BACKGROUND:** Chronic hypoparathyroidism (hypoPT) is associated with various systemic morbidities; however, its impact in thyroid cancer patients following thyroidectomy remains unclear. This study evaluated the risk of long-term morbidities in thyroid cancer patients who developed permanent postoperative hypoparathyroidism (PO-hypoPT), compared to those with preserved parathyroid function. **METHODS:** This was a retrospective cohort study using South Korea's nationwide claims data encoded in the Observational Medical Outcomes Partnership Common Data Model. Among 217,156 thyroid cancer patients who underwent thyroidectomy from 2013 to 2020, 15,592 patients with PO-hypoPT and 27,906 matched controls with preserved parathyroid function were identified after 1:2 propensity score (PS) matching. Long-term morbidities associated with hypoPT included nephrolithiasis, renal insufficiency, major adverse cardiac events (MACE), seizures, infections, cataracts, and depression. Hazard ratios (HRs) for these morbidities were estimated using Cox proportional hazards regression analysis after large-scale PS matching. **RESULTS:** The median follow-up duration in both groups was approximately 5 years. Patients with PO-hypoPT had a significantly higher risk of nephrolithiasis (HR 1.17, confidence interval [CI] 1.04-1.30), renal insufficiency (HR 1.75, [CI 1.50-2.03]), and MACE (HR 1.10, [CI 1.01-1.19]) compared to those with preserved parathyroid function. However, the risks of other long-term morbidities, including seizures, infections, cataracts, and depression, were not significantly different between the two groups. The association between PO-hypoPT and renal insufficiency remained consistent across all subgroups stratified by sex, age, and duration of calcium supplementation. **CONCLUSIONS:** PO-hypoPT in thyroid cancer patients is associated with increased long-term morbidity, particularly renal and cardiovascular complications. Long-term monitoring of renal function and cardiovascular health is warranted in this population.

PubMed-ID: [41705866](#)

DOI: [10.1177/10507256261425690](#)

**Hashimoto's Thyroiditis Beyond Thyroid Hormones: A Systematic Review of Autoimmunity, Inflammation, and Multidimensional Burden.**

*Clin Endocrinol (Oxf)*, 105(1):3-13.

G. Alfi, V. Caruso, G. Grenno, A. Gemignani, A. Antonelli, P. Fallahi and S. M. Ferrari. 2026.

**BACKGROUND:** Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease. Although levothyroxine therapy effectively normalizes thyroid-stimulating hormone (TSH) in most patients, persistent symptoms are frequently reported, suggesting that autoimmunity and inflammation contribute to reduced quality of life (QoL) independently of thyroid hormone levels. **METHODS:** According to PRISMA guidelines, we systematically searched for MEDLINE, Scopus, and Web of Science studies that assessed the association of thyroid autoimmunity, inflammatory markers, and QoL in adults with HT. Included designs were observational, interventional, and longitudinal studies that published qualified QoL outcomes and immune/inflammatory markers. **RESULTS:** Across diverse study designs, HT patients-typically euthyroid or receiving long-term levothyroxine therapy-consistently reported lower QoL compared with controls, particularly in cognitive, affective, and vitality domains. Elevated anti-thyroid antibodies (anti-TPO, anti-Tg) were negatively correlated with QoL, whereas TSH and thyroid hormone levels showed no consistent association. Interventional studies demonstrated that total thyroidectomy or therapies associated with reduced antibody titers were accompanied by improvements in fatigue and QoL. However, an important caveat must be emphasized. Some studies did not confirm a direct association between antibody levels and symptom severity, likely reflecting methodological variability and heterogeneity in QoL assessment tools. **CONCLUSION:** There is evidence that HT exerts a multidimensional impact beyond endocrine dysfunction, with chronic autoimmunity and low-grade inflammation contributing to impaired QoL. These findings should be taken into account and perhaps challenge a purely TSH-centric model and call for a broader, patient-centered approach that integrates immunological, psychological, and subjective outcomes. Properly designed longitudinal and interventional trials are required to establish causal pathways and support the personalization of therapy.

PubMed-ID: [41766594](#)

DOI: [10.1111/cen.70114](#)

### **Characteristics and outcome of pediatric and adult differentiated thyroid cancer with distant metastases.**

*Front Endocrinol (Lausanne)*, 17:1668565.

A. S. Alzahrani, L. Alobaid, E. Albasri, A. Hadadi, A. Hakami, F. Abothenain, D. Alturki, N. Ewain, A. Howaidi, H. Alhindi, G. Alskait, Y. Aljufan, S. Alghaihb, A. Alkhalifah, L. AlAyoubi and A. Abualnaja. 2026.

INTRODUCTION: Previous studies suggested differences in the histopathological and molecular characteristics and outcome between pediatric and adult differentiated thyroid cancer (DTC). In this study, we focused on the characteristics and outcome of distant metastases (DM) between pediatric and adult patients with DTC. OBJECTIVES: To compare DM between pediatric (pDTC) and adult DTC (aDTC). PATIENTS AND METHODS: We studied 35 pDTC ( $\leq 18$  years) and 79 aDTC with DM seen over 20 years. The median age was 16 and 55 years and the F:M ratio was 3.4:1 and 1.7:1, respectively. Total thyroidectomy was performed in 91.4% and 93.7% and lymph node dissection in 94.3% and 64.6% of pediatric and adult patients, respectively. Radioactive iodine (RAI) ablation/therapy was administered to all patients except one. RESULTS: pDM mostly involved a single organ (34/35), predominantly the lungs (32/35), and rarely the bone (2/35) and brain (1/35). By contrast, aDM were frequently multi-organ (45/79) involving lungs (72 patients), bone (50), brain (9), liver (10), kidneys (3), adrenal glands (2), breast (1) and soft tissues (3). Additional therapies (e.g. surgery, RAI) were administered to 28 and 78 pediatric and adult patients, respectively. At the last follow-up, only 1 (2.9%) vs. 6 (7.6%) patients had progressive metastases and 1 (2.9%) vs. 46 (58.2%) patients died due to DTC in pediatric and adult groups, respectively ( $P < 0.0001$ ). Other patients either were in an indeterminate status or had stable non-progressive metastases. CONCLUSIONS: pDM mostly involve single organs and have good outcome and rare mortality. aDM are frequently multi-organ, progressive and associated with high mortality of 58% over about 4.5 years.

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DOI: [10.3389/fendo.2026.1668565](#)

PMCID: PMC12913069

### **Molecular testing for the management of indeterminate thyroid nodules.**

*Endocr Relat Cancer*, 33(2)

I. Azaryan, C. Maxwell, D. H. Tran, J. A. Sipos and M. Endo. 2026.

Thyroid nodules are extremely common with a prevalence of up to 70% in the general population. While the majority of these are benign, 5-10% harbor a malignancy. Fine-needle aspiration has been widely implemented to stratify the cancer risk of thyroid nodules. Standardized diagnoses using the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) have aided in the triaging of nodules. While many cases are categorized with a definite diagnosis of benign (Bethesda II) or malignant (Bethesda VI) results, approximately 25% of cases are diagnosed as atypia of undetermined significance (AUS) (Bethesda III) or follicular neoplasm (Bethesda IV). These cytological categories imply an intermediate risk of malignancy ranging from 16 to 48%. These nodules, collectively defined as indeterminate thyroid nodules, pose diagnostic and management challenges. In recent years, several commercial molecular testing (MT) methods have become available to improve risk stratification, successfully helping to reduce unnecessary surgeries. In this review, we provide an overview of MT methods, present practical guidance on interpreting test results, and conclude with a discussion on future directions in the field.

PubMed-ID: [41609503](#)

DOI: [10.1530/ERC-25-0258](#)

### **Validation of molecular profiling to preoperatively predict aggressive pathologic features in differentiated thyroid cancer.**

*Surgery*, 189:109698.

J. Bauzon, J. Shin, G. Plitt, R. Perez-Soto, M. S. Lui, J. H. Choi, J. Jin, V. Krishnamurthy, E. Berber, K. B. Heiden, A. Siperstein and G. Romero-Velez. 2026.

BACKGROUND: The 2015 American Thyroid Association guidelines stratify recurrence risk of differentiated thyroid cancer using pathologic findings. Aggressive features may reclassify tumors as intermediate-to-high risk in patients initially suitable for lobectomy, warranting completion thyroidectomy. Signatures represent distinct patterns of mRNA expression on the basis of molecular pathway features. This study evaluated whether molecular expression profiles ("signatures") could preoperatively differentiate high-risk tumors and potentially guide extent of surgery. METHODS: Patients who underwent thyroid nodule molecular testing with the Afirma Genomic Sequencing Classifier and subsequent operative resection from 2017 to 2024 were identified. Using features described on surgical pathology, patients were grouped into ATA guideline-based low-risk or intermediate/high-risk cohorts. Among the signatures assessed, Invasion Score was developed to rule out extrathyroidal extension or extensive vascular invasion, whereas Sodium-Iodide Symporter Expression reflects mRNA production levels of the transmembrane glycoprotein involved in thyroid-iodine uptake.

Signatures were compared among cohorts using Mann-Whitney U and Kruskal-Wallis tests. Logistic regression was used for multivariate analysis. RESULTS: Of 445 patients analyzed, 366 were low risk and 79 were intermediate/high risk. Among 30 signatures evaluated, expression varied significantly among study cohorts in 23 (77%). Multivariate analysis demonstrated the Invasion Score signature as predictive of greater American Thyroid Association risk classification (odds ratio, 1.3; 95% confidence interval, 1.1-1.5,  $P = .005$ ) whereas Sodium-Iodide Symporter Expression was protective (odds ratio, 0.78; 95% confidence interval, 0.63-0.94,  $P = .015$ ). CONCLUSION: Multiple signature expression profiles showed marked variation among American Thyroid Association risk classes and may help enhance preoperative prognostication. Although Invasion Score mirrors greater risk pathologic features, upregulated Sodium-Iodide Symporter Expression appears to protect from greater American Thyroid Association risk class, although further studies are needed to confirm. PubMed-ID: [41058325](#)  
DOI: [10.1016/j.surg.2025.109698](#)

### **Integrating Artificial Intelligence in Thyroid Nodule Management: Clinical Outcomes and Cost-effectiveness Analysis.**

*J Clin Endocrinol Metab*, 111(2):405-17.

J. Bodoque-Cubas, J. Fernandez-Saez, S. Martinez-Hervas, M. J. Perez-Lacasta, M. Carles-Lavila, R. M. Pallares-Gasulla, J. J. Salazar-Gonzalez, J. V. Gil-Boix, M. Miret-Llaurado, A. Aulinas-Maso, I. Arguelles-Jimenez and S. Tofe-Povedano. 2026.

OBJECTIVE: The increasing incidence of thyroid nodules (TNs) raises concerns about overdiagnosis and overtreatment. This study evaluates the clinical and economic impact of KOIOS, a Food and Drug Administration-approved artificial intelligence (AI) tool for the management of TN. METHODS: A retrospective analysis was conducted on 176 patients who underwent thyroid surgery between May 2022 and November 2024. Ultrasound images were evaluated independently by an expert and novice operators using the American College of Radiology Thyroid Imaging Reporting and Data System, while KOIOS provided AI-adapted risk stratification. Sensitivity, specificity, and receiver operating (ROC) curve analysis were performed. The incremental cost-effectiveness ratio (ICER) was defined based on the number of optimal care interventions (fine-needle aspiration biopsies and thyroid surgeries). Both deterministic and probabilistic sensitivity analyses were conducted to evaluate model robustness. RESULTS: KOIOS AI demonstrated similar diagnostic performance to the expert operator [area under the curve (AUC): 0.794, 95% confidence interval (CI): 0.718-0.871 vs 0.784, 95% CI: 0.706-0.861;  $P = .754$ ] and significantly outperformed the novice operator (AUC: 0.619, 95% CI: 0.526-0.711;  $P < .001$ ). ICER analysis estimated the cost per additional optimal care decision at -euro8085.56, indicating KOIOS as a dominant and cost-saving strategy when considering a third-party payer perspective over a 1-year horizon. Deterministic sensitivity analysis identified surgical costs as the main drivers of variability, while probabilistic analysis consistently favored KOIOS as the optimal strategy. CONCLUSION: KOIOS AI is a cost-effective alternative, particularly in reducing overdiagnosis and overtreatment for benign TNs. Prospective, real-life studies are needed to validate these findings and explore long-term implications.

PubMed-ID: [40650885](#)

DOI: [10.1210/clinem/dgaf399](#)

### **A tertiary-center experience of patients with simultaneous medullary and papillary thyroid carcinomas.**

*Hormones (Athens)*, 25(1):237-47.

G. Boutzios, Z. Garoufalia, M. D. Keramida, D. Karaviti, S. A. Paschou, E. Spartalis and G. Tsurouflis. 2026.

PURPOSE: Papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma (MTC) are thyroid carcinomas of different embryological origin. Over the past few decades, several cases have been reported in which PTC and MTC coexist in the same lymph node but separated by normal tissue, this being termed mixed medullary/follicular thyroid carcinoma (MMFTC). Our study aimed to investigate the prevalence of PTC in a cohort of MTC patients in an attempt to define (a) the clinical phenotype of patients with MTC/PTC and (b) any potent association with age, carcinoembryonic antigen (CEA), calcitonin levels, gender or number of operations. MATERIALS AND METHODS: This is a single-center retrospective observational study of an endocrinology outpatient clinic at a tertiary general university hospital. All patients diagnosed with MTC/PTC between November 2017 and March 2021 were recruited. Those with positive RET were excluded. Statistical analysis was performed using SPSS software (SPSS 25. Inc. Chicago, IL). RESULTS: A total of 30 patients with MTC/PTC, either as separate tumors or as collision tumors combining MTC and PTC, were included in our study. The mean age was 58.43 +/- 12.31 years. Slightly over half of the patients were males (53.3%). Univariate analysis showed no association between MTC/PTC, either as separate tumors or as collision tumors, coexistence and age, calcitonin levels, CEA, gender, number of metastases, or number of operations. Multivariate analysis confirmed no significant associations, although the small sample size limited its scope. CONCLUSION: In our small case series, no association was demonstrated between simultaneous MTC/PTC and age, CEA, calcitonin levels, gender, or number of operations. This entity likely represents a primary tumor with an incidental pathologic finding of a second malignancy.

PubMed-ID: [41348279](#)

DOI: [10.1007/s42000-025-00725-4](#)

**Navigating the lymphatic labyrinth: insights into lateral cervical metastasis patterns in papillary thyroid carcinoma a multicenter study.**

*Int J Surg*,

T. Cai, Z. Jiao, Y. Guo, Y. Yu, K. Ning, B. Zou, M. Jiang, Z. Yang, T. Liu, W. Chen, T. Wu and A. Yang. 2025.

INTRODUCTION: Papillary thyroid carcinoma (PTC) often spreads to lateral cervical lymph nodes (LNs), but research on their distribution and drainage is limited. Delphian lymph node (DLN) metastasis is a key indicator of regional lymph node (LN) involvement and recurrence in PTC, yet its exact role in predicting regional LN metastasis and its effect on other regional LNs is unclear. METHODS: A total of 3,356 patients who had surgery at \*\*\*, \*\*\*, and \*\*\* were enrolled. PTC subspecialized pathologists independently evaluated the primary tumors and eight regions of the involved LNs. T test, Chi-square test, Kaplan-Meier survival analysis, propensity-score matching, and multivariate Cox regression were used. RESULTS: This study is the first to propose a reticular structure model for lateral cervical LNs, with each region being interconnected, first-station LN metastasis may occur within any of these regions, and we conduct a mapping of LN metastasis. In addition, compared to DLN- patients, DLN + patients had a significantly higher rate of metastasis in both central and lateral cervical regions. There was a notable rise in metastatic regions, total metastatic LNs, and particularly contralateral cervical metastasis in DLN + patients. DLN exhibit a close relationship with other regional lymph nodes and play a significant role in prognostic assessments. Researchers further discussed the correlation between the DLN and lateral cervical LNs, providing anatomical evidence for this association: the DLN positioned at the hub of lateral cervical LNs reticular structure, functions as a hub connecting with other LNs. CONCLUSION: This study focuses on the reticular structure of cervical LNs, identifying the DLN as the central component of this structure, with significant connectivity to other Levels.

PubMed-ID: [41399131](#)

DOI: [10.1097/JS9.0000000000004437](#)

**Procalcitonin Doubling Time for Postoperative Monitoring of Medullary Thyroid Carcinoma: A Comparative Kinetic Analysis.**

*Clin Endocrinol (Oxf)*, 105(2):252-8.

A. Campenni, P. P. Ovcaricek, A. Posabella, R. M. Ruggeri and L. Giovanella. 2026.

BACKGROUND: Calcitonin doubling time (CT-DT) is an established prognostic tool in medullary thyroid carcinoma (MTC), yet CT measurement can be affected by analytical variability and assay interference. Procalcitonin (PCT) has shown promise as a complementary biomarker, but data on PCT doubling time (PCT-DT) remain scarce. METHODS: Longitudinal CT and PCT were measured using Elecsys immunoassays in 25 MTC patients followed for up to 24 months after thyroidectomy. Doubling times were estimated using log-linear regression and a rolling-window approach. Agreement was assessed using Spearman correlation, Bland-Altman analysis, and Cohen's kappa across predefined DT categories. RESULTS: CT and PCT kinetics showed clear separation across response categories. In progressive disease, CT-DT and PCT-DT were strongly correlated with minimal systematic bias and substantial categorical agreement (kappa = 0.76). Short DT values clustered in structural incomplete responders. CONCLUSIONS: PCT-DT closely mirrors CT-DT and may serve as a complementary kinetic marker in the postoperative monitoring of MTC, particularly when CT interpretation is uncertain; however, these findings should be considered exploratory and warrant confirmation in larger prospective cohorts before clinical implementation.

PubMed-ID: [42013286](#)

DOI: [10.1111/cen.70147](#)

**Risk of Complications in Patients Undergoing Thyroidectomy for Graves' Disease (LUNA Study).**

*Otolaryngol Head Neck Surg*, 175(1):78-85.

G. L. Canu, F. Medas, F. Cappellacci, G. Lanzolla, L. Rossi, G. Di Filippo, A. Chorti, I. Pliakos, G. Lazzari, E. Morelli, K. Dekova, L. Sacco, L. Fantina, N. de Manzini, F. Boi, S. Bakkar, C. Dobrinja, T. Papavramidis, G. Materazzi, P. G. Calo and L. S. C. Group. 2026.

OBJECTIVE: To evaluate the risk of complications in patients with Graves' disease undergoing thyroidectomy by high-volume surgeons. STUDY DESIGN: Retrospective, multicenter, international study. SETTING: Data were obtained from 5 centers in Europe. METHODS: Patients undergoing total thyroidectomy between 2019 and 2023 were analyzed. Enrolled patients were divided in 2 groups: GD Group, including those with Graves' disease, and C Group (control group). Complications were assessed after performing propensity score matching (1:1). RESULTS: Based on inclusion/exclusion

criteria, 8518 patients were enrolled: 1067 in GD Group and 7451 in C Group. Following propensity score matching, the study population consisted of 1068 patients: 534 in GD Group and 534 in C Group. In GD Group, there were 84 (15.73%) cases of postoperative hypoparathyroidism (65, 12.17%, temporary and 19, 3.56%, permanent), 15 (2.81%) unilateral recurrent laryngeal nerve lesions, 1 (0.19%) bilateral recurrent laryngeal nerve lesion, 15 (1.40%) temporary recurrent laryngeal nerve lesions, 2 (0.19%) permanent recurrent laryngeal nerve lesions, 22 (4.12%) neck hematomas (17, 3.18%, managed conservatively and 5, 0.94%, requiring surgical revision of hemostasis), and 2 (0.37%) wound infections. Overall postoperative hypoparathyroidism, permanent hypoparathyroidism, unilateral recurrent laryngeal nerve injury, and temporary recurrent laryngeal nerve injury were significantly greater in GD Group. Other complications were comparable. CONCLUSION: Complications were greater in patients with Graves' disease, however occurrence rates were low. Based on our findings, it can be stated that thyroidectomy in patients with Graves' disease, even for high-volume surgeons, represents a more challenging procedure, but it can nevertheless be considered a valid therapeutic option.

PubMed-ID: [42015597](#)

DOI: [10.1002/ohn.70253](#)

**A commentary on "Autofluorescence alone is not enough: a combined strategy for accurate identification of parathyroid tissue in thyroidectomy specimens".**

*Int J Surg*, 112(4):10902-3.

J. H. Cao, W. Li and B. Zhang. 2026.

PubMed-ID: [41532466](#)

DOI: [10.1097/JS9.0000000000004728](#)

PMCID: PMC13105671

**Robotic thyroidectomy using the da Vinci SP surgical system.**

*Surg Endosc*, 40(3):1876-86.

Y. W. Chang. 2026.

BACKGROUND: This study aimed to summarize the current clinical evidence, technical advances, and practical insights related to robotic thyroidectomy using the da Vinci SP (Single-Port) surgical system, with an emphasis on the evolution of surgical approaches and outcomes based on the author's institutional experience and literature review. METHODS: A focused narrative review of studies published between 2019 and 2025 was conducted to evaluate the safety, feasibility, and clinical performance of single-port robotic thyroidectomy. Five representative SP approaches (single-port transoral robotic thyroidectomy [SP-TORT], single-port transaxillary robotic thyroidectomy [SP-TART/START], retroauricular approach using the da Vinci SP system [RA-SP], single-port robotic areolar approach [SPRA], and gas-insufflation one-step single-port transaxillary [GOSTA]) were compared in terms of operative technique, ergonomics, and postoperative outcomes. RESULTS: Across multiple institutions, SP robotic thyroidectomy demonstrated operative times, complication rates, and lymph node yields comparable to those of conventional multi-port or open surgery while providing distinct cosmetic and ergonomic advantages. Transient recurrent laryngeal nerve palsy and hypocalcemia were the most common complications, with low overall morbidity. Recent reports have extended the SP technology to modified radical neck dissection (MRND) through the START, SPRA, and GOSTA approaches, confirming the oncologic feasibility of comprehensive nodal dissection within a confined workspace. CONCLUSION: The da Vinci SP system represents a meaningful advancement in minimally invasive endocrine surgery by enabling single-port robotic thyroidectomy through various remote-access approaches. Current evidence supports its safety, feasibility, and favorable cosmetic outcomes when applied to appropriately selected patients. However, further refinement of instrumentation, optimization of surgical techniques, and accumulation of long-term clinical data are required to expand its indications and to define its role in advanced thyroid diseases more clearly.

PubMed-ID: [41721029](#)

DOI: [10.1007/s00464-026-12644-5](#)

**Comment on "Evaluating the necessity of prophylactic lateral neck dissection in medullary thyroid carcinoma based on preoperative calcitonin levels: a multicenter retrospective cohort study".**

*Int J Surg*, 112(4):10825-6.

Y. Chen, S. Hong and Y. Chen. 2026.

PubMed-ID: [41537339](#)

DOI: [10.1097/JS9.0000000000004663](#)

PMCID: PMC13105524

**A synergistic drug combination that aids our battle against anaplastic thyroid carcinoma: a case report and discussion.**

*Hormones (Athens)*, 25(1):267-71.

E. Chumbiauca, I. Valdes Calero, J. M. Lopez Picazo, M. Moreno-Jimenez, A. Argueta, M. D. Lozano, L. Duntas and J. C. Galofre. 2026.

BACKGROUND: Anaplastic thyroid carcinoma (ATC) is a rare and highly aggressive malignancy historically associated with a poor prognosis and a median survival of only 3.16 months. However, recent advances in molecular profiling and immunotherapy are improving outcomes. CASE PRESENTATION: We report the case of a 68-year-old man diagnosed with stage IVC ATC who achieved sustained disease stabilisation and long-term survival. Initial treatment with chemotherapy and radiotherapy led to partial remission of the primary tumour, although there was progression of metastatic disease. The patient was subsequently enrolled in a clinical trial investigating an anti-PD-L1 antibody with positive test results, followed by treatment with pembrolizumab. The latter resulted in nearly 11 years of disease control without significant adverse effects, an exceptional outcome in the context of ATC. CONCLUSION: This case underscores the transformative potential of immunotherapy in the management of advanced ATC and highlights the importance of continued research into combinatorial therapeutic strategies and predictive biomarkers to optimise treatment outcomes.

PubMed-ID: [41288952](#)

DOI: [10.1007/s42000-025-00738-z](#)

PMCID: PMC13013152

**Premedication with Lugol's solution in total thyroidectomy for graves' disease and toxic multinodular goiter: is it still indicated?**

*Updates Surg*, 78(1):343-50.

D. Ciriotto, S. Bernardi, R. Eramo, V. Calabro, A. Modica, N. de Manzini and C. Dobrinja. 2026.

Premedication with Lugol's solution (LS) has traditionally been used to reduce the vascularization and friability of the thyroid gland before total thyroidectomy in patients with Graves' disease (GD) and toxic multinodular goiter (TMNG) with thyrotoxicosis and/or with undetectable serum TSH. However, the effectiveness and applicability of this treatment remain subjects of debate. This study aims to evaluate the surgical and postoperative outcomes in patients premedicated with LS compared to those who were not premedicated. Data from 100 patients who underwent total thyroidectomy for GD and TMNG at our center from 2014 to 2024 were analyzed. Patients were divided into two groups: Lugol+, premedicated with LS (n = 57), and Lugol-, not premedicated (n = 43). Variables analyzed included thyroid diameter, thyroid weight, operative time, postoperative hemorrhage, hypocalcemia, recurrent laryngeal nerve palsy, length of hospital stay, rate of reintervention for hemorrhage, intraoperative thyroid consistency. No statistically significant differences were found between the groups regarding postoperative hemorrhage (1.7% in Group Lugol+ vs. 2.3% in Group Lugol-), operative time (median: 95 vs. 85 min), immediate postoperative complications such as transient hypoparathyroidism (15.8% vs. 9.3%) and transient recurrent laryngeal nerve (RLN) palsy (3.5% vs. 2.3%), nor the other variables analyzed. Our data suggest that routine preoperative preparation with LS may not be mandatory. This study supports the thesis that patients with GD and TMNG who cannot be premedicated due to inability to obtain LS, insufficient time for preoperative preparation, or lesser compliance by patient, may still be eligible for surgery.

PubMed-ID: [41419724](#)

DOI: [10.1007/s13304-025-02475-9](#)

PMCID: PMC12909308

**Autoimmune Thyroid Disease in a Cohort of Children With Increased Genetic Susceptibility to Type 1 Diabetes: The Environmental Determinants of Diabetes in the Young Study.**

*Clin Endocrinol (Oxf)*, 104(4):394-404.

J. L. Clasen, B. Jonsdottir, J. Toppari, S. Johnson, C. Andren Aronsson, M. Lundgren, K. Vehik, M. J. Haller, H. Elding Larsson and T. S. Group. 2026.

OBJECTIVE: Clinical autoimmune thyroid disease (AITD), presenting as either hypo- or hyperthyroidism, can occur at any

age. Autoantibodies against thyroid peroxidase or thyroglobulin precede the onset of clinical AITD. We aimed to assess factors associated with AITD in children and determine if risk factors for AITD differ among the subset who have developed thyroid autoantibodies. DESIGN: Prospective cohort study. PATIENTS: The TEDDY Study is a cohort of 8676 children with increased genetic susceptibility for type 1 diabetes, followed to age 15 years. MEASUREMENTS: Hypothyroidism and hyperthyroidism clinical diagnoses as well as medications used for treating AITD were reported to study staff at every visit, 2 to 4 times per year. Children were screened for thyroid autoantibodies at ages 9 and 14, and if positive, previously collected samples were retrospectively analyzed to determine the age when autoantibodies first appeared. RESULTS: Of 5203 children screened for thyroid autoantibodies, 99 were diagnosed with AITD. Female sex, human leukocyte antigen (HLA) haplogenotype, and family history of hypothyroidism, hyperthyroidism, type 1 diabetes, and celiac disease were associated with risk of AITD. Among the 575 children positive for thyroid autoantibodies, HLA remained associated with AITD, while the estimates for family history were attenuated, and no association was present for sex. CONCLUSIONS: Female sex, family history of autoimmune disease, and HLA haplogenotype are risk factors for AITD in genetically high-risk children, but these trends differ for progression from thyroid autoimmunity to AITD.

PubMed-ID: [41395711](#)

DOI: [10.1111/cen.70070](#)

PMCID: PMC12824991

### **Precision medicine in thyroid nodules: current strategies, challenges, and future directions.**

*Hormones (Athens),*

M. J. Concepcion-Zavaleta, J. M. Fuentes-Mendoza, C. A. Rojas-Hipolito, D. Sanchez-Mejia, M. A. Lopez-Torres, L. Concepcion-Urteaga, C. D. Armas and J. Paz-Ibarra. 2026.

Thyroid nodules represent a common clinical challenge, with ultrasound studies detecting them in 20-76% of adults. Although the majority are benign, malignancy occurs in approximately 5-15% of cases. Current diagnostic strategies integrate high-resolution ultrasound (e.g., TI-RADS), fine-needle aspiration cytology (Bethesda system), and molecular testing. For indeterminate nodules (Bethesda III/IV), classifiers such as Afirma(R) GSC and ThyroSeq(R) v3 show a 90-95% negative predictive value, which could reduce unnecessary surgeries by 30-33%. However, challenges remain, including limited accessibility, variable cost-effectiveness (USD 4,234-14,277 per avoided surgery), and difficulties in interpreting variants of uncertain significance. Emerging technologies show particular promise, including artificial intelligence (AI) applications in ultrasound interpretation (achieving 68-82% sensitivity, although performance decreases in external validation cohorts) and novel biomarkers like circulating tumor DNA and microRNA (miRNA) profiles. Precision medicine approaches now enable more tailored management, with active surveillance recommended for low-risk nodules and molecular profiling guiding surgical decision-making. Future directions include liquid biopsy techniques, improved dynamic risk stratification models, and enhanced integration of multiomics data. These advances aim to maintain excellent oncologic outcomes while minimizing overtreatment of indolent lesions. The field continues to evolve toward increasingly personalized care paradigms that balance diagnostic accuracy with quality-of-life considerations.

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### **Relationship between vascular density and microenvironment in medullary thyroid carcinoma.**

*Endocr Relat Cancer*, 33(3)

M. E. de Castro, J. F. Mariano, M. M. L. Kizys, L. Ceolin, R. Natal, H. Carneiro, R. N. Ramos, N. O. S. Camara, C. P. Camacho, F. de Oliveira Facuri Valente, S. C. Lindsey, D. D. Dos Santos, C. D. Gil, J. R. M. Martins, S. de Alcantara Rodrigues, L. S. Ward, F. A. Soares, R. Monteiro de Barros Maciel and L. L. Cunha. 2026.

This study explored the interplay between vascular density and the immune microenvironment in medullary thyroid carcinoma (MTC) to elucidate their impact on tumor behavior. Using tissue microarray (TMA) analysis of 24 histopathologically confirmed MTC cases, we assessed immune cell infiltration (CD68+ macrophages, CD3+/CD4+/CD8+/CD20+ lymphocytes, granzyme B, and FOXP3+) and vascular markers (D2-40, CD31, and ERG) across tumor regions: center, interface, adjacent normal tissue, and metastases. Vascular density was quantified using ImageJ, while immune markers were analyzed using the QuPath software. The key findings revealed distinct spatial heterogeneity in the vascular distribution. D2-40+ lymphatic vessel density was significantly elevated in adjacent normal tissue compared to the tumor center ( $P < 0.05$ ), whereas ERG+ microvessel density was the highest at the tumor interface. ERG+ vascular density at the interface was positively correlated with mast cell infiltration (Spearman = 0.571,  $P = 0.009$ ). D2-40+ density in the tumor center was associated with CD8+ T-cell infiltration (Spearman = 0.488,  $P = 0.025$ ), while interface D2-40+ density was correlated with CD3+ (Spearman = 0.584,  $P = 0.009$ ), CD8+ (Spearman = 0.508,  $P = 0.022$ ), and granzyme B+ cells (Spearman = 0.482,  $P = 0.031$ ). CD31+ vascular density in adjacent normal tissues showed a positive relationship with

FOXP3+ regulatory T cells (Tregs) (Spearman = 0.456,  $P = 0.05$ ). Patients with distant metastases exhibited a higher D2-40+ density in tumor centers than non-metastatic cases ( $P = 0.024$ ). These results underscore the dynamic relationship between vascular architecture and immune infiltration in MTC, highlighting region-specific interactions that may influence tumor progression. The elevated D2-40+ density in metastatic cases and distinct immunovascular correlations suggest potential prognostic markers and therapeutic targets.

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#### **Cryoablation of bone metastases in thyroid and adrenocortical cancers.**

*Endocr Relat Cancer*, 33(1)

R. M. C. de Freitas, A. O. Hoff, M. Fragoso, A. M. Sousa, D. L. S. Danilovic, L. A. de Castroneves, T. R. Grigio, M. H. Tsunemi, C. A. Buchpiguel and J. Caldas. 2026.

**ABSTRACT:** The purpose of this study is to assess the feasibility, efficacy and safety of cone-beam computed tomography (CBCT)-guided cryoablation of bone metastases in thyroid and adrenocortical cancers. Adult patients with bone metastases and at least 1 skeletal-related event (pain, risk of fracture, spinal cord compression or hypercalcemia) at baseline were enrolled in a prospective, single-arm, single-center IRB-approved study (ClinicalTrials: NCT03986593). Brief Pain Inventory - Short Form (BPI-SF) and morphine-equivalent daily dose (M-EDD) were recorded at baseline and weekly during the first 8 weeks and 3, 6, 12 and 24 months post-cryoablation. Adverse events (AEs) and pre- and post-treatment cross-sectional (CT or MR) and functional imaging with PET/CT were analyzed. Seventeen patients (mean age of 58.3 +/- 16.2 years old; 11 women) with either differentiated ( $n = 8$ ; 47.1%) or medullary thyroid cancer ( $n = 6$ ; 35.6%), or adrenocortical cancer ( $n = 3$ ; 17.3%) were enrolled. CBCT-guided cryoablation of 24 bone metastases reached 100% technical success rate. An overall drop of 4.8 points ( $P < 0.05$ ) in the worst pain in the last 24 h and M-EDD overall intake decrease ( $P < 0.05$ ) were observed. In addition to pain improvement, no patients required surgery. Three patients (17.6%) required radiotherapy due to refractory or recurrent pain over a follow-up of 14.9 +/- 14.0 (median +/- IQR) months. No grade 4 or 5 AE was reported. One grade 3 AE (5.9%) and two grade 2 AEs (11.8%) occurred. PET/CT imaging showed a 52% reduction in FDG uptake immediately after cryoablation. Cryoablation of bone metastases in thyroid and adrenocortical cancers was safe and effective, providing rapid and long-lasting pain relief and improving quality of life. ClinicalTrials.gov: NCT03986593. **CLINICAL RELEVANCE STATEMENTS:** Cryoablation led to a sustained reduction in pain with a mean improvement of 7.2 points on a 1-10 scale of the Brief Pain Inventory - Short Form (BPI-SF) after 54 weeks. Pain relief and quality-of-life improvement (assessed by the BPI-SF) were observed in 81.3% of bone metastases just one week after cryoablation with an overall pain score reduction of 4.8 points. Cryoablation of bone metastases from endocrine cancers was safe and effective, providing long-lasting pain relief.

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DOI: [10.1530/ERC-25-0306](#)

#### **Vocal Fold Immobility After Radiofrequency Ablation of Thyroid Nodules: A Survey of Laryngologists and an Algorithm for Peri-procedural Voice Assessment.**

*Head Neck*, 48(3):821-6.

V. K. Dhillon and C. F. Sinclair. 2026.

**BACKGROUND:** Rates of vocal fold motion impairment (VFMI) during and after thermal ablative treatments for thyroid nodules have not been well documented. This study surveys a large group of laryngologists to assess the rate of VFMI and dysphonia referral patterns after thermal ablation. A peri-procedural voice assessment algorithm for proceduralists performing thermal ablation for thyroid nodules is presented. **METHODS:** Thirteen-question-survey related to VFMI postablation. **RESULTS:** Sixty-one respondents completed the survey. One-third of total respondents affirmed a VFMI after thermal ablation, with 81% documenting evidence on laryngeal examination. Immediate dysphonia was the most common presenting symptom. Referral patterns varied, but a large portion of patients were referred more than one week postprocedure despite the proceduralist having knowledge of potential VFMI. **CONCLUSION:** VFMI is a risk during thermal ablation of thyroid nodules. Greater attention to voice during ablation and use of a procedural voice assessment algorithm may mitigate the risk of injury and potentially improve outcomes.

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DOI: [10.1002/hed.70081](#)

**Skip metastases in papillary thyroid carcinoma: evidence from a multicenter European retrospective study.**

*Front Endocrinol (Lausanne)*, 17:1712563.

G. Di Filippo, G. L. Canu, G. Gobbo, F. Medas, L. Rossi, F. Cappellacci, P. Papini, M. Paternoster, A. Chorti, I. Pliakos, M. Moysidis, G. Lazzari, E. Morelli, D. Serbusca, A. Ruzzenente, T. Papavramidis, G. Materazzi and P. G. Calo. 2026.

INTRODUCTION: Papillary thyroid carcinoma (PTC) frequently involves cervical lymph nodes. Lateral nodal involvement without central compartment disease (Skip Metastasis, SM) poses diagnostic and staging challenges. We aimed to characterize clinicopathological features of SM in a large multicenter European cohort comparing SM+ (lateral only) and SM- (central + lateral) disease. MATERIALS AND METHODS: We conducted a retrospective study across four high-volume European centers (01/2020-12/2022). Adults with histologically proven PTC, confirmed lateral cervical metastases, and both central (level VI) and lateral (levels II-IV) dissections were included. Additional subanalyses among pT1a and cases with >2 central nodes retrieved were employed to control for confounders. RESULTS: Among 283 patients, 48 (17.0%) were SM+. SM+ patients were older (47 vs 39 years,  $p=0.006$ ) and had smaller primaries (12 vs 16 mm,  $p=0.008$ ), fewer microfoci (2 vs 3,  $p=0.013$ ), fewer lateral nodes retrieved (22 vs 25,  $p=0.004$ ), fewer positive nodes (2 vs 4,  $p<0.001$ ), and smaller largest metastatic node (14.5 vs 18.5 mm,  $p=0.010$ ). Follicular variant was prevalent in SM+ (18.8% vs 4.3%;  $p=0.001$ ). Features of aggressiveness were less frequent in SM+: multifocality (62.5% vs 74.9%,  $p=0.016$ ), bilaterality (37.5% vs 52.8%,  $p=0.024$ ), microscopic ETE (33.3% vs 52.3%,  $p=0.016$ ), LVI (14.6% vs 47.7%,  $p<0.001$ ), and extranodal extension (8.3% vs 20.4%,  $p=0.043$ ). Findings persisted in different subanalyses (>2 central nodes;  $n=252$ . pT1a tumors  $n=73$ ). In multivariable analysis, central nodal yield (OR 1.13,  $p=0.003$ ) and LVI (OR 6.5,  $p=0.005$ ) were associated with SM-, whereas follicular variant was inversely associated (OR 0.24,  $p=0.028$ ). CONCLUSION: SM were not uncommon and associated with a less aggressive clinicopathologic profile and increased proportion of follicular variant. While limited central nodal yield may pose false positive risks, key associations persisted after adjustment. Prospective studies are warranted to refine risk stratification and surgical planning.

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PMCID: PMC12900679

**Comparison of the application value of bipolar electrocoagulation and ultrasonic scalpel in robot-assisted thyroid carcinoma surgery: a single-center study based on perioperative indicator and short-term prognosis.**

*Front Surg*, 13:1764805.

Y. Dong, L. Huo, L. Wang, J. Gu, B. Xie and X. Xu. 2026.

OBJECTIVE: To study the effectiveness of bipolar electrocoagulation cutting technology and traditional ultrasonic scalpel cutting technology in Da Vinci robot-assisted thyroid carcinoma surgery. METHODS: We retrospectively reviewed 154 patients with thyroid carcinoma who had undergone ultrasonic scalpel (US,  $n = 81$ ) or Maryland bipolar electrocoagulation (MB,  $n = 73$ ) cutting in Da Vinci robotic surgery. The operation time, complications, efficacy and other clinical indicators were compared between the two groups. RESULTS: The operation time of the MB group was significantly reduced ( $p < 0.05$ ), and the drainage volume was significantly higher than that of the US group ( $p < 0.05$ ). The postoperative PTH and serum calcium levels of total thyroidectomy in the MB group were higher than those in the US group ( $p < 0.05$ ), which were (US:  $2.07 \pm 1.51$ , MB:  $2.42 \pm 1.46$ ) and (US:  $2.15 \pm 0.14$ , MB:  $2.20 \pm 0.13$ ). CONCLUSION: Bipolar coagulation cutting technology is more precise. Its application in robotic thyroid surgery can significantly shorten the operation time and protect parathyroid function, which has better clinical application prospects.

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DOI: [10.3389/fsurg.2026.1764805](#)

PMCID: PMC12936032

**The clinical value and learning curve analysis of the modified areolar approach for endoscopic thyroidectomy.**

*Surg Endosc*, 40(4):3174-84.

A. Du, L. An, J. Wang, X. Li, N. Zhao, Z. Ge and G. Ding. 2026.

OBJECTIVE: To compare the clinical outcomes and learning curve characteristics of the traditional bilateral areolar approach (BAA) and the modified areolar approach (MAA) in endoscopic thyroidectomy and to assess the advantages and potential for clinical dissemination of the modified technique. METHODS: We retrospectively reviewed 79 female patients who underwent endoscopic radical thyroidectomy for thyroid cancer. Patients were assigned to the BAA group or the MAA group according to the incision placement. Perioperative parameters were compared between groups, such as operative time, intraoperative blood loss, number of lymph nodes harvested, incidence of postoperative complications, and patient satisfaction. A cumulative sum analysis (CUSUM) was performed to construct learning curves and evaluate the progression of surgical proficiency. RESULTS: Compared with the BAA group, the MAA group demonstrated a significantly

shorter operative time ( $P < 0.001$ ), reduced intraoperative blood loss ( $P = 0.029$ ), and a lower rate of short-term postoperative complications ( $P = 0.05$ ). The CUSUM learning curve inflection point occurred earlier in the MAA group (20th case vs. 26th case), indicating more rapid acquisition of the technique. **CONCLUSION:** By optimizing incision placement and instrument alignment, the modified areolar approach shortens operative time, minimizes intraoperative trauma, and decreases complication rates. Its shorter learning curve and greater procedural stability facilitate faster mastery of endoscopic thyroidectomy, supporting its wider clinical adoption.

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### **Preoperative and Intraoperative Assessment of Extrathyroidal Extension in Unilateral Papillary Thyroid Carcinoma: Does It Necessitate Total Thyroidectomy?**

*J Surg Oncol*, 133(7):901-8.

K. Fei, Z. Bin and Y. Song. 2026.

**BACKGROUND:** The optimal surgical extent for papillary thyroid carcinoma (PTC) with extrathyroidal extension (ETE) suspected on ultrasound or intraoperative exploration remains debated. This study evaluated the diagnostic accuracy of clinical ETE (cETE) assessment and compared oncologic outcomes after lobectomy between cETE-positive and cETE-negative patients. **METHODS:** This single-center retrospective study enrolled 213 patients with PTC who underwent lobectomy. cETE was defined as tumor extension beyond the thyroid capsule on preoperative ultrasound or intraoperative exploration. Pathologically confirmed ETE served as the gold standard for determining the sensitivity, specificity, and accuracy of both ultrasound and intraoperative ETE assessments. Recurrence-free survival was compared between groups by different ETE features. **RESULTS:** Preoperative/intraoperative ETE assessments exhibited limited sensitivity (12.3% and 33.6%), limited accuracy (49.3% and 55.9%), and high specificity (98.9% and 85.7%). With a mean follow-up duration of 63.5 +/- 11.7 months, the recurrence rates were recorded at 1.6% (1/61) in Group cETE+ in comparison to 2.0% (3/152) in Group cETE- ( $p = 0.871$ ). **CONCLUSION:** Clinical ETE assessment has limited accuracy but high specificity. Lobectomy offers comparable oncologic outcomes regardless of cETE status, supporting its feasibility in selected PTC patients without mandating total thyroidectomy.

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DOI: [10.1002/jso.70238](#)

PMCID: PMC13352319

### **Learning curve for direct nasofibrolaryngoscopy in an endocrine surgery unit.**

*Surg Endosc*, 40(2):1288-96.

N. C. Fernandez, M. R. Cardona, A. J. Silvestre, R. A. Ballester, R. M. M. Fernandez and M. L. Rodriguez. 2026.

**BACKGROUND:** Injury to the recurrent laryngeal nerve (RLN) is a specific complication of thyroid surgery. Flexible direct nasofibrolaryngoscopy (DNFL) is the gold standard for evaluating vocal cord mobility, although its systematic use and learning curve among endocrine surgeons remain poorly defined. The aim of this study is to identify factors related to the final result and how explorer experience or patient characteristics could influence in the evolution of the learning curve. **METHODS:** Retrospective observational study included 110 consecutive patients who underwent thyroid surgery between June 2022 and February 2024. A total of 123 DNFL procedures were performed by junior and senior endocrine surgeons, all of them without prior experience in the technique. Variables analyzed included demographic and clinical data, exploration time, and procedural success. Comparative statistical analysis, multivariate linear regression, and cumulative sum (CUSUM) analysis were used to evaluate the learning curve. **RESULTS:** DNFL was successfully completed in 93.5% of cases, with no complications reported. The mean exploration time was 75.28 +/- 58.23 s. Significant differences were observed in relation to study period ( $p < 0.01$ ) and surgeon experience ( $p < 0.01$ ); but not with pathology or patient characteristics. The regression model confirmed a gradual reduction in exploration time with increased experience. CUSUM analysis identified three learning phases and showed that performance stabilized after 35-40 procedures, regardless of the surgeon's level of experience. **CONCLUSION:** DNFL was safe with a short and well-defined learning curve. Its integration into endocrine surgery practice may be feasible even for surgeons without prior experience.

PubMed-ID: [41249536](#)

DOI: [10.1007/s00464-025-12359-z](#)

### **Comparative Analysis of Incidental and Non-Incidental Papillary Thyroid Microcarcinoma Outcomes: Implications on Management Recommendations.**

*Clin Endocrinol (Oxf)*, 105(1):100-7.

E. A. Finnegan, J. M. Hintze, A. McGowan, J. Gibney, C. W. R. Fitzgerald, J. Kinsella and M. L. Healy. 2026.

**INTRODUCTION:** Papillary thyroid microcarcinomas (PTMC) are defined by the World Health Organisation (WHO) as tumours measuring  $\leq 10$  mm. Incidental PTMCs, or lesions discovered postoperatively on histological examination, are less extensively studied compared with lesions diagnosed preoperatively through cytology, particularly in terms of demographics, histopathological features and long-term outcomes. This study aimed to compare outcomes between these patients. **METHODS:** A single-centre retrospective cohort analysis of data from the St. James's University Hospital Head and Neck tumour board spanning from 2013 to 2023 was conducted. A total of 152 patients diagnosed with PTMCs and neck nodes  $\leq 1$  cm were identified during this period. Of these, 55 were incidental and 47 were non-incidental PTMCs included in the final analysis. **RESULTS:** Significant differences were observed between the two subgroups in terms of the size of the largest tumour focus (7.8 mm vs. 3.9 mm,  $p < 0.001$ ), the presence of aggressive histologic variants (9.2% vs. 0.9%,  $p = 0.002$ ) and the frequency of neck dissections (8.8% vs. 0.0%,  $p < 0.001$ ). However, no recurrences occurred in either group. **CONCLUSION:** This comprehensive 10-year retrospective review found few differences in the presentation of incidental and non-incidental microcarcinoma, with low recurrence rates and excellent outcomes. These findings, with overall low numbers, provide hypothesis-generating evidence that this group may be suitable for discharge to primary care for further follow-up.

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### **Management of Retropharyngeal Lymph Node Metastases in Thyroid Cancer.**

*Head Neck*, 48(1):237-45.

I. Fournier, A. V. Bandi, S. Hamidi, P. Iyer, N. L. Busaidy, M. E. Cabanillas, R. Dadu, M. I. Hu, S. G. Waguespack, U. N. Basmaci, M. D. Williams, M. Mansour, M. G. Monroe, N. D. Gross, R. P. Goepfert, N. D. Perrier, V. Banuchi, J. R. Wang, A. Maniakas and M. E. Zafereo. 2026.

**BACKGROUND:** Retropharyngeal lymph node (RPLN) metastases in thyroid cancer are rare, with optimal management underreported. **METHODS:** Retrospective study of consecutive thyroid cancer patients with RPLN metastases treated at MD Anderson Cancer Center between 2000 and 2024. **RESULTS:** One hundred and sixty-seven patients (75% differentiated, 21% medullary, 4% poorly differentiated thyroid cancer) were divided into three groups: active surveillance (AS) (13%), surgery (56%), and nonsurgical treatment (31%). In the AS group (median follow-up 2.3 years), RPLN metastases grew a median 3% (range: 0-56) or 0.02 cm (range: 0-0.7) per year. Surgical therapy included transcervical (73%), transoral robotic (14%), transoral (12%), and transmandibular (1%) approaches. Median RPLN metastasis size was 1.7 cm (interquartile range: 1.3-2.2) at surgery. Three months post-operatively, 11% had dysphagia and 1% had velopharyngeal insufficiency. Nonsurgical treatments included radioactive iodine (10%), radiation therapy (11%), and systemic targeted therapy (79%). **CONCLUSION:** RPLN metastases grow slowly, and those  $\geq 1$  cm typically undergo surgical resection without significant long-term morbidity.

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DOI: [10.1002/hed.70027](#)

PMCID: PMC12703554

### **Ethanol Ablation of Metastatic Lymph Nodes in Patients With Papillary Thyroid Carcinoma-Predictors of Clinical Outcome.**

*J Clin Endocrinol Metab*, 111(1):e185-e94.

P. S. Frich, E. Sigstad, A. E. Berstad, E. M. Opsahl, K. H. Fagerlid, K. K. Groholt, T. Bjoro, K. H. Hole and L. I. Flinder. 2025.

**CONTEXT:** Ethanol ablation (EA) is a treatment option in recurrent or persistent metastatic lymph nodes (MLNs) from papillary thyroid carcinoma. **OBJECTIVE:** This work aimed to assess whether ultrasonographic characteristics of the MLN, history of lymph node surgery, aggressive histological subtype, or BRAFV600E mutation in the primary tumor predict long-term response from EA. **METHODS:** Seventy-five patients who received EA at a tertiary referral center were included. We evaluated treatment response from the most recent clinically indicated examination, or a study-specific examination. BRAFV600E analysis and review of histological subtypes in the primary tumor were conducted. **RESULTS:** Median interval from initial surgery to follow-up was 119 months (range, 39-471 months). Pure cystic MLN had a better outcome than the solid and partially cystic MLN (13/13, 100% vs 90/121, 74%;  $P = .039$ ). Small MLNs ( $\leq 0.5$  mL) had a higher response rate compared to larger lesions (71/92, 77% vs 10/19, 53%;  $P = .045$ ). We observed no difference in EA response between patients with or without the BRAFV600E mutation (80/99, 81% vs 17/25, 68%;  $P = .181$ ) or an aggressive subtype (22/24, 92% vs 75/100, 75%;  $P = .099$ ) in their primary tumors. EA achieved similar rates of locoregional disease control in neck regions with or without previous lymph node surgery (66% vs 63%,  $P = .825$ ). **CONCLUSION:** EA was highly effective in pure cystic MLNs. Partially cystic or noncystic MLNs over 0.5 mL were less responsive, though many of these MLNs still showed a lasting response. BRAFV600E mutation, aggressive histological subtype, or absence of prior lymph node surgery did not

negatively affect EA response.

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PMCID: PMC12712947

**Letter to editor on "Navigating the Lymphatic Labyrinth: Insights into Lateral Cervical Metastasis Patterns in Papillary Thyroid Carcinoma: A multicenter study".**

*Int J Surg*,

Y. Fu. 2026.

PubMed-ID: [41563020](#)

DOI: [10.1097/JS9.0000000000004896](#)

**Are Total Thyroidectomy and Adjuvant Radioactive Iodine Treatment Required in All Patients with N1b Intermediate-High Risk Papillary Thyroid Carcinoma?**

*Thyroid*, 36(1):36-45.

T. Fujiwara, N. Kofuji, Y. Kishimoto, K. Hamaguchi, S. Shinohara, M. Kikuchi, R. Asato, H. Ishida, Y. Kitani, S. Otsuki, J. Kusano, T. Tsujimura, H. Harada, K. Yasuda, H. Tamaki and K. Omori. 2026.

BACKGROUND: The optimal extent of surgery and the role of radioactive iodine (RAI) in patients with papillary thyroid carcinoma (PTC) with lateral neck metastasis (cN1b) remain controversial. We aimed to evaluate the oncologic outcomes of lobectomy with lateral neck dissection, total thyroidectomy with lateral neck dissection, and total thyroidectomy with lateral neck dissection followed by adjuvant RAI in patients with intermediate-risk cN1b PTC. METHODS: In this multicenter retrospective cohort study, we included patients with cT1-3N1bM0 PTC who underwent thyroidectomy with therapeutic lateral neck dissection between 2010 and 2022. Recurrence-free survival (RFS) and disease-specific survival (DSS) were compared across three treatment groups using Kaplan-Meier. Multivariable cox proportional hazards models were also used to identify independent risk factors for recurrence. RESULTS: We included 593 patients (60.6% female; median age, 58.0 years) who had a median follow-up duration of 71.5 months. We observed no significant differences in RFS ( $p = 0.19$ ) or DSS ( $p = 0.40$ ) among the treatment groups of lobectomy, total thyroidectomy, and total thyroidectomy with RAI. Although the total thyroidectomy with RAI group showed a trend toward worse RFS, this was not statistically significant ( $p = 0.19$ ). In multivariable analysis, older age (hazard ratio [HR] 1.024 per year, confidence interval [CI] 1.007-1.041,  $p = 0.006$ ), larger primary tumor size (HR 1.026 per mm, CI 1.012-1.041,  $p < 0.001$ ), larger metastatic lymph node size (HR 1.020 per mm, CI 1.003-1.036,  $p = 0.017$ ), and extranodal extension (HR 1.741, CI 1.046-2.898,  $p = 0.033$ ) were independently associated with shorter RFS. CONCLUSIONS: RAI may improve RFS in selected patients with extensive nodal disease, but its routine use in all cN1b PTC cases may be unnecessary. Lobectomy or total thyroidectomy without RAI could be appropriate options in lower risk cN1b patients. Further studies are warranted to refine treatment strategies in intermediate-risk cN1b PTC.

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DOI: [10.1177/10507256251401241](#)

**Laryngeal ultrasound-guided adhesive transcutaneous electrodes versus conventional endotracheal electrodes for intraoperative neuromonitoring during thyroid and neck surgery.**

*Surgery*, 189:109709.

M. H. M. Fung, C. C. Cheng, Y. Luk and B. H. H. Lang. 2026.

INTRODUCTION: Conventional intraoperative neuromonitoring during thyroid surgery commonly uses electromyography electrodes embedded in endotracheal tubes. Adhesive transcutaneous electrodes may be a novel, noninvasive and low-cost alternative, but its accuracy and limitations remain less known. This prospective study compared the accuracy of adhesive transcutaneous electrodes placed under laryngeal ultrasound guidance to that of conventional endotracheal tube electrodes and assessed the factors associated with success in adhesive transcutaneous electrodes intraoperative neuromonitoring. METHODS: Consecutive patients undergoing open thyroid and neck surgery in a tertiary endocrine surgery unit were prospectively recruited. Before skin incision, the position of vocal cords relative to the thyroid cartilage was marked with laryngeal ultrasonography, and a pair of adhesive transcutaneous electrodes was placed on the overlying skin. Endotracheal tube electrode was used simultaneously. Standardized vagus and recurrent laryngeal nerve stimulation protocol was followed. On each stimulation, electromyography signals were simultaneously recorded by adhesive transcutaneous electrodes and endotracheal tube electrodes and later verified by postoperative flexible laryngoscopy. RESULTS: From 2023 to 2024, 300 nerves at risk from 216 patients were analyzed. Median age was 59 (50-70) years; 72.7% were female. Adhesive transcutaneous electrode electromyography had lower amplitudes for both recurrent laryngeal

nerve and vagus nerve ( $P < .001$ ). All 4 vocal cord vocal cord paresis (1.33%, transient and unilateral) were detected by adhesive transcutaneous electrodes and endotracheal tube electrodes, that is, 100% sensitivity and negative predictive value for vocal cord vocal cord paresis. Adhesive transcutaneous electrodes had slightly lower specificity (91.6% vs 96.5%) and accuracy (91.8% vs 96.6%), and lower positive predictive value (14.3% vs 28.6%). Signal interference in adhesive transcutaneous electrodes occurred in 6 patients (2.8%). Higher body mass index (BMI) was the only factor associated with false results from adhesive transcutaneous electrodes ( $P = .002$ , odds ratio 1.176, 95% confidence interval 1.060-1.305). Accuracy of adhesive transcutaneous electrodes (94.6%) became comparable to endotracheal tube electrodes in patients with body mass index  $<25$ . Adhesive transcutaneous electrodes cost less than endotracheal tube electrodes (32 vs 427 US dollars) for each surgery. Two patients with misplaced endotracheal tube electrodes (false endotracheal tube electrodes signal loss) had normal recurrent laryngeal nerve function correctly predicted by adhesive transcutaneous electrodes. **CONCLUSION:** Laryngeal ultrasound-guided adhesive transcutaneous electrode intraoperative neuromonitoring has comparable sensitivity and negative predictive value to endotracheal tube electrodes and may resolve false endotracheal tube electrodes signal loss. Lower body mass index was associated with improved and comparable accuracy to endotracheal tube electrodes. Adhesive transcutaneous electrodes may be a reliable, low-cost replacement to endotracheal tube electrodes in patients with body mass index  $<25$ .

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### **A prospective comparison of sequential versus interval retreatment with radiofrequency ablation for predominantly solid, large-volume benign thyroid nodules.**

*Surgery*, 189:109763.

M. H. M. Fung, Y. Luk and B. H. H. Lang. 2026.

**BACKGROUND:** Radiofrequency ablation is an effective treatment for benign thyroid nodules. For large nodules  $\geq 20$  mL, retreatment within 6 months would lead to a higher volume reduction rate at 12 months than a single treatment. However, the optimal timing of retreatment within the 6-month period has not been determined. This prospective study compared sequential versus interval retreatment with radiofrequency ablation for predominantly solid, large benign thyroid nodules  $\geq 20$  mL and identified factors associated with a better volume reduction rate. **METHODS:** Consecutive patients with predominantly ( $>80\%$ ) solid, cytologically benign large thyroid nodules ( $\geq 20$  mL) that were undergoing radiofrequency ablation at a tertiary endocrine surgery center were recruited for a planned, 2-session radiofrequency ablation treatment. Group I received sequential retreatment in  $<1$  month, whereas group II received interval retreatment in 4-6 months. For each session, the entire nodule was ablated until it was fully covered with echogenic bubbles. The primary outcome was 18-month volume reduction rate = (baseline volume - 18-month volume)/baseline volume  $\times 100\%$ . Complications, compressive symptoms, and cosmetic symptoms were compared. **RESULTS:** From 2022 to 2023, 31 nodules (group I: 15, group II: 16) from 30 patients were recruited for a total of 62 ablation sessions. Baseline characteristics including nodule volumes (33.5 [25-40] vs 37.2 [23.9-56.1] mL) and symptoms were comparable ( $P < .05$ ). The overall 12-month and 18-month volume reduction rates were 75.7% (60.4%-80.9%) and 82.7% (64.7%-87.6%). No significant difference in 18-month volume reduction rate was observed between groups (group I: 84.1% [68.1%-88.3%] vs group II: 79.4% [64.7%-87.6%],  $P = .608$ ). Both groups had significant further nodule shrinkage from 12 months to 18 months ( $P < .05$ ), at comparable rates ( $P > .05$ ), and significant improvement in cosmetic and compressive symptoms ( $P < .001$ ). A higher energy per unit volume delivered at the second ablation session was the only factor associated with an 18-month volume reduction rate of  $\geq 80\%$  ( $P = .038$ , odds ratio: 88.3 [1.47-532]). No vocal cord palsy or hematoma occurred, and all patients were discharged on the same day after each treatment session. **CONCLUSION:** Continued shrinkage beyond 12 months was observed in large, predominantly solid benign thyroid nodules that received 2-session radiofrequency ablation within 6 months. Varying the time interval to retreatment within 6 months did not affect treatment efficacy. A higher energy per unit volume delivered at the second ablation session was associated with greater volume reduction.

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DOI: [10.1016/j.surg.2025.109763](#)

### **Is it possible to predict functional recovery of vocal folds palsy? Role of intraoperative neuromonitoring and laryngostroboscopy findings.**

*Surgery*, 189:109712.

P. Gallucci, P. F. Procopio, F. Pennestri, L. Revelli, A. D'Amore, A. Martullo, G. Marincola, M. R. Marchese, L. D'Alatri, C. De Crea and M. Raffaelli. 2026.

**BACKGROUND:** Vocal fold palsy is a common reason for claims after thyroidectomy. We evaluated the prognostic role of

intraoperative neuromonitoring and postoperative flexible fiberoptic laryngostroboscopy findings in patients with type I or type II loss of signal, indicating the injury in an exact point of recurrent laryngeal nerve and whether the damage level cannot be determined, respectively. METHODS: Among 4,526 intraoperative neuromonitoring-assisted thyroidectomies (2021-2024), all cases of loss of signal were prospectively analyzed. Flexible fiberoptic laryngostroboscopy was performed in first, 15th, 45th, and 180th postoperative day for the evaluation of arytenoid motility and arytenoid inward rotation. On the basis of vocal fold motility at postoperative day 180, patients were categorized into a recovery group and nonrecovery group. Predictive factors for vocal fold palsy were assessed using univariable and multivariable analyses. RESULTS: Of 104 included patients, 87 (83.6%) patients recovered vocal fold motility within postoperative day 180. After univariable analysis, type I loss of signal ( $P = .001$ ) and postoperative day 15 arytenoid inward rotation ( $P = .001$ ) were significantly more frequent in the nonrecovery group, whereas postoperative day 15 arytenoid motility was more frequent in the recovery group ( $P = .001$ ). Type I loss of signal, absence of arytenoid motility, and presence of arytenoid inward rotation at postoperative day 15 were associated with recovery in 1 case ( $P = .001$ ), whereas type II loss of signal with presence of arytenoid motility and absence of arytenoid inward rotation related to recovery in all cases ( $P = .001$ ). Multivariable analysis showed preserved arytenoid motility as a protective factor for persistent vocal fold palsy ( $P = .010$ ), whereas the presence of arytenoid inward rotation increased the risk of persistent vocal fold palsy ( $P = .002$ ). CONCLUSION: This study results support the prognostic role of loss of signal type and postoperative day 15 arytenoid features on vocal fold palsy persistence 6 months after surgery. The identification of these parameters may help clinicians to address patients to early management of vocal fold palsy.

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#### **18F-DOPA-PET/CT role in medullary thyroid cancer patients with biochemical incomplete response.**

*Eur J Endocrinol*, 194(5):663-73.

C. Gambale, A. Faranda, A. Ambrogio, A. Prete, E. Minaldi, V. Cappagli, D. Volterrani, R. Elisei and A. Matrone. 2026.

OBJECTIVE: Several patients with medullary thyroid carcinoma (MTC) are not cured after surgery. Disease persistence/recurrence is monitored by measuring calcitonin (CTN) and carcinoembryonic antigen (CEA) and by imaging. The role of 18F-fluoro-dihydroxyphenylalanine positron emission tomography/computed tomography (18F-DOPA-PET/CT) in identifying structural disease in patients with biochemical incomplete response (BiR) remains debated. This study aimed to evaluate the capability of 18F-DOPA-PET/CT to identify structural disease in MTC patients with BiR. METHODS: We performed 18F-DOPA-PET/CT in 91 MTC patients with BiR without evidence of structural disease or indeterminate lesions on neck ultrasound (US) and total-body computed tomography (CT). RESULTS: 18F-DOPA-PET/CT showed pathological uptake in 16/37 (43.2%) CT-negative cases and in 43/54 (79.6%) CT-indeterminate cases. Of these, 23/43 (53.5%) cases showed concordance between 18F-DOPA-PET/CT uptake and CT-scan indeterminate lesions, 4/43 (9.3%) cases showed discordance, and 16/43 (37.2%) cases showed partial concordance. Moreover, 18F-DOPA-PET/CT showed pathological uptake in cervical lymph nodes in 33/91 (36.3%) cases, of whom 9 (27.3%) had no lesions at neck US, and 24 (72.7%) had indeterminate findings. Patients with positive 18F-DOPA-PET/CT showed higher median CTN and CEA values. Management of patients with positive 18F-DOPA PET/CT uptake did not change, except for those with bone metastases. CONCLUSIONS: 18F-DOPA-PET/CT demonstrates good diagnostic accuracy for identifying structural disease in MTC patients with BiR, particularly when indeterminate lesions are present on neck US and CT. However, in most BiR patients, the results of 18F-DOPA-PET/CT did not change their management.

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DOI: [10.1093/ejendo/lvag078](#)

#### **Percutaneous Laser Ablation for Thyroid Nodules: Efficacy and Safety in 1492 Patients With Median Follow-up of 10 Years or More.**

*J Clin Endocrinol Metab*, 111(4):e1023-e8.

G. Gambelunghé, P. Del Sindaco, F. Morettini, S. Ristagno and P. De Feo. 2026.

CONTEXT: Previous studies have shown the efficacy and safety of percutaneous laser ablation for the treatment of nontoxic and toxic benign thyroid nodules; however, data on long-term follow-up are limited. OBJECTIVE: This work aimed to evaluate the long-term efficacy and safety of percutaneous, ultrasound-guided laser ablation of benign thyroid nodules. METHODS: Between May 2009 and July 2024, 1492 patients underwent a single treatment with laser ablation (nontoxic nodules,  $N = 1291$ ; toxic nodules,  $N = 201$  [211 nodules]). Nodule volume was assessed before treatment, then every 6 months in the first 3 years and annually thereafter. RESULTS: Median durations of follow-up were 10.4 years (range, 1-18 years) for nontoxic nodules and 11.4 years (range, 3-15 years) for toxic nodules. For nontoxic nodules, median volume reduction (VRR) was 70.7% at 1 year, reducing to 64.1% at 10 years. For toxic nodules, the corresponding VRR values were

63.8% and 56.9%, respectively ( $P < .001$  vs pretreatment at all time points). No cases of benign nodule regrowth of 25% or greater occurred during the first 3 years of follow-up. The percentage of patients discontinuing methimazole treatment decreased with increasing nodule volume, from 100% for nodules smaller than 5 mL to 33.3% for nodules larger than 25 mL. No major complications were reported; overall, minor complications consisted of fever (15% of patients), pain (7%), and hematoma (1%). **CONCLUSION:** In the largest cohorts reported to date, ultrasound-guided laser ablation of thyroid lesions showed long-term efficacy and safety for treatment of nontoxic and toxic nodules, based on median follow-ups of 10 years or more.

PubMed-ID: [41132004](#)

DOI: [10.1210/clinem/dgaf581](#)

### **Can Immunotherapy Improve Neoadjuvant Response and Allow Surgical Resection in Locally Advanced Anaplastic Thyroid Cancer?**

*Ann Surg Oncol*, 33(7):5935-6.

A. R. Glover. 2026.

PubMed-ID: [41811395](#)

DOI: [10.1245/s10434-026-19385-8](#)

### **Better with a buddy: A multidisciplinary approach to starting a thyroid radiofrequency ablation (RFA) program.**

*Am J Surg*, 254:116736.

C. E. Graves and S. Naderi. 2026.

PubMed-ID: [41318339](#)

DOI: [10.1016/j.amjsurg.2025.116736](#)

### **Long-term Survivors of Anaplastic Thyroid Cancer: A Genomic Predictive Model.**

*J Clin Endocrinol Metab*, 111(2):382-7.

B. C. Greenspun, D. A. Metzger, S. Lee, B. E. Pearson, J. H. Li, S. Chen, R. Zarnegar, T. J. Fahey Iii and B. M. Finnerty. 2026.

**CONTEXT:** Longer-term survival is possible for some patients with anaplastic thyroid cancer (ATC). However, genomic factors associated with improved survival are poorly characterized. **OBJECTIVE:** To develop a mathematical model to predict mutation-based survival risk in ATC. **DESIGN:** Retrospective cohort study of 204 ATC samples from the cBioPortal database, divided into 80% training and 20% validation cohorts. Multivariate analysis identified prognostic genes, used to construct a point-based risk model. KEGG pathway enrichment and BRAF subanalyses were performed. **SETTING:** Multi-institutional, international genomic database. **PATIENTS OR OTHER PARTICIPANTS:** Samples were included if sequencing and survival data were available ( $n = 204$ ). **INTERVENTION(S):** Not applicable. **MAIN OUTCOME MEASURE(S):** The prespecified primary outcome was overall survival. **RESULTS:** Fourteen genes were associated with increased risk: TET1, MAPK12, ATP10A, PIK3CA, MUC4, PNPLA2, PLD4, EGLN2, BSN, FLNC, RADIL, ZMYND8, FRAS1, RECQL4. More aggressive ( $n = 37$ ) and less aggressive cohorts ( $n = 128$ ) were determined using the maximally selected rank statistic, yielding a point threshold of 0.27. The predictive performance of the risk model demonstrated a C-index of 0.74. On Kaplan-Meier analysis, 1-year survival differed for more aggressive patients (0%) compared to less aggressive patients (32%). For the validation cohort, survival remained significantly different between risk cohorts and on BRAF subanalysis. Each risk cohort subsequently underwent KEGG pathway enrichment analysis, which showed significantly increased enrichment across several pathways for more aggressive tumors. **CONCLUSION:** This model identifies mutated genes that are associated with the most aggressive ATCs and thus may aid in preoperative risk assessment when evaluating patients for surgery for curative intent.

PubMed-ID: [40663630](#)

DOI: [10.1210/clinem/dgaf391](#)

PMCID: PMC13233113

### **The impact of minimal extrathyroidal extension on survival outcomes in patients with pT1 and pT2 differentiated thyroid cancer.**

*Surgery*, 190:109820.

H. Guo, H. Yang, Z. Yang and M. Zhu. 2026.

**BACKGROUND:** Minimal extrathyroidal extension, detected only through histologic examination, remains a topic of ongoing debate regarding the prognostic importance of differentiated thyroid cancer. **METHODS:** Patients with pT1 and pT2 differentiated thyroid cancer from 2004 to 2015 were collected from the Surveillance, Epidemiology, and End Results database on 3 March 2025. The median follow-up period was 129 months for both patients with pT1 and pT2. Multivariate

analyses were conducted to evaluate differences in lymph node involvement or distant metastasis, as well as survival outcomes between patients with pT1 and pT2 differentiated thyroid cancer with and without minimal extrathyroidal extension. RESULTS: Patients with pT1 and pT2 with minimal extrathyroidal extension had a significantly greater risk of lymph node involvement or distant metastasis compared with those without in the multivariate logistic analysis (pT1: adjusted odds ratio, 4.15; 95% confidence interval, 3.83-4.48;  $P < .001$ ; pT2: adjusted odds ratio, 4.69; 95% confidence interval, 4.23-5.20;  $P < .001$ ). Patients with pT1 with minimal extrathyroidal extension experienced a similar hazard risk of cancer-specific death to those without in the multivariate Cox analysis (adjusted hazard ratio, 1.41; 95% confidence interval, 0.91-2.21;  $P = .127$ ) and the multivariate competing risk model (adjusted subdistribution hazard ratio, 1.44; 95% confidence interval, 0.92-2.27;  $P = .111$ ) whereas patients with pT2 with minimal extrathyroidal extension experienced a significantly greater risk of cancer-specific death than those without in the multivariate Cox analysis (adjusted hazard ratio, 2.48, 95% confidence interval, 1.77-3.49;  $P < .001$ ) and the multivariate competing risk model (adjusted subdistribution hazard ratio, 2.50; 95% confidence interval, 1.72-3.63;  $P < .001$ ). CONCLUSION: Minimal extrathyroidal extension was an independent risk factor of lymph node involvement or distant metastasis in patients with pT1 and pT2. Minimal extrathyroidal extension did not significantly affect survival in patients with pT1, but it was an independent prognostic factor for survival in patients with pT2. Therefore, more aggressive treatment strategies are warranted for patients with differentiated thyroid cancer with minimal extrathyroidal extension, particularly those classified as pT2. PubMed-ID: [41172883](#) DOI: [10.1016/j.surg.2025.109820](#)

### **Determining Thyroid Biopsy Appropriateness: A Retrospective Study Integrating Clinical Context and Ultrasound Features.**

*J Clin Endocrinol Metab*, 111(4):e1014-e22.

S. Habib, G. Perez Rodriguez Garcia, Z. Zhang, A. Roy, Y. Wu, J. P. Brito and N. M. Singh Ospina. 2026.

CONTEXT: Thyroid nodules are common in clinical practice, and inappropriate selection of patients for thyroid biopsy can contribute to thyroid cancer overdiagnosis or delayed diagnosis. OBJECTIVE: This work aimed to evaluate the frequency of inappropriate thyroid biopsies in practice, following a framework that integrates thyroid nodule ultrasound (US) features and patient-specific clinical factors. METHODS: This cross-sectional study was conducted at a single academic center in the United States. Participants included adult patients who underwent their first thyroid fine-needle aspiration (FNA) biopsy between January 1, 2016, and December 31, 2023, at the University of Florida. Data collection included thyroid US characteristics, clinical factors (eg, comorbidities, patient preferences), and context for biopsy decision-making. Main outcome measures included the appropriateness of thyroid biopsy assessed using a tiered framework incorporating US features and additional clinical factors. RESULTS: A total of 899 patients were evaluated, with 441 meeting the inclusion criteria and undergoing 481 thyroid biopsies. Of these, 388 of 481 (80.7%) were classified as likely appropriate (L-APP) based on the American College of Radiology Thyroid Imaging Reporting and Data System criteria. In 34 of 481 (7%) of cases, clinical factors such as thyroid cancer risk features, comorbidities, symptoms, or patient preferences led to reclassification from likely inappropriate (L-INAP) to L-APP. In 50 of 481 (10%) of cases, limited life expectancy (eg, chemotherapy, end-stage disease) led to reclassification from L-APP to possibly or extremely inappropriate (EXT-INAP). EXT-INAP biopsies occurred in only 0.8% (4/481) of cases. CONCLUSION: This study underscores the value of integrating US findings with clinical context to guide thyroid biopsy decisions and enhance patient-centered care.

PubMed-ID: [41133765](#)

DOI: [10.1210/clinem/dgaf577](#)

PMCID: PMC13016818

### **Genomic Characterization of Oncocytic Carcinoma of the Thyroid Using a Large Multi-Institutional Database.**

*Otolaryngol Head Neck Surg*, 174(3):696-704.

B. Hsia, R. Dongre, V. D. Veluvolu, J. Kuzniar, G. Bitar, S. A. Alshaka, A. J. Bastien, V. A. Patel and A. Khaku. 2026.

OBJECTIVE: Characterize the somatic mutations in Oncocytic Carcinoma of the Thyroid (OCA) using a large, multi-institutional database to identify potential therapeutic targets and gain insights into tumor biology. STUDY DESIGN: Cross-sectional study. SETTING: Retrospective nationwide database review. METHODS: Genomic data from 130 OCA samples, representing 124 adult patients, were retrieved from the American Association for Cancer Research (AACR) Project Genomics, Evidence, and Neoplasia Information Exchange (GENIE) database (v17.0-public). Analysis focused on nonsynonymous somatic mutations identified via whole-genome, whole-exome, or targeted panel sequencing after standardized filtering. Mutation frequencies, enrichment based on gender and metastatic status (primary vs. metastatic), and patterns of co-occurrence or mutual exclusivity were statistically evaluated. RESULTS: The most frequently mutated genes were TERT (33.1%, predominantly promoter mutations), TP53 (20.0%), DAXX (16.2%), KMT2D (13.1%), NF1 (12.3%),

and PTEN (10.0%). Significant gender-specific enrichment was identified, notably MST1R mutations exclusive to females (10.7%) and PRKDC mutations exclusive to males (16.7%). Mutations in PC, PCLO, MEN1, and TSC2 were significantly enriched in metastatic samples. DAXX and CDKN1A mutations exhibited significant co-occurrence, whereas TERT mutations were mutually exclusive with DAXX alterations. CONCLUSION: The genomic landscape of OCA is marked by frequent TERT promoter mutations and distinct mutational patterns associated with patient gender and tumor metastatic status. These findings highlight potential molecular subtypes, reveal pathways potentially driving metastasis (eg, involving MEN1/TSC2), and identify novel sex-specific alterations (MST1R, PRKDC), offering avenues for improved development of targeted therapeutic strategies for OCA.

PubMed-ID: [41582704](#)

DOI: [10.1002/ohn.70115](#)

#### **Clinicopathologic predictors of incidental thyroid cancer in Graves' disease: a single-center retrospective cohort study.**

*Updates Surg*, 78(1):319-25.

W. Huang and W. H. Chen. 2026.

The necessity of total thyroidectomy for Graves' disease (GD) remains a subject of debate due to lifelong thyroxine replacement therapy. However, total thyroidectomy is a definitive treatment and allows for the detection of incidental thyroid cancer (ITC), which may necessitate further surgical intervention if not initially treated. This study aimed to investigate the prevalence, clinicopathological characteristics, and risk factors associated with ITC in GD patients undergoing total thyroidectomy. We conducted a retrospective cohort study of 86 GD patients who underwent total thyroidectomy from January 2016 to December 2022. Clinical and pathological characteristics were analyzed to determine potential risk factors associated with ITC. The incidence of ITC was 15.1% (13/86), predominantly papillary thyroid microcarcinoma (PTMC) at 9.3% (8/86). Patients with ITC were significantly older (mean age 45.2 years vs. 36 years,  $p = 0.017$ ) and more frequently presented thyroid nodules on ultrasound (84.6% vs. 45.2%,  $p = 0.014$ ). Multivariate analysis identified thyroid volume as a significant protective factor, with each 1 mL increase reducing ITC risk by approximately 6% ( $p = 0.009$ ). Older age, smaller thyroid volume, and the presence of thyroid nodules on ultrasound were significantly associated with increased ITC risk. A larger thyroid volume may be associated with a lower risk of ITC. Careful preoperative evaluation, including assessment of thyroid nodules on ultrasound, is advised in older patients and those with smaller glands. Surgical decisions should be guided by individual risk factors and shared decision-making.

PubMed-ID: [41102412](#)

DOI: [10.1007/s13304-025-02435-3](#)

#### **Sprayable pH-sensitive near-infrared fluorophore for rapid, bright, specific, and safe visualization of human thyroid cancer in orthotopic mouse models.**

*Surgery*, 189:109703.

S. Jaiswal, A. Yamashita, S. Lee, S. Amirfakhri, J. Ser, S. Kashiwagi, G. Lin, R. M. Hoffman, M. Henary, H. S. Choi and M. Bouvet. 2026.

BACKGROUND: Surgery is the primary treatment for thyroid cancer. However, incomplete resection of thyroid cancer can result in local, regional, and distant recurrences that are life threatening. We hypothesized that a topically applied, pH-sensitive near-infrared fluorophore in spray form (PH10) could offer rapid labeling of thyroid tumors, enabling better visualization of the tumor and its margins. METHODS: Cellular uptake inhibition and cytotoxicity studies using PH10 were performed on TPC-1 papillary and TT medullary thyroid cancer cells. Subcutaneous or orthotopic tumors were established by injecting TPC-1 cells in the flanks or thyroid glands of nude mice, respectively, and sprayed with PH10. Fluorescence of the tumor was compared to surrounding tissues. Tumors were harvested for pathologic analysis. RESULTS: The organic anion transporter peptide mediated uptake of PH10 in TPC-1 and TT cells was determined. PH10 exhibited an IC<sub>50</sub> value of 13.18 and 17.28  $\mu$ M in TPC-1 and TT cells, respectively. Both subcutaneous and orthotopic tumors displayed strong near-infrared fluorescence upon spraying PH10 at a concentration of 10  $\mu$ M on the tumor sites, within 1 minute, contrasting with surrounding tissues. The effective PH10 dose for tumor visualization was well below the IC<sub>50</sub>. The average tumor to background ratios were 5.5 (+/-1.47) for subcutaneous tumors ( $n = 5$ ) and 9.4 (+/-2.59) for orthotopic tumors ( $n = 5$ ). Hematoxylin and eosin staining confirmed the tumor characteristics. CONCLUSION: The pH-sensitive near-infrared fluorophore PH10 brightly, rapidly, specifically, and safely labeled thyroid cancer in mouse models by spraying, demonstrating future clinical promise as a useful agent for improved visualization of thyroid cancer.

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DOI: [10.1016/j.surg.2025.109703](#)

PMCID: PMC12961585

**Factors Associated with Receiving Thyroid Cancer Care From High-Volume Surgeons: Analysis of a State-Wide Claims Registry.**

*J Am Coll Surg*, 242(3):572-80.

C. B. Jensen, C. M. Jackson, S. Xie, A. Sinha, E. M. Bacon, L. N. Krumeich, H. J. Underwood, D. T. Hughes, P. G. Gauger, H. Nathan and S. C. Pitt. 2026.

BACKGROUND: High-volume thyroid surgeons (HVTs) provide quality care with fewer adverse outcomes, yet access to these surgeons can be challenging. This study aimed to assess factors associated with receiving care from an HVT for thyroid cancer. STUDY DESIGN: This retrospective cohort study analyzed adults with thyroid cancer who underwent thyroidectomy in a state-wide multipayer claims registry (2015 to 2022). Surgeons were classified as high (greater than 25 per year) or low volume (25 per year or less; LVTS). Logistic regression evaluated demographics; distance between home, surgical facility, and closest endocrinologist; and ZIP code-level census data in association with surgery by an HVT.

RESULTS: Overall, 357 surgeons performed thyroidectomies on 3,839 patients with thyroid cancer: 17 (4.8%) were HVTs and 340 (95.2%) were LVTS. Most thyroidectomies were performed by LVTS (53.9%, 2,068). Patients treated by HVTs traveled an average of 4.8 miles farther to their treating surgeons (33.7 +/- 44.4 miles vs 28.9 +/- 44.3 miles to LVTS,  $p < 0.001$ ). Factors significantly ( $p < 0.05$ ) associated with an increased likelihood of treatment by an HVT included: having Medicare Advantage through a preferred provider organization and living further from their treating surgeon. Patients who were significantly ( $p < 0.05$ ) less likely to have surgery by an HVT were male, had Medicare insurance without an advantage plan, lived in a ZIP code with low educational attainment, and lived further from an endocrinologist.

CONCLUSIONS: This study identified several factors independently associated with decreased odds of having thyroidectomy by an HVT for thyroid cancer treatment in the state of Michigan. These results underscore the continued existence of inequities in access within our healthcare system.

PubMed-ID: [41358606](#)

DOI: [10.1097/XCS.0000000000001703](#)

**Statewide episode spending variation of thyroidectomy for lower-risk thyroid cancer.**

*Am J Surg*, 253:116816.

C. B. Jensen, S. Xie, A. Sinha, E. M. Bacon, H. J. Underwood, H. Nathan and S. C. Pitt. 2026.

BACKGROUND: This study aimed to evaluate variation in spending for thyroidectomy for patients with thyroid cancer.

METHODS: This retrospective cohort study analyzed risk-adjusted, price-standardized Michigan-based claims data from 2015 to 2022 and included patients who underwent thyroidectomy for lower-risk thyroid cancer. The primary outcome was 90-day spending. A mixed linear model with facility as a random effect identified factors associated with spending variability. RESULTS: In total, 2516 patients underwent thyroidectomy at 81 facilities. Unadjusted 90-day spending ranged from \$5917 to \$25,630 across facilities (median \$8993). Spending was lowest for lobectomy (median \$7755) and highest for lobectomy followed by completion thyroidectomy (median \$14,181). On regression, factors significantly associated with increased spending were patient age and readmission. The interaction between occurrence of post-operative complications and lengths of stay  $>2$  nights contributed to dramatically higher spending. CONCLUSIONS: Reducing complications and associated length of stay as well hospital readmissions represent opportunities to improve the value of thyroidectomy.

PubMed-ID: [41539038](#)

DOI: [10.1016/j.amisurg.2025.116816](#)

**Non-Neural Post-Thyroidectomy Dysphonia: Long-Term Voice Outcomes in 527 Patients.**

*Otolaryngol Head Neck Surg*, 174(4):963-72.

J. Y. Ji, S. Y. Kim, J. Yoon, Y. Park, G. H. Kim, Y. W. Lee, J. Kim, J. H. Chang, W. J. Jeong and W. Cha. 2026.

OBJECTIVE: To characterize non-neural post-thyroidectomy dysphonia (PTD) by analyzing long-term voice outcomes in patients with no evidence of nerve injury on postoperative laryngoscopy and electromyography (EMG). STUDY DESIGN: Retrospective cohort study. SETTING: Tertiary referral center. METHODS: We reviewed 527 post-thyroidectomy patients with intact vocal fold mobility and normal EMG results at 2 to 3 months postoperatively. Voice evaluations, including acoustic analysis, voice range profile, aerodynamic study, and VHI-10, were performed preoperatively and 3 days, 2 weeks, 1, 3, 6, and 12 months postoperatively. Linear mixed models and machine learning were used to assess the effects of sex, age, surgical extent, and preoperative fundamental frequency ( $F_0$ (pre)) on voice parameters. RESULTS: Fundamental frequency ( $F_0$ ) and speaking fundamental frequency (SFF) declined immediately after surgery, with more prolonged reduction in older patients ( $\geq 45$  years) and those with high  $F_0$ (pre). VHI-10 increased during the early postoperative period, particularly after total thyroidectomy, but returned to near-baseline by 6 to 12 months. Older age was associated with delayed VHI-10 recovery. Maximum frequency ( $F$ (max)) decreased in the early period after total

thyroidectomy. F0(pre) and age were main predictors of F0 and SFF at 1 and 3 months, while surgical extent predicted VHI-10 and F(max) at 1 month. CONCLUSIONS: Voice changes may occur even when the recurrent laryngeal nerve and the external branch of the superior laryngeal nerve are preserved during thyroidectomy. Although most alterations improve over time, some voice parameters may not fully recover, with outcomes influenced by sex, age, surgical extent, and F0(pre). These findings may aid in counseling patients with non-neural PTD.

PubMed-ID: [41810852](#)

DOI: [10.1002/ohn.70168](#)

**Thyrotrophin Receptor Antibody: Objective and Quantitative Inflammatory Indicator in Patients With Thyroid Eye Disease.**

*J Clin Endocrinol Metab*, 111(1):e260-e9.

G. Jing, J. Tang, Y. Li, Y. Li, R. Ma, X. Kang, Q. Yang, B. Wang, S. Wang, X. Tang, S. Fu, X. Yang and W. Wu. 2025.

CONTEXT: Accurate assessment of the inflammatory status in thyroid eye disease (TED) is crucial for diagnosis and treatment; however, this assessment remains challenging. OBJECTIVES: To study whether thyrotrophin receptor antibody (TRAb) can be utilized as a quantitative and objective indicator of the inflammatory status in patients with TED. METHODS: We gathered and analyzed TRAb and clinical characteristics from 226 consecutive TED patients. Additionally, we examined 27 inflammatory cytokines in the orbital adipose tissue of 41 patients and assessed the alterations in TRAb following IV methylprednisolone (IVMP) therapy in 40 patients. RESULTS: The 226 TED patients included 116 females and 110 males, with a mean age of 46.4 +/- 12.2 years. The correlation between TRAb and clinical activity score (CAS) was the most pronounced ( $r = 0.427$ ;  $P < .001$ ). TRAb was identified as the most influential factor for CAS. Subsequent investigation into the relationship between TRAb and pathological inflammation revealed that TRAb exhibited a significant positive correlation with 7 proinflammatory cytokines [Interleukin (IL)-8, chemokine (C-C motif) ligand 3 (CCL-3), serpin E1, platelet-derived growth factor (PDGF)-AB, IL-12p70, IL-21, and PDGF-BB] and a significant negative correlation with 1 anti-inflammatory cytokine [bone morphogenetic protein 7 (BMP-7)]. IL-8, CCL-3, serpin E1, PDGF-AB, and IL-1beta were significantly upregulated in the orbital adipose tissue of TRAb-positive patients compared to TRAb-negative patients. In contrast, BMP-7 demonstrated an opposite trend. Additionally, TRAb and CAS significantly decreased following IVMP therapy, with a significant correlation between the extent of reduction in TRAb and CAS. CONCLUSION: TRAb significantly correlated with both CAS (clinical inflammation indicator) and inflammatory cytokines (pathological inflammation marker). Consequently, we propose, for the first time, that TRAb may serve as an objective and quantitative biomarker for assessing inflammation in TED.

PubMed-ID: [40344181](#)

DOI: [10.1210/clinem/dgaf273](#)

**Improvement in Thyroid-Specific Quality of Life After Radio Frequency Ablation of Symptomatic Benign Solitary Thyroid Nodules: A Prospective Cohort Study.**

*Head Neck*, 48(3):856-62.

M. Kaltoft, J. R. Sorensen, P. K. Cramon, T. Todsén and C. H. Hahn. 2026.

BACKGROUND: Radio frequency ablation (RFA) is an effective and safe treatment for thyroid nodules, with a volume reduction ratio of 60%-80%. However, only limited reports include validated disease-specific outcome measures. Using the validated Thyroid-Related Patient Reported Outcome (ThyPRO), we aimed to investigate changes in disease-specific quality of life (QoL) following RFA treatment. METHODS: In this prospective clinical study, we compared ThyPRO questionnaires from baseline and after RFA treatment with a previously collected sample from the general population. RESULTS: Fifty-four patients completed RFA. At baseline, ThyPRO scores were significantly worse than scores from the general population. After treatment, a large and significant improvement was observed on the Goiter Symptoms scale, and moderate improvements were seen on the Cosmetic Complaints and ThyPRO overall QoL scales. At 12 months, patients still had higher scores than the general population on most scales. CONCLUSION: RFA treatment significantly improves goiter-related symptoms and overall disease-specific QoL.

PubMed-ID: [41159382](#)

DOI: [10.1002/hed.70086](#)

**Improvement in Thyroid-Specific Quality of Life After Radio Frequency Ablation of Symptomatic Benign Solitary Thyroid Nodules: A Prospective Cohort Study.**

*Head Neck*, 48(3):856-62.

M. Kaltoft, J. R. Sorensen, P. K. Cramon, T. Todsén and C. H. Hahn. 2026.

BACKGROUND: Radio frequency ablation (RFA) is an effective and safe treatment for thyroid nodules, with a volume reduction ratio of 60%-80%. However, only limited reports include validated disease-specific outcome measures. Using the

validated Thyroid-Related Patient Reported Outcome (ThyPRO), we aimed to investigate changes in disease-specific quality of life (QOL) following RFA treatment. **METHODS:** In this prospective clinical study, we compared ThyPRO questionnaires from baseline and after RFA treatment with a previously collected sample from the general population. **RESULTS:** Fifty-four patients completed RFA. At baseline, ThyPRO scores were significantly worse than scores from the general population. After treatment, a large and significant improvement was observed on the Goiter Symptoms scale, and moderate improvements were seen on the Cosmetic Complaints and ThyPRO overall QOL scales. At 12 months, patients still had higher scores than the general population on most scales. **CONCLUSION:** RFA treatment significantly improves goiter-related symptoms and overall disease-specific QoL.

PubMed-ID: [41159382](#)

DOI: [10.1002/hed.70086](#)

### **Communication of Cost in Thyroidectomy: A Mixed-Methods Analysis of Financial Toxicity.**

*Otolaryngol Head Neck Surg*, 174(6):1457-67.

D. D. Kao, E. V. Crowley, C. B. Jensen, E. M. Bacon, S. E. Bradley, J. D. Thomas and S. C. Pitt. 2026.

**OBJECTIVE:** To assess cost information provided to patients undergoing thyroidectomy. **STUDY DESIGN:** Explanatory sequential mixed-methods study. **SETTING:** Single academic medical center. **METHODS:** Adults who underwent thyroidectomy between 1/2021 and 1/2024 completed a survey about financial toxicity. Purposive sampling identified survey respondents for semi-structured interviews to explore experiences related to cost communication. Qualitative data were thematically analyzed. **RESULTS:** Of 167 survey respondents, most were female (77.8%), white (83.8%), and underwent total thyroidectomy (65.3%). Nearly one-third experienced moderate to severe financial toxicity. Forty-one percent felt "not at all" informed about costs, while 20% sought preoperative cost information, most commonly from insurers (82.4%). Education was significantly associated with feeling cost-informed, while lowest- and highest-income, younger, and female patients trended toward greater cost-seeking behavior. Thirty-five respondents were invited for an interview; 20 consented. Almost all participants recalled no cost discussion with their care team. Several felt like they "had to" have surgery, regardless of cost, and many were surprised by copays, missed work, and medication costs. Some wished they had received estimates or information about financial resources. Participants identified insurers as a source for cost information but received vague communication regarding coverage. A few stated that while better cost information would not have changed their treatment decision, it would have better prepared them for the financial impact. **CONCLUSION:** Patients undergoing thyroidectomy appear to be insufficiently informed of costs before surgery. Improved cost communication by care teams and hospital systems could improve preparedness and mitigate financial toxicity, as reliance on insurers alone appears inadequate.

PubMed-ID: [41940688](#)

DOI: [10.1002/ohn.70203](#)

### **Outcome of routine discharge after a 4-hour postanesthesia care stay following thyroid lobectomy.**

*Surgery*, 191:109968.

A. M. Kara, S. M. Conte, A. Turza, R. C. Semanate, A. R. Sehgal and C. R. McHenry. 2026.

**BACKGROUND:** Patients who undergo thyroid lobectomy are routinely observed for 4 hours in the postanesthesia care unit and are discharged if there is no evidence of neck hematoma. The aim of this study was to determine the outcome of routine discharge after a 4-hour observation following thyroid lobectomy. **METHODS:** A retrospective review of consecutive patients who underwent thyroid lobectomy from 2008 to 2023 was completed. Patients were evaluated for neck hematoma requiring urgent evacuation, emergency department visits, and hospital readmission. Univariate analysis and multivariate regression analysis were used to analyze potential factors associated with an unsuccessful discharge after 4 hours of observation. **RESULTS:** A total of 494 patients underwent thyroid lobectomy; 330 (67%) were discharged after a 4-hour postanesthesia care unit stay (group I), and 164 (33%) were observed overnight (group II). Neck hematoma occurred in 2 (0.4%) patients before they were both discharged. Thirty-seven (7%) patients presented to the emergency department, 23 (7%) from group I and 14 (9%) from group II ( $P = .53$ ). Six (1%) patients were readmitted, 3 (1%) from groups I and 3 (2%) from group II ( $P = .38$ ). Factors independently associated with an overnight stay and their odds ratio and confidence interval were dependent status (10.76, 2.18-53.07), American Society of Anesthesiologists class  $\geq 3$  (5.32, 2.04-13.86), increased blood loss (4.00, 1.04-2.45), age  $>50$  years (2.68, 1.38-5.20 years), and substernal extension (1.60, 1.04-2.45). **CONCLUSION:** Discharge to home after 4 hours of observation is safe after thyroid lobectomy. However, patients who are older, dependent, have an American Society of Anesthesiologists score  $\geq 3$ , or undergo a more difficult operation should be prepared for overnight observation.

PubMed-ID: [41387057](#)

DOI: [10.1016/j.surg.2025.109968](#)

### **Rare metastatic sites in three patients with RAI-refractory differentiated thyroid cancer (DTC).**

*Hormones (Athens)*, 25(1):261-6.

O. Karapanou, G. Effraimidis, E. Petinellis, M. Michalaki, M. Krokidis and K. Saltiki. 2026.

**PURPOSE:** While the majority of patients with differentiated thyroid cancer (DTC) have favourable outcomes, less than 5% may have metastatic disease that is refractory to radioiodine (RAI) treatment. Distant metastases from thyroid cancer usually involve the lungs and bones. However, it is essential to accurately identify and treat rare sites of metastasis.

**METHODS:** In this report, we present three cases of rare metastatic sites originating from RAI-refractory DTC. The first patient had a cystic calcaneous metastasis, the second patient developed bilateral metachronous renal metastases, and the third patient presented with a large thigh metastasis, which was later followed by a large pelvic mass. **RESULTS:** None of the patients had a targetable mutation. A multidisciplinary therapeutic approach was implemented for their treatment, incorporating both local and systemic therapies. **CONCLUSION:** Managing cases with unusual metastases can be particularly challenging, especially in patients with advanced disease. The combination of local and systemic treatments is crucial, as it may help prolong survival.

PubMed-ID: [40627327](#)

DOI: [10.1007/s42000-025-00694-8](#)

### **Safety of Oxidized Regenerated Cellulose and Gelatin Sponge Application in Thyroidectomy.**

*World J Surg*, 50(2):461-3.

L. Kathir, D. Suresh, N. Kuppurajan and M. Dhiwakar. 2026.

Cohort study of 777 patients (1238 sides at risk) shows that both oxidized regenerated cellulose and gelatin sponge (topical hemostatic agents) are safe to use in thyroidectomy. Adverse events are nil and the incidence of RLN palsy and permanent hypoparathyroidism are low.

PubMed-ID: [41514482](#)

DOI: [10.1002/wjs.70225](#)

### **Thyroglobulin Cutoffs after Total Thyroidectomy Without Radioiodine in Low- to Intermediate-Risk Thyroid Cancer: A Multicenter Cohort Study.**

*Thyroid*, 36(1):46-56.

M. Kim, E. K. Lee, K. J. Kim, S. M. Shin, J. Jang, J. Y. Shin, M. Jin, J. S. Bae, K. Kim, W. G. Kim, M. J. Jeon, S. H. Kang, H. K. Kim, J. H. Yoon, Y. E. Kang, H. Y. Ahn, Y. J. Park and B. H. Kim. 2026.

**Background:** The prognostic value of unstimulated serum thyroglobulin (Tg) levels for structural recurrence in patients with low- to intermediate-risk differentiated thyroid cancer (DTC) who underwent total thyroidectomy but did not receive radioactive iodine (RAI) therapy remains unclear. This study aimed to determine Tg cutoff values and evaluate the role of dynamic Tg monitoring in risk stratification in these patients. **METHODS:** We retrospectively analyzed 9753 patients with low- to intermediate-risk DTC who underwent total thyroidectomy without RAI at 11 Korean tertiary hospitals. Serum Tg levels were measured under thyrotropin suppression ( $<2$  mIU/L) at 6, 12, and 24 months postoperatively using high-sensitive assays (functional sensitivity,  $<0.2$  ng/mL). Optimal Tg cutoffs were determined by receiver operating characteristic curves and survival analyses. **RESULTS:** Higher postoperative unstimulated Tg levels consistently predicted structural recurrence, with an optimal cutoff of 0.3 ng/mL (area under the curve: 0.815, 0.772, and 0.816 at 6, 12, and 24 months, respectively). A Tg  $\geq 0.2$  ng/mL, the Korean Thyroid Association (KTA) guideline cutoff for biochemical remission (excellent response), showed high sensitivity for recurrence. Tg  $\geq 5.0$  ng/mL at 6 months, a KTA-defined threshold for a biochemical incomplete response, independently predicted an elevated recurrence risk. Kaplan-Meier curves showed stepwise declines in recurrence-free survival with increasing Tg levels. Notably, even Tg  $< 0.2$  or  $< 0.3$  ng/mL were associated with recurrence if levels rose over time. **CONCLUSION:** Unstimulated Tg levels are strongly associated with the risk of structural recurrence in patients with DTC who have undergone total thyroidectomy without RAI. The current cutoff values of 0.2 ng/mL and 5.0 ng/mL were clinically relevant, and Tg kinetics over time further improved risk stratification. These findings provide the first large-scale evidence from an East Asian cohort and underscore the importance of early, serial Tg assessment in this growing patient population.

PubMed-ID: [41467912](#)

DOI: [10.1177/10507256251409134](#)

### **Value of TERT Promoter Mutations for Early Outcomes in Papillary Thyroid Cancer.**

*Endocr Relat Cancer*,

M. J. Kim, D. Kim, H. S. Lee, S. H. Park, E. J. Kim, J. K. Kim, S. W. Kang, J. Lee, J. J. Jeong, W. Y. Chung and K. H. Nam. 2026.

Telomerase reverse transcriptase (TERT) promoter mutations are associated with aggressive clinicopathological features of papillary thyroid cancer (PTC). However, their independent prognostic value remains unclear. This study aimed to evaluate the prognostic significance of TERT promoter mutations (TPMs) in predicting early treatment outcomes and event-free survival (EFS) in patients with PTC. We retrospectively analyzed a prospective cohort; patients underwent surgery at a single tertiary referral center between 2019 and 2022. Patients underwent thyroidectomy, selective postoperative radioactive iodine ablation, and levothyroxine suppression therapy. Propensity score matching (PSM, 1:1) was applied to adjust for baseline clinicopathological differences. Of 10,642 patients with available molecular data, 115 (1.1%) harbored TPMs. After PSM, 90 matched pairs of patients with TERT-wild-type and TERT-mutant tumors were analyzed. Early treatment responses at 1 and 2 years post-treatment and EFS were evaluated. Early treatment responses did not differ significantly between groups at 1 year ( $P = 0.212$ ) and 2 years ( $P = 0.571$ ). However, patients with TERT-mutant tumors had fewer excellent responses and higher rates of structural incomplete response. During follow-up, the TERT-mutant group experienced more recurrences and one disease-specific death. Cumulative EFS was significantly poorer in TERT-mutant group than TERT-wild-type group ( $P = 0.022$ ). Despite their low prevalence, TPMs were independently associated with adverse oncological outcomes, including higher rates of recurrence and mortality. TPMs may serve as valuable prognostic markers for early risk stratification in PTC.

PubMed-ID: [41989876](#)

DOI: [10.1530/ERC-25-0424](#)

### **Sonographic and pathologic features of malignant hot thyroid nodules: A multi-institutional study.**

*Surgery*, 189:109710.

E. L. Koelliker, L. N. Krumeich, T. Kravchenko, M. M. Keamy Blanco, A. S. Letica-Kriegel, I. Hsu and R. M. Gartland. 2026. BACKGROUND: Prior studies indicate that approximately 5% of hot thyroid nodules harbor malignancy. Hot nodules often exhibit suspicious sonographic features despite their typical benign pathology. This study examines the incidence, sonographic characteristics, and surgical pathology of malignancy within hot nodules to guide workup of these nodules, including preprocedure workup for thermal ablation. METHODS: Patients at 5 tertiary care centers with solitary toxic nodules or toxic multinodular goiters undergoing thyroidectomy (2017-2024) were included. Using thyroid uptake scan and ultrasonography, hot nodules were matched with sonographic characteristics. Nodules <1 cm and patients without either imaging were excluded. Sonographic features and indications for biopsy were assessed using the Thyroid Imaging Reporting and Data System classification. Kruskal Wallis and tests of proportions were used for analysis. RESULTS: Among 257 patients with 323 hot nodules, 11 (3.4%) nodules were malignant: 9 of 124 (7.3%) solitary toxic nodules and 2 of 199 (1.0%) in multinodular goiters ( $P = .003$ ). Compared with benign hot nodules, malignant hot nodules were more often solid (90.9% vs 51.6%,  $P = .01$ ), isoechoic/hyperechoic (81.8% vs 48.4%,  $P = .04$ ), and biopsied (81.8% vs 41.7%,  $P = .008$ ). Pathology of malignant hot nodules revealed papillary and follicular cancers with BRAF positivity (36.4%), lymphovascular invasion (45.5%), multifocality (36.4%), and tall cell features (33.3%). Providers recommended completion thyroidectomy for 2 patients and postoperative radioactive iodine for 3. CONCLUSIONS: Solitary toxic nodules harbor a higher risk of malignancy than toxic multinodular goiters, and these malignancies can exhibit poor prognostic pathologic features. The 7.3% malignancy rate in resected solitary toxic nodules may support existing recommendations for biopsy prior to thermal ablation of these nodules.

PubMed-ID: [41062395](#)

DOI: [10.1016/j.surg.2025.109710](#)

### **Patient preferences in papillary thyroid microcarcinoma management are driven by aversion toward complications rather than treatment pathway.**

*Surgery*, 189:109694.

R. Kowalski, K. Carlisle, A. N. Park, S. Ricci, R. Don, C. Cunningham, J. F. Slejko, C. D. Mullins and Y. Hu. 2026. BACKGROUND: Papillary thyroid microcarcinomas carry an excellent prognosis, making patient preferences and cost-effectiveness important determinants of treatment selection. To conduct cost-effectiveness analyses, quality-adjusted life year weights for papillary thyroid microcarcinoma treatments must be derived. Our objective was to estimate the quality-adjusted life year weights of common papillary thyroid microcarcinoma treatment scenarios. METHODS: This study used 10 previously published papillary thyroid microcarcinoma clinical vignettes describing active surveillance, radiofrequency ablation, partial thyroidectomy, and total thyroidectomy, along with potential complications (progression, vocal cord palsy, hypocalcemia). Quality-adjusted life year weights were derived using a time trade-off instrument administered to thyroid cancer survivors. Quality-adjusted life year weights were compared using within-subjects repeated measures analysis of variance and paired Wilcoxon rank-sum tests. The cohort was powered to detect a minimal important difference with an effect size of 0.5 (ie, 0.04 quality-adjusted life year). RESULTS: Data from 101 thyroid cancer survivors

were collected. Median quality-adjusted life year weights for uncomplicated treatment scenarios ranged from 0.975 to 0.992 and were not significantly different between treatments ( $P = .15$ ). Treatment complications resulted in significantly lower quality-adjusted life year weights across all treatment strategies ( $P < .01$ ) except active surveillance ( $P = .72$ ). CONCLUSION: Quality-adjusted life year weights were comparable between the uncomplicated versions all 4 treatment pathways, suggesting that patient treatment preferences for papillary thyroid microcarcinoma are driven by aversion to treatment complications, rather than an inclination toward the experience of the treatments themselves. These quality-adjusted life year weights may be readily incorporated into value assessments for papillary thyroid microcarcinoma treatments.

PubMed-ID: [41006152](#)

DOI: [10.1016/j.surg.2025.109694](#)

PMCID: PMC13222115

### **Thermal Ablation for Papillary Thyroid Microcarcinoma: Promise, Pitfalls, and Perspective.**

*JAMA Surg*, 161(4):315-6.

J. H. Kuo and Q. Y. Duh. 2026.

This Viewpoint discusses thermal ablation as a treatment option for papillary thyroid microcarcinoma, including technical challenges, patient perceptions, and costs compared with active surveillance.

eng.

PubMed-ID: [41706465](#)

DOI: [10.1001/jamasurg.2025.6720](#)

### **Autofluorescence alone is not enough: a combined strategy for accurate identification of parathyroid tissue in thyroidectomy specimens.**

*Int J Surg*,

T. C. Kuo, K. Y. Chen, C. W. Lai, M. T. Lin, C. H. Chang and M. H. Wu. 2025.

IMPORTANCE: Inadvertent excision of parathyroid glands (PTGs) during thyroidectomy remains a common and significant surgical complication, potentially leading to hypoparathyroidism. While near-infrared autofluorescence (NIRAF) imaging enhances intraoperative PTG identification, its specificity and real-world diagnostic accuracy remain uncertain. OBJECTIVE: To evaluate the diagnostic accuracy of NIRAF imaging in identifying inadvertently excised PTGs in thyroidectomy specimens and to assess the added value of intraoperative tissue parathyroid hormone (PTH) washout testing. DESIGN, SETTING, AND PARTICIPANTS: This was a prospective diagnostic accuracy study conducted at a university hospital between 28 February 2024, and 28 February 2025. Consecutive adult patients undergoing conventional or endoscopic thyroidectomy were included. NIRAF imaging was performed on all excised thyroid lobes prior to pathological examination. Autofluorescent (AF)-positive areas were assessed using intraoperative tissue PTH washout testing, with histopathology serving as the reference standard. MAIN OUTCOMES AND MEASURES: The primary outcome was the diagnostic performance (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) of NIRAF imaging for identifying parathyroid tissue. Secondary outcomes included inadvertent parathyroid excision rate and diagnostic accuracy of the tissue PTH washout test. RESULTS: Among 672 patients (mean age, 46.8 years; 82.7% female), 1,144 thyroid lobes were examined, yielding 224 AF-positive areas. Of these, 197 had PTH  $\geq 100$  pg/mL and were confirmed as PTGs; 27 had PTH  $< 100$  pg/mL, of which 2 were confirmed as PTGs on histopathology. The sensitivity and specificity of NIRAF imaging were 100.0% (95% CI, 98.1%-100.0%) and 97.9% (95% CI, 96.7%-98.7%), respectively; PPV was 88.8% and NPV was 100.0%. The inadvertent parathyroid excision rate was 8.7% (199/2,288). The tissue PTH washout test showed 99.1% overall diagnostic accuracy (95% CI, 97.3%-99.8%), with sensitivity 99.0% (95% CI, 96.2%-99.9%), specificity 100.0% (95% CI, 86.3%-100.0%), PPV 100.0% (95% CI, 98.1%-100.0%), and NPV 92.6% (95% CI, 75.7%-98.9%).

CONCLUSIONS AND RELEVANCE: NIRAF imaging is highly sensitive for detecting inadvertently excised parathyroid glands, but false-positive signals from non-parathyroid tissues limit its specificity. Combining NIRAF with intraoperative tissue PTH measurement can improve diagnostic accuracy and guide timely autotransplantation. Further studies are needed to refine tissue PTH thresholds and validate broader clinical applicability.

PubMed-ID: [41287871](#)

DOI: [10.1097/JS9.0000000000004025](#)

### **Professor Petros S. Kokkalis (1896-1962) and the evolution of thyroid disease understanding in early 20th century Greek medicine.**

*Hormones (Athens)*,

K. Laios, P. Lytsikas-Sarlis, K. G. Apostolou, A. Paspala, G. Tsourouflis, N. Voloudakis, I. Koutelidakis, D. Zisiadis, G. Tsoucalas

and D. Schizas. 2026.

This article presents a comprehensive historical analysis of thyroid gland pathology as described by Professor Petros S. Kokkalis (1896-1962), drawing on original early 20th century clinical observations and the foundational Greek medical literature of the era. It explores the transformation in medical understanding from viewing thyroid disorders as localized organ dysfunctions to recognizing their systemic nature, particularly in the context of hyperthyroidism and Basedow's (Graves') disease. The review synthesizes Kokkalis's meticulous clinical classifications, pathophysiological insights, and pioneering therapeutic protocols, including the adoption of iodine-based therapies and advances in surgical technique. It further contextualizes his work within the broader international landscape by comparing his findings and approaches to those of contemporaneous European and American researchers, such as Neisser, Plummer, Marine, and Mayo, who collectively advanced the field of endocrinology. The article demonstrates that Kokkalis's contributions were not only consistent with but also emblematic of the most progressive medical thought of his time. This historical perspective underscores the enduring importance of detailed clinical observation, systematic documentation, and international collaboration in shaping the scientific foundations of modern thyroid disease management.

PubMed-ID: [41699377](#)

DOI: [10.1007/s42000-026-00764-5](#)

### **Calculation of postoperative parathyroid hormone level using indocyanine green angiography during robotic total thyroidectomy: equivalent function hypothesis.**

*Surg Endosc*, 40(3):2189-98.

J. K. Lee, Y. Kong, E. Kim, S. Yun, H. W. Yu and J. Y. Choi. 2026.

**BACKGROUND:** Postoperative hypoparathyroidism remains a common complication following total thyroidectomy. Although anatomical preservation of the parathyroid glands (PGs) is routinely attempted, functional outcomes are often unpredictable. To address this gap, we developed a novel physiology-based model to predict postoperative parathyroid hormone (PTH) levels by incorporating preoperative hormonal status and intraoperative perfusion assessment using indocyanine green (ICG) angiography. **METHODS:** This retrospective study included 37 patients who underwent bilateral axillo-breast approach robotic total thyroidectomy between July 2024 and February 2025. Intraoperative ICG angiography was used to classify each PG as well-perfused, poorly perfused, or unidentifiable. Based on our hypotheses that each PG contributes to total PTH levels equally under normal physiology and that PG's functional viability can be evaluated by ICG angiography, postoperative PTH levels were calculated using the following formula: Calculated PTH = (Preoperative PTH / 4 x n(well)) + (1 x n(poor)), where n(well) and n(poor) represent the number of well- and poorly perfused PGs, respectively. **RESULTS:** Postoperative-to-preoperative PTH ratios exhibited distinct clustering at 0.25, 0.50, and 0.75, consistent with the hypothesis that each PG contributes approximately one-quarter to overall PTH production. Calculated PTH values were strongly correlated with measured postoperative levels (Spearman's rho = 0.60, p < 0.001), and 73.0% of patients had calculated values within +/- 5 pg/mL of the actual result. Transient hypoparathyroidism occurred in 13 patients (35.1%) and was associated with significantly lower actual and calculated postoperative PTH levels compared to those without hypoparathyroidism. **CONCLUSIONS:** Our physiology-based model enables accurate intraoperative estimation of postoperative PTH levels by incorporating preoperative PTH values and ICG angiography-based perfusion status. This approach may serve as a rapid and effective indicator of post-thyroidectomy hypoparathyroidism, particularly in day surgery settings or in institutions where routine postoperative laboratory monitoring is not feasible.

PubMed-ID: [41410748](#)

DOI: [10.1007/s00464-025-12462-1](#)

### **Impact of Subtype Variability on Clinical Features in Papillary Thyroid Cancer.**

*J Clin Endocrinol Metab*, 111(3):648-55.

J. S. Lee, N. K. Kim, H. J. Jeong, H. J. Yun, H. Chang, S. M. Kim, Y. S. Lee and H. S. Chang. 2026.

**CONTEXT:** Thyroid cancer comprises multiple subtypes and is broadly classified as aggressive or nonaggressive. While many studies have analyzed the clinical features of aggressive and nonaggressive subtypes, to the best of our knowledge, no study has focused on patients having more than 1 subtype concomitantly. **OBJECTIVES:** We investigated the clinical features manifested when these subtypes and conventional types of thyroid cancer occur simultaneously in the same patient. **METHODS:** In this single-center, cross-sectional study, we analyzed 26 449 patients with thyroid cancer who underwent surgery for papillary thyroid cancer (PTC) between March 2009 and December 2021 in Korea. We categorized the patients into 5 groups according to the subtypes of PTC (conventional, aggressive, nonaggressive, conventional with aggressive, and conventional with nonaggressive). We compared the patient characteristics and clinical features among the groups and analyzed them statistically. **RESULTS:** Significant differences among the groups were observed based on the PTC subtypes. Patients with both conventional and aggressive subtypes exhibited more aggressive clinical features

compared to those with the conventional subtype alone. In the same context, patients with both conventional and nonaggressive subtypes showed aggressive features compared to those with the nonaggressive subtype alone. CONCLUSION: We concluded that patients with mixed subtypes had clinical features that were more severe than those with a single subtype, suggesting that postoperative management warrants caution.

PubMed-ID: [41259122](#)

DOI: [10.1210/clinem/dgaf531](#)

#### **Risk of post-contrast thyroid dysfunction in non-toxic goiter: a matched cohort study.**

*Eur J Endocrinol*, 194(4):555-65.

W. Lee, C. T. Kor and Y. T. Liu. 2026.

OBJECTIVE: To quantify the risk of post-iodinated contrast media (ICM) thyroid dysfunction and identify clinical predictors in adults with nontoxic goiter. DESIGN: Single-center retrospective cohort study. METHODS: We conducted a retrospective cohort study (2010-2023) of adults with intravenous ICM exposure after  $\geq 1$ -year ICM-free baseline. Nontoxic goiter was identified via ICD codes, with ultrasound as sensitivity analysis. Goiter cases were 1:8 propensity score matched to controls by age, sex, comorbidities, and medications. The primary outcome was thyroid-stimulating hormone (TSH)-defined thyroid dysfunction within 2 years after ICM exposure. Additional sensitivity analyses included cases with concurrent abnormal free T4 or T3 levels, and cases with subsequent thyroid-related medication use. Adjusted odds ratios (aORs) were estimated using logistic regression, and repeated ICM exposure during follow-up was examined as a risk factor. RESULTS: After matching, 1347 goiter cases and 10 776 controls were analyzed. TSH-defined dysfunction occurred in 4.8% vs 1.4% within 2 years (OR, 3.46; 95% CI, 2.57-4.66). Sensitivity analyses using stricter definitions showed consistent results. In adjusted models, nontoxic goiter remained independently associated with dysfunction (aOR, 3.10; 95% CI, 2.39-4.02). Additional predictors included amiodarone use (aOR, 11.34; 95% CI, 8.60-14.94), repeated ICM exposure (aOR, 1.54; 95% CI, 1.34-1.77), and female (aOR, 1.96; 95% CI, 1.69-2.22). Findings were consistent when goiter was defined sonographically (309 vs 2472; OR, 3.76; 95% CI, 2.22-6.38). CONCLUSION: Nontoxic goiter was linked to a 3-fold increased risk of thyroid dysfunction post-ICM, supporting targeted screening, and TSH monitoring in high-risk populations.

PubMed-ID: [42012254](#)

DOI: [10.1093/ejendo/lvag069](#)

#### **The triglyceride-glucose body mass index paradox: dual metabolic effects on tumor aggressiveness and recurrence risk in 11 317 papillary thyroid carcinoma patients.**

*Int J Surg*, 112(2):4356-65.

C. Li, G. Dionigi, H. Guan, H. Sun and J. Zhang. 2026.

OBJECTIVE: To investigate the linear and nonlinear relationships between the triglyceride-glucose body mass index (TyG-BMI) and aggressiveness and risk of recurrence in papillary thyroid carcinoma (PTC). METHODS: This retrospective single-center cohort study included 11 317 patients with PTC. The associations between the TyG-BMI and PTC aggressiveness as well as moderate-to-high recurrence risk were analyzed with binary logistic regression and odds ratios (ORs). Linear and nonlinear relationships between the TyG-BMI and these outcomes were evaluated with restricted cubic spline and smoothed curve-fitted logistic risk regression models. Key factors contributing to TyG-BMI prediction outcomes were weighted with machine learning algorithms. RESULTS: After adjusting for confounding factors, higher TyG-BMI was associated with a significantly increased risk for tumors with a maximum diameter of  $>1$  cm (OR adjust = 1.35,  $P < 0.001$ ), multifocality (OR adjust = 1.42,  $P < 0.001$ ), and extrathyroidal extension (OR adjust = 1.53,  $P < 0.001$ ). Conversely, higher TyG-BMI was associated with a significantly decreased risk for positive lymph nodes with a maximum diameter of  $>0.2$  cm (OR adjust = 0.36,  $P < 0.001$ ) and intermediate-to-high risk of PTC recurrence (OR adjust = 0.68,  $P < 0.001$ ). TyG-BMI exhibited a linear relationship with the risk of tumors with a maximum diameter of  $>1$  cm and multifocality, but a nonlinear relationship with extrathyroidal extension and intermediate-to-high recurrence risk of PTC. TyG-BMI showed a positive linear correlation with free triiodothyronine (FT3) and thyroglobulin (Tg); a negative linear correlation with free thyroxine (FT4), thyroid peroxidase antibody (TPOAb), and thyroglobulin antibody (TgAb); and no linear relationship with thyroid-stimulating hormone (TSH). Among the components of the TyG-BMI and potential confounding factors, machine learning algorithms consistently identified triglyceride (TG) level as the primary contributor when predicting PTC aggressiveness and intermediate-to-high risk of PTC recurrence. CONCLUSION: This study reveals complex relationships, both linear and nonlinear, between the TyG-BMI, PTC aggressiveness and intermediate-to-high risk of PTC recurrence, with TG playing a pivotal role within the TyG-BMI. There were linear correlations between the TyG-BMI and thyroid function.

PubMed-ID: [41287894](#)

DOI: [10.1097/JS9.0000000000003887](#)

**Prognostic Value of Hematological Inflammatory Indices (PLR, NLR, SII) in Medium and High-Risk Papillary Thyroid Carcinoma: A Multicenter Cohort Study.**

*Clin Endocrinol (Oxf)*, 104(3):255-69.

C. Li, S. Li, Y. Zhao, D. Zhang, Y. Fu, L. Zhou, J. Li, F. Li, R. Du, N. Liang and H. Sun. 2026.

BACKGROUND: Patients with medium and high-risk papillary thyroid carcinoma (PTC) demonstrate significantly poorer clinical outcomes compared to their low-risk counterparts. However, current prognostic stratification for this patient population remains suboptimal due to the absence of reliable biomarkers. This investigation aims to evaluate the clinical utility and prognostic potential of three hematological inflammatory indices: the platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII) in medium and high-risk PTC cases.

METHODS: This study analyzed 1070 PTC patients from the "DTCC study" (2014-2016), a multicenter prospective cohort investigating the initial management of differentiated thyroid cancer (DTC) in China. Preoperative hematological parameters (including PLR, NLR, and SII) and baseline clinical characteristics were evaluated to assess their prognostic significance. RESULTS: In medium and high-risk PTC patients, PLR  $\leq$  115.6 predicted increased recurrence risk (OR = 4.579, 95% CI: 1.863-11.255,  $p$  = 0.001) and worse disease-free survival (DFS;  $p$  = 0.001). Multivariate Cox regression confirmed PLR  $\leq$  115.6 as an independent prognostic factor for reduced DFS (HR = 3.080, 95% CI: 1.115-8.507,  $p$  = 0.030). Notably, this association persisted in intermediate-risk patients. Among high-risk PTC patients, however, SII  $\leq$  360.9 (rather than PLR) demonstrated stronger predictive value for recurrence (OR = 15.154, 95% CI: 1.873-122.640,  $p$  = 0.011). Consistently, multivariate analysis identified SII  $\leq$  360.9 as an independent risk factor for shorter DFS (HR = 14.399, 95% CI: 1.823-113.730,  $p$  = 0.011). CONCLUSION: Our findings demonstrate that PLR and SII emerged as risk stratification-specific prognostic biomarkers: PLR independently predicted prognosis in intermediate-risk cases, while SII showed superior predictive value for prognosis in high-risk patients. The differential utility of these indices-PLR for intermediate-risk stratification patients and SII for high-risk stratification patients-highlights their complementary roles in clinical decision-making. As routinely available, cost-effective inflammatory markers, PLR and SII may enhance risk-adapted surveillance strategies, though further validation is warranted to standardize cutoff values and integrate them into existing clinical management systems. TRIAL REGISTRATION: The trial was registered at ClinicalTrials.gov under the identifier NCT02638077.

PubMed-ID: [41102848](#)

DOI: [10.1111/cen.70046](#)

**Reflections on prevention and treatment of post-thyroidectomy hypoparathyroidism: current management approaches and future prospects.**

*Front Endocrinol (Lausanne)*, 17:1768391.

J. Li, Z. Hu, Z. Ma, G. Feng, L. Zhang, S. Zhu, J. Hu, W. Han and T. Li. 2026.

Postoperative hypoparathyroidism (hypoPT) is one of the predominant and severe complications of thyroid surgery. This condition manifests as suboptimal circulatory levels of parathyroid hormone (PTH), engendering multifaceted systemic perturbations. This comprehensive review elucidates the underlying pathophysiological mechanisms and clinical presentations associated with hypoparathyroidism. Moreover, methodologies for the precise recognition and preservation (naked eye, near-infrared autofluorescence, indocyanine green, carbon nanoparticles, and mitoxantrone hydrochloride) of the parathyroid gland during thyroid surgery have been explored, along with recent therapeutic innovations (palopecteriparatide and parathyroid organoids). Finally, this review prospects and interventions via organoids are contemplated. The aim of the literature is to recapitulate the knowledge and the gaps in this field, increasing awareness of postoperative hypoparathyroidism, and improve the prognosis for patients afflicted with hypoparathyroidism.

PubMed-ID: [41847457](#)

DOI: [10.3389/fendo.2026.1768391](#)

PMCID: PMC12990180

**Thyroid cancer in adolescents and young adults: a population-based study in 185 countries worldwide.**

*Lancet Diabetes Endocrinol*, 14(2):112-22.

M. Li, L. Dal Maso, M. Pizzato, H. Rumgay and S. Vaccarella. 2026.

BACKGROUND: Cancer burden among adolescents and young adults (AYAs) aged 15-39 years has increased during the past two decades, with thyroid cancer being a major contributor. We aimed to comprehensively evaluate trends and the current burden of thyroid cancer among AYAs globally. METHODS: We obtained annual incidence and mortality data of

thyroid cancer from the Cancer Incidence in Five Continents Plus and the WHO Mortality databases. Temporal trends were displayed using the average annual percent changes of age-standardised incidence rates estimated during 2003-2017. The national estimates of incidence and mortality of thyroid cancer and other cancer types for 185 countries in 2022 were obtained from the GLOBOCAN platform. Incidence-to-mortality ratios were compared by cancer type. We estimated the correlation of human development index (HDI) with thyroid cancer incidence and mortality. **FINDINGS:** Thyroid cancer incidence rates among AYAs have increased rapidly since the 2000s in most countries, whereas mortality rates remained stably low. Notable increases in incidence were found in South Korea, Cyprus, Ecuador, and Türkiye, with particularly pronounced rises in China. During 2003-2017, the average annual percent changes of thyroid cancer incidence were greater than 10% in six countries and greater than 5% in 19 countries. In 2022, there were approximately 237 000 new cases and around 2100 deaths from thyroid cancer, ranking among the top three most diagnosed cancers in 100 countries for females and in 26 countries for males. By 2022, thyroid cancer accounted for 20.3% of all new cancer cases in female AYAs and 13.6% in male AYAs, ranking as the second most diagnosed cancer among female AYAs, after breast cancer, and the most common cancer among male AYAs. Thyroid cancer incidence rates varied greatly by country, continent, and HDI, while mortality rates were less variable. The incidence-to-mortality ratios for thyroid cancer among AYAs exceeded 3300 for females and 600 for males (<100 for other cancer types) in some countries. HDI was strongly and positively correlated with thyroid cancer incidence, whereas its association with mortality was negative but weak. **INTERPRETATION:** The epidemiological profile of thyroid cancer among AYAs indicates a large expansion of overdiagnosis to younger populations. Increased efforts are required to prevent unnecessary diagnosis and treatment due to overuse of diagnostic procedures. **FUNDING:** Guangzhou Science and Technology Project, Guangdong Basic and Applied Basic Research Foundation, Italian Association for Cancer Research, Italian Ministry of Health, and Young Talents Program of Sun Yat-sen University Cancer Center.

PubMed-ID: [41274302](#)

DOI: [10.1016/S2213-8587\(25\)00289-X](#)

#### **Endoscopic surgical treatment of thyroid cancer: clinical application and future prospects.**

*Int J Surg,*

M. Li and X. Yu. 2026.

Endoscopic thyroid cancer surgery, as a typical representative of minimally invasive surgical techniques, has made remarkable progress in surgical approaches, functional protection, complication control, and indication expansion in recent years. This article reviews the technical evolution, clinical efficacy, and future development direction of endoscopic thyroid cancer surgery, with a focus on analyzing the advantages and disadvantages of different approaches, optimizing surgical indications, and improving strategies for complication management, with the aim to provide a reference basis for clinical practice.

PubMed-ID: [41556189](#)

DOI: [10.1097/JS9.0000000000004496](#)

#### **Effect of Radioactive Iodine Therapy on Cancer-Specific Survival of Papillary Thyroid Carcinoma With T4aM0 Stage.**

*Clin Endocrinol (Oxf),* 105(1):93-9.

P. Li, Y. Tong, Y. Zhang, Y. Fan, G. Yang, W. Zhao, T. Wei and X. Wang. 2026.

**CONTEXT:** Papillary thyroid carcinoma (PTC) with T4aM0 stage, which involves extrathyroidal extension without distant metastasis, presents challenges in treatment management. While radioactive iodine (RAI) therapy has been shown to benefit certain high-risk thyroid cancer patients, its effect on cancer-specific survival (CSS) in T4aM0 PTC patients remains unclear. **OBJECTIVE:** We aim to evaluate the impact of RAI therapy on CSS in T4aM0 PTC patients following total thyroidectomy. **METHODS:** 1938 PTC patients with T4aM0 stage who underwent total thyroidectomy in the SEER database were identified. Clinical-pathological and CSS data were systematically collected. Patients were stratified into the RAI-treated group and the non-RAI-treated group. Propensity score matching (PSM) was implemented with 1:1 nearest-neighbour matching to balance baseline covariates. Intergroup comparisons of demographic and clinical characteristics were performed in the entire cohort and PSM cohort. Subset analyses were conducted to indicate the effect of RAI therapy on CSS in different subgroups. Cox proportional hazards regression models were employed to evaluate CSS outcomes. **RESULTS:** After PSM, 472 pairs of patients were included in the analysis. In both the entire cohort and the PSM cohort, no significant difference in CSS was observed between RAI-treated and non-RAI-treated patients (HR = 0.797, 95% CI: 0.540-1.175,  $p = 0.252$ ; HR = 0.709, 95% CI: 0.437-1.151,  $p = 0.709$ ). Subgroup analysis also showed no survival benefit of RAI across various clinical characteristics. **CONCLUSION:** RAI therapy does not significantly improve cancer-specific survival in T4aM0 PTC patients after total thyroidectomy. These findings suggest that RAI may not be necessary for this subgroup, advocating for more individualised treatment approaches.

PubMed-ID: [41796710](#)  
DOI: [10.1111/cen.70123](#)

**Short-term outcomes in radiofrequency ablation for the primary treatment of T1N0M0 papillary thyroid carcinomas.**

*Am J Surg*, 253:116702.

R. Liou, L. Slattey, Y. Hu, E. J. Kuo, C. McManus, J. A. Lee and J. H. Kuo. 2026.

Radiofrequency ablation (RFA) has been gaining traction for treating benign thyroid nodules, but its use for papillary thyroid carcinomas (PTCs) remains uncommon. We conducted a single institution prospective cohort study of patients who underwent RFA for biopsy-proven PTC(s) 1.5 cm in greatest diameter. Primary outcomes included volume reduction ratio (VRR) at 1, 3, 6, and 12 months and rate of complications. We performed RFA on 46 PTCs in 41 patients. With a median follow-up of 8 months (IQR:6-12.3), we achieved complete sonographic disappearance of 85 % of tumors. Median VRR was -107.5 % (IQR: 322.3 - 6.0), 18.8 % (IQR: 75 - 54.12), and 100 % (IQR:70.7-100) at 1, 3, and 12- months follow-up. Four patients (9.8 %) experienced minor complications. Preliminary findings suggest that RFA is a safe and effective treatment modality for patients with PTCs. Additional enrollment and further surveillance are necessary to assess the long-term efficacy of RFA for PTCs.

PubMed-ID: [41224560](#)

DOI: [10.1016/j.amjsurg.2025.116702](#)

**Meningeal metastatic tumor with bone destruction from follicular thyroid carcinoma: a case report and literature review.**

*Front Surg*, 12:1708113.

W. Liu, L. Su, Q. Zhang and Y. Liu. 2025.

BACKGROUND: Follicular thyroid carcinoma (ftc) is a malignant neoplasm arising from thyroid follicular epithelial cells and is the second most common thyroid cancer after papillary thyroid carcinoma. meningeal metastasis from ftc with calvarial destruction is exceedingly rare and is often misdiagnosed clinically as meningioma. we reviewed previously reported cases in the literature and, in addition, report and include one case of meningeal metastasis from ftc treated at our center.

METHODS: Using the keywords "meningioma," "follicular thyroid carcinoma," and "cerebral metastatic tumor," we searched PubMed/MEDLINE and Web of Science to identify relevant publications. We extracted patient age, sex, tumor location and size, treatment modalities, and follow-up outcomes. In parallel, we provide a detailed description and analysis of the clinical course of the present case. RESULTS: A total of 10 patients were included, comprising the cases reported in the literature and the index case in this study. The mean age was 60.5 years, and most lesions were solitary epidural or dural-based masses. Headache was the most common presenting symptom. All patients underwent surgical resection; postoperative recurrence occurred in two cases, and the longest survival on follow-up was 7 years.

CONCLUSIONS: Meningeal metastasis from FTC is rare and typically presents as a dural-based mass that readily mimics meningioma. Gross-total resection can achieve favorable initial disease control, although recurrence may still occur. Given the small number of reported cases, the long-term prognosis remains uncertain and warrants further investigation.

PubMed-ID: [41568262](#)

DOI: [10.3389/fsurg.2025.1708113](#)

PMCID: PMC12816310

**Correction: Meningeal metastatic tumor with bone destruction from follicular thyroid carcinoma: a case report and literature review.**

*Front Surg*, 13:1782451.

W. Liu, L. Su, Q. Zhang and Y. Liu. 2026.

[This corrects the article DOI: 10.3389/fsurg.2025.1708113.].

PubMed-ID: [41660495](#)

DOI: [10.3389/fsurg.2026.1782451](#)

PMCID: PMC12875087

**Positive predictive value of the Afirma gene sequencing classifier for evaluation of the indeterminate thyroid nodule: An institutional experience.**

*Am J Surg*, 252:116759.

S. Lyon, A. Turza, S. Ganesan and C. R. McHenry. 2026.

BACKGROUND: The purpose of this study was to determine the positive predictive value (PPV) and false positive (FP) rate for the Afirma Gene Sequencing Classifier (GSC). METHODS: The GSC was analyzed in patients with indeterminate thyroid

nodules (ITN). True positive (TP), FP and PPV were determined and were correlated with pathology. RESULTS: From June 2023-January 2025, 75 ITN were evaluated with the GSC and it was suspicious for cancer in 21 (28 %); 15 patients with 16 suspicious nodules underwent thyroidectomy. There were 7 TP and 9 FP results for a PPV of 44 %. The final pathology was papillary cancer 6 and oncocytic carcinoma 1 with TP GSC and follicular/oncocytic adenoma 4, follicular nodule 2, NIFTP 2 and Hashimoto thyroiditis 1 with FP GSC. CONCLUSIONS: A PPV of 44 % for the GSC has implications for the extent of surgery and for reducing overtreatment of patients with ITN.

PubMed-ID: [41343883](#)

DOI: [10.1016/j.amisurg.2025.116759](#)

#### **Real-world data show limited efficacy of sequential cabozantinib treatment in RAIR-(P)DTC.**

*Endocr Relat Cancer*, 33(2)

Y. M. Machlah, L. M. Srasra, S. Theurer, F. Weber, D. Kersting, H. Lahner, D. Fuhrer and T. Brandenburg. 2026.

Cabozantinib has significantly improved progression-free survival (PFS) in patients with radioiodine-refractory differentiated thyroid cancer (RAIR-DTC) after lenvatinib and/or sorafenib pretreatment in the phase 3 COSMIC-311 trial, leading to its approval for sequential treatment. Real-world evidence of cabozantinib remains limited, particularly in poorly differentiated thyroid cancer (PDTC). In this retrospective analysis, we included adult patients with RAIR-DTC or PDTC treated with cabozantinib as further-line treatment at the Essen Endocrine Tumor Center (June 2022-July 2025). All patients had received prior targeted therapy and had documented progressive disease at cabozantinib initiation. Best overall response, PFS, overall survival (OS) and adverse events were assessed. Nineteen patients (7 DTC and 12 PDTC) were included in the safety analysis, and 17 patients were included in the efficacy assessment. Under sequential cabozantinib treatment, partial response (PR) was observed in 4/17 (24%): 3/4 in patients switched due to lenvatinib toxicity and 1/13 in those switched due to progression. Median PFS was 5.4 months in DTC and 3.6 months in PDTC. Median OS from cabozantinib initiation was 13.5 months in DTC and 15.8 months in PDTC. Dose reductions or interruptions were required in 6/19 (31.6%), and 3/19 (15.8%) permanently discontinued cabozantinib due to toxicity. In this real-world cohort, further-line cabozantinib showed limited efficacy in RAIR-(P)DTC, especially in PDTC. Responses were more favorable when cabozantinib was initiated due to prior treatment toxicity rather than progression. The substantial toxicity highlights the need for careful management and improved therapeutic strategies in this population.

PubMed-ID: [41543029](#)

DOI: [10.1530/ERC-25-0461](#)

#### **Segmental Tracheal Resection for Thyroid Cancer: Perioperative Morbidity, Locoregional Control, and Survival.**

*Head Neck*, 48(3):644-9.

A. Maniakas, D. C. Wilde, I. Fournier, E. K. Hyde, L. Xu, J. R. Wang, N. D. Gross, E. M. Sturgis, V. Banuchi, N. L. Busaidy, M. E. Cabanillas, P. Iyer, R. Dadu, S. G. Waguespack, M. I. Hu, G. B. Gunn, M. Kwon, S. Ahmed, M. D. Williams and M. E. Zafereo. 2026.

BACKGROUND: Segmental tracheal resection is rarely needed for advanced thyroid cancer but is among the most complex, high-risk thyroid surgeries. METHODS: Retrospective study of patients undergoing segmental tracheal resection for thyroid cancer at MD Anderson Cancer Center (2005-2024). RESULTS: We identified 120 patients with a median follow-up of 4.6 years (range 0.02-16.38). Papillary thyroid cancer was most common (68%). The median number of tracheal rings resected was 4 (range 1-9). Seventeen (14%) patients had a new tracheostomy placed at the time of surgery, with 11 (9%) remaining trach-dependent at last follow-up. Twenty-six (22%) patients had a return to the operating room within 30 days, while 3 (3%) patients suffered perioperative mortality. The more common postoperative complications included tracheostomy tube placement (10%), hematoma (7%), and anastomotic air leak (6%). Median hospitalization was 6 days (range 2-67). Locoregional control (LRC) and overall survival (OS) were 79% and 77% at 5 years, respectively. CONCLUSIONS: Segmental tracheal resection for advanced thyroid cancer is technically complex and high-risk, but most patients stay recurrence-free 5 years post-surgery.

PubMed-ID: [41059669](#)

DOI: [10.1002/hed.70045](#)

PMCID: PMC12891758

#### **Long-term phonation status after recurrent laryngeal nerve reconstruction.**

*Surgery*, 189:109695.

A. Matsunaga, A. Miyauchi, S. Adachi, S. Kawano, M. Yamamoto, T. Sasaki, M. Fujishima, H. Masuoka, T. Higashiyama, M. Kihara, N. Onoda, Y. Ito and A. Miya. 2026.

BACKGROUND: Patients undergoing recurrent laryngeal nerve resection and reconstruction usually recover phonatory

function within a year. However, their long-term outcomes remain unclear. This study assessed phonatory function over more than 10 years. **METHODS:** Data of a cohort of 212 patients (165 female, 47 male) who underwent recurrent laryngeal nerve reconstruction between February 2005 and August 2022 were retrospectively analyzed. Maximum phonation time and mean flow rate were measured preoperatively and, periodically, postoperatively. The Voice Handicap Index-10 questionnaire was administered at patients' final visits. Postoperative periods were divided into period I (>6 months-2 years), period II (>2-10 years), and period III (>10 years). **RESULTS:** Preoperatively, 100 patients (47.2%) had vocal cord paralysis. For both sexes, patients with preoperative vocal cord paralysis had significantly longer maximum phonation times and smaller mean flow rates in period I than they had preoperatively; these values further improved in period II, with improvements maintained in period III. Patients without vocal cord paralysis showed recovery in voice after recurrent laryngeal nerve reconstruction; however, in both sexes, their maximum phonation times and mean flow rates in period I did not reach preoperative levels. Maximum phonation time and mean flow rate improved in period II in both sexes, with these improvements being maintained in period III. The Voice Handicap Index-10 score improved over time in all patients except female patients without preoperative vocal cord paralysis, whose best score was obtained in period I.

**CONCLUSIONS:** In patients who required recurrent laryngeal nerve resection, reconstructive surgery restored phonatory function early. Further modest improvement was observed over 10 years, persisting beyond 10 years.

PubMed-ID: [41027747](#)

DOI: [10.1016/j.surg.2025.109695](#)

### **Nrf2 shapes response to lysosomal inhibition of radiation-induced senescent thyroid cancer cells.**

*Endocr Relat Cancer*, 33(2)

B. Mazzoleni, M. Mazzoni, D. Vergaro, T. Di Marco, S. Pagliardini and A. Greco. 2026.

Therapy-induced senescence (TIS) is a potential outcome of anti-cancer treatments, characterized by a stable cell cycle arrest. However, it is now widely accepted that this process acts as a double-edged sword: in fact, senescent cells are active drivers of cancer relapse, aggressiveness and metastasis, through the release of pro-inflammatory factors and the ability to resume proliferation. Therefore, selectively targeting TIS cells, a strategy named one-two punch approach, is crucial to avoid their harmful effects. This may become particularly important for those aggressive tumors that currently lack effective therapeutic options, such as dedifferentiated thyroid tumors. To this purpose, identifying targetable characteristics of TIS cells is essential for the development of new senotherapeutics. TIS is often associated with variations of the autophagic flux, therefore, we investigated the interplay between autophagy and TIS in thyroid cancer cells, to explore a new potential target for senotherapy. We demonstrate that TIS thyroid cancer cells do not always exhibit a sufficient enlargement of the lysosomal compartment to maintain autophagy function. The deficiency in lysosomal biogenesis is driven by the inability of TFEB, the master regulator of this process, to properly enter and remain inside the nucleus. The disruption of the autophagic flux leads to the accumulation of SQSTM1/p62, which in turn activates the Nrf2 pathway. In contrast to cells with functional autophagy, Nrf2-activated cells display a higher tolerance to oxidative stress, making them resistant to the senolytic activity of lysosomal inhibitors.

PubMed-ID: [41553296](#)

DOI: [10.1530/ERC-25-0291](#)

### **Designing a SPIKES-based protocol for communicating uncertainty in indeterminate thyroid cytology: a mixed-method analysis within a pilot study.**

*Updates Surg*, 78(1):75-87.

R. Melcarne, F. Consorti, G. Grani, T. D. Engel, E. Iannuzzi, C. Ammendolia, L. Giacomelli, C. Durante and M. Biffoni. 2026. Indeterminate thyroid cytology presents a significant diagnostic challenge, often leading to difficult treatment decisions for both physicians and patients. Effective communication of these uncertainties is crucial, especially in a surgical setting, where decisions can have long-lasting impacts. This is particularly important for younger surgeons who may lack extensive clinical experience. This study aimed to plan, develop, implement, and pilot a communication protocol designed for surgeons, particularly those in training, to navigate uncertainty and build trust with their patients. Additionally, it documented the reactions of patients managed using this approach. Fifty-two patients diagnosed with indeterminate thyroid cytology were enrolled between March 2023 and January 2024 at the Endocrine Surgery Unit of "Azienda Ospedaliera Universitaria Policlinico Umberto I" in Rome, Italy. A communication protocol based on the SPIKES model (Setting, Perception, Invitation, Knowledge, Emotion, Strategy), a six-step protocol for guiding difficult conversations, was designed to structure discussions around uncertain diagnoses. Patient consultations were conducted in three phases: the initial outpatient visit, pre-surgery admission, and a follow-up one week after surgery. During each encounter, patients' emotional responses were recorded using open-ended questions. To ensure clarity, a Decision Aid (DA) tool was introduced during the K-Knowledge phase of SPIKES, to better explain the risks and treatment options. A mixed-methods

approach was used to analyze both qualitative and quantitative data from patient feedback. The adapted protocol was found to be effective in enhancing patient comprehension and emotional response. Approximately 80% of patients reported emotional relief after the first consultation, and by the third encounter, 91% expressed a sense of well-being or trust. The most frequently reported emotional states across all three encounters were serenity, reassurance, and trust. A small subset of patients continued to experience concern or fatigue. Additionally, 96% of participants rated the communication as clear, and 88.5% considered the final therapeutic decision as the correct one. This pilot study suggests that a structured SPIKES-based communication protocol can help address gaps in patient understanding, trust, and satisfaction when managing indeterminate thyroid cytology. Implementing such protocols may streamline communication in surgical settings, improve patient-centered care, and support physicians, particularly trainees, in managing complex patient interactions.

PubMed-ID: [40864410](#)

DOI: [10.1007/s13304-025-02346-3](#)

PMCID: PMC12909332

#### **Data-driven thresholds for tumor size and nodal involvement in oncocytic thyroid carcinoma: A population-based analysis.**

*Am J Surg*, 255:116874.

M. Milan, S. M. Thomas, C. V. Lindsay, T. W. Frieze, R. P. Scheri and H. S. Kazaure. 2026.

INTRODUCTION: We sought to identify prognostically meaningful thresholds for tumor size and lymph node (LN) metastasis as a first step toward developing a dedicated staging system for oncocytic thyroid carcinoma (OTC). METHODS: Using SEER (2004-2022), tumor size and LN thresholds for OTC were analyzed using restricted cubic splines; Cox models estimated association with overall (OS) and disease-specific survival (DSS). RESULTS: Among 4114 patients, median tumor size was 34 mm, and 1410 (34.3%) had  $\geq 1$  LN examined. Tumor size showed a linear relationship with OS and DSS (no prognostic threshold). LN positivity showed thresholds of 2.42 positive LNs for OS and 2.14 for DSS; thus,  $\geq 3$  positive LNs was considered a prognostic threshold. Patients with  $\geq 3$  vs  $< 3$  positive LNs had lower adjusted DSS (HR 3.32;  $p < 0.001$ ) and OS (HR 2.65;  $p < 0.001$ ). CONCLUSION: For OTC,  $\geq 3$  positive LNs constituted a prognostic threshold, while tumor size conferred continuous risk.

PubMed-ID: [41763177](#)

DOI: [10.1016/j.amisurg.2026.116874](#)

#### **Day case and inpatient elective thyroid lobectomy across England: observational study of variation in practice and safety.**

*Br J Surg*, 113(2)

M. Monaghan, W. K. Gray, M. Cheetham, P. Dent, T. W. R. Briggs and M. Lansdown. 2026.

BACKGROUND: Day case elective surgery is becoming increasingly common across a range of procedures. The aim of this study was to investigate the safety of day case thyroid lobectomy, a procedure with low uptake in the UK. METHODS: This study analysed the Hospital Episode Statistics administrative data set for all first-time elective thyroid lobectomies performed on adults in England from 1 April 2017 to 31 March 2024. The primary outcome was 30-day emergency readmission and secondary outcomes were 30-day emergency readmission for complications and specifically for haemorrhage. The primary exposure variable was whether patients were day case patients or inpatients. Models were adjusted for the demographic and frailty characteristics of the patients. RESULTS: Over the 7-year interval, 41 518 elective thyroid lobectomies were performed by 127 different hospital trusts. The day case rate was 9.9% (4125 patients) across all hospital trusts. Rates in the 118 hospital trusts conducting  $>20$  procedures during the 7 years varied from 0% to 74.6%. Day case surgery was associated with a lower 30-day emergency readmission rate (OR 0.73 (95% c.i. 0.56 to 0.96);  $P < 0.021$ ), with no evidence of association with poorer outcomes. There was no evidence that trusts with day case rates  $>30\%$  had poorer outcomes than trusts with day case rates  $<1\%$ . CONCLUSION: In low-risk patients, day case thyroid lobectomy is safe.

PubMed-ID: [41738922](#)

DOI: [10.1093/bjs/znaf299](#)

#### **Early familial non-medullary thyroid cancer: differences with late-onset and sporadic forms.**

*Eur J Endocrinol*, 194(4):510-8.

C. Mura, S. Corrias, M. Lecca, M. L. Lai, G. L. Canu, F. Medas, S. Mariotti, P. G. Calo, P. Caria, G. Lanzolla and F. Boi. 2026.

OBJECTIVE: This study aimed to compare clinicopathological features of familial non-medullary thyroid cancer (FNMT) and sporadic non-medullary thyroid cancer (sNMTC) and assess whether age at onset contributes to the different behavior

of these 2 entities. DESIGN: A retrospective study including 31 patients with FNMTC, and 31 age- and sex-matched patients with sNMTC. METHODS: Histological variant, multifocality, tumor infiltration, angioinvasion, TNM stage, lymph node metastasis, BRAF and p53 expression, ATA risk stratification, and the presence of chronic lymphocytic thyroiditis (CLT) were compared between groups. Then, we identified a cutoff age to stratify patients by age of onset ( $\leq 35$  vs  $>35$  years). RESULTS: FNMTC presented at a more advanced stage at diagnosis compared to sNMTC, with a higher proportion of medium-high TNM stages. Among FNMTC, early-onset ( $\leq 35$  years) cases showed higher BRAF expression, more frequent lymph node metastases, a higher proportion of medium-high TNM stages, and intermediate-to-high ATA risk compared to late-onset cases ( $>35$  years). Medium-high TNM stage, BRAF expression, and lymph node metastases were observed more frequently in early onset FNMTC than in age-matched sNMTC. Late-onset FNMTC patients exhibited a higher prevalence of CLT than early-onset FNMTC and late-onset sNMTC patients. CONCLUSIONS: These findings underscore the relevance of age at disease onset in shaping the clinical phenotypes of FNMTC. The distinct pathological features of early-onset vs late-onset FNMTC suggest different pathophysiological mechanisms, with the former likely driven by direct genetic/oncogenic alterations, and the latter influenced by autoimmune thyroiditis-related carcinogenesis, a hypothesis that warrants further investigation in larger prospective studies.

PubMed-ID: [41988787](#)

DOI: [10.1093/ejendo/lvag059](#)

### **Initial Evaluation of Radioiodine Therapy Using Imaging for Long-term Prognosis in Thyroid Cancer: A Retrospective Study.**

*J Clin Endocrinol Metab*, 111(4):1004-20.

R. Nakatani, T. Watabe, A. Fukuhara, T. Takano, T. Kamiya, H. Sasaki, H. Kurakami, Y. Nakata, M. Otsuki, Y. Hidaka and I. Shimomura. 2026.

OBJECTIVE: Radioactive iodine (RAI) is an established therapy for thyroid cancer (TC). The aim of this study was to evaluate the prognosis and disease characteristics based on initial RAI therapy using image findings. METHODS: We reviewed the clinical records of 290 TC patients who received initial therapeutic RAI therapy following total thyroidectomy for ablation and treatment between 2010 and 2021. Patients were classified into 3 groups based on the 131I whole-body scintigraphy (WBS) combined with morphological imaging records: non-DM, RAI-non-avid DM, and RAI-avid DM. Progression-free survival (PFS) and overall survival were assessed in each group. Normalized indices were calculated automatically using dedicated software for each patient on WBS. 131I-avid lesions were defined as areas with uptake exceeding the mean + 2 SDs of the reference regions of interest placed at the head-cervical, thoracic, and abdominal-pelvis regions, Watabe proposed. RESULTS: The 5-year and 7-year survival rates for the non-DM, RAI-non-avid DM, and RAI-avid DM groups were 98% to 95%, 86% to 78%, and 82% to 82%, respectively. Average count of 131I-avid area was identified as a significant prognostic factor for PFS, being independent of age, distant metastatic pattern, histological subtype, and T classification. Retreatment was preferably performed within 2 years after the initial RAI therapy, as this period appears to be critical for efficacy. Additionally, the site of metastases was a strong prognostic determinant. CONCLUSION: Precise imaging evaluation of the initial RAI therapy may help predict the prognosis during the first 5 years, contributing to more effective comprehensive treatment approaches for long-term management.

PubMed-ID: [41092239](#)

DOI: [10.1210/clinem/dgaf568](#)

### **Multifocality in sporadic medullary thyroid carcinoma is associated with low tumor grade and no difference in somatic driver mutations or overall survival when compared with unifocal tumors.**

*Surgery*, 189:109764.

A. Nigam, M. A. Mederos, Y. A. Aksoy, B. Alzumaili, M. A. Bani, T. Fuchs, A. Al Ghuzlan, A. J. Gill, A. R. Glover, A. Papachristos, A. Repaci, A. De Leo, G. Tallini, S. Ahmadi, B. Clausen, F. Najdawi, J. Barletta, A. R. Shaha, P. Spanheimer, R. M. Tuttle, R. J. Wong, B. Xu, R. A. Ghossein, I. Ganly and B. R. Untch. 2026.

BACKGROUND: Total thyroidectomy for patients with sporadic medullary thyroid carcinoma is often recommended because of multifocality. The International Medullary Thyroid Carcinoma Grading System is established as a predictor of disease-specific outcomes. We aimed to study multifocality and its association with index tumor grade and somatic mutations. METHODS: A retrospective cohort analysis of 5 high-volume medullary thyroid carcinoma centers was performed between January 1, 1986, and January 1, 2018. Thyroidectomy specimens were evaluated for multifocality. Molecular profiling was assessed with RET germline testing and/or targeted exome sequencing of specimens with matched normal DNA. Outcomes evaluated were risk of local recurrence, distant recurrence, and survival within 15 years. RESULTS: Among 270 patients with nongermline medullary thyroid carcinoma, 207 (77%) were unifocal and 63 (23%) multifocal ( $P < .05$ ). A similar proportion of patients were low-grade (unifocal: 75% vs multifocal: 79%;  $P = .45$ ) although a

significantly greater proportion of multifocal patients demonstrated C-cell hyperplasia (48% vs 9%;  $P < .001$ ). Molecular profiling identified no differences among driver mutations. The median size of multifocal lesions was 0.60 cm (interquartile range: 0.3-1.0 cm) with 74% harboring multiple foci. The ratio of positive lymph nodes in dissected compartments was similar (multifocal: 0.37, interquartile range: 0-0.66 vs unifocal: 0.27, interquartile range: 0-0.43;  $P = .23$ ). Local recurrence ( $P = .25$ ) and overall survival ( $P = .31$ ) were not statistically different between cohorts. **CONCLUSION:** Subcentimeter multifocality is common in sporadic medullary thyroid carcinoma. In this study cohort, no differences were observed in tumor grade, lymph node burden, overall survival, or somatic driver mutations compared with unifocal tumors. Multifocality in patients with sporadic medullary thyroid carcinoma is not associated with adverse overall survival. PubMed-ID: [41073156](#)  
DOI: [10.1016/j.surg.2025.109764](#)

### **The dynamic changes and precise classification of parathyroid function within 1 year after thyroid cancer surgery.**

*Int J Surg*, 112(2):3633-42.

K. Ning, Y. Liang, T. Cai, J. Zhou, L. Hong, Y. Yu, Y. Guo, Z. Jiao, Y. Wu, B. Zou, Z. Luo, Q. Chen, Z. Zhang, J. Bu, T. Wu, Y. Chen, M. Jiang, M. Fang, T. Liu, Z. Yang and A. Yang. 2026.

**BACKGROUND:** Postoperative parathyroid dysfunction is a common complication of thyroid surgery. However, the temporal pattern of postoperative parathyroid function and standardized clinical interventions remains poorly defined. This study systematically characterizes the dynamic changes in postoperative parathyroid hormone (PTH) following thyroid cancer surgery and proposes a clinically applicable classification system with corresponding management strategies. **MATERIALS AND METHODS:** A total of 12 664 patients who underwent thyroid cancer surgery between 2012 and 2022 across three tertiary hospitals were included. Changes in postoperative PTH were analyzed using locally estimated scatterplot smoothing regression. Logistic regression analysis was performed to identify independent risk factors associated with different postoperative PTH trajectories. **RESULTS:** Based on 38 949 postoperative PTH measurements from 12 664 patients, we observed that PTH levels declined sharply after surgery, reached the lowest point around 1 week [defined as valley value PTH (vvPTH)], and then rose rapidly and stabilized after 1 month [defined as new baseline PTH (nbPTH)]. Importantly, postoperative PTH did not fully recover to preoperative levels. Five distinct postoperative PTH trajectory types were identified based on vvPTH and nbPTH: I (normal function), II (subclinical injury), IIIA (sufficiently recovered hypoparathyroidism), IIIB (insufficiently recovered hypoparathyroidism), and IIIC (refractory hypoparathyroidism). Multivariate analysis identified operation type, lymph node dissection, parathyroid autotransplantation, and preoperative PTH as independent predictors, which were integrated into a predictive nomogram. Patients with type III disease require intensive monitoring and calcium supplementation within the first month, whereas type IIIC patients require long-term management. **CONCLUSION:** Parathyroid function does not fully return to preoperative levels within 1 year after thyroid surgery. This large-scale study establishes a precise classification system for postoperative parathyroid function, which may provide a valuable framework to guide clinical management and optimize patient outcomes.

PubMed-ID: [41255296](#)

DOI: [10.1097/JS9.0000000000003996](#)

### **Molecular and Biological Features of Invasive Lobular Carcinoma: Toward New Treatment Strategies.**

*Ann Surg Oncol*, 33(1):146-58.

N. Ozawa, E. Takeyama, H. Sakai, A. Katayama, M. Onishi, R. Kizawa, Y. Matsunaga, K. Nozawa, N. Umezaki, R. Mitsueda, K. Tanabe, C. Sekine, M. Golshan, E. A. Rakha, J. Horiguchi and S. Kurozumi. 2026.

**INTRODUCTION:** Invasive lobular carcinoma (ILC) is the second most common type of invasive breast cancer, following invasive breast cancer of no special type (IBC-NST). Due to the absence of cell adhesion factors, ILC is characterized by reduced cell adhesion and a linear or single-cell growth pattern. As a result, previous studies have frequently reported that ILC tends to spread more extensively than preoperative imaging evaluations suggest, often presents with multicentric lesions, and exhibits distinct recurrence and metastasis patterns compared with conventional invasive breast cancer. **METHODS:** We conducted a comprehensive literature search in PubMed, and performed a full-text screening for articles that met the inclusion criteria. Key information from each eligible study, including study design, population characteristics, primary outcomes, and conclusions were extracted. **RESULTS:** Recent translational research has identified several genes and molecular pathways associated with ILC progression and metastasis, with particular focus on the role of cancer-associated fibroblasts and the tumor microenvironment, including tumor-infiltrating immune cells. **CONCLUSION:** While no specific treatment strategy for ILC has been established, its clinical, molecular, and morphological characteristics differ from those of IBC-NST, highlighting the need to develop targeted treatment approaches for ILC. This review examined the clinical, molecular, and morphological characteristics of ILC from a clinical perspective, incorporating recent findings from

translational research.

PubMed-ID: [40940597](#)

DOI: [10.1245/s10434-025-18259-9](#)

**Evaluating the necessity of prophylactic lateral neck dissection in medullary thyroid carcinoma based on preoperative calcitonin levels: a multicenter retrospective cohort study.**

*Int J Surg*, 112(1):1332-9.

S. J. Pak, D. Kwon, B. C. Kim, W. W. Kim, T. Y. Sung, K. W. Chung, Y. M. Lee and J. J. Jeong. 2026.

**BACKGROUND:** The need for prophylactic lateral neck dissection (LND) in medullary thyroid carcinoma (MTC) patients without clinically evident lateral lymph node (LN) metastasis remains controversial, particularly in those with elevated preoperative calcitonin levels. This study investigated the prognostic impact of prophylactic LND in MTC patients with preoperative calcitonin levels >200 pg/mL, but without clinically suspicious lateral LNs. **MATERIALS AND METHODS:** This multicenter retrospective cohort study included 103 patients with MTC treated between January 1980 and December 2022 at two tertiary hospitals in Seoul, South Korea. Patients had preoperative calcitonin levels above 200 pg/mL and no clinical evidence of lateral LN metastasis. They were divided into two groups based on whether LND was performed, and their long-term oncological outcomes were compared. **RESULTS:** The median follow-up duration was 90 months. The LND group had significantly larger tumors and higher preoperative calcitonin levels. Although the biochemical cure rate was higher in the LND group than in the No LND group (95.2% vs 82.5%), this difference was not statistically significant (P = 0.074). No significant differences were observed between the groups in biochemical recurrence, structural recurrence, overall survival, or disease-specific survival. Subgroup analyzes based on preoperative calcitonin levels showed comparable results. **CONCLUSION:** Prophylactic LND did not significantly impact long-term oncologic outcomes in MTC patients without clinically evident lateral LN metastasis, even among those with elevated preoperative calcitonin levels above 200 pg/mL. Although prophylactic LND was associated with higher biochemical cure rates, this did not translate into reduced recurrence rates or improved survival. Routine prophylactic LND may not be necessary, and the decision to perform it should be carefully individualized based on patient-specific factors.

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DOI: [10.1097/JS9.0000000000003557](#)

PMCID: PMC12825659

**No prognostic or molecular disparity between synchronous and metachronous metastases in differentiated thyroid cancer: insight from middle eastern cohort.**

*Int J Surg*,

S. K. Parvathareddy, A. K. Siraj, R. Bu, P. Annaiyappanaidu, W. Haqawi, M. Al-Rasheed, S. S. Al-Sobhi, F. Al-Dayel and K. S. Al-Kuraya. 2025.

**BACKGROUND:** Whether synchronous (SDM) and metachronous (MDM) metastases in differentiated thyroid cancer (DTC) differ in clinical behavior or molecular profiles remains unclear. Prior studies suggest poorer outcomes in metachronous cases but regional molecular profiles and clinical outcome are not well defined. We aimed to assess whether molecular alterations, immune landscape, metastatic sites and survival outcomes differ between SDM and MDM DTC in a large Middle Eastern cohort. **MATERIALS AND METHOD:** Among 1,822 DTC patients, 178 developed distant metastases-88 (4.8%) SDM and 90 (4.9%) MDM. Clinicopathological features, mutational status, PD-L1 expression and radioactive iodine (RAI) response were compared. Kaplan-Meier analysis assessed overall survival (OS) and thyroid cancer-specific survival (TCSS). **RESULTS:** Molecular alterations were largely similar between SDM and MDM groups. TERT mutation alone occurred in 16.9% of SDM vs. 19.7% of MDM. BRAF V600E mutation alone was significantly higher in MDM cases (22.2% vs 10.4%). TERT and BRAF V600E co-mutations were comparable (22.1% vs 30.9%) between the two groups. NRAS, HRAS and TP53 mutations showed no significant difference. RAI refractoriness was 57.9% (SDM) vs 67.8% (MDM) and PD-L1 high expression was 42.2% (SDM) vs 54.5% (MDM). Cancer-specific mortality was 8.6% in SDM and 13.8% in MDM groups. Metastatic patterns revealed the lung as the most common site (69.3% SDM vs. 84.4% MDM), followed by bone (37.5% vs. 26.7%), brain (5.7% vs. 3.3%) and liver (1.1% in synchronous only). Multiple-organ metastasis were observed in 11.4% of SDM and 13.3% MDM patients. However, Kaplan Meier curves showed no statistically significant differences in OS or TCSS by metastatic timing or metastatic site. **CONCLUSION:** In this Middle Eastern cohort, no consistent molecular or clinical disparities across most parameters. These findings suggest the timing of metastasis may not independently influence prognosis and highlight the relevance of individualized, biology-driven management strategies.

PubMed-ID: [41399287](#)

DOI: [10.1097/JS9.0000000000004272](#)

**Machine learning: predicting lymph node metastasis around the entrance point to the recurrent laryngeal nerve in cN0 papillary thyroid carcinoma.**

*Front Endocrinol (Lausanne)*, 17:1721148.

J. Peng, J. Zhou, Y. Deng, Q. Xiao, X. Su and C. Deng. 2026.

**BACKGROUND:** Owing to the limited characterization of lymph nodes around the entrance point of the recurrent laryngeal nerve (LN-epRLN) in clinical lymph node negative (cN0) papillary thyroid carcinoma (PTC), this study sought to develop machine learning (ML) models to predict LN-epRLN metastasis, identify the optimal model, and improve interpretability using explainable artificial intelligence techniques. **METHODS:** We retrospectively reviewed 1,800 patients with cN0-PTC who underwent central lymph node dissection (CLND) with systematic LN-epRLN sampling. Histopathological evaluation confirmed metastatic status. Patients were randomly divided into training and testing sets at a 7:3 ratio. Nine ML models were constructed and optimized through 10-fold cross-validation and grid search. Performance was assessed using 11 metrics, including AUC, accuracy, sensitivity, and specificity. The best-performing model was compared against traditional nomograms via probability-based ranking analysis (PMRA). **RESULTS:** LN-epRLNs were identified in 149 out of 1800 PTC patients, with a metastasis rate of 19.46%. The Random Forest (RF) model outperformed others, achieving training/testing scores of 0.914/0.911 accuracy, 0.956/0.919 AUC, 0.993/0.974 specificity, and 0.609/0.500 sensitivity. A simplified model incorporating seven key predictors-total central lymph node metastasis number and ratio, pretracheal lymph node metastasis number and ratio, tumor size, age, and paratracheal lymph node metastasis number-retained high predictive performance. SHAPley Additive exPlanations (SHAP) analysis highlighted central compartment metastasis burden (number and ratio) as the most influential predictors. **CONCLUSION:** The interpretable ML model developed in this study, leveraging the RF, provides a reliable tool for preoperative and intraoperative prediction of LN-epRLN metastasis in cN0 PTC patients. This approach has the potential to guide individualized surgical planning, optimizing the balance between oncological resection completeness and functional preservation.

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DOI: [10.3389/fendo.2026.1721148](#)

PMCID: PMC12989384

**Predicting central lymph node metastasis in papillary thyroid microcarcinoma: a study of ultrasound and clinical features.**

*Front Endocrinol (Lausanne)*, 17:1752405.

X. Peng, J. Zhang, Y. Lin and R. Li. 2026.

**BACKGROUND:** Papillary thyroid microcarcinoma (PTMC) generally has a favorable prognosis. Early central lymph node metastasis (CLNM) can significantly impact treatment strategy and prognosis. However, CLNM lacks typical ultrasound features. Accurate preoperative prediction of CLNM remains challenging. This study aims to develop and validate a high-accuracy tool for preoperatively assessing the risk of lymph node metastasis in PTMC patients. **METHODS:** We retrospectively analyzed clinical and ultrasound data from 534 PTMC patients who underwent initial thyroidectomy with central lymph node dissection. Patients were randomly divided into training (n=373) and validation (n=161) cohorts. We calculated high-throughput radiomics features, including tumor size, tumor shape, margin, capsular contact, microcalcifications, and peritumoral echogenicity features. A combined feature selection strategy was then used to identify features with the greatest discriminatory power for lymph node status. A Logistic Regression machine classifier was employed to build and validate the prediction model. Additionally, ultrasound ACR TI-RADS and clinical variables were evaluated. Univariate and multivariate logistic regression was used to identify independent predictors, which were further incorporated into a nomogram model. The area under the operating characteristic curves (AUCs) was used to draw comparisons between different models and the decision curve analysis was conducted to assess their clinical utility. **RESULTS:** In the clinical model based solely on clinical and conventional ultrasound features, multivariate analysis identified five independent predictors of CLNM: age <46.5 years, male sex, capsular contact  $\geq 50\%$ , peritumoral hyperechogenicity and heterogeneous echotexture (AUC: 0.857 in the training set and 0.840 in the validation set). By further integrating a radiomics score with all univariately significant clinical variables, a combined clinical-radiomics nomogram was developed. In this combined model, age, transverse diameter of tumor, capsular contact, peritumoral echo changes, and the radiomics score were identified as independent predictors. The combined model achieved an improved AUC of 0.900 in the validation set, demonstrating superior predictive performance and higher clinical net benefit than the clinical model alone. **CONCLUSION:** The proposed clinical-radiomics nomogram, which incorporates conventional ultrasound features and radiomics signatures, outperforms the standalone clinical model in predicting CLNM. This non-invasive approach provides superior pre-operative risk assessment in optimizing treatment strategies for PTMC patients.

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DOI: [10.3389/fendo.2026.1752405](#)  
PMCID: PMC13106017

**Targeted RNA sequencing of thyroid tumors from individuals with PTEN hamartoma tumor syndrome reveals a unique transcriptome with a predominantly RAS-like expression profile.**

*Surgery*, 189:109697.

G. Plitt, T. Mitzukami, L. Yehia, L. Rabinowitz, C. C. Griffith, G. Romero-Velez, A. Siperstein and C. Eng. 2026.

BACKGROUND: Differentiated thyroid cancer is typically caused by a single oncogenic driver alteration. In PTEN hamartoma tumor syndrome, a pathogenic germline PTEN alteration results in a predisposition to thyroid cancer and adenomatous thyroid nodules. This provides a unique model to study thyroid carcinogenesis in the setting of a baseline "hit" to the PI3K/AKT/mTOR pathway, implicated in RAS-like thyroid tumors. METHODS: RNA sequencing and differential expression analysis were performed on thyroid cancers, adenomatous nodules, and background thyroid tissue in patients with PTEN hamartoma tumor syndrome. BRAF(V600E)-RAS scores were calculated and compared across histologic subtypes. RNA sequencing data were then integrated with previously published paired exome sequencing data. RESULTS: RNA sequencing was performed on 26 cancers, 27 adenomatous nodules, and 15 background thyroid samples from 20 patients with PTEN hamartoma tumor syndrome. This demonstrated 3 expression clusters: papillary architecture tumors, follicular architecture tumors, and background thyroid tissue. The majority (17, 65.4%) of cancers were RAS-like. Follicular architecture cancers were primarily RAS-like (BRAF(V600E)-RAS score +0.67) and frequently associated with biallelic PTEN alterations. Papillary architecture cancers were BRAF-like (BRAF(V600E)-RAS score -0.77), often in absence of biallelic PTEN alterations. Adenomatous nodules had indistinguishable expression profiles from follicular architecture cancers. CONCLUSIONS: PTEN hamartoma tumor syndrome-associated thyroid tumors most frequently have RAS-like expression profiles. This appears to be caused by baseline dysregulation of the PI3K/AKT/mTOR pathway, with predisposition to biallelic PTEN inactivation promoting follicular adenomatous growth and subsequent malignant transformation to follicular architecture cancers. Better understanding malignant potential and tumor progression in PTEN hamartoma tumor syndrome thyroid tissue is essential for optimizing diagnosis, enhanced surveillance, and treatment in this population.

PubMed-ID: [41027746](#)

DOI: [10.1016/j.surg.2025.109697](#)

**The rise of thyroid cancer incidence in adolescents and young adults.**

*Lancet Diabetes Endocrinol*, 14(2):94-5.

T. Porcelli and M. Schlumberger. 2026.

PubMed-ID: [41274301](#)

DOI: [10.1016/S2213-8587\(25\)00321-3](#)

**Artificial Intelligence Applications in Thyroid Cancer Care.**

*J Clin Endocrinol Metab*, 111(2):316-24.

N. Pozdeyev, S. L. White, C. C. Bell, B. R. Haugen and J. Thomas. 2026.

CONTEXT: Artificial intelligence (AI) has created tremendous opportunities to improve thyroid cancer care. EVIDENCE ACQUISITION: We used the "artificial intelligence thyroid cancer" query to search the PubMed database until May 31, 2025. We highlight a set of high-impact publications selected based on technical innovation, large generalizable training datasets, and independent and/or prospective validation of AI. EVIDENCE SYNTHESIS: We review the key applications of AI for diagnosing and managing thyroid cancer. Our primary focus is on using computer vision to evaluate thyroid nodules on thyroid ultrasound, an area of thyroid AI that has gained the most attention from researchers and will likely have a significant clinical impact. We also highlight AI for detecting and predicting thyroid cancer neck lymph node metastases, digital cyto- and histopathology, large language models for unstructured data analysis, patient education, and other clinical applications. We discuss how thyroid AI technology has evolved and cite the most impactful research studies. Finally, we balance our excitement about the potential of AI to improve clinical care for thyroid cancer with current limitations, such as the lack of high-quality, independent prospective validation of AI in clinical trials, the uncertain added value of AI software, unknown performance on non-papillary thyroid cancer types, and the complexity of clinical implementation. CONCLUSION: AI promises to improve thyroid cancer diagnosis, reduce health care costs and enable personalized management. High-quality, independent prospective validation of AI in clinical trials is lacking and is necessary for the clinical community's broad adoption of this technology.

PubMed-ID: [40997161](#)  
DOI: [10.1210/clinem/dgaf530](#)

**Long-term outcomes of robotic vs. open thyroidectomy for differentiated thyroid cancer: efficacy, safety, and quality of life.**

*Int J Surg*, 112(2):4036-46.

X. Qin, X. Liu, L. Zeng, X. Cao, J. Luo, J. Zhao, H. Tang, T. Zhang, X. Xiong, Y. Chen, G. Tang, Y. Zhang and L. Fan. 2026.

**OBJECTIVE:** To compare robotic vs. open thyroidectomy's (OT) long-term safety, efficacy, and quality of life for differentiated thyroid cancer (DTC). **BACKGROUND:** Early research showed that robotic thyroid surgery better preserves parathyroid glands and nerves compared to open surgery, but its long-term efficacy and safety remain uncertain. Comparative studies across various extents of thyroidectomy should be enhanced to include long-term follow-up, large sample sizes, and robust evidence from extensive clinical experience. **METHODS:** This retrospective cohort study included 6249 patients who underwent open or robotic thyroidectomy (RT) in 2014-2024 at a 3:1 ratio (aged 15-80 years; 4659 females and 1590 males) from a cohort of 11 733 who underwent OT or RT were analyzed. Postoperative complications were recorded, and patients were assessed using quality of life and aesthetic outcome scales. Patients were evaluated using Short Form-36, voice/swallowing/neck impairment scales, and the SCAR-Q questionnaire. Clinical-pathological characteristics, postoperative complications, quality of life, and aesthetic outcome scores were compared. **RESULTS:** Compared to the RT group, the OT group had a higher recurrence rate [135 (2.29%) vs. 29 (1.82%);  $P = 0.02$ ], transient and permanent hypoparathyroidism ( $P < 0.001$ ) and permanent hoarseness rate ( $P = 0.002$ ). The OT group showed a marked decline in recurrence-free survival probability after 100 months postsurgery, falling below that of the RT group ( $P = 0.027$ ). The OT group had higher swallowing and voice impairment scores than the RT group ( $P < 0.001$ ) and performed worse in physiological function, body pain, general health, vitality, social function, mental health, health change, and SCAR-Q scores ( $P < 0.001$ ) after surgery. **CONCLUSIONS:** Besides its well-recognized cosmetic benefits, RT demonstrated superior elegance, effectiveness, and safety across various surgical scopes, significantly enhancing the long-term postoperative quality of life for patients with DTC. These findings affirm RT as a valuable surgical option, particularly for those seeking enhanced cosmetic outcomes and requiring complex procedures.

PubMed-ID: [41255276](#)

DOI: [10.1097/JS9.0000000000003835](#)

**Association of long-term quality of life, safety, and efficacy: robotic vs. open thyroidectomy for benign thyroid nodules.**

*Int J Surg*, 112(1):1244-51.

X. Qin, X. Liu and Y. Zhang. 2026.

**OBJECTIVE:** To compare the safety, efficacy, and quality of life (QoL) of robotic thyroidectomy (RT) and open thyroidectomy (OT) for benign thyroid nodules. **BACKGROUND:** Traditional OT lacks aesthetic advantages, while endoscopic thyroidectomy has limitations for larger nodules. Advances in RT provide a minimally invasive option, offering improved aesthetics and efficacy for larger benign thyroid nodules. **METHODS:** This retrospective cohort study included 1614 benign thyroid nodules patients from 2014 to 2024. Following propensity score matching (1:2 ratio), 1079 patients who underwent OT or RT were analyzed. Postoperative complications were recorded, and patients were assessed using QoL and aesthetic outcome scales. **RESULTS:** In the OT group, 186 patients (25.34%) had inadvertent parathyroid resection vs. none in the RT group ( $P < 0.001$ ). Transient hypoparathyroidism affected 129 OT patients (17.57%) vs. 36 RT patients (10.43%), respectively ( $P = 0.002$ ). Swallowing Impairment Score and Voice Impairment Score were higher in the OT group after 5 years ( $P < 0.001$ ). The RT group showed better "general health" and "vitality" at 0.5-3 years and >5 years, and better "social function," "mental health," and "role emotional" at >5 years ( $P < 0.05$ ). Scar lengths were shorter in the RT group at all time points ( $P < 0.001$ ), while SCAR-Q appearance scores were higher in the OT group ( $P < 0.001$ ). **CONCLUSION:** Robotic thyroidectomy demonstrated superior cosmetic outcomes, lower complication rates, and minimal impact on postoperative QoL compared to open surgery for benign thyroid nodules, including larger ones. Therefore, with appropriate patient selection, robotic thyroidectomy may be the preferred approach for benign thyroid disease.

PubMed-ID: [41159403](#)

DOI: [10.1097/JS9.0000000000003540](#)

PMCID: PMC12825542

**Surgical management of retrosternal thyroid disease: a decennial retrospective analysis.**

*Front Endocrinol (Lausanne)*, 17:1739552.

F. Quaglini, D. Galetta, L. Cestino, F. Festa, S. Ruscio, G. Carbonaro, M. Breda, G. Gavello and S. Cannazza. 2026.

**INTRODUCTION:** Thyroid disease with retrosternal extension lacks a universally accepted definition in the literature,

contributing to significant variability in the reported prevalence across series. This study aims to present the experience of a high-volume center in the management of retrosternal thyroid pathology and to identify potential predictive factors that may assist in surgical planning. **MATERIALS AND METHODS:** Between 1 January 2014 and 31 December 2024 we performed 1347 thyroidectomies: 355 (26,3%) thyroid surgical procedures were performed in patients whose thyroid pathology was identified intra-operatively as retrosternal extension. We analyzed patient comorbidities, any pre-operative treatments, pre-operative imaging, the type of surgical procedure performed, the surgical approach adopted, and post-operative complications. Four definitions of retrosternal thyroid pathology, selected among those most frequently cited in the literature and deemed applicable in clinical practice, were compared. **RESULTS:** Benign retrosternal goiter accounted for 84.2% of cases, thyroid malignancies represented 6.2% of the cohort, while retrosternal goiters with indeterminate cytology comprised 9.6% of the total. Total thyroidectomy was performed in 80% of patients. Among the 355 patients operated on, a classical cervical approach (Kocher incision, optionally with split cutaneous layer) was used in 99.2% of cases; only 0.8% required an additional thoracic approach. Pre-operative diagnosis of malignancy and the type of surgical procedure performed emerged as the principal factors associated with the development of recurrent laryngeal nerve palsy and hypocalcaemia in the postoperative period. **CONCLUSIONS:** A universally recognized definition of retrosternal thyroid pathology remains elusive. In high-volume centers the cervical approach is sufficient and the rates of thoracic surgical approach is less than 1%. Computed tomography (CT) or magnetic resonance imaging (MRI) of the cervical region are the modalities of choice for investigating the retrosternal component of the thyroid, as they allow accurate assessment of mediastinal extension and facilitate surgical planning. In our study, the integration of the Huins classification and the Cohen & Cho classification proved to be a valid predictive factor for identifying cases that may require a surgical approach beyond the classical Kocher-type cervicotomy. We recommend that retrosternal thyroid pathologies be managed in referral centers equipped with multidisciplinary expertise and adequate surgical experience to ensure optimal outcomes. PubMed-ID: [41837129](#)  
DOI: [10.3389/fendo.2026.1739552](#)  
PMCID: PMC12982106

**Thyroid Volume Measurement With AI-Assisted Freehand 3D Ultrasound Compared to 2D Ultrasound-A Clinical Trial.**  
*Head Neck*, 48(1):64-70.

K. B. Rask, F. Makouei, M. H. J. Wessman, T. T. Kristensen and T. Todsén. 2026.

**BACKGROUND:** Accurate thyroid volume assessment is critical in thyroid disease diagnostics, yet conventional high-resolution 2D ultrasound has limitations. Freehand 3D ultrasound with AI-assisted segmentation presents a potential advancement, but its clinical accuracy requires validation. **METHOD:** This prospective clinical trial included 14 patients scheduled for total thyroidectomy. Preoperative thyroid volume was measured using both 2D ultrasound (ellipsoid method) and freehand 3D ultrasound with AI segmentation. Postoperative thyroid volume, determined via the water displacement method, served as the reference standard. **RESULTS:** The median postoperative thyroid volume was 14.8 mL (IQR 8.8-20.2). The median volume difference was 1.7 mL (IQR 1.2-3.3) for 3D ultrasound and 3.6 mL (IQR 2.3-6.6) for 2D ultrasound ( $p = 0.02$ ). The inter-operator reliability coefficient for 3D ultrasound was 0.986 ( $p < 0.001$ ). **CONCLUSION:** These findings suggest that freehand 3D ultrasound with AI-assisted segmentation provides superior accuracy and reproducibility compared to 2D ultrasound and may enhance clinical thyroid volume assessment. **TRIAL REGISTRATION:** ClinicalTrials.gov identifier: NCT05510609.

PubMed-ID: [40778496](#)  
DOI: [10.1002/hed.28267](#)  
PMCID: PMC12703570

**Comparable Outcomes of Differentiated Thyroid Cancer in Immunocompromised Versus Immunocompetent Patients.**  
*J Clin Endocrinol Metab*, 111(4):1075-83.

A. Ritter, A. Eagan, H. Levyn, R. M. Tuttle, S. Patel and I. Ganly. 2026.

**BACKGROUND:** Differentiated thyroid cancer (DTC) is generally a highly treatable malignancy with low mortality and a favorable prognosis. However, the impact of immunodeficiency on DTC outcomes remains poorly understood, with research largely limited to organ transplant recipients. This study aimed to address this gap by comparing the clinical characteristics and outcomes of DTC in immunocompromised patients with a propensity-matched cohort of immunocompetent individuals. **METHODS:** The study compared adult patients with DTC and preexisting immunodeficiencies treated at Memorial Sloan-Kettering Cancer Center between 1987 and 2020 to a propensity-matched control group of immunocompetent patients, with a 5:1 comparison ratio. Data on demographics, disease characteristics, and outcomes were analyzed. **RESULTS:** Among 8534 DTC patients, 130 (1.5%) were immunocompromised. After propensity score matching, 650 immunocompetent patients were included for comparison. Recurrence-free survival did

not differ significantly between groups ( $P = .94$ ), with recurrence rates remaining below 10% in both cohorts over 180 months. At 10 years, disease-specific survival was also similar ( $P = .34$ ), with rates of 100% for immunocompromised and 98% for immunocompetent patients. CONCLUSION: DTC has a comparable prognosis in immunocompetent and immunocompromised patients.

PubMed-ID: [41054817](#)

DOI: [10.1210/clinem/dgaf550](#)

#### **Cost analysis in thyroid cancer clinical trials: Toward value-based oncology care.**

*Am J Surg*, 252:116772.

J. L. Rogers, S. Henostroza, A. Fahey and C. C. Solorzano. 2026.

BACKGROUND: Clinical trials are crucial in advancing novel therapies for thyroid cancer. Given the increased cost of modern healthcare, cost considerations in clinical trials are important yet remain under-reported. METHODS: A search of ClinicalTrials.gov identified thyroid cancer studies including cost in the trial description or as an outcome. Data collected included trial information, cost outcomes, and cost-effectiveness analyses. RESULTS: Among 46 thyroid cancer-focused clinical trials, only 28 (60.8 %) mentioned cost in any capacity, of which 21 (75 %) included cost outcomes and 7 (25 %) included cost-effectiveness analyses. Overall, cost was a primary outcome in 1 (2.2 %) trial, secondary outcome in 20 (43.5 %) trials, and exploratory outcome in 7 (15.2 %) trials. CONCLUSION: The inclusion of cost analysis in thyroid cancer clinical trials is limited. Given rising cost pressures in modern healthcare systems, the low prevalence of cost endpoints and cost-effectiveness analyses underscores the need for increased awareness and investment in this domain.

PubMed-ID: [41386062](#)

DOI: [10.1016/j.amjsurg.2025.116772](#)

#### **Redefining the prevalence of different clinical variants in MEN2A and their correlation with RET germline mutations: a single-center series and experience.**

*Endocr Relat Cancer*, 33(1)

C. Romei, T. Ramone, R. Ciampi, R. Casalini, A. Prete, V. Bottici, V. Cappagli, L. Agate, E. Molinaro, C. Gambale, S. Brogioni, A. Matrone and R. Elisei. 2026.

Multiple endocrine neoplasia type 2 (MEN2) is caused by germline RET mutations and is characterized by the presence of medullary thyroid cancer (MTC) associated or not with other endocrine neoplasias. MEN2 is classified as MEN2A, including different variants, and MEN2B. The aim of the present study was to evaluate the impact of the RET genetic screening in redefining the prevalence of the different MEN2 variants inside the MEN2A group. This study included 223 MEN2 families: 202 MEN2A (55 MEN2A classical, 3 MEN2A + lichen cutaneous amyloidosis (CLA), 5 MEN2A + Hirschsprung disease (HD) and 139 FMTC variants) and 21 MEN2B. RET germline mutations found in MEN2A classical variant, as well as in MEN2A + CLA and MEN2A + HD, were the 'high-risk' category in most cases, while only 5/139 RET-mutated FMTC families showed a 'high-risk' category mutation. The most frequent mutation in the FMTC variant was the p.Val804Met (62/139). Among all, 116 families had a known history of hereditary disease (group A) at diagnosis and 107 had an apparently sporadic form of MTC (group B). Different MEN2A variants and RET ATA risk level category mutations were observed in the two groups. In conclusion, we demonstrated that the FMTC is the most prevalent MEN2A variant; 'moderate-risk' RET mutations, particularly non-cysteine mutations, are almost exclusively present in the FMTC variant; about 50% of hereditary MTC kindreds are primarily discovered by the RET genetic screening, confirming the clinical utility of performing this analysis in all cases of MTC.

PubMed-ID: [41404851](#)

DOI: [10.1530/ERC-25-0244](#)

#### **Highly-selected sporadic, apparently unifocal cN0 MTC may benefit from unilateral surgery. A proof of concept in a high-volume institution.**

*Surgery*, 189:109699.

L. Rossi, A. Matrone, L. Torregrossa, C. Becucci, A. De Palma, G. Frustaci, C. E. Ambrosini, C. Ugolini, G. Materazzi and R. Elisei. 2026.

BACKGROUND: This study aimed to evaluate the incidence of multifocality, bilaterality, and central compartment lymph node involvement (both ipsilateral and contralateral) in patients with apparently unifocal sporadic medullary thyroid carcinoma cN0. METHODS: Patients with sporadic medullary thyroid carcinoma cN0 were prospectively enrolled between February 2022 and December 2024. To confirm the sporadic form of medullary thyroid carcinoma, the search for RET germline mutation was performed in all cases. All patients underwent total thyroidectomy with central compartment neck dissection. Ipsilateral and contralateral central compartment lymph nodes were harvested separately for histopathologic

examination. RESULTS: A total of 54 patients were included in the study. The median age was 60 years, with a female predominance of 55.6%. Preoperative median calcitonin levels were 112.5 pg/mL. Median tumor size was 1.1 cm. Three patients (5.6%) presented with multifocal sporadic medullary thyroid carcinoma, but only 1 had bilateral sporadic medullary thyroid carcinoma (1.9%). The median number of central compartment lymph nodes removed was 10. Twelve patients (22.2%) had lymph node metastasis, including 2 patients (3.7%) with lymph node metastases in both the ipsilateral and contralateral central compartments. All metastatic lymph nodes measured  $\leq 5$  mm. In multivariate analysis, no independent risk factor for lymph node metastasis was found among age ( $P = .589$ ), sex ( $P = .069$ ), calcitonin ( $P = .953$ ), tumor size ( $P = .644$ ), and desmoplasia  $>20\%$  ( $P = .087$ ). CONCLUSION: Sporadic medullary thyroid carcinoma cN0 harbors a unilateral disease in 94.4% of cases. Contralateral lymph node involvement is extremely rare in highly selected cases, although ipsilateral central compartment lymph node metastases occur in 22.2% of cases. In this cohort of patients, unilateral surgery (hemithyroidectomy with ipsilateral central compartment neck dissection) may be the treatment of choice.

PubMed-ID: [40998592](#)

DOI: [10.1016/j.surg.2025.109699](#)

### **TERT promoter mutations and recurrence patterns in differentiated thyroid carcinoma.**

*Endocr Relat Cancer*, 33(2)

H. J. Ryu, J. H. Yoo, D. E. Leem, C. S. Ki, J. H. Shin, Y. L. Oh, J. H. Kim, J. E. Jun, K. J. Ahn, J. Ahn, S. W. Kim, J. H. Chung, T. H. Kim and Y. I. Son. 2026.

Telomerase reverse transcriptase promoter mutations (TERT) are known prognostic factors associated with poor outcomes in differentiated thyroid carcinoma (DTC). We analyzed differences in DTC recurrence patterns over time according to TERT. A retrospective review was conducted on DTC patients who achieved remission after total thyroidectomy and/or radioactive iodine treatment at Samsung Medical Center between 1994 and 2004. The sites and patterns by time of recurrence in the patients were reviewed. In total, 367 patients with a median follow-up of 14 years (interquartile range, 12-17 years) were included. Recurrence occurred in 91 patients, wherein 56 had lymph node recurrence and 35 had either local or distant recurrence. TERT and tumor size  $<2$  cm were independent factors for recurrence in the Cox proportional hazards analysis. In cases of TERT-wild type (WT), the recurrence rate decreased significantly over time after diagnosis, whereas in TERT-mutant type (MT), a consistently high recurrence rate was observed. In the Kaplan-Meier analysis, TERT-MT exhibited a significantly poorer disease-free survival, with continuous recurrence over time, whereas in TERT-WT, the curve showed a gradual decline. Further analysis of the overall survival among the 91 patients revealed that TERT-MT was significantly associated with a higher risk of mortality, whereas TERT-WT exhibited a slowly decreasing curve. In conclusion, TERT-MT was a significant adverse prognostic factor wherein continuous recurrence necessitates long-term follow-up. For TERT-WT, the recurrence rate decreased compared to TERT-MT, and even in cases of recurrence, the treatment outcomes are favorable.

PubMed-ID: [41604294](#)

DOI: [10.1530/ERC-25-0273](#)

PMCID: PMC12921681

### **Comment on 'Second Primary Papillary Thyroid Carcinoma: Insights From Competing Risk Analysis and Post-RAIT'.**

*Clin Endocrinol (Oxf)*, 104(1):75.

A. N. Sanli and D. E. Tekcan Sanli. 2026.

PubMed-ID: [40988346](#)

DOI: [10.1111/cen.70040](#)

### **Durability of Active Surveillance in Thyroid Cancer-Reply.**

*JAMA Surg*, 161(2):209.

A. M. Sawka, S. Ghai and D. P. Goldstein. 2026.

PubMed-ID: [41405987](#)

DOI: [10.1001/jamasurg.2025.5513](#)

### **Patient-Reported Outcomes Three Years After Deciding on Surgery or Active Surveillance for Small, Low-Risk Papillary Thyroid Cancer: Results of a Prospective Cohort Study.**

*Thyroid*, 36(4):385-96.

A. M. Sawka, S. Ghai, L. Rotstein, J. C. Irish, J. D. Pasternak, K. Lajkosz, W. Xu, J. M. Jones, A. Gafni, N. N. Baxter, D. P. Goldstein and G. Canadian Active Surveillance Study. 2026.

**BACKGROUND:** Long-term quality of life is an important consideration of patients in deciding on disease management options for low-risk papillary thyroid cancer (PTC). **METHODS:** We conducted a prospective cohort study of Canadian patients who were diagnosed with small (<2 cm in maximal diameter), low-risk papillary thyroid cancer (PTC) and were given the choice of active surveillance (AS) or immediate surgery. We report the results of a self-administered questionnaire on patient-reported outcomes (PROs) that was completed approximately three years after the initial disease management choice. PROs included overall and subscale scores from questionnaires, including those on quality of life (EORTC QLQ-C30, EORTC THY-34), the Assessment of Survivor Concerns, the Decision Regret Scale, and the Generalized Anxiety Disorder 7-item Scale. We compared the results according to the initial disease management choice and according to the disease management status at the time of questionnaire completion. **RESULTS:** The participant response rate was 64% (120/188), including 98 individuals who chose AS and 22 who chose immediate surgery. The median duration of follow-up at the time of questionnaire completion was 42 months (interquartile range [IQR] = 39, 46). After statistical adjustment for multiple comparisons, there were no significant differences in the overall scores or subscales of any of the questionnaires between patients who chose AS and those who chose immediate surgery. However, in a secondary analysis, patients who crossed over from AS to surgery experienced greater cancer-related worry as well as overall worry ( $p = 0.021$  for each) and decision regret ( $p = 0.031$ ) as compared with patients who remained under AS and those who initially chose surgery. **CONCLUSIONS:** We observed that PROs do not significantly differ between patients who chose AS and those who chose immediate surgery a few years after the initial disease management choice. However, patients who crossover from AS to surgery may experience greater cancer-related worry and decision regret.

PubMed-ID: [41816978](#)

DOI: [10.1177/10507256251408857](#)

#### **Diagnostic Utility of Genetic Testing in Hyperthyroxinemia With Non-Suppressed TSH.**

*Clin Endocrinol (Oxf)*, 104(6):693-701.

H. Sekizkardes, M. Eltan, S. Demir, D. Giray, Z. Yavas Abali and S. Abali. 2026.

**BACKGROUND:** Hyperthyroxinemia with non-suppressed thyroid-stimulating hormone (TSH) is a complex clinical entity that presents significant diagnostic challenges. Inherited causes include resistance to thyroid hormone beta (RTHbeta), characterised by highly variable clinical presentation, and familial dysalbuminemic hyperthyroxinemia (FDH), a form of assay interference caused by pathogenic variants in the ALB gene leading to pseudo elevation of free thyroxine (FT4). This study aimed to characterise the clinical, laboratory, and molecular features of a paediatric cohort presenting with hyperthyroxinemia and non-suppressed TSH, and to identify clinical parameters that may aid in differential diagnosis.

**METHODS:** In this retrospective observational study, 25 children from 19 unrelated families with elevated FT4 and non-suppressed TSH were evaluated. Clinical history, anthropometric data, physical examination findings, vital signs, laboratory results, radiological imaging, and sequencing data of the THRB and/or ALB genes were reviewed. **RESULTS:** THRB gene sequencing was performed in 21 children from 18 families, identifying pathogenic or likely pathogenic variants in six patients from six unrelated families, including a novel variant c.997 G > C, p.(Glu333Gln), consistent with a diagnosis of RTHbeta in 33.3% of those tested. Among these patients, tachycardia was observed in three cases (50%). ALB gene sequencing was completed in 16 children from 13 families, revealing the hotspot variant c.725 G > A, p.(Arg242His) in 12 patients from six unrelated families, corresponding to FDH in 46.2% of those tested. None of the FDH-confirmed patients exhibited tachycardia or other signs of thyroid dysfunction. FT4 and TSH levels were similar between RTHbeta and FDH groups; however, FT3 levels tended to be lower in FDH, although FT3/FT4 ratio did not differ significantly. **CONCLUSION:** Our findings highlight the critical role of molecular testing in accurately diagnosing the underlying cause of elevated FT4 with non-suppressed TSH and in preventing unnecessary interventions. Hotspot analysis of the ALB gene is recommended as a first-line test, particularly in asymptomatic individuals.

PubMed-ID: [41800491](#)

DOI: [10.1111/cen.70126](#)

#### **Outcomes in Surgical Management of Graves' Disease: Transcervical Versus Transoral Thyroidectomy.**

*Otolaryngol Head Neck Surg*, 174(1):105-11.

S. Seo, O. Wei, M. Plitt, N. Nagururu, A. S. Ding, D. R. Trakimas, K. Frazier, A. Mathur, L. Morris-Wiseman, R. P. Tufano and J. O. Russell. 2026.

**OBJECTIVE:** To compare surgical outcomes of patients with Graves' disease undergoing total thyroidectomy through the transoral endoscopic thyroidectomy vestibular approach versus the transcervical approach. **STUDY DESIGN:** Retrospective cohort study. **SETTING:** Tertiary care academic institution. **METHODS:** Patients were offered a choice of either approach, undergoing surgery between September 2016 (when TOETVA was first offered) and March 2024. Patients were excluded if they were under 18 years old or received a neck dissection or re-operation. Collected data includes demographics, clinical

and surgical variables, pathology, and postoperative complications. RESULTS: In total, 152 transcervical and 81 transoral cases were included. The transoral group was younger (36.1 vs 45.3 years,  $P < .0001$ ) and had more females (95.1% vs 77.0%,  $P = .0003$ ) but had comparable body mass index to the transcervical group. There were no significant differences in the median maximum lobe size (5.9 (transcervical) vs 5.6 (transoral) cm,  $P = .647$ ). Complication rates were similar between groups. Of the minor complications, temporary hypoparathyroidism was the most prevalent with 12 (7.9%) cases in the transcervical and 7 (8.6%) in the transoral groups. There were 2 (1.3%) and 4 (5.0%) cases of major complications in transcervical and transoral groups, respectively. Multivariable regression for age, sex, length of admission, and surgery duration confirmed no significant associations between approach and complication rates. CONCLUSION: Transcervical and transoral approaches for surgical management of Graves' disease show statistically comparable rates of minor and major complications, even early in the learning curve. The choice of approach should involve shared decision-making between surgeon and patient, as highly motivated patients may not be excellent candidates.

PubMed-ID: [41353724](#)

DOI: [10.1002/ohn.70076](#)

#### **Durability of Active Surveillance in Thyroid Cancer.**

*JAMA Surg*, 161(2):208-9.

R. H. Shahid, M. A. Khan and M. Shahid. 2026.

PubMed-ID: [41405982](#)

DOI: [10.1001/jamasurg.2025.5510](#)

#### **Nomogram prediction for central lymph node metastasis in papillary thyroid microcarcinoma of the isthmus based on clinical and ultrasound features.**

*Front Surg*, 13:1728250.

Y. Shi, L. Qian, J. Huang, T. Ma, X. Cui and J. Zhang. 2026.

AIM: To better predict the central lymph node metastasis (CLNM) of patients with isthmic papillary thyroid microcarcinoma (IPTMC) before surgery, we developed a new predictive nomogram based on clinical and ultrasound features and validate its reliability. METHODS: Our study included 160 patients who were hospitalized from January 2016 to December 2024, underwent thyroidectomy with lymph node dissection, and were pathologically diagnosed with IPTMC. These patients were randomly divided into a training group of 112 cases and a validation group of 48 cases. Clinical and ultrasound characteristic data of the patients were collected. Univariate and multivariate logistic regression analyses were conducted on the training group to determine the independent risk factors for CLNM, and a nomogram was established based on these factors to predict the risk of CLNM in patients with IPTMC. The predictive performance of the nomogram was verified using the validation group. RESULTS: Among the clinical and ultrasound features in the training cohort, we identified four independent risk factors for CLNM: age, tumor size, multifocality, and calcification. A predictive nomogram was developed based on the above four risk factors. The predictive nomogram showed excellent calibration in predicting CLNM, with an area under the curve (AUC) of 0.811 and a concordance index (C-index) of 0.783. The calibration curve of the nomogram was close to the ideal diagonal. In addition, decision curve analysis (DCA) proved that the model had significantly greater net benefits. The validation group verified the reliability of the prediction nomogram. CONCLUSIONS: The nomogram model developed in this study can effectively predict the risk of CLNM in patients with IPTMC before surgery and provide a reference for selecting surgical procedures.

PubMed-ID: [41660496](#)

DOI: [10.3389/fsurg.2026.1728250](#)

PMCID: PMC12872766

#### **Neoadjuvant Combination Therapy with Tyrosine Kinase and Immune Checkpoint Inhibitors in Anaplastic Thyroid Cancer: A Single-Center, Real-World Experience.**

*Ann Surg Oncol*, 33(7):5950-7.

Y. Song, Y. Zhang, J. Wang, K. Fei, G. Xu, T. Wang and B. Zhang. 2026.

BACKGROUND: Most patients with anaplastic thyroid carcinoma (ATC) present with surgically unresectable disease. The use of combined kinase inhibitors and immunotherapy in the neoadjuvant setting for ATC remains relatively unexplored. METHODS: The authors conducted a single-center, retrospective case study assessing combination neoadjuvant therapy for patients with stages IVb and IVc ATC. The primary outcomes comprised the rate of conversion to surgery, changes in tumor size and surgical morbidity parameters, as well as recurrence-free survival and overall survival. RESULTS: Of the 27 ATC patients treated with combination kinase inhibitors and immunotherapy, 11 (40.7%) achieved R0/R1 surgical resection. The median reduction in the largest tumor diameter was 54%. Mean surgical complexity scores decreased from

baseline to surgery. According to the postoperative pathology, five patients achieved a complete response. Several major complications were observed, including one perioperative death. Neither median recurrence-free survival nor median overall survival were reached during a median follow-up period of 36 months. CONCLUSIONS: Neoadjuvant combination therapy followed by surgery enhances resectability and provides a potential curative option for patients with ATC. However, postoperative complications remain a significant concern and warrant careful attention.

PubMed-ID: [41933241](#)

DOI: [10.1245/s10434-026-19139-6](#)

#### **Real-time detection of parathyroid glands during surgery using a highly sensitive autofluorescence-based system.**

*Int J Surg,*

J. Sun, H. Zhao, B. Song, Z. Wu, L. Yu, B. Lv, Y. Jiang and C. Jiang. 2025.

BACKGROUND: The question of how to quickly and accurately identify and localize living parathyroid tissue, protect its functional integrity, and reduce the risk of intraoperative parathyroid function damage is a great challenge for clinicians and a technical challenge for researchers in the healthcare field. METHODS: This prospective basic research designed a laser-induced fluorescence detection system that utilizes the intrinsic fluorescence of tissues and conducted a single-center clinical validation study from 28 May 2025 to 2 July 2025 which was registered with ISRCTN. The parathyroid gland detection data were obtained. A total of 106 patients aged between 18 and 99 representing different racial and gender backgrounds participated in this study. All the participating patients signed the informed consent form. This study mainly determines whether the tissue is a parathyroid gland by measuring the fluorescence intensity values of the relevant human tissues during surgery under the laser-induced fluorescence detection system. RESULTS: The fluorescence detection module designed employs an innovative algorithm, which can effectively overcome the interference from complex environmental light sources such as shadowless surgical lights, thereby significantly improving the accuracy of fluorescence imaging of tissue contrast agents. System performance was evaluated using serial dilutions of indocyanine green (ICG) to simulate PG autofluorescence, achieving a minimum detectable concentration of  $8 \times 10^{-10}$  mol/L and a limit of detection (LoD) of  $1.24 \times 10^{-10}$  mol/L. The clinical verification of over 100 cases of in situ PG detection showed that the detection accuracy rate was 98.3% (higher than 96% of the PTeye system and the naked eye recognition of clinicians respectively), confirming its reliability in surgical environments. CONCLUSIONS: This parathyroid gland detection system can accurately identify parathyroid glands, providing an effective solution for the real-time localization of intraoperative PG, which may improve intraoperative decision making and patient prognosis.

PubMed-ID: [41295885](#)

DOI: [10.1097/JS9.0000000000004078](#)

#### **Diagnostic value of molecular testing for evaluating thyroid nodules greater than 4 centimeters.**

*Am J Surg,* 252:116755.

N. Swaminathan, Z. Song, C. Wu, R. Akhund, J. Fazendin, B. Lindeman, H. Chen and A. Gillis. 2026.

BACKGROUND: Molecular testing (MT) aids in reducing unnecessary thyroidectomy for indeterminate thyroid nodules, primarily due to its high negative predictive value (NPV). However, its reliability in large nodules ( $\geq 4$  cm), which carry a higher malignancy risk, remains unclear. METHODS: We performed a retrospective study of patients with thyroid nodules  $\geq 4$  cm who underwent fine-needle aspiration (FNA) at a tertiary care center from 2015 to 2023. Cytology was categorized using the Bethesda system. Molecular results (Afirma GEC and GSC) were matched with surgical pathology. Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) was classified as malignant. RESULTS: A total of 231 patients were included (mean age 52  $\pm$  16 years; 69.7 % female). The median nodule size was 5.0 cm (IQR: 4.4-5.8). Malignancy was identified in 28.1 % of cases. Malignancy rates by Bethesda category were 4.3 % (Bethesda II), 33.8 % (III), and 50.0 % (IV), all Bethesda V and VI nodules were malignant. Among 96 patients with Bethesda III or IV cytology, 79 (82.3 %) underwent MT, 30 with GEC and 47 with GSC. GEC yielded 91.7 % sensitivity, 33.3 % specificity, and NPV of 85.7 %. GSC showed 88.9 % sensitivity, 58.6 % specificity, and NPV of 89.5 %. Malignancy occurred in 40.0 % (GEC) and 38.3 % (GSC) of tested nodules. False negatives included anaplastic carcinoma, oncocytic carcinoma, and NIFTP. Mutation testing revealed malignancy in 41.4 % of BRAF-negative and 44.8 % of RET/PTC-negative patients. CONCLUSION: Molecular testing in nodules  $\geq 4$  cm may underestimate malignancy risk. Clinicians should interpret benign MT results in this subgroup with caution.

PubMed-ID: [41352294](#)

DOI: [10.1016/j.amjsurg.2025.116755](#)

### **Feasibility and Efficacy of Indocyanine Green Angiography in Transoral Robotic Thyroidectomy: A Pilot Study.**

*Head Neck*, 48(1):71-81.

K. Tae, V. C. Nguyen, H. W. Choi, D. W. Lee, K. N. Kim and G. W. Randolph. 2026.

**BACKGROUND:** This study aimed to evaluate the feasibility and effectiveness of indocyanine green (ICG) angiography in transoral robotic thyroidectomy (TORT). **METHODS:** A total of 130 patients with papillary thyroid carcinoma who underwent TORT with ICG angiography (ICG group, 65 patients) and without ICG angiography (control group, 65 patients) were analyzed. **RESULTS:** The parathyroid detection rate did not differ between the control and ICG groups. Among patients with total thyroidectomy, the incidence of postoperative transient hypoparathyroidism did not differ between the control (7/20, 35%) and ICG (4/20, 20%) groups. Pearson's correlation coefficients between the total ICG perfusion score and postoperative changes in serum intact parathyroid hormone and calcium levels showed statistical significance. **CONCLUSIONS:** ICG angiography is feasible in TORT. Although it did not improve the parathyroid detection rate or reduce the incidence of hypoparathyroidism, ICG angiography was able to predict postoperative parathyroid function, as assessed by the total ICG perfusion score.

PubMed-ID: [40778482](#)

DOI: [10.1002/hed.70011](#)

### **Guiding Management of Bethesda V Thyroid Nodules: The Role of Molecular Testing.**

*Clin Endocrinol (Oxf)*, 104(1):67-74.

I. Tessler, G. B. Morand, N. A. Gecel, A. Dotan, T. Yamin, E. E. Alon, R. J. Payne and G. Avior. 2026.

**OBJECTIVE:** The 2023 Bethesda System update introduced molecular testing as a management option for Bethesda V cytology nodules, aiming to guide surgical decision-making. This study investigates the correlation between molecular profiling and malignancy aggressiveness. **DESIGN:** We conducted a retrospective multicenter study involving patients with Bethesda V cytology and confirmed malignant pathology who underwent molecular profiling between 2018 and 2021. **PATIENTS:** A total of 156 patients with Bethesda V cytology and final malignant histology were included. **MEASUREMENTS:** Malignancy aggressiveness was assessed based on histopathological features following 2015 ATA guidelines. Demographic data, pathology results, and genetic variants were analyzed. Molecular profiling results were stratified according to variant risk levels. **RESULTS:** We identified 161 Bethesda V nodules, of which 153 (95.0%) were malignant on final pathology. Genetic stratification revealed no detected mutations in 39.7% (n = 56), low-risk (n = 49, 31.4%), and intermediate-risk variants (n = 45, 28.8%). Only one patient had a high-risk variant. Patients with intermediate-risk variants had a sixfold risk of aggressive disease compared to those with low-risk variants (49% vs. 8.2%, p < 0.001). RAS mutations were the most common among the low-risk group (68.8%) and BRAF V600E predominated in the intermediate-risk group (93.3%). **CONCLUSIONS:** Our findings suggest that molecular profiling offers insights into risk stratification for Bethesda V thyroid lesions, demonstrating a very low incidence of aggressive pathology in the low-risk molecular group.

PubMed-ID: [40964868](#)

DOI: [10.1111/cen.70032](#)

PMCID: PMC12669814

### **Artificial Intelligence Applications in Thyroid Cancer Diagnosis: 2026 Update.**

*Thyroid*, 36(2):133-40.

J. Thomas and F. N. Tessler. 2026.

**BACKGROUND:** In this updated review, we will discuss the role of artificial intelligence (AI) in the assessment of thyroid nodules, cervical lymph nodes, and cytology or histology specimens, followed by guidance for practices wishing to install AI systems. **SUMMARY:** To date, six AI platforms for assessing sonograms of thyroid nodules have been cleared by the United States Food and Drug Administration, with generally good performance, especially when compared with that of less-experienced physicians. Multimodality large language models have also been tested in this context, but with less impressive results so far. Software to evaluate lymph nodes and biopsy or surgical specimens shows promise, though no systems have yet reached the marketplace. The process of evaluating and installing an AI system in a practice requires consideration in five areas: information technology, vendor support, effectiveness, usability, and finance. Engagement of people with subject matter expertise in all these domains is recommended, beginning with product selection. **CONCLUSIONS:** AI tools for the evaluation of thyroid nodules continue to proliferate, and commercial software to assess lymph nodes and slide specimens may soon become available. Attention to detail is critical for successful implementation and operation.

PubMed-ID: [41791884](#)

DOI: [10.1177/10507256251412316](#)

### **Radiofrequency ablation for nodal recurrence in papillary thyroid carcinoma.**

*Am J Surg*, 256:116920.

A. Thornton, E. Kuo, J. Lee, Y. Hu and J. Kuo. 2026.

The optimal management of recurrent papillary thyroid carcinoma (PTC) in cervical lymph nodes remains a clinical challenge. Lymphadenectomy is the gold standard, but reoperative procedures have a well-documented increase in morbidity. Radiofrequency ablation (RFA) has emerged as a promising alternative for the management of nodal metastases. In this study, nine patients with ten sites of PTC nodal recurrence were treated with RFA. At one month, there was a statistically significant reduction in nodule size ( $P = .022$ ). By the end of follow-up, all patients achieved a volume reduction ratio (VRR)  $> 90\%$ , and three-quarters demonstrated complete sonographic resolution. One patient experienced transient voice change. No major complications occurred. These findings support RFA as a safe and effective therapy that can play a complementary role to surgery and radioactive iodine in the management of nodal recurrence of PTC.

PubMed-ID: [41865451](#)

DOI: [10.1016/j.amisurg.2026.116920](#)

### **Follow up or FNAB?: Malignancy Rates of ACR TI-RADS 4 and 5 Thyroid Nodules <10 mm in Diameter.**

*Otolaryngol Head Neck Surg*, 174(2):366-74.

E. Tobcu, E. Karavas, G. T. Yilmaz and Z. Tobcu. 2026.

**OBJECTIVE:** The aim of this study is to ascertain the rate of malignancy in nodules that are less than 10 mm in diameter in the TR-4 and TR-5 categories, as defined by the American College of Radiology Thyroid Imaging and Reporting Data System 2017 whitepaper and to open a discussion on the strategy of approach to PTMCs. **STUDY DESIGN:** Prospective cohort study. **SETTING:** Single academic medical center. **METHODS:** All thyroid ultrasound examinations were performed by 2 senior radiologists with consensus. The fine-needle aspiration biopsy procedure was performed under the guidance of ultrasound. All patients underwent surgery, except for those with benign cytology. **RESULTS:** Among 60 nodules, 15 nodules (25%) were classified as TR-4 and 45 nodules (75%) as TR-5. Based on cytological analysis, 12 of the 15 nodules classified in the TR-4 category (80%) were benign, while 3 nodules (20%) were classified as nonbenign. In the assessment of 45 TR-5 nodules, 30 (66.7%) were identified as nonbenign, while the remaining 15 (33.3%) were classified as benign. Surgery was performed on all 33 patients with nonbenign FNAB results, and the histopathological results confirmed malignancy in 3 TR-4 nodules (20%) and in 29 TR-5 nodules (64.4%). **CONCLUSION:** Our study highlights that TR-4 and TR-5 thyroid nodules smaller than 10 mm exhibit high malignancy rates. Despite limitations such as small sample size and single-center design, our findings support the consideration of FNAB in selected  $<10$  mm nodules, particularly when active surveillance is unsuitable.

PubMed-ID: [41353734](#)

DOI: [10.1002/ohn.70084](#)

### **Endocrine and metabolic late effects in childhood cancer survivors in Germany: the VersKiK study.**

*Eur J Endocrinol*, 194(2):102-13.

P. Trocchi, E. Swart, E. Aleshchenko, H. Merzenich, C. Ronckers, K. Baust, G. Calaminus, T. Langer, P. Ihle, J. Kupper-Nybelen, C. Lupkes, P. Droge, T. Ruhnke, D. Horenkamp-Sonntag, U. Marschall, M. Klein, C. Spix, C. Apfelbacher and J. Gebauer. 2026.

**OBJECTIVE:** Endocrine and metabolic diseases are known to be common late effects in childhood cancer survivors (CCS). We assessed the prevalence of these diseases in a large German CCS cohort, and a matched comparison population, using health claims data. **DESIGN:** The cohort study was based on record linkage between the nationwide German Childhood Cancer Registry and claims data from 13 major German statutory health insurances. **METHODS:** The monitored insurance period covered the years 2017-2021. We assessed the frequencies of endocrine and metabolic diseases among 11 863 five-year CCS, diagnosed 1991-2021, with continuous insurance coverage and a matched comparison group of 35 589 insured persons without a history of childhood cancer. We present prevalence and prevalence ratios (PR) with corresponding 95% confidence intervals (95% CI). **RESULTS:** At least one endocrine or metabolic disease was recorded in 31.3% of survivors ( $n = 3716$ ) and in 16.4% of the comparison group ( $n = 5819$ ,  $PR = 1.9$ ; 95% CI: 1.8-2.0). The frequency of diseases was higher among females than among males in both groups. The PR was 2.4 (95% CI: 2.3-2.5) for males and 1.6 (95% CI: 1.5-1.7) for females. The frequency of at least one disease increased with increasing attained age. The disease with the highest frequency among CCS was hypothyroidism (15.85%), and the highest PR was estimated for patients with primary thyroid cancer (43.5; 95% CI: 24.2-78.1). **CONCLUSIONS:** Our study highlights the increased vulnerability of CCS to endocrine and metabolic diseases compared to the general population and underscores the need for risk-adapted surveillance during the whole survivorship trajectory.

PubMed-ID: [41636640](#)

DOI: [10.1093/ejendo/lvag010](#)

**Preoperative Lugol's solution and surgical outcomes in Graves' disease: a single-center retrospective study.**

*Front Surg*, 13:1755477.

M. T. Unlu, O. Caliskan, I. Cetinoglu, Z. Sengul, H. Arikan, D. Gercelman, N. Aygun and M. Uludag. 2026.

INTRODUCTION: Basedow Graves disease (BG) is the most common cause of hyperthyroidism. Lugol's solution (LS) is used preoperatively to inhibit thyroid hormone production, decrease thyroid gland vascularity and ensure a safer surgical field. This study aims to evaluate efficacy of the LS and its association with surgical complications in patients with BG.

MATERIALS AND METHODS: Patients with total thyroidectomy for BG between 2019 and 2024 were retrospectively included. Preoperative calcium (Ca), alkaline phosphatase (ALP), parathyroid hormone (PTH) levels, operative time, resected thyroid specimen weights, postoperative complications were analyzed. RESULTS: Among 128 patients, 38(29.6%) received LS (Group1), while 90 (70.3%) did not (Group2). No significant difference was found between groups regarding preoperative Ca, ALP, PTH ( $p = 0.780$ ,  $p = 1.000$ ,  $p = 1.000$ , respectively). Mean operative times were 147.79 +/- 64.66 min in Group1, 146.19 +/- 35.69 min in Group2 ( $p = 0.225$ ). Mean thyroid specimen weights were 36.83 +/- 26.47 g in Group1, 43.16 +/- 30.81 g in Group2 ( $p = 0.246$ ). The rates of incidental parathyroidectomy were 21.1% ( $n = 8$ ) in Group1 and 15.6% ( $n = 14$ ) in Group2 ( $p = 0.456$ ). Transient hypoparathyroidism rate was slightly higher in Group1 (34.2%,  $n = 13$ ) than in Group2 (23.3%,  $n = 21$ ) ( $p = 0.292$ ). Permanent hypoparathyroidism occurred in 2.63% of Group1 and 8.89% of Group2 patients ( $p = 0.375$ ). The rates of postoperative vocal cord paralysis, adjusted for the number of nerves at risk, were comparable between the groups (9.21%, 8.89%;  $p = 1.000$ ). CONCLUSION: The primary endpoint of postoperative hypocalcemia/hypoparathyroidism did not differ significantly between groups. Although the incidence of transient hypoparathyroidism was slightly higher in the LS group, no statistically significant difference was observed. Additionally, no significant difference was found regarding intraoperative or long-term outcomes. Present study did not demonstrate a protective effect of preoperative LS on surgical complications in patients with BG.

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DOI: [10.3389/fsurg.2026.1755477](#)

PMCID: PMC12979558

**Long-Term Outcomes of Patients Diagnosed With Differentiated Thyroid Cancer in Childhood and Young Adulthood.**

*J Clin Endocrinol Metab*, 111(3):e715-e24.

A. Valenciaga, S. Liyanarachchi, P. L. Brock and M. D. Ringel. 2026.

CONTEXT: Rates of pediatric differentiated thyroid cancer (DTC) in the United States have been increasing while studies on this population remain limited by inconsistent age cutoffs, short follow-up periods, or relative lack of clinical data.

OBJECTIVE: This work aimed to report long-term outcomes in patients diagnosed with DTC at age 20 years and younger.

METHODS: A retrospective study was conducted of patients diagnosed with DTC at age 20 years or younger with long-term follow-up. RESULTS: A total of 155 patients were included with a median age at diagnosis of 17 years (9-20 years). The frequency of distant metastasis and larger tumor size were inversely related to age at diagnosis (overall stage  $P = .045$ ; T-stage (size of the primary tumor +/- invasion);  $P = .001$ ). The median duration of follow-up was 16 years (1-63 years) and at last follow-up, 52.3% of patients had excellent response and disease specific mortality was 0%. There was no difference in response to therapy based on histologic subtype or birth sex; however, younger age at diagnosis was associated with worse response ( $P = .046$ ). Patients with more than 50 years of follow-up ( $n = 9$ ) had a median of 36 years of stability, with progression occurring in 6 out of 9 (67%) patients. CONCLUSION: Patients diagnosed with DTC as children or young adults have outstanding long-term survivorship, but may experience disease progression later in life, suggesting that long-term follow-up might be appropriate for this population. Younger age at diagnosis was identified as a risk factor for distant metastases and poorer response to therapy.

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DOI: [10.1210/clinem/dgaf522](#)

PMCID: PMC13051342

**Long-term calcitonin after thyroidectomy for medullary thyroid cancer in MEN2A.**

*Endocr Relat Cancer*, 33(1)

M. L. van den Berg, D. J. van Beek, M. F. M. van den Broek, L. Lodewijk, A. A. Verrijn Stuart, S. Terwisscha van Scheltinga, R. S. van Leeuwen, I. H. M. Borel Rinkes and M. R. Vriens. 2026.

Thyroidectomy is recommended for patients with multiple endocrine neoplasia type 2A (MEN2A). American Thyroid Association 2015 guidelines recommend follow-up of calcitonin values after thyroidectomy. The aim of this study was to

determine the natural course of calcitonin levels after total thyroidectomy (TTx) in MEN2A patients. Patients with MEN2A who underwent TTx between 1993 and 2019 and had multiple postoperative calcitonin measurements were retrospectively included from our referral center. Long-term serial calcitonin measurements and clinical outcomes were correlated to the first postoperative calcitonin, histopathology and type of TTx (prophylactic versus non-prophylactic). Fifty-two patients underwent TTx after 1993 at a median age of 10 years (range 0-71). Of these, 23 (44%) had no MTC and 29 (56%) had MTC. The median follow-up time was 12 years (range 3-30). Thirty-eight patients had an 'undetectable' first postoperative calcitonin, seven 'within reference range' and seven 'above reference range'. Of the 38 patients with an 'undetectable' first postoperative calcitonin, 32 remained 'undetectable'. All 21 patients without MTC and 'undetectable' first postoperative calcitonin remained 'undetectable'. Of the 17 patients with MTC and 'undetectable' first postoperative calcitonin, 11 remained 'undetectable' and none developed structural recurrence. Twenty-two of the 25 patients undergoing prophylactic thyroidectomy had repeated 'undetectable' measurements. Persistent MTC or structural recurrence occurred in six patients; all had MTC, had a detectable first postoperative calcitonin and underwent non-prophylactic TTx. In conclusion, the long-term serial calcitonin values remain undetectable in the majority of the patients with an undetectable first postoperative calcitonin. Biochemical follow-up for patients without MTC and an undetectable first postoperative calcitonin may not be necessary.

PubMed-ID: [41498511](#)

DOI: [10.1530/ERC-25-0366](#)

PMCID: PMC12910569

#### **Transoral Endoscopic Thyroidectomy via Vestibular Approach in Young Pediatric Patient.**

*Laryngoscope*, 136(2):994-6.

J. M. Walsh, J. A. Hurly and J. Russell. 2026.

Transoral endoscopy thyroidectomy by vestibular approach (TOETVA) provides the opportunity for thyroidectomy without cervical scarring. This procedure has yet to be widely studied in younger pediatric patients. We provide a case report of the youngest patient at our institution to successfully undergo TOETVA.

PubMed-ID: [40799123](#)

DOI: [10.1002/lary.70048](#)

#### **Comment on "Deep learning habitat radiomics based on ultrasound for predicting preoperative locally progression and postoperative recurrence risk of thyroid cancer: a multicenter study".**

*Int J Surg*,

B. Wan and W. Lu. 2026.

PubMed-ID: [41632014](#)

DOI: [10.1097/JS9.0000000000004818](#)

#### **Responses to Comment on 'Second Primary Papillary Thyroid Carcinoma: Insights From Competing Risk Analysis and Post-RAIT'.**

*Clin Endocrinol (Oxf)*, 104(1):76.

M. Wang, W. Chen, P. Li and Y. Gong. 2026.

PubMed-ID: [40993971](#)

DOI: [10.1111/cen.70043](#)

#### **Second Primary Papillary Thyroid Carcinoma: Insights From Competing Risk Analysis and Post-RAIT.**

*Clin Endocrinol (Oxf)*, 104(1):53-66.

M. Wang, W. Chen, P. Li and Y. Gong. 2026.

**BACKGROUND:** Improved cancer survival rates have highlighted second primary malignancies (SPMs), with the thyroid gland being one of the most common organs developing SPMs in cancer survivors. Second primary papillary thyroid carcinoma (2-PTC) is the predominant type, yet it remains poorly understood. This study aims to delineate the clinicopathological features and survival outcomes of 2-PTC and assess the efficacy of postoperative radioactive iodine therapy (post-RAIT) in reducing mortality risks in intermediate-risk 2-PTC patients. **METHODS:** Using the SEER-17 database (2004-2019), we identified 6399 2-PTC patients as Cohort 1 to analyze characteristics and outcomes, and 1743 as Cohort 2 to examine post-RAIT effects. Competing risk regression models were applied to assess mortality risks from prior primary malignancies (PPMs) and other causes. Propensity score matching and stabilized inverse probability treatment weighting with 500 bootstrap samples were used for robust analysis. **RESULTS:** Predominant demographic characteristics of 2-PTC patients included older age, female sex, and white ethnicity. Breast (25.5%), prostate (9.8%), and skin cancer (6.7%) were

the most common PPMs. Unfavorable PPMs were found in 6.3% of patients. Despite lower cumulative mortality from 2-PTC compared to PPMs and other causes, post-RAIT did not significantly reduce mortality risks in Cohort 2, even among patients aged  $\geq 55$  years, with clinical stage IV disease, or unfavorable PPMs. Sensitivity analyses confirmed these findings. CONCLUSION: The survival prognosis for 2-PTC patients is generally favorable, and post-RAIT does not significantly affect mortality in intermediate-risk cases, indicating a need for reevaluation of its use.

PubMed-ID: [40916361](#)

DOI: [10.1111/cen.70031](#)

#### **Learning curve and functional safety in robotic thyroidectomy via bilateral axillo-breast approach: a prospective study of 537 cases.**

*Surg Endosc*, 40(1):530-40.

S. S. Wang, Z. H. Tang, W. Y. Huang, X. Lin, S. F. He, M. T. Lin, N. Xu, B. Han, Z. Wang, S. Hua, A. H. A. Ahmed, G. W. Randolph, W. X. Zhao and B. Wang. 2026.

AIM: Robotic thyroidectomy via the bilateral axillo-breast approach (BABA) provides excellent cosmetic outcomes, but its adoption is limited by a steep learning curve and concerns about functional safety. This study aimed to define the learning curve trajectory and evaluate functional safety outcomes-with the primary endpoint of intraoperative RLN adverse events and secondary endpoints of inadvertent parathyroidectomy and PTH recovery. METHODS: A prospective cohort study was conducted at a high-volume endocrine surgery center from March 2018 to March 2024. A total of 537 consecutive patients with differentiated thyroid carcinoma underwent robotic BABA thyroidectomy with central neck dissection. Intraoperative refinements included real-time recurrent laryngeal nerve (RLN) monitoring, intraoperative parathyroid-hormone (PTH) testing, and nanocarbon lymph node mapping. Learning phases were defined by cumulative sum analysis. Primary outcomes were intraoperative RLN adverse events and inadvertent parathyroidectomy; secondary outcomes included operative time, lymph node yield, PTH recovery, complication rates, and tracheal injury. RESULTS: Among 537 patients (401 women, 74.7%; median age 43 years), operative time decreased from 189.9 to 129.3 min ( $P < 0.001$ ), with plateaus at 152 and 352 cases. RLN adverse events declined from 16.7% (95% CI 7.9-30.2%) to 1.6% (95% CI 0.3-4.8%), and inadvertent parathyroidectomy decreased from 23.8% (95% CI 12.0-39.5%) to 1.6% (95% CI 0.3-4.8%). Six-month PTH levels improved from 3.15 to 4.14 pmol/L, and lymph node yield increased from 9.9 to 13.3 ( $P = 0.019$ ). Three patients (0.6%) developed tracheal fistula. CONCLUSIONS: Robotic BABA thyroidectomy demonstrates a structured learning curve in which functional safety improves with surgical experience and intraoperative standardization. These data-driven milestones may inform structured training and credentialing frameworks for robotic thyroid surgery.

PubMed-ID: [41152529](#)

DOI: [10.1007/s00464-025-12331-x](#)

PMCID: PMC12823686

#### **Defining the ATA-2025 'consider RAIT' zone in older patients with N1b PTC.**

*Endocr Relat Cancer*, 33(1)

Z. Wang, X. Song, T. Wang, Y. Xie, Q. Du, W. Zhang, N. Liu, R. Li and J. He. 2026.

The aim of this study was to quantify the cancer-specific death (CSD) benefit of radioactive iodine therapy (RAIT) in older patients with N1b differentiated thyroid carcinoma, a population designated by the ATA-2025 guideline as a 'consider RAIT' zone despite unproven mortality benefit, and to translate this recommendation into clinically actionable subgroups using a competing-risks framework. We used data from the Surveillance, Epidemiology, and End Results (SEER) programme (2004-2015) and analysed papillary thyroid carcinoma (PTC) cases aged  $\geq 55$  years with N1b, M0. After 1:1 propensity score matching, cumulative incidence function and Fine-Gray models evaluated associations between RAIT and CSD. Stratifications included tumour size, positive lymph node burden (PLN  $> 5$ ), and ETE. A nomogram was developed for 1-, 3-, and 5-year CSD prediction, and absolute risk reduction (ARR) and number needed to treat (NNT) were estimated. Among 1,142 patients, 648 were matched ( $n = 324$ /group; median follow-up = 69 months). Five-year CSD was 14.1% without RAIT versus 5.1% with RAIT ( $P = 0.001$ ), yielding ARR approximately 9% and NNT approximately 11. RAIT was independently protective (SHR 0.33, 95% CI: 0.14-0.76). Benefit concentrated in tumours 2-4 cm, PLN  $> 5$ , and ETE-positive strata. The nomogram showed strong discrimination and calibration. In patients aged  $\geq 55$  years with N1b PTC, RAIT confers measurable mortality benefit, most evident in 2-4 cm, PLN  $> 5$ , or ETE-positive disease. Integrating ARR, NNT, and a validated nomogram, this study converts the conceptual 'consider RAIT' into clinically actionable 'RAIT-favoured' and 'RAIT-optional' pathways.

PubMed-ID: [41543025](#)

DOI: [10.1530/ERC-25-0420](#)

PMCID: PMC12910568

### **Risk Analysis Index Outperforms the Modified Frailty Index in Predicting Outcomes in Thyroidectomy and Parathyroidectomy.**

*Otolaryngol Head Neck Surg*, 174(3):705-14.

A. Warriar, S. Ranganathan, D. Montgomery, J. Tawil, A. Istambouli, C. Bowers, R. K. Gurgel and H. McCrary. 2026.

**OBJECTIVE:** In an aging population, patients undergoing thyroidectomy and parathyroidectomy are at an increased risk of adverse outcomes; thus, measuring patient frailty is a key metric to assess risk. This study innovatively compares the utility of the Risk Analysis Index (RAI) with the 5-factor Modified Frailty Index (mFI-5) in predicting adverse postoperative outcomes. **STUDY DESIGN:** Retrospective cohort. **SETTING:** US hospitals. **METHODS:** Patients undergoing thyroidectomy or parathyroidectomy procedures were selected from the 2005 to 2020 NSQIP data set. RAI and mFI-5 frailty scores were calculated and stratified: non-frail (RAI: <21/mFI-5: <1), pre-frail (RAI: 21-30/mFI-5: 1), frail (RAI: 31-40/mFI-5: 2), and severely frail (RAI: 40+/mFI-5: 3-5) categories. Univariate and multivariate analyses were conducted, followed by receiver operating characteristic (ROC) curves, to evaluate the comparative discriminative thresholds of the indices. **RESULTS:** A cohort of 30,362 patients was identified with a median age of 56 years. Multivariate odds ratios showed that both indices were significant independent predictors of mortality (RAI: 15.508,  $P < .001$ ; mFI-5: 10.713,  $P < .001$ ), extended length of stay (eLOS) (RAI: 9.480,  $P < .001$ ; mFI-5: 7.952,  $P < .001$ ), non-home discharge (RAI: 15.897,  $P < .001$ ; mFI-5: 9.346,  $P < .001$ ), and Clavien-Dindo (CD) II complications (RAI: 7.130,  $P < .001$ ; mFI-5: 3.760,  $P < .001$ ). ROC analysis demonstrated significantly superior discrimination by the RAI for mortality (0.769 vs 0.650,  $P = .022$ ), eLOS (0.712 vs 0.596,  $P < .001$ ), non-home discharge (0.763 vs 0.639,  $P < .001$ ), CD II (0.739 vs 0.566,  $P < .001$ ), CD IIb (0.644 vs 0.587,  $P = .002$ ), CD IV (0.707 vs 0.622,  $P < .001$ ), and organ/space infection (0.719 vs 0.519,  $P < .001$ ). **CONCLUSION:** Both the RAI and mFI-5 frailty indices are comparable, significant predictors of adverse events in thyroidectomy/parathyroidectomy. The RAI demonstrated superior discrimination for predicting postoperative morbidity across most outcomes, indicating it may be a superior clinical tool for identifying high-risk patients. The RAI may better inform perioperative decision-making, patient counseling, and resource allocation.

PubMed-ID: [41553036](#)

DOI: [10.1002/ohn.70125](#)

PMCID: PMC12948393

### **Identifying Failure Predictors in Thyroid Nodule Radiofrequency Ablation Using Multivariate Analysis: A Single-Centre Experience.**

*Clin Endocrinol (Oxf)*, 105(1):85-92.

S. Wechsler, T. Shcherbaeva, J. Pitaro and L. M. Kalmovich. 2026.

**BACKGROUND:** Radiofrequency ablation (RFA) has become an established minimally invasive treatment for benign thyroid nodules (BTN), offering excellent safety and efficacy. However, factors predicting treatment success and post-procedural thyroid dysfunction remain incompletely understood. This study aimed to perform a preliminary evaluation of clinical, procedural, and biochemical predictors of RFA outcomes in a real-world consecutive patient cohort. **STUDY DESIGN AND METHODS:** A retrospective analysis was conducted on consecutive patients who underwent ultrasound-guided RFA for cytologically benign thyroid nodules between January 2018 and March 2024 at a single tertiary medical centre.

Demographic, sonographic, procedural, and biochemical variables, including thyroid-stimulating hormone (TSH), thyroglobulin (Tg), and anti-Tg antibodies, were analysed. The primary endpoint was the Volume Reduction Ratio (VRR), with  $\geq 50\%$  defined as procedural success. **RESULTS:** Sixty-two patients (mean age 52.6 years; 85.5% female) were included. The median best VRR achieved was 61.9% (IQR 46.6-74.5), with 71% of patients attaining  $\geq 50\%$  reduction. Higher pre-treatment Tg levels were significantly associated with reduced VRR ( $p < 0.001$ ) and remained independently associated with procedural failure in an exploratory multivariable model (OR 0.87 per 10 ng/mL increase,  $p = 0.011$ ).

Pretreatment TSH levels showed a univariate positive trend but did not reach statistical significance on multivariate analysis. Two patients (3.2%) developed hypothyroidism post-RFA, both with positive anti-Tg antibodies (total 13 patients had positive anti Tg Ab). The overall complication rate was 6.5%, with no major adverse events. **CONCLUSIONS:** Our results suggest that pre-treatment thyroglobulin levels may serve as a potential biochemical predictor of RFA success in benign thyroid nodules, while antibody positivity may suggest susceptibility to post-ablation hypothyroidism. While most existing literature focuses on imaging features (e.g., sonographic features) or surgeon technique, our findings highlight the unique importance of biochemical characteristics. Incorporating biochemical profiling into pre-procedural assessment could refine patient selection and enhance individualised treatment planning. Future prospective studies are warranted to validate Tg as a biomarker of RFA response.

PubMed-ID: [41797266](#)

DOI: [10.1111/cen.70125](#)

**Deep learning habitat radiomics based on ultrasound for predicting preoperative locally progression and postoperative recurrence risk of thyroid cancer: a multicenter study.**

*Int J Surg*,

L. Wenwu, Z. Di, W. Wei, D. Wenbo, W. Xin, X. Xiang, C. Weibo, W. Tao, H. Song, L. Boyuan, Z. Wang and Z. Chaoxue. 2025. BACKGROUND: Locally advanced thyroid cancer (LATC), characterized by lymph node metastasis or extrathyroidal extension, is associated with increased surgical complexity and worse prognosis compared to intrathyroidal cancer (ITC). Accurate preoperative identification of LATC is critical for optimizing surgical and postoperative management. This study aimed to develop a deep learning-based habitat radiomics (DLH) model using ultrasonographic features to predict LATC and assess recurrence risk. METHODS: A retrospective cohort of 1881 thyroid cancer patients from nine medical centers. 1383 patients from eight centers were divided into a training cohort and an internal test cohort at a 7:3 ratio, while 498 patients from the remaining center served as the external test cohort. An additional prospective cohort of 130 patients serving as validation. The inclusion criteria required preoperative ultrasound examination and postoperative pathological confirmation of thyroid cancer, with exclusion of cases lacking complete clinical data. Patients were classified as LATC or intrathyroidal cancer based on postoperative pathology. Ultrasound tumor regions were manually segmented, and intratumoral subregions were delineated using K-means clustering to capture spatial heterogeneity. Peritumoral regions were generated by isotropic expansion of tumor regions of interest (ROIs). Radiomic features from intra- and peritumoral regions were used to train the DLH model. A clinical-radiomic nomogram incorporating DLH and clinical variables was constructed. Model performance was assessed using area under the curve (AUC), and recurrence-free survival (RFS) was evaluated via Kaplan-Meier and Cox regression analyses. RESULTS: DLH was an independent predictor for both RFS and LATC ( $P < 0.05$ ). The nomogram achieved robust performance in preoperative LATC identification (AUC: 0.852 in the internal test cohort and 0.897 in the external test cohort). Cox regression identified DLH, tumor size, surgical approach, and lymph node metastasis count as significant RFS predictors. CONCLUSION: Our multicenter model effectively predicts LATC and RFS based on routine ultrasound, with potential to guide individualized treatment planning. Further validation in diverse clinical settings and longer follow-up are warranted.

PubMed-ID: [41363706](#)

DOI: [10.1097/JS9.0000000000004415](#)

**Vitamin D Supplementation to Prevent Post-Thyroidectomy Hypocalcemia.**

*Clin Endocrinol (Oxf)*, 105(2):259-66.

J. I. A. Willems, D. J. L. van Twist, K. M. Pickwell, P. L. H. van Battum, R. Bianchi, A. M. Pijnenburg, J. van Bastelaar, M. Medici, R. P. Peeters and R. F. A. Tummers-de Lind van Wijngaarden. 2026.

OBJECTIVE: Hypocalcemia is the most common complication following thyroidectomy. Previous studies yielded inconsistent results on whether vitamin D(3) prevents postoperative hypocalcemia and were conducted in non-European countries with different dietary habits and baseline vitamin D levels. Therefore, we explored the effect of preoperative vitamin D(3) on post-thyroidectomy hypocalcemia in a Dutch cohort. METHODS: Patients undergoing thyroidectomy between 2023 and 2025 received 100,000 IU vitamin D(3) 1 week before surgery ("vitamin D group") and were compared to a historical cohort (2019-2022) without vitamin D(3) supplementation ("control group"). Outcomes included incidence of hypocalcemia (albumin-adjusted calcium  $< 2.00$  mmol/L), need for postoperative supplementation, time until normocalcemia, length of hospital stay, and readmissions. RESULTS: Fifty patients received preoperative vitamin D(3) and were compared to 154 controls (82.8% female, median age: 55 years [IQR: 43-66]). Vitamin D(3) supplementation was associated with a reduced risk of biochemical hypocalcemia at all postoperative time points (OR 0.28, 95% CI: 0.11-0.68,  $p = 0.005$ ), corresponding to a number needed to treat of five patients to prevent one case of hypocalcemia. As compared to controls, the need for postoperative supplementation and time to recover from hypocalcemia were lower in the vitamin D group (32.0% vs. 53.9%,  $p = 0.007$ ; and 0 [0-2] vs. 3 [0-11] days,  $p = 0.002$ , respectively). No differences were observed in length of hospital stay or readmissions. CONCLUSIONS: Although larger randomized trials are needed to confirm these observations, preoperative vitamin D(3) was associated with a significant reduction in post-thyroidectomy hypocalcemia in this observational cohort study. Given its low costs, this intervention may be considered for routine implementation in thyroidectomy patients.

PubMed-ID: [42059053](#)

DOI: [10.1111/cen.70152](#)

PMCID: PMC13326965

**Lateral laryngeal ultrasound for vocal cord evaluation in neck surgery: A mutually double-blind comparative study with laryngoscopy.**

*Surgery*, 192:110074.

J. W. Woo, J. H. Lee, H. S. Lee, H. Suh and E. J. Jung. 2026.

**BACKGROUND:** Vocal cord dysfunction is a significant complication after thyroid surgery, typically evaluated with invasive laryngoscopy. This study assessed diagnostic accuracy and feasibility of lateral laryngeal ultrasound as a noninvasive alternative. **METHODS:** In a prospective, double-blind study at Gyeongsang National University Changwon Hospital (February 2016 to June 2023), 718 patients underwent preoperative and postoperative vocal cord assessment using laryngoscopy and lateral laryngeal ultrasound. Both patients and assessors were blinded to the counterpart modality. Sensitivity, specificity, and visualization rates were analyzed. **RESULTS:** Lateral laryngeal ultrasound visualized vocal cords in 99.6% of cases (715/718), with 100% sensitivity and 99.5% specificity for detecting vocal cord paralysis compared with laryngoscopy. No adverse effects were reported. **CONCLUSIONS:** Lateral laryngeal ultrasound is a reliable, noninvasive tool for perioperative vocal cord evaluation, offering a patient-friendly alternative that may reduce the need for laryngoscopy in thyroid surgery.

PubMed-ID: [41564746](#)

DOI: [10.1016/j.surg.2025.110074](#)

**Sensory changes in the chin and lower lip after transoral endoscopic thyroidectomy.**

*Surg Endosc*, 40(2):1572-80.

K. Woo, D. K. Lee, P. S. Chung and S. H. Woo. 2026.

**BACKGROUND:** Minimally invasive thyroid surgery offers cosmetic benefits over traditional approaches, but mental nerve injury risk affecting the chin and lower lip persists. Transoral endoscopic thyroidectomy within a defined safety zone is a scarless alternative that may cause transient sensory changes. **METHODS:** In this prospective observational study, 77 patients with benign thyroid conditions were enrolled; after exclusions, 37 underwent transoral endoscopic thyroidectomy and 40 underwent conventional transcutaneous thyroidectomy. Baseline chin and lower lip sensation was quantified preoperatively and postoperatively at 1 week, 1 month, and 2 months using a monofilament evaluator, measuring the area of sensory deficit at 1 mm intervals. The conventional group served as a control, as this approach is not associated with mental nerve injury. **RESULTS:** Baseline sensation was normal in both groups. The mean patient age was 32.5 +/- 8.9 years (53% female). Operative times were significantly longer in the transoral group. All 37 transoral patients experienced transient sensory disturbances immediately postoperatively. The area of sensory deficit decreased at 1 and 2 months compared with 1 week ( $p = 0.028$ ), and 5 of 37 patients achieved complete recovery by 2 months, while the remaining patients demonstrated progressive reduction in affected area. No sensory changes occurred in the conventional group at any time point. **CONCLUSIONS:** Transoral endoscopic thyroidectomy within a defined safety zone induces early transient sensory disturbances that improves or resolves by 2 months postoperatively. These findings support its use as a safe, cosmetically superior alternative to conventional thyroidectomy, with minimal long-term compromise to mental nerve integrity.

PubMed-ID: [41326731](#)

DOI: [10.1007/s00464-025-12407-8](#)

**On-demand l -thyroxine replacement therapy in post-lobectomy papillary thyroid cancer: a prospective nonrandomized controlled study.**

*Int J Surg*, 112(2):3467-73.

S. Xu, L. Liao, K. Xian, K. Wang, C. Xing, R. Liu, Z. Zhang, H. Guan and J. Liu. 2026.

**BACKGROUND:** The necessity of thyrotropin (TSH) suppression therapy for papillary thyroid cancer (PTC) after lobectomy has been challenged. This study aims to evaluate on-demand l -thyroxine replacement therapy for post-lobectomy PTC. **METHODS:** This prospective study cohort included adult patients with low- to intermediate-risk PTC, who underwent lobectomy (2021-2023). l -Thyroxine supplementation was given after surgery only if serum TSH exceeded the upper limit of the reference range ( $>5.91$  mU/L). Retrospective controls were selected from the institute database (2000-2014) after being matched with prospective patients and treated according to the guideline (TSH, 0.5-2 mU/L). The primary endpoint was prognosis, including structural recurrence and biochemical response. The secondary endpoint was the euthyroidism rate without thyroxine. The Kaplan-Meier curve was used to estimate recurrence-free survival (RFS) and euthyroidism rates, and compared using the log-rank test. **RESULTS:** Among 381 patients who were enrolled in the present study (median age 39 years, 70.6% female), no new cases were detected requiring l -thyroxine for elevated TSH at greater than year post surgery. In the prognostic evaluation, 333 cases were included, with a mean follow-up of 17 months, and 72.3% never underwent l -thyroxine supplementation. Comparison with the historical control group was conducted in 204 pairs

of cases. No significant difference was observed in either 2-year RFS (test group vs. control group, 99.4% vs. 98.5%,  $P = 0.917$ ) or biochemical responses among patients with negative thyroglobulin (Tg) antibody (rate of patients with increasing Tg, 21.6% vs. 21.6%,  $P > 0.05$ ). CONCLUSIONS: On-demand l-thyroxine replacement therapy benefit three-fourths of post-lobectomy low- to intermediate-risk PTC patients avoid l-thyroxine supplementation, while preserving equivalent short-term treatment response and RFS.

PubMed-ID: [41208784](#)

DOI: [10.1097/J9.0000000000003905](#)

### **Surgical efficiency, safety, and quality of life among four various approaches for T1 stage papillary thyroid carcinoma: a prospective cohort study.**

*Surg Endosc*, 40(3):1984-98.

T. Xu, X. Zheng, Y. Fan, G. Yang, A. Su, X. Wang, W. W. Hu and T. Wei. 2026.

OBJECTIVE: This study aims to comprehensively evaluate surgical efficiency and quality of life (QoL) differences among Conventional open thyroidectomy (COT), gasless endoscopic thyroidectomy trans-axillary approach (GETTA), transoral endoscopic thyroidectomy vestibular approach (TOETVA), and endoscopic thyroidectomy via bilateral-areolar approach (ETBAA) in T1 papillary thyroid carcinoma (T1-PTC) patients. STUDY DESIGN: Prospective observational cohort study. SETTING: Tertiary academic center. METHODS: 463 female patients with T1-PTC were stratified into four cohorts: GETTA ( $n = 122$ ), TOETVA ( $n = 108$ ), COT ( $n = 128$ ), and ETBAA ( $n = 105$ ). Perioperative time periods were divided into five parts for analysis. Level VI lymph node dissection was routinely performed, and the yield is reported. QoL was assessed using Voice Impairment Score (VIS), Swallowing Impairment Score (SIS), Scar Cosmesis Assessment and Rating (SCAR-Q), European Organization for Research and Treatment of Cancer QoL Questionnaire-Core 30 (EORTC QLQ-C30), and Symptom Checklist-90 (SCL-90). Longitudinal QoL trends were evaluated during postoperative recovery. RESULTS: Significant intergroup disparities were observed in surgical efficiency ( $P < 0.001$ ); COT demonstrated superior time efficiency. All cohorts experienced transient postoperative QoL declines, with endoscopic groups showing accelerated recovery trajectories in physical, psychological, and cosmetic domains ( $P < 0.001$ ). CONCLUSION: Four techniques are safe and effective. COT remains the most time-efficient approach, while TOETVA excels in cosmesis. GETTA and ETBAA offer intermediate advantages, combining reasonable efficiency with enhanced recovery profiles. Clinical decision-making should prioritize patient-specific factors, including cosmetic preferences and recovery priorities.

PubMed-ID: [41350787](#)

DOI: [10.1007/s00464-025-12437-2](#)

### **Clinical Significance of Successful Ablation in Follicular Thyroid Carcinoma.**

*J Clin Endocrinol Metab*, 111(1):84-92.

H. Yamazaki, K. Sugino, R. Katoh, K. Matsuzu, W. Kitagawa, M. Nagahama, A. Saito and K. Ito. 2025.

CONTEXT: Outcomes of postoperative ablation focused on follicular thyroid carcinoma (FTC) have not been fully investigated. OBJECTIVE: The purpose of this study is to investigate the clinical characteristics of patients with FTC who received postoperative ablation, the predictive factors for successful ablation, and the association between successful ablation and the clinical outcomes of FTC. PATIENTS: The study included 428 patients with FTC (216 in ablation group and 212 in observation group). A multivariate logistic regression model was used to identify factors independently associated with successful ablation. RESULTS: Patients in the ablation group were significantly older ( $P < .001$ ), had a higher prevalence of widely invasive-FTC histology ( $P < .001$ ), had vascular invasion  $\geq 2$ , and had a higher rate of antithyroglobulin antibody positivity ( $P = .007$ ) than patients in the observation group. Among the 116 patients with postoperative ablation following diagnostic I-131 scintigraphy, 65 (56%) achieved successful ablation. In the multivariate analysis, the thyroglobulin level at ablation was the only independent predictor of successful ablation (odds ratio 0.952; 95% CI 0.909-0.996;  $P = .034$ ). Among the ablation group, the 10-year cause-specific survival (CSS) rates of patients with ( $n = 65$ ) and without successful ablation ( $n = 151$ ) were 100% and 98.4% ( $P = .246$ ), respectively. None of the patients with successful ablation died during the follow-up period. The 10-year distant-metastasis-free survival (DMFS) rates of patients with and without successful ablation were 100% and 81.7% ( $P < .001$ ), respectively. None of the patients with successful ablation experienced distant metastatic recurrence during the follow-up period. CONCLUSION: Patients with FTC with successful ablation achieved excellent 10-year CSS and DMFS rates of 100%. Therefore, careful follow-up may be unnecessary for these patients even if they have negative prognostic factors.

PubMed-ID: [40464652](#)

DOI: [10.1210/clinem/dgaf326](#)

**Understanding the Factors That Influence Shared-Decision Making Around Surgical Resection of Low-Risk Thyroid Cancers: A Prospective Qualitative Study.**

*Thyroid*, 36(1):81-8.

W. Yang, O. Skan, S. N. Rogers, S. Wheelwright and D. S. Kim. 2026.

**BACKGROUND:** International guidelines now recommend adopting individualized approaches which consider patient preferences when deciding the extent of surgical resection for low-risk differentiated thyroid carcinoma (LRDTC). Information-sharing must be methodical to help patients make informed decisions without feeling overwhelmed by information. Understanding the factors influencing decision-making is therefore essential. **METHODS:** Semi-structured interviews were conducted between May 2023 and June 2024 at two large tertiary referral centers in England, United Kingdom. Consecutive sampling via the multidisciplinary team meetings was used to identify patients newly diagnosed with LRDTC measuring 1-4 cm without adverse features, choosing between hemithyroidectomy and total thyroidectomy, or, if diagnosed following hemithyroidectomy, active surveillance and total thyroidectomy. Clinicians directly involved in their care were approached and recruited, with six consultant thyroid surgeons (five male, one female), and two thyroid cancer nurse specialists (both female), agreeing to participate. All had experience managing over 10 LRDTC patients annually. Transcripts were analyzed using the framework method of thematic analysis. **RESULTS:** Twenty-four patients were identified, and 19 agreed to participate (13 female, 6 male). Information-sharing was often perceived as a didactic process, leaving patients overwhelmed with complex clinical details. Both groups emphasized tailoring information to meet patients' needs and delivering it in bite-sized portions to enhance comprehension. Key factors influencing individual decisions included a desire among most patients to minimize the number of, and extent of, surgical procedures, the need to preserve the thyroid gland and avoid hormone supplementation, and the patient's ability to accept the cancer recurrence risk. Although autonomy was paramount for patients, providers' recommendations still significantly impacted the final decision. Some clinicians expressed concern that multiple treatment options might confuse patients, instead entrusting decision-making to the multidisciplinary team meetings. **CONCLUSIONS:** This study identified essential information needs for LRDTC treatment decision-making, which can help inform the development of decision-support tools. Multidisciplinary team discussions may need to evolve to allow greater flexibility and support individualized decision-making.

PubMed-ID: [41467962](#)

DOI: [10.1177/10507256251408856](#)

**Omitting Radioactive Iodine after Therapeutic Lateral Neck Dissection May Be the Next Step in De-Escalating Initial Treatment of Papillary Thyroid Cancer.**

*Thyroid*, 36(1):1-2.

M. W. Yeh. 2026.

PubMed-ID: [41916262](#)

DOI: [10.1177/10507256251408734](#)

**A Study of Time to Recovery Following Loss of Neuromonitoring Signal of the Recurrent Laryngeal Nerve in Thyroid Surgery.**

*World J Surg*, 50(3):660-7.

J. Yu, R. Ragavan, C. Nysten, A. Aniss, S. Sidhu, A. Papachristos, D. Novakovic, T. Stewart, K. Ng, H. Ozoran and M. Sywak. 2026.

**BACKGROUND:** Injuries of the recurrent laryngeal nerve (RLN) during thyroidectomy although infrequent can lead to major morbidity. Permanent RLN injury is uncommon; however, temporary neurapraxia and loss of signal (LOS) during intraoperative neuromonitoring (IONM) are seen more frequently. This study aimed to identify factors associated with type I (segmental) and II (global) LOS of the RLN during thyroid surgery and to analyze time to recovery of vocal cord function. **METHODS:** This observational retrospective cohort study included 3806 patients (2924 female, 76.8% and 882 male, 23.2%) who underwent hemi or total thyroidectomy in a tertiary center between January 2015 and March 2021. Regression analyses determined factors associated with LOS. Postoperative fiberoptic laryngoscopy was used to measure time to recovery of vocal cord function. **RESULTS:** RLN LOS occurred in 167 (2.7%) of 5983 nerves at risk during surgery. The rate of Type I and Type II LOS per nerve at risk was 1.4% and 1.3%, respectively. Compared with an indication of malignancy, toxic nodule was associated with 96% increased odds of LOS independent of age and sex ( $P < 0.001$ ). Time to recovery was reduced for those with a Type II LOS (median 4 weeks) compared to Type I LOS (median 8 weeks and  $p = 0.04$ ). Female sex and increasing age were independently associated with a longer duration to return of vocal cord function. **CONCLUSIONS:** Time to recovery of RLN function is significantly reduced for patients with Type II LOS. Toxic thyroid nodules were associated with a higher risk of LOS, and female sex and age are significantly associated with a

longer time to recovery.  
PubMed-ID: [41697196](#)  
DOI: [10.1002/wjs.70254](#)  
PMCID: PMC13006785

**Intraglandular Dissemination Is a Risk Factor for Lymph Node Metastasis and Recurrence in Papillary Thyroid Carcinoma: A Propensity Score Matching Analysis.**

*Head Neck*, 48(3):665-79.

T. Yu, Z. Liu, J. Ma, P. Su, X. Ji, N. Liu, C. Ding, Z. Yang, W. Liang and B. Lv. 2026.

BACKGROUND: Intraglandular dissemination (ID) is an important clinicopathological feature, but the statistical evidence of its relationship with lymph node metastasis (LNM) and the prognosis of papillary thyroid carcinoma (PTC) has not been widely reported in the literature. The purpose of this study was to investigate the potential correlation between ID, LNM, and prognosis in PTC patients. METHODS: Patients with PTC were retrospectively collected from Qilu Hospital of Shandong University from 2017 to 2019 and categorized into two groups based on postoperative routine pathology: intraglandular dissemination group (ID group) and the non-intraglandular dissemination group (NID group). The propensity score matching (PSM) was used to analyze and compare the differences in LNM and prognosis between groups. RESULTS: Among the 2845 patients included in the study, 6.85% had ID. After PSM matching, ID was associated with an increased risk of LNM (OR: 2.143, 95% CI: 1.279-3.591,  $p = 0.004$ ) and recurrence in PTC patients (HR: 6.585, 95% CI: 1.782-24.335,  $p = 0.005$ ). Kaplan-Meier curves showed that the recurrence-free survival (RFS) of the ID group before and after PSM was worse than that of the NID group (95.3% vs. 99.0%,  $p < 0.001$ ; 95.0% vs. 99.0%,  $p = 0.011$ ). CONCLUSION: ID is an independent risk factor for LNM (includes microscopic metastasis) and postoperative recurrence in PTC patients. The recurrence rate of ID-PTC patients with markers of aggressive disease is higher than that of ID-PTC patients alone. Patients with ID-PTC require more intensive follow-up to monitor for recurrence. The necessity of more extensive lymph node dissection for these patients may need to be validated by future multi-center, prospective studies.

PubMed-ID: [41059576](#)

DOI: [10.1002/hed.70058](#)

**Glucagon-like peptide-1 receptor agonists & thyroid cancer: What thyroid surgeons should know.**

*Am J Surg*, 257:116975.

L. Yuan and S. M. Wiseman. 2026.

PubMed-ID: [41990629](#)

DOI: [10.1016/j.amjsurg.2026.116975](#)

**A commentary on "Long-term outcomes of robotic vs. open thyroidectomy for differentiated thyroid cancer: efficacy, safety and quality of life".**

*Int J Surg*, 112(4):10870-1.

B. Zhang, W. Li and J. H. Cao. 2026.

PubMed-ID: [41537366](#)

DOI: [10.1097/JS9.0000000000004667](#)

PMCID: PMC13105533

**Fibrosis-Driven Surgical Risk After Thyroid Nodule Ablation: Quantitative Clinicopathological Determinants of Complications in Post-Ablative Thyroidectomy-A Retrospective Cohort Study.**

*World J Surg*, 50(4):914-23.

D. Zhang, A. Boero, G. Gazzano, A. Satta, L. Fugazzola, C. Colombo, F. Brucchi and G. Dionigi. 2026.

BACKGROUND: Thermal ablation is increasingly used for selected benign and low-risk thyroid nodules, yet some patients still require thyroidectomy for regrowth, persistent symptoms, or new oncologic concern. The surgical and pathological impact of ablation-induced remodeling remains incompletely defined. We aimed to characterize postablation thyroidectomy outcomes and identify histological correlates of perioperative morbidity. METHODS: We conducted a single-center retrospective cohort study of patients undergoing thyroidectomy after radiofrequency or ethanol ablation (2021-2025). Clinical and ablation-related variables were collected, and intraoperative neuromonitoring was routinely used. Primary outcomes were recurrent laryngeal nerve (RLN) palsy, reoperative hematoma, and hypoparathyroidism. Surgical specimens underwent blinded dual-pathologist assessment with semiquantitative scoring of sclerosis, necrosis, and residual viability, from which a maturation index was derived. Associations with complications were analyzed using nonparametric methods. Outcomes were descriptively compared with a contemporaneous nonablated cohort for

contextual purposes. RESULTS: Thirty-one patients were included. Postoperative complications occurred in 22.6% of ablated cases. Histological analysis demonstrated moderate sclerosis (19.2%), necrosis (14.6%), and high residual viability (66.1%), with frequent pericapsular inflammatory changes and preserved capsule integrity. Sclerosis was the only parameter significantly associated with postoperative complications (30.0% vs. 16.9% and  $p = 0.008$ ), whereas nodule size, ablation-to-surgery interval, and incidental carcinoma were not predictive. The maturation index increased with time after ablation but did not discriminate complication risk. Exploratory fibrosis-weighted metrics suggested potential risk thresholds, although these findings remain hypothesis-generating given the limited sample size. CONCLUSIONS: Thyroidectomy after prior ablation is feasible in experienced centers but may be technically demanding and associated with modestly increased procedural complexity. Mature sclerosis represents the principal histological correlate of perioperative morbidity, linking fibrotic remodeling to operative risk. These findings support centralization of postablation thyroid surgery in high-volume units with routine neuromonitoring and specialized pathology and highlight the need for larger prospective studies to validate fibrosis-based risk stratification tools.

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DOI: [10.1002/wjs.70300](#)

PMCID: PMC13070446

### **Standardizing cervical lymph node evaluation in papillary thyroid carcinoma: diagnostic accuracy of Node-RADS on ultrasound.**

*Front Endocrinol (Lausanne)*, 17:1709522.

H. Zhang, D. He, M. Mao, R. Li, T. Yin, B. W. Zheng, J. Zheng, T. Wu, J. Ren and Z. Xu. 2026.

OBJECTIVES: To assess the diagnostic performance of the Node Reporting and Data System (Node-RADS) in ultrasonographic evaluation of cervical lymph node (LN) metastasis in papillary thyroid carcinoma (PTC) and compare it with conventional suspicious sonographic features. MATERIALS AND METHODS: This retrospective study included 227 PTC patients (269 LNs) who underwent preoperative cervical LN ultrasound and biopsy (September 2022-December 2023). Two radiologists independently assigned Node-RADS scores (1-5) based on LN size and morphologic features (shape, border, echogenicity). Diagnostic performance was evaluated using ROC analysis, with histopathology as the reference standard. Node-RADS was compared to five American Thyroid Association (ATA)-defined suspicious features (microcalcifications, cystic changes, etc.). Multivariable analysis assessed an integrated model combining Node-RADS with peripheral vascularity. RESULTS: Metastatic LNs (63.9%, 172/269) exhibited higher Node-RADS scores (malignancy rates: 35.7% for score 1 vs. 88.2% for score 5). Node-RADS achieved an AUC of 0.720 (95% CI: 0.662-0.773), surpassing individual features (best AUC: 0.703 for peripheral vascularity). Inter-reader agreement was good ( $\kappa = 0.67$ ). A combined Node-RADS and peripheral vascularity model significantly improved diagnostic performance (AUC: 0.825,  $p < 0.01$ ). CONCLUSIONS: Node-RADS offers standardized, reproducible risk stratification for cervical LN metastasis in PTC, with moderate diagnostic accuracy. Integration with peripheral vascularity enhances performance, supporting its potential clinical utility in preoperative assessment.

PubMed-ID: [41685242](#)

DOI: [10.3389/fendo.2026.1709522](#)

PMCID: PMC12890614

### **Chinese language patients' perceptions on thyroid disease and treatment: A qualitative study.**

*Am J Surg*, 254:116842.

J. Zhang, J. J. Wong, T. Peng, Y. V. Mao, E. G. Hughes, A. M. Sawka, M. J. Livhits, M. W. Yeh and J. X. Wu. 2026.

BACKGROUND: Chinese language speakers comprise a significant proportion of the United States patient population. This qualitative study seeks to characterize health beliefs among Chinese-speaking patients with thyroid disease to inform culturally competent care. METHODS: Thirteen Chinese-speaking patients (mean age 47; 12 female) participated in semi-structured interviews exploring beliefs about thyroid disease and its management. RESULTS: Participants reported limited knowledge of thyroid disease and desired more accessible education. Thyroid disease was viewed as minimally disruptive relative to other diseases or malignancies with family history, environmental exposures, and stress as contributors to development. Experiences with conventional thyroid treatment were marked by logistical and relational challenges. While modern medicine was seen as effective, some perceived it to be overly aggressive and believed Traditional Chinese Medicine (TCM) may have a valuable, complementary role in management. CONCLUSIONS: Future research may seek to investigate the integration of TCM and conventional thyroid care to improve therapeutic relationships and health outcomes for Chinese-language patients.

PubMed-ID: [41619347](#)

DOI: [10.1016/j.amisurg.2026.116842](#)

**A comparative study of transoral and submental versus vestibular endoscopic thyroidectomy in patients with papillary thyroid carcinoma.**

*Surg Endosc*, 40(1):512-8.

Y. Zhang, H. Hu, J. T. Tan, T. J. Yao and L. Y. Qian. 2026.

**BACKGROUND:** Transoral endoscopic thyroidectomy vestibular approach (TOETVA) is widely adopted for its cosmetic advantage but is associated with postoperative oral discomfort and mental nerve injury. This study aimed to evaluate whether a modified technique, transoral and submental endoscopic thyroidectomy (TOaST), improves perioperative outcomes in patients with papillary thyroid carcinoma (PTC). **METHODS:** A retrospective study was conducted on 136 patients with PTC who underwent either TOaST (n = 51) or TOETVA (n = 85). Key outcomes included operative time, time to oral intake, postoperative pain, swallowing function, incidence of chin numbness, complications, and cosmetic satisfaction. **RESULTS:** TOaST was associated with shorter operative time (123.05 +/- 19.45 vs. 143.89 +/- 22.68 min,  $P < 0.001$ ), earlier oral intake (3.12 +/- 0.82 vs. 5.22 +/- 1.49 h,  $P < 0.001$ ), and lower pain scores at 24 and 48 h ( $P < 0.001$ ). Swallowing function on day 3 was better in the TOaST group ( $P < 0.001$ ). Chin numbness occurred in 17.6% of TOETVA patients but none in the TOaST group ( $P = 0.001$ ). Overall complication rates and cosmetic satisfaction were similar between the groups. **CONCLUSIONS:** TOaST demonstrates advantages in surgical efficiency, pain control, and early functional recovery without compromising aesthetic results, making it a favorable alternative to TOETVA in selected PTC patients.

PubMed-ID: [41145699](#)

DOI: [10.1007/s00464-025-12253-8](#)

**Surgical Optimization in Preoperatively Low-risk cN1a PTC: A Predictive Model for High-Volume Central Lymph Node Metastasis.**

*Ann Surg Oncol*, 33(2):1307-18.

Y. Zhou, Z. Guo, J. Long, H. Xu, M. Liang, Y. Hu, R. Li, Z. Ke, W. Chen and X. Xu. 2026.

**BACKGROUND:** Accurate preoperative identification of high-volume central lymph node metastasis (hv-CLNM; defined as more than 5 central lymph node metastases) is critical for guiding surgical decisions-lobectomy or total thyroidectomy-in patients with papillary thyroid carcinoma (PTC) clinically diagnosed with central neck lymph node metastasis (cN1a). Total thyroidectomy is generally preferred for patients with hv-CLNM. In contrast, lobectomy may be sufficient for patients with low-volume metastasis (5 or fewer lymph node metastases). This study aimed to identify predictors of hv-CLNM in preoperatively low-risk cN1a and to develop a predictive model to estimate the risk of hv-CLNM, thereby optimizing surgical decision-making. **METHODS:** A total of 707 patients with pathologically confirmed PTC and classified as preoperatively low-risk cN1a were retrospectively enrolled. Clinical and ultrasound features were collected. Variables were selected using least absolute shrinkage and selection operator regression, followed by multivariate logistic regression to construct a predictive model. Internal validation was performed. Recurrence-free survival was compared between lobectomy and total thyroidectomy groups using propensity score matching. **RESULTS:** Hv-CLNM occurred in 13.4% (96/707) of patients. Independent predictors of hv-CLNM included age, sex, tumor size, tumor location, and lymph node calcification. The nomogram demonstrated good discrimination (area under the plasma concentration-time curve = 0.75) and calibration. After adjustment, recurrence-free survival did not significantly differ between surgical groups. **CONCLUSIONS:** This nomogram, based on readily available clinical and ultrasound features, effectively predicts the risk of hv-CLNM in preoperatively low-risk cN1a PTC. This tool may facilitate individualized surgical planning. Lobectomy appears to be a safe and appropriate option for most patients in this subgroup.

PubMed-ID: [41125985](#)

DOI: [10.1245/s10434-025-18569-y](#)

PMCID: PMC12765736

**Comprehensive analysis of learning curve and surgical outcomes of endoscopic thyroidectomy for papillary thyroid carcinoma: a prospective study.**

*Langenbecks Arch Surg*, 411(1)

Y. Zhou, M. Jiang, Y. Zhang, Y. Cai, D. Zeng, W. Wang, X. Li, W. Deng, T. Liu and C. Li. 2026.

**BACKGROUND:** Endoscopic thyroid cancer surgery has been widely carried out in the world, however, the learning curve of the technique is undetermined due to a lack of prospective and large sample-size studies. This study aims to prospectively evaluate the learning curve of endoscopic thyroidectomy in papillary carcinoma from multidimension and assess the outcomes. **MATERIALS AND METHODS:** Data from 351 consecutive patients who underwent gasless transaxillary endoscopic thyroidectomy (GTET) were collected. Cumulative sum (CUSUM) analysis was applied to identify

the learning curve of the operation time, number of retrieved lymph node(LN) and weight of dissection lymphatic tissue (WDLT). The differences in surgical outcome, surgical trauma, parathyroid gland(PG) function protection and quality of life (QOL) between learning phases were analyzed. RESULTS: Females predominated (86.7%) with a mean age of 34 years. Postoperative pathology in most cases was T1 (98.6%) and N0 (70.9%). The transition points of the operation time, space building time, thyroidectomy with central neck dissection time, and number of retrieved LN were 110, 133, 91 and 205 patients respectively. According to the CUSUM curves, there were 3 phases in the learning: phase 1 (patients 1-110), phase 2 (patients 111-205), and phase 3 (from patients 206). There were significant differences in operation time, blood loss, recovery, WDLT, PG function protection, surgical trauma and short-term QOL among the phases. CONCLUSION: The learning curve identified in our study was divided into 3 stages. We indicated that GTET is safe and feasible for indication-based selected patients.

PubMed-ID: [41920361](#)

DOI: [10.1007/s00423-026-04020-7](#)

PMCID: PMC13167826

### **Risk factors and clinical courses of chylous fistula following lateral neck dissection: a decade-long cohort study in head and neck malignancies.**

*Eur J Surg Oncol*, 52(1):111191.

Y. Zhou, A. Wang, L. Ma, Y. Cai, X. Zhang, X. Wang, T. Liu, Y. Li, S. Dong, C. Shui, D. Zeng, S. Zhang, J. Jiang, R. Sun, S. Wang and C. Li. 2026.

INTRODUCTION: Chylous fistula (CF) is a serious complication after lateral (ND) in patients with head and neck malignancies. Due to the low incidence of this complication, its risk factors and clinical courses remain unclear. The aim of this study is to provide dependable results regarding these aspects through the largest sample size and comprehensive indicators. METHODS: A retrospective study was conducted at our hospital from 2014 to 2024. Univariate and multivariate regression analyses were used to identify the risk factors for CF. RESULTS: A total of 3819 consecutive neck dissections in 3733 patients were analyzed. The overall incidence of CF was 7.5 %. Logistic regression analysis revealed that alcohol use, poorly differentiated carcinoma, recurrence in lateral neck, retrieval of additional lateral lymph nodes (LNs), clinical extranodal extension (ENE) level IV and intraoperative identification of CF were independent risk factors. In subgroup analysis, alcohol use, recurrence in lateral neck, clinical ENE level IV and intraoperative identification of CF were independent risk factors for CF in papillary thyroid carcinoma, whereas retrieval of additional LNs of the lateral neck and surgical measures in the venous angle were more statistically significant in squamous cell carcinoma (SCC). The clinical courses of CF in the left neck and SCC were more severe. There were no independent risk factor for high-volume CF. CONCLUSION: The incidence of CF after ND in head and neck malignancies was higher than expected. The risk factors for CF included variations in the lymphatic system, patient-specific clinicopathological characteristics and surgical factors.

PubMed-ID: [41308400](#)

DOI: [10.1016/j.ejso.2025.111191](#)

### **Comparative study of surgical outcomes and quality of life between endoscopic and robotic thyroidectomy for differentiated thyroid cancer patients.**

*Int J Surg*,

Y. Zhou, B. Zhou, Y. Wang, X. Tan, X. Wu, G. Zhang, H. Tian, N. Sun, Y. Liu, C. Wang, X. Qi, L. Ren and Y. Zhang. 2025.

BACKGROUND: Robotic and endoscopic thyroidectomy have increasingly been performed for patients with differentiated thyroid cancer (DTC). However, the advantages of robotic surgery over endoscopic surgery remain enigmatic, hence, the controversy about which is the optimal minimally-invasive surgery is hotly debated. This study compared the surgical outcomes and health-related quality of life (HRQOL) between robotic and endoscopic thyroidectomy in DTC patients. METHODS: This study included 1,476 DTC patients, divided into endoscopic (n = 698) and robotic groups (n = 778). The patients were further subdivided into those undergoing total thyroidectomy (TT) and thyroid lobectomy (TL). Considering the differences in baseline characteristics among patients undergoing TL, propensity score matching (PSM) was performed. Intraoperative outcomes, postoperative outcomes, follow-up results, and HRQOL were compared between the two groups. RESULTS: The operation time was longer in the endoscopic group compared to the robotic group for both TT and TL ( $P < 0.05$ ). The robotic group also had a higher number of dissected lymph nodes, lower incidence of parathyroid gland mis-resection, and smaller changes in parathyroid hormone levels ( $P < 0.05$ ). For TT patients, the robotic group exhibited a lower incidence of transient and permanent hypoparathyroidism ( $P < 0.05$ ). Over 32 months of follow-up, there was a significant difference in postoperative serum thyroglobulin levels ( $1.70 \pm 3.50$  vs  $0.35 \pm 1.81$ ,  $P < 0.001$ ). One patient in the robotic group developed lung metastasis, while four experienced local or regional recurrence in the endoscopic group. Patients undergoing robotic TT reported significantly better thyroid cancer-specific QOL and less fear of

disease progression compared to those undergoing endoscopic TT. CONCLUSIONS: Robotic thyroidectomy offers significant advantages for DTC patients over endoscopic thyroidectomy, particularly in TT procedures.

PubMed-ID: [41403261](#)

DOI: [10.1097/JS9.0000000000004414](#)

## Parathyroids

### Meta-Analyses

#### **Quality of Life After Parathyroidectomy in Chronic Kidney Disease-Related Hyperparathyroidism: A Systematic Review and Meta-Analysis.**

*World J Surg*, 50(1):94-104.

W. Alves Filho, M. D'Elboux Guimaraes Brescia, F. F. Magnabosco, M. Catafesta das Neves, S. S. Arap, R. O. Santos, J. de Almeida Mota Ramalho, F. Luiz de Menezes Montenegro and M. R. Studart da Fonseca. 2026.

BACKGROUND: Secondary and tertiary hyperparathyroidism (SHPT and THPT) are frequent complications of chronic kidney disease and kidney transplantation, often impairing quality of life (QoL) through bone pain, fatigue, and pruritus.

Parathyroidectomy is the definitive treatment for refractory cases, yet its impact on patient-reported QoL outcomes remains uncertain. METHODS: We conducted a systematic review and meta-analysis in accordance with PRISMA

guidelines (PROSPERO CRD42025108038). Nine studies (n = 675) with validated QoL assessments and  $\geq 6$  months of follow-up were included. QoL was measured using SF-36, KDQOL, and Pasieka's parathyroid assessment of symptoms

(PAS). Standardized mean differences (SMDs) were calculated, with analyses of physical (PCS) and mental (MCS) component summary scores. Meta-regression evaluated preoperative parathyroid hormone (PTH), calcium, and

phosphorus as predictors of QoL change. RESULTS: Parathyroidectomy significantly improved global QoL (Hedges'  $g = 1.05$ ; 95% CI: 0.42-1.69;  $p = 0.0011$ ), PCS (SMD = 0.85; 95% CI: 0.32-1.37;  $p < 0.001$ ), and MCS (SMD = 0.40; 95% CI: 0.11-0.69;  $p = 0.001$ ).

PAS scores also improved (SMD = -1.66; 95% CI: -2.72 to -0.60;  $p = 0.004$ ). Preoperative PTH, calcium, and phosphorus were not associated with postoperative QoL gains ( $p = 0.71, 0.54, 0.47$ ).

Both subtotal and total parathyroidectomy provided comparable benefits ( $p = 0.76$ ). CONCLUSION: Parathyroidectomy leads to meaningful QoL improvements in CKD-related hyperparathyroidism, regardless of surgical technique. Baseline biochemical markers do not predict postoperative gains. Standardized, long-term studies of patient-reported outcomes are needed to guide surgical decision-making.

PubMed-ID: [41419434](#)

DOI: [10.1002/wjs.70211](#)

PMCID: PMC12831522

#### **Extent of Surgical Resection and Predictors of Outcomes in MEN1-related Hyperparathyroidism: A Systematic Review and Meta-analysis.**

*J Clin Endocrinol Metab*, 111(1):291-301.

W. Alves Filho, F. Filho, V. M. C. Morais, V. B. Goncalves, M. D. G. Brescia, F. L. M. Montenegro, C. B. d'Alva, A. R. P. Quidute and M. R. Studart da Fonseca. 2025.

CONTEXT: Primary hyperparathyroidism (PHPT) is the earliest and most frequent manifestation of multiple endocrine neoplasia type 1 (MEN1). The optimal surgical extent remains controversial due to the tradeoff between recurrence and permanent hypoparathyroidism. OBJECTIVE: To evaluate outcomes of different surgical approaches in MEN1-related PHPT

and assess preoperative biochemical predictors through systematic review and meta-analysis. DATA SOURCES: MEDLINE, PubMed, Embase.com, LILACS, and CENTRAL were searched from inception to April 2025, following PRISMA guidelines (PROSPERO: CRD420251027970). STUDY SELECTION: We included studies on adult MEN1-related PHPT patients

undergoing parathyroidectomy with reported recurrence, hypoparathyroidism, and preoperative biochemical data. DATA EXTRACTION: Two reviewers independently extracted data and assessed study quality. Random-effects models were used

to pool risk ratios (RR) with 95% confidence intervals (CI). Meta-regression evaluated associations with preoperative PTH, calcium, and phosphorus. DATA SYNTHESIS: Thirteen studies (915 patients) were included. Less-than-subtotal

parathyroidectomy (<STPT) had higher recurrence than subtotal parathyroidectomy (STPT) (RR = 1.26; 95% CI: 1.16-1.36) and total parathyroidectomy with autotransplantation (PTX) (RR = 1.35; 95% CI: 1.22-1.49). STPT showed slightly higher recurrence than PTX (RR = 1.12; 95% CI: 1.02-1.24). <STPT had lower hypoparathyroidism than STPT (RR = 0.90; 95% CI: 0.82-0.98) and PTX (RR = 0.76; 95% CI: 0.63-0.90). Grouping < STPT vs STPT/PTX confirmed higher recurrence (RR = 1.23; 95% CI: 1.03-1.46) and lower hypoparathyroidism (RR = 0.86; 95% CI: 0.78-0.96). No significant associations were found for preoperative PTH, calcium, or phosphorus with outcomes. CONCLUSION: Conservative surgery reduces hypoparathyroidism but increases recurrence. Personalized surgical strategies are essential in MEN1-related PHPT.

PubMed-ID: [40891326](#)

DOI: [10.1210/clinem/dgaf492](#)

#### **Diagnostic performance of AI-assisted intraoperative imaging for parathyroid identification: a systematic review.**

*Am J Surg*, 254:116853.

D. Gomez-Carrillo, R. Roy, A. Izhar, N. Swaminathan, H. Arain, J. Kasmirski, S. Dream, A. Gillis, B. Lindeman and H. Chen. 2026.

BACKGROUND: Intra-operative identification of parathyroid glands might be technically challenging and is a major source of hypocalcemia and nerve injury. Artificial-intelligence (AI)-based computer-vision systems have emerged as a potential adjunct. METHODS: A comprehensive search strategy was performed to identify studies using any machine-learning or deep-learning model for intraoperative parathyroid localization or viability assessment in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The protocol on PROSPERO: CRD420251104234. RESULTS: From 1124 records, 12 studies met inclusion criteria. Among the included studies, nine focused on localization of abnormal glands, while others addressed normal gland identification or perfusion assessment. AI systems utilized various imaging modalities including near infrared autofluorescence, red-blue-green surgical video, and indocyanine green angiography. These models have achieved high diagnostic accuracy, with most systems demonstrating >85% sensitivity and specificity for parathyroid identification. CONCLUSIONS: AI-driven systems demonstrate promising diagnostic performance for intraoperative parathyroid identification across multiple imaging modalities. Although results are encouraging, multicenter datasets, surgeon trust and workflow integration, and trials linking AI guidance to clinical outcomes are essential before routine adoption.

PubMed-ID: [41650512](#)

DOI: [10.1016/j.amisurg.2026.116853](#)

#### **Parathyroid hormone guided protocols for hypocalcemia management after thyroidectomy: A systematic review.**

*Am J Surg*, 251:116669.

R. Roy, N. Swaminathan, J. Kasmirski, S. ZhiXing, A. Babu, O. E. Anyagwa, A. Gillis, B. Lindeman, S. Dream and H. Chen. 2026.

INTRODUCTION: Hypocalcemia following total thyroidectomy remains a clinical challenge, often leading to preventable readmissions. Standardized PTH-based protocols offer a structured approach to postoperative management. This study examines institutional variations in such protocols and evaluates their effectiveness in minimizing unnecessary hospital visits. METHODS: A detailed search of published Parathyroid Hormone (PTH) based protocols at various institutions was conducted across Pubmed, Web of Science, Embase and Scopus. Variables such as mean hospital stay, PTH and calcium thresholds, supplementation guidelines, discharge criteria, ED visits and hospital readmissions were collected. This systematic review was PROSPERO registered with the ID CRD42024615865. RESULTS: Of 1178 studies screened, 10 met inclusion criteria. Most protocols recommended PTH measurement within 4 h postoperatively, without routine postoperative calcium testing. Risk stratification typically used thresholds of 10-15 pg/mL, with some adopting tiered PTH categories. Effective protocols avoided supplementation in low-risk patients while standardizing calcium carbonate (1000 mg TID) +/- calcitriol (0.25-0.5 mcg BID) for medium/high-risk patients. Severe or refractory hypocalcemia was managed with intravenous calcium +/- magnesium. Follow-up was typically within 1-4 weeks, with same-day discharge feasible in select low-risk patients. Reported readmission rates ranged from 0 to 7.0 %, with most <1 %. CONCLUSIONS: PTH-based protocols reduce readmissions after total or completion thyroidectomy by combining early PTH measurement, defined risk thresholds, selective supplementation, and timely follow-up. Adoption of these shared components across institutions could minimize unnecessary supplementation, improve safety, and standardize care.

PubMed-ID: [41151297](#)

DOI: [10.1016/j.amisurg.2025.116669](#)

#### **Preoperative 25(OH)D>=75 Nmole/L is associated with a reduced risk of hypocalcemia after parathyroidectomy: evidence from a meta-analysis.**

*Int J Surg,*

Y. Yu, F. Xu, D. Dai, Y. Ding, R. Sun, Y. Ling, L. Qiu, A. Xiong, X. Cai and Z. Xie. 2025.

**IMPORTANCE:** Postoperative hypocalcemia is a significant complication in patients with primary hyperparathyroidism (PHPT) after parathyroidectomy. While vitamin D supplementation is a commonly used as a preventive strategy, the optimal preoperative 25-hydroxyvitamin D [25(OH)D] level for this population remains unclear. Some guidelines recommend 25(OH)D >75 nmol/L as the optimal threshold, while others suggest that correcting vitamin D deficiency, typically defined as achieving levels above 50 nmol/L, is sufficient. **OBJECTIVES:** This meta-analysis aimed to determine whether preoperative 25(OH)D levels  $\geq$ 50 nmol/L or  $\geq$ 75 nmol/L are necessary to reduce the risk of hypocalcemia in PHPT patients after parathyroidectomy, in order to provide information for evidence-based prevention strategies. **DATA SOURCES:** PubMed, Embase, Web of Science, Scopus and the Cochrane Library were systematically searched from inception to December 2024, without language restrictions. **STUDY SELECTION:** Eight observational studies (N = 4,120) met the inclusion criteria of 1917 initially identified records. **DATA EXTRACTION AND SYNTHESIS:** Two investigators independently extracted data from eligible studies, including characteristics of study design, preoperative baselines of 25(OH)D levels, calcium and PTH levels, postoperative calcium levels, and hypocalcemia outcomes. The meta-analysis was conducted by the inverse variance model. Risk Ratio (RR) were used for dichotomous outcome event, standardized mean difference (SMD) was calculated for continuous data. Data was presented with 95% confidence interval (CI). The I<sup>2</sup> index was used for heterogeneity assessment. **RESULTS:** PHPT patients with preoperative 25(OH)D levels 50-75 nmol/L showed no significant reduction in hypocalcemia risk compared to those <50 nmol/L (RR 0.65, 95% CI 0.39-1.07, I<sup>2</sup> = 72%, p = 0.028). However, PHPT patients with preoperative 25(OH)D levels  $\geq$ 75 nmol/L exhibited 44% lower risk of postoperative hypocalcemia compared to those with 25(OH)D levels <75 nmol/L (RR 0.56, 95% CI, 0.32-0.99; I<sup>2</sup> = 65%; p = 0.02). In addition, compared to patients with preoperative 25(OH)D levels <75 nmol/L, patients with preoperative 25(OH)D levels > 75 nmol/L showed no significant increase in preoperative serum calcium levels (SMD 0.01, 95% CI -0.29-0.32, I<sup>2</sup> = 92.3%, p<0.001). **CONCLUSION:** Preoperative 25(OH)D levels  $\geq$ 75 nmol/L are associated with a reduced risk of hypocalcemia after parathyroidectomy, whereas levels between 50 and 75 nmol/L are not. Notably, achieving a 25(OH)D level  $\geq$ 75 nmol/L is not associated with increased preoperative serum calcium levels, supporting its safety in clinical practice.

PubMed-ID: [41342520](#)

DOI: [10.1097/JS9.0000000000004163](#)

## Randomized controlled trials

-None-

## Consensus Statements/Guidelines

**"Albumin-adjusted" calcemia: time to move on for chronic hypoparathyroidism patients?**

*Eur J Endocrinol*, 194(1):L3-L5.

J. P. Bertocchio, A. Hecini and C. Ghander. 2026.

PubMed-ID: [41435905](#)

DOI: [10.1093/ajendo/lvaf258](#)

## Other Articles

**The Impact of Adjuvant Radiotherapy Administration on Disease-Specific Survival in Patients with Parathyroid Carcinoma.**

*Ann Surg Oncol*, 33(1):707-14.

H. Al Asadi, H. Najah, J. A. Greenberg, B. Greenspun, N. Salehi, D. Aykan, B. M. Finnerty, T. J. Fahey and R. Zarnegar. 2026.

**INTRODUCTION:** The effect of adjuvant radiotherapy (AR) on disease-specific survival (DSS) in patients with parathyroid carcinoma remains unclear. We explored the impact of AR on DSS. **METHODS:** Patients with parathyroid carcinoma were

identified in SEER and categorized based on AR administration. To address confounding factors affecting the nonrandom allocation of radiotherapy, we conducted propensity score matching. We then employed Kaplan-Meier survival analysis to estimate DSS. RESULTS: In total, 549 patients were included, with 64 (11.6%) receiving AR. Those who received AR had larger tumors, measuring 3.2 (interquartile range 2.3-4.5) cm compared with 2.7 (interquartile range 1.8-3.5) cm than those who did not receive AR ( $p = 0.01$ ). Patients who received AR exhibited improved 10- (90.3% vs. 72.2%,  $p = 0.02$ ) and 20 year DSS (90% vs. 68%,  $p = 0.03$ ). Our multivariable Cox regression confirmed that patients who did not receive AR had poorer DSS [3.2, 95% CI 1.3-10.1]. Furthermore, non-Hispanic ethnicity [Hispanic patients: 0.13, 95% CI 0.007-0.7], extraparathyroidal extension (EPE) [2.7, 95% CI 1.1-6.9], and positive lymph node status [10.2, 95% CI 1.6-47.8] were linked to diminished DSS. CONCLUSIONS: Using propensity-score matching in a large database, AR in patients with parathyroid carcinoma was associated with improved DSS compared with matched patients who did not receive AR. Notably, the lack of AR administration was identified as an independent factor linked to poorer DSS [3.2, 95% CI 1.3-10.1]. These findings indicate that AR should be considered by clinicians when dealing with these rare tumors and prospective studies are warranted to further assess its role.

PubMed-ID: [40802086](#)

DOI: [10.1245/s10434-025-18036-8](#)

### **Ultrasound-Guided Radiofrequency Ablation for the Treatment of Primary Hyperparathyroidism in Elderly Patients.**

*Clin Endocrinol (Oxf)*, 105(1):34-41.

S. Alkan, S. C. Guney, C. Akcura, B. Sunbul, A. Alsac, S. Tarhan, N. Ozdemir and Z. Hekimsoy. 2026.

AIM: This study aimed to assess the efficacy and safety of ultrasound-guided radiofrequency ablation (RFA) in elderly patients with primary hyperparathyroidism (PHPT). METHODS: This retrospective cohort study included patients aged  $\geq 60$  years with PHPT who underwent ultrasound-guided RFA at a single center between May 2021 and May 2025. A total of 36 patients were analyzed. Laboratory parameters, including serum calcium and intact parathyroid hormone (iPTH), were assessed before and after the procedure. All patients were followed for at least 6 months. Cure was defined as normalization of both serum calcium and iPTH levels during follow-up. Procedural outcomes, complications, and factors associated with treatment response were evaluated. RESULTS: The mean age of the cohort was 70.4 ( $\pm 8.69$ ) years. After a single RFA session, 28 of 36 patients achieved a cure. When repeat procedures were included, the overall cure rate increased to 83.3% (30/36). The key procedure-related adverse events were postoperative mild pain and hoarseness. Hoarseness was transient in most cases; permanent hoarseness occurred in one patient. No major life-threatening complications were observed. Baseline characteristics did not differ significantly between cured and non-cured patients. Patients who developed hoarseness were older and had lower baseline magnesium levels than those without hoarseness. CONCLUSIONS: Ultrasound-guided RFA appears to be an effective and safe minimally invasive treatment option for selected elderly patients with PHPT, achieving acceptable cure rates with a favorable safety profile. RFA may represent a valuable alternative for elderly or frail patients who are at increased surgical risk. Prospective studies with larger cohorts and longer follow-up are warranted to confirm these findings.

PubMed-ID: [41928071](#)

DOI: [10.1111/cen.70138](#)

### **Continuous subcutaneous administration of teriparatide as a therapeutic option in chronic hypoparathyroidism: retrospective study in three tertiary care centers of the epi-hypo study.**

*Eur J Endocrinol*, 194(1):K1-K7.

A. Attia, M. Briere, P. Kamenicky, A. L. Lecoq, L. Maione, P. Houillier, C. Buffet, J. P. Bertocchio and C. Ghander. 2026.

CONTEXT: Chronic hypoparathyroidism (cHP) is a rare endocrine disorder characterized by hypocalcemia secondary to the insufficient secretion of the parathyroid hormone. Despite the good observance of oral treatment with calcium salts and active vitamin D analogs, and even after adding intermittent subcutaneous injections of teriparatide (IST), some patients are still uncontrolled. Previous studies have suggested that continuous subcutaneous administration of teriparatide (CSAT) may be an option in such cases. OBJECTIVE: The aim of this study was to assess the evolution of biological parameters with CSAT in comparison to previous treatment. DESIGN: Retrospective observational study including all patients who received CSAT from 3 tertiary care centers of the Epi-Hypo study. METHODS: Blood calcium, phosphate, bone remodeling markers, urine calcium, and the evolution of oral treatment were captured from electronic medical records. Quality of life (QoL) was assessed using the Hypoparathyroid Patient Questionnaire (HPQ28). RESULTS: Twenty patients were included, 85% were women, and 75% had post-surgery cHP. Total calcium concentration was significantly higher with CSAT than with IST for 73% patients. HPQ28 showed an improvement in three out of the five patients for whom it was assessed. Osteocalcin increased significantly with IST ( $P = .003$ ), but no difference was observed after initiating CSAT. CONCLUSION: CSAT may be an option for patients with uncontrolled cHP. Further studies need to investigate bone consequences and better

characterize the improvement of QoL among these patients.

PubMed-ID: [41439459](#)

DOI: [10.1093/ejendo/lvaf257](#)

#### **Assessing parathyroid function requires both parathyroid hormone and calcaemia assessments.**

*Br J Surg*, 113(2)

J. P. Bertocchio and C. Ghander. 2026.

PubMed-ID: [41667407](#)

DOI: [10.1093/bjs/znaf297](#)

#### **Primary hyperparathyroidism incidence in northeastern Italy: A large population-based study.**

*J Endocrinol Invest*, 49(1):143-51.

S. Censi, L. Salmaso, G. Voltan, F. Ceccato, U. Fedeli, M. Iacobone, L. Bertazza, C. Clausi, F. Torresan, C. Mian, M. Saia and V. Camozzi. 2026.

**PURPOSE:** Population-based studies of trends in the incidence of primary hyperparathyroidism (PHPT) in Italy were still lacking. Our aim was to estimate the incidence of PHPT in the Veneto region over the period 2012-2023. **METHODS:** A retrospective, population-based study conducted in Veneto using the population registry and administrative health databases. Only subjects  $\geq 18$  years of age were included. We documented incident PHPT from 2013 to 2023 to exclude prevalent cases and calculated standardised incidence rates (IR) per 10,000 person-years by age and sex. We also made a sub analysis of only surgical cases. **RESULTS:** We identified 5,276 incident cases (IR: 1.17). Overall, the incidence of PHPT was stable from 2013 to 2023, although there was a declining trend in males, at the limits of statistical significance with the standardised IR decreasing from 0.77 (95% CI: 0.64;0.91) in 2013 to 0.67 in 2023 (95% CI: 0.55;0.78) ( $p = 0.056$ ). The overall female-to-male incidence ratio was 2.55, with females predominating, and reached a peak in the 50-54 age group (ratio: 3.94) and a nadir in 25-29 age group (ratio: 0.54). Median age was 65 years (IQR: 56-76 years) and was lower among females than males (64 vs 68 years) ( $p < 0.0001$ ). Among the surgical cases, the percentage distribution of incident cases by age was almost the same for females and males, median age was similar (61 years for females, 62 years for males), while the rates remained higher for females than for males. **CONCLUSION:** Our study shows that over the past decade there has been a general stability in the incidence of PHPT in our Region. A higher incidence was observed in postmenopausal females and a different pattern of incidence emerged from our analysis of surgical cases.

PubMed-ID: [41108501](#)

DOI: [10.1007/s40618-025-02723-0](#)

PMCID: PMC12847158

#### **Multiple endocrine neoplasia type 5: emerging evidence and clinical perspectives.**

*Endocr Relat Cancer*, 33(2)

N. Charoenngam and M. Mannstadt. 2026.

Multiple endocrine neoplasia type 5 (MEN5) is a newly proposed hereditary syndrome caused by heterozygous germline loss-of-function mutations in the MAX gene, which encodes MYC-associated factor X (MAX). Initially only linked to pheochromocytoma/paraganglioma (PCC/PGL) syndrome, MAX mutations have also been associated with other tumors. This review synthesizes current knowledge on the discovery, pathogenesis, clinical features, diagnosis, and management of MEN5. The pathogenesis of MEN5 involves disruption of tumor suppressor MAX-MXD heterodimers in the context of MAX loss, leading to increased cell proliferation. Tumor development in MAX-associated disease is consistent with the two-hit mechanism, in which a heterozygous germline mutation is followed by somatic inactivation of the remaining allele. Clinically, MEN5 is characterized by a diverse tumor spectrum, with PCC/PGL and pituitary adenoma being the most common manifestation. Other reported conditions include primary hyperparathyroidism, renal oncocytoma, and neuroblastoma, but the connection between the mutation and development of some of these tumors has not been definitively proven. Evidence from published reports suggests a parent-of-origin effect, with higher penetrance more commonly observed when the pathogenic variant is paternally inherited. Despite recent progress, the epidemiology, penetrance, and genotype-phenotype associations of MEN5 require further investigation. Taken together, MEN5 represents a novel hereditary endocrine neoplasia syndrome with a broader tumor spectrum than initially suspected. The MAX gene is included in several diagnostic gene panels, and endocrinologists should be aware of the associated disorders. The limitations of current knowledge highlight the need for further research to better characterize its clinical features, pathogenesis, and management.

PubMed-ID: [41685558](#)

**Intraoperative Parathyroid Hormone in Minimally Invasive Parathyroidectomy (MIP) for Primary Hyperparathyroidism With Concordant Localisation.***Otolaryngol Head Neck Surg*, 174(6):1434-41.

B. M. H. Chew, S. S. A. Lim, T. R. X. Gan, S. W. H. Sim, J. W. L. Lau, H. B. Oh, Y. J. Chai, W. K. Cheah and M. H. Tang. 2026.

**OBJECTIVE:** There is increasing use of intraoperative parathyroid hormone (ioPTH) in minimally invasive parathyroidectomy (MIP). While ioPTH has improved cure rate, there is little evidence to suggest effectiveness in primary hyperparathyroidism (PHP) with concordant preoperative localisation. This study aims to determine if ioPTH improves cure rates in such cases. **DATA SOURCES:** A search of PubMed, Embase, and Cochrane databases identified studies that compared MIP with and without ioPTH, in patients with concordant preoperative imaging of ultrasonography and technetium-99m sestamibi (MIBI) scans. Inclusion criteria were comparative studies between years 2000 and 2023. **REVIEW METHODS:** Analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines. Primary outcome was the overall cure rate. Secondary outcomes analyzed include operative duration, and conversion to neck exploration. **RESULTS:** Six studies involving 884 patients were eligible for inclusion. The overall cure rate was 97.3%, higher in those that had ioPTH than without, but this was not statistically significant (98.3% vs 96.0%,  $P = .18$ ). Operative duration was reported in 2 studies, showing significantly longer duration in the ioPTH group. Overall conversion rate to bilateral neck exploration was 6.64% in the ioPTH group, with a success rate of 4.80%. **CONCLUSION:** Use of ioPTH in MIP with concordant localization did not result in statistically significant higher cure rates. Operative time is potentially longer with use of ioPTH. It is difficult to justify the routine use of ioPTH for such cases based on cure rates alone; considerations should also be given to center-specific case volume, surgical experience, and overall cost outcomes.

PubMed-ID: [41904980](https://pubmed.ncbi.nlm.nih.gov/41904980/)DOI: [10.1002/ohn.70218](https://doi.org/10.1002/ohn.70218)**Implementation of a perioperative protocol for parathyroidectomy reduces postoperative hypocalcaemia and healthcare utilization.***Br J Surg*, 113(1)

P. C. R. Dahmen, J. C. Hol, J. Feenstra, A. B. Francken and A. D. van Dalsen. 2025.

PubMed-ID: [41557348](https://pubmed.ncbi.nlm.nih.gov/41557348/)DOI: [10.1093/bjs/znaf301](https://doi.org/10.1093/bjs/znaf301)**Autofluorescence enhances intraoperative detection of parathyroid glands: a single-center comparative study.***Front Endocrinol (Lausanne)*, 17:1788568.

J. B. Dubuis, J. Meyer, M. Mavromati, S. Leboulleux, F. Triponez and M. S. Demarchi. 2026.

**INTRODUCTION:** Permanent hypoparathyroidism after total thyroidectomy remains a major complication, occurring in close to 10% of cases and increasing risks of cardiac, renal, and metabolic morbidity. Near-infrared autofluorescence (NIRAF) imaging has emerged as a promising adjunct to improve parathyroid gland (PG) identification and preservation. This study evaluates the efficacy of NIRAF in enhancing intraoperative PG detection compared to conventional visual inspection. **METHODS:** This single-center retrospective cohort study included 349 patients undergoing total thyroidectomy. Outcomes were compared between a control group managed with visual PG identification alone ( $n = 126$ , 2014-2016) and a NIRAF-assisted group using Fluobeam LX((R)) imaging ( $n = 223$ , 2021-2023). The primary outcome was the mean number of PGs identified intraoperatively. Secondary outcomes included postoperative calcium and parathyroid hormone (PTH) levels, rates of PG autotransplantation, and inadvertent PG removal. **RESULTS:** NIRAF use was associated with significantly improved intraoperative PG identification, with a higher mean number of glands visualized compared to controls ( $2.91 \pm 0.98$  vs.  $2.59 \pm 1.02$ ;  $p = 0.004$ ). Postoperative PTH levels were significantly higher in the NIRAF group ( $3.64 \pm 1.72$  vs.  $3.03 \pm 1.40$  pmol/L;  $p < 0.001$ ). Although postoperative calcium levels were lower in the NIRAF group ( $2.21 \pm 0.11$  vs.  $2.29 \pm 0.12$  mmol/L;  $p < 0.001$ ), the incidence of severe hypocalcemia ( $\leq 2.0$  mmol/L) was low and comparable between groups (3.1% vs. 1.6%;  $p = 0.497$ ). Rates of postoperative PTH  $< 1.1$  pmol/L, PG autotransplantation, and reimplantation did not differ significantly. Inadvertent PG removal was more frequent in the NIRAF group (20.6% vs. 5.6%;  $p < 0.001$ ). **DISCUSSION:** NIRAF imaging improves intraoperative identification of PG and is associated with higher early postoperative PTH levels. Although hypoparathyroidism did not differ between the two groups, the effect of NIRAF on permanent hypoparathyroidism requires prospective evaluation, particularly when combined with perfusion assessment using indocyanine green (ICG) angiography. Standardized use and surgeon training are necessary to optimize

clinical outcomes.

PubMed-ID: [41987894](#)

DOI: [10.3389/fendo.2026.1788568](#)

PMCID: PMC13076167

### **Parathyroid autofluorescence: A conditionally cost-effective tool to reduce postoperative hypocalcemia after total thyroidectomy.**

*Surgery*, 190:109853.

K. B. Fergus, P. C. Conroy, J. Thiesmeyer, A. Kannan, J. Gosnell and Q. Y. Duh. 2026.

**BACKGROUND:** Postoperative hypocalcemia due to parathyroid removal/injury remains a major source of morbidity after thyroidectomy. Technologies using autofluorescence for parathyroid identification allow for parathyroid preservation. We aimed to determine if imaging-based autofluorescence was associated with decreased postoperative hypocalcemia and cost-effective. **METHODS:** Randomized controlled trials examining patients undergoing total/completion thyroidectomy with versus without imaging-based autofluorescence were identified through a systematic review. Exclusion criteria included non-English language, total events <5, or missing 24-hour postoperative hypocalcemia and number of parathyroids on pathology. Meta-analysis was performed using inverse variance method for fixed and random effects models. For cost-effectiveness analysis, fixed upfront device plus recurring costs for the autofluorescence group were summed. Postoperative hypocalcemia rates were used as a proxy for effectiveness and overnight hospitalization likelihood. **RESULTS:** Ten studies (2019-2024) with a pooled cohort of 1,878 patients (77% female, mean age 50 years) were included. Autofluorescence was associated with reduced inadvertent parathyroidectomy (odds ratio 0.42, 95% confidence interval 0.19-0.92) and postoperative hypocalcemia (odds ratio 0.59, 95% confidence interval 0.43-0.81). We calculated 17% of cases without and 11% with autofluorescence would have transient hypocalcemia. At high-volume centers ( $\geq 200$  thyroidectomies/year), the incremental cost of device purchase at 1 year is +\$36,458; at 10 years it saves - \$382,413. In moderate-volume centers ( $\geq 50$  thyroidectomies/year) the incremental costs were +\$71,365 at 1 year and a savings of -\$33,353 at 10 years. **CONCLUSIONS:** Imaging-based autofluorescence was associated with reduced risk of postoperative hypocalcemia after thyroidectomy and was conditionally cost-saving over extended device usage periods. Future studies examining the cost-effectiveness of other applications are warranted.

PubMed-ID: [41237690](#)

DOI: [10.1016/j.surg.2025.109853](#)

### **Risk of bone overstimulation in long-term PTH(1-34) therapy for hypoparathyroidism.**

*Eur J Endocrinol*, 194(4):500-9.

R. Fischler, A. L. Lecoq, P. Houillier, M. Verdoux, M. C. Vantyghem, K. Briot, F. L. Besson, N. Pierquet-Ghazzar, A. Beron, S. Viengchareun, S. Trabado, A. Lecoivre, C. Bordet, C. Goujard, S. Salenave, S. Leboulleux, E. Carreira, C. Chabrolle, B. Corvilain, P. Chanson, J. Young, A. Linglart, G. Grimon and P. Kamenicky. 2026.

**OBJECTIVE:** PTH(1-34), used off-label, effectively controls serum calcium in patients with chronic hypoparathyroidism inadequately managed by standard-of-care therapy. PTH(1-34) also strongly stimulates bone remodeling and often raises bone turnover markers above normal levels. This study aimed to visually assess the risk of excessive bone stimulation associated with prolonged PTH(1-34) replacement therapy. **DESIGN:** An observational study (N degrees 20201026100318) was conducted in adults with chronic hypoparathyroidism treated with PTH(1-34) for over 2 years at 3 referral centers. **METHODS:** Patients underwent whole-body 99mTc-methylenediphosphonate scintigraphy, biochemical evaluation, and bone mineral density assessment. The primary endpoint was the proportion of patients with pathological increases in bone tracer uptake. **RESULTS:** Forty-one patients received a mean daily dose of 29.9 microg [Q1; Q3 22.5; 39.9] of PTH(1-34) for a duration of 57 months [40; 70], representing an exposure of 218.3 patient-years. Median age at imaging was 44 years [30; 55]; 31 (75.6%) were women. Pathological bone uptake was observed in 25 (61%) patients despite serum calcium predominantly in the target therapeutic values. Osteoarticular pain did not differentiate affected individuals. These patients had higher weight-adjusted PTH(1-34) doses (0.44 microg/kg [0.32; 0.56] vs 0.34 microg/kg [0.24; 0.40],  $P = .045$ ), elevated bone remodeling markers, lower serum magnesium, and increased urinary calcium excretion. A score combining serum C-telopeptides of collagen I, osteocalcin, and magnesium correctly classified 97% of patients (95% CI: 91%-100%). **CONCLUSION:** Long-term PTH(1-34) therapy in chronic hypoparathyroidism is frequently associated with excessive bone remodeling despite adequate calcemic control. Careful monitoring is therefore essential, especially in patients with elevated bone remodeling markers and hypomagnesemia.

PubMed-ID: [41985052](#)

DOI: [10.1093/ajeendo/lvag053](#)

### **Surgery for normocalcemic hyperparathyroidism is safe and effective.**

*Surgery*, 189:109707.

C. C. Frye, Z. Song, S. Balachandra, N. Swaminathan, A. Gillis, J. Fazendin, B. Lindeman and H. Chen. 2026.

**BACKGROUND:** The ideal management of normocalcemic primary hyperparathyroidism is controversial and is not discussed in recent guidelines as a result of limited published data. To help fill this knowledge gap, we aimed to report the outcomes of a large case series of patients with normocalcemic primary hyperparathyroidism who underwent parathyroidectomy. **METHODS:** A retrospective review of a prospectively maintained database was conducted to identify patients with normocalcemic primary hyperparathyroidism who underwent parathyroidectomy from 2000 to 2023. A small subset of patients participated in a prospective quality of life pilot study. **RESULTS:** In 554 patients with normocalcemic primary hyperparathyroidism who underwent parathyroidectomy, 89% had clinical manifestations and 58% were caused by multigland disease. Intraoperative parathyroid hormone decrease >50% was achieved in 99% and normal parathyroid hormone levels at 6 months were achieved in 81% of patients. Serious complications were rare. Younger patients had greater rates of transient postoperative hypocalcemia ( $P < .01$ ). Patients undergoing bilateral exploration were more likely to be Black ( $P < .01$ ). In participating patients ( $n = 18$ ), median overall quality of life improved significantly from 29 (interquartile range, 18) preoperatively to 2 (interquartile range, 18) at 2 weeks' postoperatively ( $P < .001$ ). Each of the individual quality of life subsections including the pain, activities of daily living, occupation, mobility, leisure, general health, and mental function domains all improved significantly after parathyroidectomy ( $P < .05$ ). **CONCLUSION:** We have herein reported the largest institutional case series of patients with normocalcemic primary hyperparathyroidism undergoing parathyroidectomy. Surgery for normocalcemic primary hyperparathyroidism was safe, effective, and, in a prospective pilot study, was associated with significant improvements in quality of life at 2 weeks postoperatively. These findings further support that parathyroidectomy may play an important role in the management of normocalcemic primary hyperparathyroidism.

PubMed-ID: [41015676](#)

DOI: [10.1016/j.surg.2025.109707](#)

PMCID: PMC12479090

### **Influence of Hashimoto's thyroiditis on intraoperative probe-assisted near-infrared autofluorescence detection of parathyroid glands: A cross-sectional study.**

*Surgery*, 190:109848.

X. X. Gan, J. Zhang, W. H. Jian, L. K. Zhong, Z. Chen, H. L. Tang, W. S. Cai, R. Y. Zhong and B. Xu. 2026.

**BACKGROUND:** Probe-assisted near-infrared autofluorescence has emerged as a promising technique for intraoperative identification of parathyroid glands. However, the influence of Hashimoto's thyroiditis on detection of parathyroid glands with probe-assisted near-infrared autofluorescence remains unclear. This study aimed to evaluate the influence of Hashimoto's thyroiditis on probe-assisted near-infrared autofluorescence fluorescence signal features in type A parathyroid glands during thyroidectomy. **METHODS:** This single-center cross-sectional study included patients who underwent thyroidectomy between June and November 2024. Clinical data, including baseline demographic and laboratory characteristics and intraoperative probe-assisted near-infrared autofluorescence measurements, were collected for analysis. Parathyroid glands were categorized into type A and type B based on their anatomic location. Probe-assisted near-infrared autofluorescence fluorescence detected values were measured intraoperatively for each suspicious parathyroid gland. Comparative analyses were performed between type A and type B parathyroid glands to evaluate differences in fluorescence detected value. Further, patients were stratified into Hashimoto's thyroiditis and non-Hashimoto's thyroiditis groups to evaluate differences in clinical characteristics. We also investigated the influence of Hashimoto's thyroiditis on the specific anatomic and fluorescence signal features of type A parathyroid glands. Univariable and multivariable linear regression analyses were conducted to identify independent variables of fluorescence-detected value and ratio (detected/baseline). To evaluate the relative contribution of covariates, variable importance was further assessed using least absolute shrinkage and selection operator regression. Lastly, we conducted receiver operating characteristic curve analysis to assess diagnostic performance of the models. **RESULTS:** Compared with the non-Hashimoto's thyroiditis group, the Hashimoto's thyroiditis group showed significantly lower probe-assisted near-infrared autofluorescence fluorescence detected values and baseline and preoperative parathyroid hormone levels ( $P < .05$ ) in type A parathyroid glands. In multivariate models, thyroid peroxidase antibody and baseline were identified as independent impact variables of probe-assisted near-infrared autofluorescence fluorescence detected values ( $P < .001$ ). For ratio, sex and baseline were significant impacted variables ( $P < .05$ ). Least absolute shrinkage and selection operator regression revealed sex, Hashimoto's thyroiditis, thyroid peroxidase antibody, and baseline as the top predictors for detected value, whereas gender and thyroid peroxidase antibody were key for ratio. Receiver operating characteristic curve analysis indicated that the presence of Hashimoto's thyroiditis did not compromise the performance of probe-assisted near-

infrared autofluorescence in identifying parathyroid glands (all-group analysis area under the curve  $\geq 0.945$ ). The ratio-based model demonstrated superior sensitivity and maintained high specificity, achieving 100% sensitivity in the Hashimoto's thyroiditis subgroup. CONCLUSION: Hashimoto's thyroiditis reduces probe-assisted near-infrared autofluorescence fluorescence detected value in type A parathyroid glands, yet the ratio remains stable. Despite autoimmune interference, this technique consistently enables accurate intraoperative identification of parathyroid glands, supporting its reliable use in patients with Hashimoto's thyroiditis.

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### **Use of a Best Practice Advisory to increase the detection rate of hyperparathyroidism.**

*Surgery*, 189:109706.

R. S. Gates, K. McCoy, J. Stewart, A. J. Behnke, A. Bankole, T. Vallia, M. S. Nussbaum and D. Tershak. 2026.

**BACKGROUND:** Timely diagnosis and treatment of primary hyperparathyroidism requires a high index of suspicion and collaboration across specialties. The diagnosis often is overlooked. This study aimed to determine whether the introduction of a screening algorithm for primary hyperparathyroidism would increase diagnosis and treatment rates.

**METHODS:** An electronic health record Best Practice Advisory was launched in 2022, encouraging parathyroid hormone testing for patients with hypercalcemia (calcium  $\geq 11$  mg/dL). Parathyroid hormone testing, specialist referrals, and parathyroidectomy were examined pre- and postintervention.

**RESULTS:** There were 902 and 893 patients with hypercalcemia in the pre- and postintervention groups, respectively. Parathyroid hormone testing increased from 24.61% to 38.75% after the Best Practice Advisory was implemented ( $P < .01$ ). Specialist referrals and rates of parathyroidectomy were unchanged between the pre- and postintervention groups (referrals in 41.44% vs 41.04% of those with parathyroid hormone testing,  $P = .93$ ; parathyroidectomy in 27.17% vs 26.76% of those referred,  $P = 1.00$ ). Parathyroid hormone testing was performed more commonly in older patients (69.63 vs 59.01 years,  $P < .01$ ). Patients referred to a specialist were younger (67.59 vs 71.05 years,  $P = .04$ ). Patients with primary hyperparathyroidism-associated comorbidities were more likely to undergo parathyroid hormone testing, with no differences in rates of specialist referrals ( $P = .11$ ) or parathyroidectomy ( $P = .60$ ). **CONCLUSION:** An electronic health record Best Practice Advisory was effective in increasing primary hyperparathyroidism screening, but did not result in a higher rate of specialist referrals or parathyroidectomies. Reflex parathyroid hormone testing as well as increased education about primary hyperparathyroidism may further improve screening, referrals, and treatment.

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### **Current state of autofluorescence technology in parathyroid identification.**

*Am J Surg*, 253:116701.

D. Gomez-Carrillo and C. C. Frye. 2026.

PubMed-ID: [41193366](#)

DOI: [10.1016/j.amjsurg.2025.116701](#)

### **Fiber-Based Near-Infrared Autofluorescence, Parathyroid Gland Identification, and Outcomes.**

*JAMA Surg*, 161(2):205-6.

Y. Huang and Z. Tian. 2026.

PubMed-ID: [41335452](#)

DOI: [10.1001/jamasurg.2025.5276](#)

### **Prevalence of parathyroid multiglandular disease in Asian population.**

*Am J Surg*, 254:116613.

J. A. Kasmirski, R. Roy, Z. Song, C. Wu, S. Balachandra, M. C. McLeod, A. Gillis, J. Fazendin, B. Lindeman and H. Chen. 2026.

PubMed-ID: [40998671](#)

DOI: [10.1016/j.amjsurg.2025.116613](#)

### **Surgical intervention for primary hyperparathyroidism is associated with a reduction in new-onset neuropsychiatric disorders.**

*Surgery*, 189:109867.

J. A. Kasmirski, Z. Song, N. Swaminathan, I. Chaudhary, S. Balachandra, A. Gillis, J. Fazendin, B. Lindeman and H. Chen. 2026.

**BACKGROUND:** Primary hyperparathyroidism has been linked to an increased prevalence of neuropsychiatric disorders. However, there is sparse literature to determine if parathyroidectomy improves the development of new-onset conditions when compared to nonoperative management. This project aims to assess the impact of parathyroidectomy on new-onset neuropsychiatric disorders. **METHODS:** Using data from a multi-institutional database, a retrospective cohort was conducted on patients classified with an International Classification of Diseases, Tenth Revision, of primary hyperparathyroidism (E21.0) aged 18 years or older with at least 3 years of follow-up after diagnosis. The study compared those with a previous parathyroidectomy (Current Procedural Terminology code 60500) to those with nonsurgical management. A regression analysis was conducted to compare cohorts and calculate the hazard ratio of developing neuropsychiatric disorders based on International Classification of Diseases, Tenth Revision, codes. **RESULTS:** The initial

query identified 51,983 patients with primary hyperparathyroidism. After matching, 37,194 patients were included and were predominantly White (73.4%, n = 27,324) and female (74.1%, n = 27,582). The parathyroidectomy and nonsurgical groups both contained 18,597 patients, with an average age of 60 +/- 13 years. Patients who underwent parathyroidectomy had significantly lower rates of anxiety (hazard ratio 0.72, 95% confidence interval 0.67-0.78), depression (0.76, 0.70-0.84), mania or bipolar disorder (0.45, 0.30-0.67), and mild cognitive decline (0.73, 0.58-0.91) than their nonsurgical counterparts. There was no difference between the groups regarding new-onset schizophrenia (hazard ratio 0.81, 95% confidence interval 0.37-1.80), somnolence (0.87, 0.74-1.02), and suicidal ideation (0.65, 0.41-1.02). CONCLUSIONS: Parathyroidectomy was associated with significantly lower rates of new-onset neuropsychiatric disorders in patients with primary hyperparathyroidism compared with medical management.

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### **Surgery for kidney-related hyperparathyroidism: A review.**

*Am J Surg*, 254:116854.

J. A. Kasmirski, N. Swaminathan, R. Roy, A. Gillis, B. Lindeman, H. Chen and S. Dream. 2026.

Secondary hyperparathyroidism often occurs as a result of a disruption in calcium and phosphorus homeostasis caused by chronic kidney disease (CKD). While some individuals experience a remission of parathyroid gland disease subsequent to kidney transplantation due to the restoration of calcium homeostasis, a subset continues to exhibit elevated parathyroid hormone due to autonomous secretion, a condition otherwise known as tertiary hyperparathyroidism. This review aims to investigate the intricacies of diagnosis, presentation, medical treatment, state-of-the-art surgical options, and strategies to potentially improve the cure rates of parathyroidectomy in cases of secondary and tertiary hyperparathyroidism.

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### **Revisiting parathyroid carcinoma through the lens of the 2022 WHO classification.**

*Hormones (Athens)*,

E. P. Koroglu, G. U. Kocabas, Y. Ertan, M. Ozdemir, I. Y. Simsir and P. B. S. Yurekli. 2026.

PURPOSE: Parathyroid carcinoma is a rare endocrine malignancy. This study aimed to evaluate the clinical characteristics, treatment approaches, and follow-up data of patients diagnosed with parathyroid carcinoma. Additionally, pathological findings were reassessed according to the 2022 World Health Organization (WHO) classification to examine its clinical implications. METHODS: The medical records of patients who were pathologically diagnosed with parathyroid carcinoma at the Endocrinology Clinic of a University Hospital between March 2013 and June 2024 were retrospectively reviewed. Clinical characteristics, demographic data, and laboratory findings were recorded. Pathological features were also obtained retrospectively from medical charts and records. RESULTS: We reported eight patients with surgical and pathological diagnoses of parathyroid carcinoma. Six of the patients were females and two were males. The ages of the patients ranged from 43 to 85, with a mean age of 61. The follow-up periods after diagnosis varied from 6 to 132 months. The calcium levels at diagnosis ranged from 11.7 mg/dL to 18.4 mg/dL, with a median of 16.0 mg/dL (normal range 8.6-10.2 mg/dL). The median PTH level at admission was 1609 ng/L (487.7-3035 ng/L) (normal range: 15-65 ng/L). Re-evaluation of all patients based on the 2022 WHO classification revealed no changes in initial diagnoses. CONCLUSIONS: Surgical resection remains the cornerstone of effective treatment. Accurate preoperative assessment, including detailed clinical and biochemical evaluation, is essential for optimal management. Sharing comprehensive data with pathologists enhances diagnostic accuracy. This study emphasizes the relevance of preoperative indicators and highlights that the updated WHO classification supports existing diagnostic criteria without altering clinical practice.

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### **AFBPS-ICGT-guided identification and selective removal of unhyperplastic ectopic parathyroid tissue during SHPT surgery: a retrospective cohort study.**

*Int J Surg*,

P. Kun, C. Hongcun, Y. Baozhong, L. Honglin, B. Wenzhong, L. Wenbo, S. Daiwei, S. Sailong, L. Li and L. Liang. 2025.

BACKGROUND: To evaluate the clinical utility of autofluorescence base point spectroscopy (AFBPS) combined with the immune colloidal gold technique (ICGT) for intraoperative identification and selective removal of non-hyperplastic ectopic parathyroid tissues (EPTs) in secondary hyperparathyroidism (SHPT). METHODS: This retrospective study included 100 SHPT patients who underwent surgery and were assigned to three groups: Group 1 received conventional total parathyroidectomy (TPTX) without EPTs localization; Group 2 underwent AFBPS-ICGT-guided selective resection; Group 3

received bilateral extended central neck dissection regardless of AFBPS-ICGT results. AFBPS was used to detect autofluorescence targets within central neck fibro-adipose tissues. Suspicious sites were validated by ICGT, and resection was guided accordingly. RESULTS: Surgical success was achieved in all patients. EPTs were more frequently identified in Groups 2 and 3 than Group 1 ( $P < 0.05$ ). AFBPS-ICGT achieved EPTs identification accuracies of 100% and 85.7% in Groups 2 and 3, while AFBPS alone reached 71.4% and 66.7%, respectively. ROC analysis showed base point intensity and spectral peak were strong predictors (AUCs: 0.96, 0.92; cut-offs: 172, 1092 AU). At 6 months, Group 1 had higher PTH, phosphate, and ALP levels ( $P < 0.01$ ) and a higher recurrence rate (26.7%) than Groups 2 (5.0%) and 3 (3.3%) ( $P < 0.01$ ). Refractory hypocalcemia was more frequent in Group 3 ( $P < 0.05$ ). CONCLUSION: AFBPS-ICGT enables accurate intraoperative detection and removal of EPTs, minimizing recurrence and reducing unnecessary bilateral dissection.

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DOI: [10.1097/JS9.0000000000004124](#)

### **Patient-Reported Outcome Measures Used in Primary Hyperparathyroidism: A Scoping Review.**

*Ann Surg Oncol*, 33(4):3435-48.

C. L. Leblang, M. Ahmed, C. G. Wade, N. L. Cho, G. M. Doherty, M. A. Nehs and J. B. Liu. 2026.

BACKGROUND: Standardized measuring tools, such as patient-reported outcome measures (PROMs), are needed to sufficiently measure the effect of an intervention or to describe patterns of disease. The extent to which PROMs have been used in primary hyperparathyroidism (PHPT) research is undefined. We conducted this scoping review to delineate the current landscape of PROMs used in research involving patients with PHPT. METHODS: Six databases were systematically searched, and two independent reviewers identified all primary research articles that involved patients with PHPT and used PROMs. Characteristics of the identified studies and the PROMs were collated. RESULTS: We examined 243 studies in full. Of these, 147 (49.7%) reported on symptoms or other health-related quality of life constructs that could be measured with PROMs but were not. In total, 96 (50.3%) studies used at least one PROM and were included. The median number of PROMs used per study was one (interquartile range 1-2), and 36 unique PROMs were identified. The three most frequently used PROMs were the 36-item Short Form Health Survey (42 studies), the Parathyroidectomy Assessment of Symptoms (20 studies), and the Beck Depression Inventory (12 studies). Symptoms and mental health constructs (e.g., anxiety, depression) were the most frequently assessed. Validity evidence for use in patients with PHPT was identified for only three PROMs: the 36-item Short Form Health Survey, Parathyroidectomy Assessment of Symptoms, and the Primary Hyperparathyroidism Quality of Life Questionnaire. All others were validated for use in patients without PHPT. CONCLUSIONS: There are missed opportunities in the rigor of health-related quality of life measurement in PHPT research. Future clinical research should emphasize proper application of PROMs to attain valid conclusions.

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DOI: [10.1245/s10434-026-19246-4](#)

PMCID: PMC12982322

### **Radius Bone Mineral Density Measurement Is Essential During Initial PHPT Workup: Results of a Retrospective Study on 400 Patients.**

*World J Surg*, 50(2):441-50.

M. Loison, M. Wargny, C. Caillard, P. Guillot, M. Le Bras, B. Cariou, C. Blanchard, E. Mirallie and S. Frey. 2026.

BACKGROUND: Bone mineral density (BMD) measurement at the lumbar spine, femoral neck, total hip, and distal 1/3 radius is recommended for patients with primary hyperparathyroidism (PHPT). Osteoporosis at any site justifies surgery. The distal 1/3 radius is often neglected. This study evaluated the prevalence of distal 1/3 radius measurement, the proportion of osteoporosis at this site alone, and BMD changes 1 year post-parathyroidectomy in patients with PHPT. METHODS: A total of 548 patients who underwent parathyroidectomy for PHPT between 2016 and 2024 in University Hospital Center of Nantes (France) were reviewed. Patients without pre-surgery BMD measurements at the lumbar spine or the femoral neck were excluded. BMD was assessed via dual x-ray absorptiometry before and 12-months after surgery. RESULTS: Four hundred patients (mean age 63.3  $\pm$  12.3 years, 80.5% female, and 86.2% menopausal) were included. Mean baseline serum calcium was 2.76  $\pm$  0.19 mmol/L; median PTH was 99.2 pg/mL [76.1; 138.7]. Osteoporosis was present in 47.0% of patients. Distal 1/3 radius BMD was measured in 46.2%, identifying 11.4% with forearm-only osteoporosis. They were younger (60.6  $\pm$  13.9 vs. 67.1  $\pm$  10.2 years,  $p = 0.048$ ), less frequently menopausal (66.7% vs. 95.9%,  $p = 0.001$ ) and had higher calcium levels (2.88  $\pm$  0.18 vs. 2.73  $\pm$  0.20 mmol/L,  $p = 0.002$ ) than the other osteoporotic patients. After surgery, BMD increased significantly at the lumbar spine (+0.06 g/cm<sup>2</sup>) and the total hip (+0.03 g/cm<sup>2</sup>), in a similar way to other osteoporotic patients. CONCLUSION: After measuring distal 1/3 radius BMD, performed in < 50% of PHPT patients, it was identified that 11.4% patients had forearm-only osteoporosis, who could have a bone benefit from surgery. These findings emphasize the importance of systematic measurement during PHPT

evaluation. TRIAL REGISTRATION: NCT05469087.

PubMed-ID: [41486083](#)

DOI: [10.1002/wjs.70223](#)

**Is atypical parathyroid tumor a different clinical entity than parathyroid adenoma and carcinoma? A retrospective review of a large single-center case series.**

*Updates Surg*, 78(2):543-54.

C. Maconi, A. M. Saibene, L. Castellani, P. Lozza, C. Pescia, M. Falleni and L. De Pasquale. 2026.

Primary hyperparathyroidism is primarily caused by single-gland pathology (80-85% of cases). According to the 2022 World Health Organization (WHO) guidelines (Erickson et al. in *Endocr Pathol*, 2022), single-gland pathologies include parathyroid adenoma, atypical parathyroid tumor and parathyroid carcinoma (Gurrado in *J Clin Med* 12:6297, 2023). The aim of this study is to identify differences or similarities of both pre-, intra- and post-operative characteristics between atypical parathyroid tumor and parathyroid adenoma/carcinoma, thereby establishing an appropriate follow-up protocol for atypical parathyroid tumor. We retrospectively analyzed 437 patients who underwent parathyroidectomy for primary hyperparathyroidism between 2012 and 2022 at the Thyroid Unit of ASST Santi Paolo e Carlo in Milan focusing our analysis on 352 patients with single-gland disease. Several pre-, intra-, and post-operative variables, including follow-up, were analyzed and compared using non-parametric statistical methods. Histological analysis identified 316 cases of PA (90%), 27 cases of atypical parathyroid tumor (7.7%), and 9 cases of parathyroid carcinoma (2.3%). Patients with atypical parathyroid tumor had significantly higher pre-operative PTH levels, intermediate calcium levels, falling between those of parathyroid adenoma and parathyroid carcinoma patients and larger gland diameter. No cases of disease persistence or recurrence were observed in patients with atypical parathyroid tumor after a mean follow-up of 42.8 months. APT exhibits biochemical and pathological features overlap with both PA and PC. However, the lack of recurrence or persistence suggests that APT behaves more similarly to PA than PC. The favorable evolution of APT in our case series could be a factor in favor of reducing the follow-up time for atypical tumors to a shorter period than the one recommended for carcinomas.

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DOI: [10.1007/s13304-025-02445-1](#)

PMCID: PMC13053332

**Determinants of extracellular fluid calcium concentration in patients with chronic hypoparathyroidism.**

*Eur J Endocrinol*, 194(3):326-35.

A. Michon-Colin, T. Blanchard, E. Boudierlique, G. Maruani and P. Houillier. 2026.

OBJECTIVE: To assess, in patients with chronic hypoparathyroidism, the relative contribution to serum calcium value of intestinal calcium absorption, renal tubular calcium reabsorption, and net bone calcium release, altered by parathyroid hormone (PTH) and calcitriol deficiency. DESIGN: Retrospective, single-center collection of data of consecutive patients with chronic hypoparathyroidism was performed. METHODS: Interactions between the collected variables were represented in a correlation matrix. The association of variables with serum calcium concentration was tested by multivariable linear regression. RESULTS: Data from 101 patients with hypoparathyroidism were collected. Their initial characteristics were consistent with the literature. Tubular calcium reabsorption corrected by glomerular filtration rate (TRCa/GFR), fasting calcium-to-creatinine ratio (UCa/UCr) and alfacalcidol dose were independently associated with serum ionized calcium concentration. TRCa/GFR was the most important explanatory variable, followed by UCa/UCr. Alfacalcidol dose was the only modifiable variable independently associated with TRCa/GFR and UCa/UCr. Longitudinal analysis of 33 patients showed that the increase in ionized calcium concentration due to a higher dose of alfacalcidol was mostly associated with an increase in TRCa/GFR. CONCLUSIONS: The main determinant of blood calcium levels in patients with chronic hypoparathyroidism is tubular calcium reabsorption, assessed by TRCa/GFR. Alfacalcidol is effective in correcting hypocalcemia due to its tubular effect but may lead to renal complications due to its intestinal and bone effects. The use of complementary treatment with thiazide diuretics or PTH analogs, possibly guided by the calculation of TRCa/GFR, could allow a better correction of hypocalcemia in these patients.

PubMed-ID: [41712492](#)

DOI: [10.1093/ejendo/lvag036](#)

**A prospective cohort study of intraoperative parathyroid gland management by early and advanced career surgeons based on viability assessment by visual perception and indocyanine green (ICG) fluorescence imaging.**

*Surgery*, 191:109920.

N. Oravec, R. Lahamm-Andraos, E. A. Harris, A. M. Harvey, S. A. Wolfe and C. T. Yeo. 2026.

BACKGROUND: Parathyroid gland identification and preservation during thyroidectomy has historically relied on

experienced visual acumen. Indocyanine green fluorescence imaging has demonstrated improvement in parathyroid gland preservation, but it is unclear if the benefit is limited to less-experienced surgeons. The aim of this study was to identify how often discordant parathyroid viability assessments by surgeon visual perception versus indocyanine green fluorescence resulted in changes in management, stratified by surgeon years of experience. **METHODS:** Patients undergoing thyroid surgery by high-volume endocrine surgeons were recruited. Perception of parathyroid viability was documented before and after intravenous indocyanine green administration. In cases of discordant assessments, management was at the surgeon's discretion. Rates of discordance and change in management were stratified by surgeon experience-"early career" (<5 years independent practice) and "advanced career" (>15 years independent practice). Results were analyzed using the Pearson chi(2) test. The primary outcome was the rate of change in management of the parathyroid on the basis of discordant assessments stratified by surgeon years of experience. **RESULTS:** Thirty-five patients were included and comprised 81 observations of parathyroid viability, 50 by early career surgeons and 31 by advanced-career surgeons. Early career surgeons had a discordance rate of 26.0% (n = 13/50) versus 19.3% (n = 6/31) for advanced career surgeons (chi(2) = 0.17329, P = .6722). Of the 19 discordant observations, 13 (68.4%) resulted in changes in management (early career = 10/13 = 76.9%; advanced career = 3/6 = 50.0%; chi(2) = 1.3772, P = .3093). **CONCLUSION:** These results suggest that indocyanine green fluorescence imaging is a useful adjunct to visual perception, regardless of the surgeon's years of experience.

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DOI: [10.1016/j.surg.2025.109920](#)

### **Radiofrequency ablation as an alternative treatment for hyperparathyroidism: a case study of a single parathyroid adenoma and review of the literature.**

*Hormones (Athens),*

M. C. T. Palla, A. Drosou, P. Gkousis, A. Drakopoulou, S. Kalaitzidou, E. Veniou and M. Gkeli. 2026.

Radiofrequency ablation (RFA) is a minimally invasive technique that is increasingly applied in endocrine diseases. While parathyroidectomy (PTX) is the first-line treatment for primary hyperparathyroidism (PHPT) and the standard option for secondary hyperparathyroidism (SHPT) unresponsive to medical therapy, RFA is under investigation as an alternative for high-risk or non-surgical candidates. This review included 31 studies, six of which were meta-analyses, assessing RFA in PHPT, SHPT, and tertiary hyperparathyroidism (THPT). In PHPT, complete response rates ranged from 60% to 100%, with volume reduction ratios exceeding 95%. A frequent observation was eucalcemic PTH elevation, attributed to bone turnover or release of glandular suppression, though usually without clinical consequences. In SHPT, outcomes were variable, and further investigation is required before establishing RFA as a therapeutic approach. Compared with PTX, RFA demonstrated lower rates of severe hypocalcemia and shorter recovery, though PTX achieved stronger biochemical suppression. Complications were generally mild and transient, most often hypocalcemia or hoarseness. RFA in PHPT may be used in patients not suitable for surgery under general anaesthesia. The technique should be used only as a unilateral approach whereas in bilateral hyperplasia associated with SHPT can be hazardous. Larger series are necessary to establish the RFA technique and clarify the recurrent laryngeal nerve paresis and long-term results.

PubMed-ID: [41888464](#)

DOI: [10.1007/s42000-026-00772-5](#)

### **Bilateral internal jugular vein (BIJV) sampling during surgery for primary hyperparathyroidism (PHPT) - scoping review of evidence and search for an optimal definition for lateralisation.**

*Langenbecks Arch Surg*, 411(1):56.

V. Prakash, N. Kamalakkannan and S. P. Balasubramanian. 2026.

**PURPOSE:** Accurate localisation of hyperfunctioning parathyroid glands is crucial for successful parathyroid surgery. In patients with inconclusive imaging, intraoperative bilateral internal jugular venous sampling (BIJVS) has been reported; but its utility remains unclear. The purpose of the review is to evaluate published techniques and reported effectiveness of BIJVS in parathyroid surgery. **METHODS:** PubMed, Ovid and Cochrane databases were searched for articles on intraoperative BIJVS in parathyroid surgery. All original English language human studies reporting on lateralisation rates, diagnostic accuracy or cure rates following use of intraoperative BIJVS were included. Exclusion criteria included case reports, reviews, IJV sampling in non-parathyroid pathology and IJV sampling for confirming cure. Data on patient numbers, definitions used for lateralisation and correlation with clinical outcomes were extracted by one reviewer and cross-checked by a second reviewer. The review was prospectively registered on the Open Science Framework (OSF; DOI: <https://doi.org/10.17605/OSF.IO/TSQA6> ). **RESULTS:** Of 753 screened, 12 studies including 502 patients where BIJVS was performed were included. Lateralisation definitions were reported in 7 studies. Among studies with relevant data, lateralisation gradient was defined as ranging from 5 to 20% and lateralisation rates varied from 51 to 100%. The positive

and negative predictive values ranged from 76 to 100% (6 studies) and 0-53% respectively (3 studies). Reported cure rates following BIJVS guided surgery were high (> 98%), but the definition for cure was only reported in 8 studies.

**CONCLUSIONS:** BIJVS can aid localisation in parathyroid surgery. A significant lateralisation gradient may permit unilateral surgery, but a lack of gradient does not imply bilateral disease. However, the absence of a standard definition for lateralisation and inconsistent reporting limits widespread adoption of this technique.

PubMed-ID: [41483311](#)

DOI: [10.1007/s00423-025-03957-5](#)

PMCID: PMC12816074

### **Effect of Delayed Parathyroidectomy on Risk of Future Cardiovascular and Nephrolithiasis Interventions in Adults With Primary Hyperparathyroidism.**

*Ann Surg*, 283(2):345-52.

K. M. Ramonell, R. Liou, X. Zheng, Z. Song, J. A. Lee, A. Sedrakyan and H. Chen. 2026.

**OBJECTIVE:** To determine whether the timing of parathyroid surgery impacts the risk of renal stone retreatment and cardiovascular interventions. **BACKGROUND:** Long-term, untreated primary hyperparathyroidism (pHPT) is associated with significant morbidity, including nephrolithiasis and cardiovascular disease. **METHODS:** We conducted a population-based cohort study of New York and California state-wide data from 2000 to 2020. Adult patients who underwent renal stone treatment and were subsequently diagnosed with pHPT and underwent parathyroidectomy (PTX) were included. Patients were excluded if PTX was before the index stone procedure, they underwent second stone treatment within 6 months, with stage V chronic kidney disease, with secondary or tertiary hyperparathyroidism, with prior kidney transplant or hemodialysis, or with prior cancer diagnosis. The rate of renal stone retreatment and cardiovascular interventions after PTX in patients with pHPT with nephrolithiasis who underwent parathyroid surgery at  $\leq 2$  years and  $> 2$  years after the index stone procedure was measured. **RESULTS:** We identified 2093 patients who underwent first-time stone treatment and subsequent PTX. The median time to PTX was 560 days (interquartile range: 187-1477), and follow-up was 7.4 years (interquartile range: 4.5-13.1). Delaying PTX for more than 2 years increased the risk of renal stone retreatment by 59% (HR=1.59;  $P < 0.001$ ), increased the risk of experiencing coronary disease or associated interventions by 118% (HR=2.18;  $P = 0.01$ ), and increased the risk of experiencing an overall cardiovascular event by 52% (HR=1.52;  $P < 0.01$ ). **CONCLUSIONS:** In symptomatic pHPT, delaying PTX significantly increases the risk of requiring future stone retreatment and cardiac/vascular surgical interventions. This highlights the importance of early surgical referral and multidisciplinary approaches to optimize outcomes and resource utilization in pHPT.

PubMed-ID: [39176567](#)

DOI: [10.1097/SLA.0000000000006508](#)

### **Deviating from Thyroid Imaging Reporting and Data Systems (TI-RADS) guidelines in surgical planning for patients with parathyroid disease: What is the clinical impact?**

*Surgery*, 189:109705.

S. V. Sathe, A. Chmiel, C. Jones, W. E. Gillanders, J. A. Olson, Jr. and T. C. Brown. 2026.

**BACKGROUND:** The American College of Radiology Thyroid Imaging Reporting and Data Systems standardizes thyroid nodule classification to assess malignancy risk. The use of preoperative ultrasound before parathyroidectomy often detects incidental thyroid nodules, prompting consideration of additional evaluation and/or concomitant thyroid surgery to minimize need for reoperative surgery. This study evaluated clinician adherence to Thyroid Imaging Reporting and Data Systems guidelines for patients with parathyroid disease and associated clinical outcomes. **METHODS:** A retrospective review of 992 patients undergoing parathyroidectomy (2019-2024) examined the role of Thyroid Imaging Reporting and Data Systems in preoperative planning and the clinical decision-making after incidental discovery of thyroid nodules. Descriptive and univariate statistical analyses were performed to compare guideline-concordant and discordant care. **RESULTS:** Of 957 patients with a formal preoperative ultrasound, 406 (42.4%) had at least 1 thyroid nodule with the Thyroid Imaging Reporting and Data Systems classification reported by a radiologist. Among those with a nodule, 154 (37.9%) underwent fine-needle aspiration and 56 (13.8%) underwent concomitant thyroid surgery for the nodule. Notably, 47 fine-needle aspiration procedures (30.5%) did not meet Thyroid Imaging Reporting and Data Systems criteria. Patients who received guideline-discordant fine-needle aspiration procedures were less likely to undergo thyroid surgery (12.8% vs 34.9%,  $P = .005$ ) or receive a diagnosis of thyroid cancer (4.3% vs 16.8%,  $P = .037$ ). Overall, most malignancies were low risk per American Thyroid Association guidelines ( $n = 20$ , 80.0%), regardless of Thyroid Imaging Reporting and Data Systems criteria. **CONCLUSION:** Many patients undergoing parathyroidectomy receive additional interventions for incidental thyroid nodules. However, adherence to Thyroid Imaging Reporting and Data Systems guidelines may help reduce unnecessary surgery, because most identified malignancies are low risk. The long-term impact remains unclear,

emphasizing the need for shared decision-making between surgeons and patients.

PubMed-ID: [41033888](#)

DOI: [10.1016/j.surg.2025.109705](#)

#### **A PTH Value at 6 Hours Postsurgery Predicts the Diagnosis of Transient and Permanent Hypoparathyroidism.**

*J Clin Endocrinol Metab*, 111(2):375-81.

A. Segarra-Balao, J. D. Barranco-Ochoa, M. de Damas-Medina, B. A. Sanchez-Arquelladas, E. Antonaya-Rubia, C. Rosa-Garrido, M. J. Martinez-Ramirez and A. J. Moreno-Carazo. 2026.

CONTEXT: PTH+ levels after thyroid surgery are generally used to detect patients at risk of developing postoperative hypoparathyroidism. However, there is still a lack of consensus about the threshold value regarding its evaluation, the definition of gland function recovery, and the classification of hypoparathyroidism as permanent. OBJECTIVE: PTH levels (determined 6 hours after total thyroidectomy) could be effective for early prediction of the risk of postsurgical hypocalcemia and IV calcium requirements during hospitalization, comparing it with the predictive capacity of serum calcium levels at 24 and 48 hours after surgery. We also aim to study the efficacy of the measurement of PTH levels for the predictive diagnosis of permanent hypoparathyroidism. DESIGN: Prospective cohort study between September 2021 and November 2023. SETTING: A public tertiary care hospital (Jaen, Spain). PATIENTS: We collected data on 105 patients undergoing total thyroidectomy. MAIN OUTCOME MEASURES: PTH levels were measured 6 hours postoperatively. Additionally, corrected calcium levels, adjusted for total protein, were measured at 24 hours and 48 hours postsurgery. RESULTS: In our study, a PTH value at 6 hours postsurgery  $<10.10$  pg/mL suggests, with high sensitivity and specificity, to be a very effective measure for identifying patients who would develop either transient [area under the curve (AUC) = 0.991, 95% confidence interval (CI) 0.978-1] and permanent hypoparathyroidism (AUC = 0.961, 95% CI 0.952-0.997). CONCLUSION: Measuring PTH levels at 6 hours postthyroidectomy is an accurate method for predicting which patients are at risk of developing transient and/or permanent hypoparathyroidism.

PubMed-ID: [40671592](#)

DOI: [10.1210/clinem/dgaf416](#)

PMCID: PMC12819874

#### **Setting yourself up for reoperative surgical success: Lessons learned from a 10-year experience with selective venous sampling for reoperative parathyroidectomy.**

*Surgery*, 189:109708.

E. R. Smith, E. Cooper, J. Pinchot and R. S. Sippel. 2026.

BACKGROUND: Accurate preoperative localization is critical in preparing for reoperative parathyroidectomy. Given the limitations of noninvasive imaging modalities, we examined how parathyroid selective venous sampling aided in identification of hyperactive parathyroid tissue and facilitated operative cure in challenging parathyroidectomy cases. METHODS: We performed a retrospective review of patients who underwent selective venous sampling prior to reoperative parathyroidectomy between 2014 and 2024. Operative reports, imaging studies, and selective venous sampling results were analyzed to evaluate the utility of venous sampling for reoperative parathyroidectomy. RESULTS: 83 patients underwent selective venous sampling prior to reoperative parathyroidectomy. Before undergoing selective venous sampling, all patients underwent a neck ultrasonography and a 4-dimensional computed tomography, and 49% (n = 41) also underwent Tc-99m sestamibi scan. Imaging was negative or inconclusive in all patients. Selective venous sampling results showed lateralization to one side of the neck in 77% (n = 64), clear mediastinal location facilitating thoracic approach in 6% (n = 5), inferior location without lateralization in 11% (n = 9), multigland disease in 2% (n = 2), and equivocal results in 4% (n = 3). After reviewing the selective venous sampling results, potential targets were identified on noninvasive imaging in 62% (n = 51) of cases. Overall, 92% (n = 76) proceeded with further surgical exploration based on the selective venous sampling. At the time of reoperative surgery, an abnormal parathyroid gland concordant with selective venous sampling localization was found in 81% (n = 62) of patients. CONCLUSIONS: Selective venous sampling can be a useful adjunct in reoperative parathyroidectomy when less invasive imaging modalities are inconclusive. Selective venous sampling requires significant expertise to do well and interpretation is nuanced and should be done in the context of additional imaging and a thorough understanding of patients' prior operations.

PubMed-ID: [41015677](#)

DOI: [10.1016/j.surg.2025.109708](#)

#### **Fiber-Based Near-Infrared Autofluorescence, Parathyroid Gland Identification, and Outcomes-Reply.**

*JAMA Surg*, 161(2):206-7.

C. C. Solorzano and A. Mahadevan-Jansen. 2026.

PubMed-ID: [41335410](#)

DOI: [10.1001/jamasurg.2025.5279](#)

**Parathyroidectomy is associated with lower mortality and fewer cardiac complications in patients with secondary hyperparathyroidism.**

*Surgery*, 189:109851.

Z. Song, J. Kasmirski, S. Balachandra, C. Wu, A. Gillis, J. Fazendin, B. Lindeman and H. Chen. 2026.

BACKGROUND: Secondary hyperparathyroidism can be treated with calcimimetics such as cinacalcet or surgically with parathyroidectomy. The adoption of cinacalcet has reduced the frequency of surgical management. This study evaluates the long-term outcomes of parathyroidectomy versus cinacalcet in patients with renal-origin secondary hyperparathyroidism who previously received conventional therapy. METHODS: We conducted a retrospective analysis using electronic health records (2004-2025) from the TriNetX platform. Patients with renal-origin secondary hyperparathyroidism and a medication history of vitamin D or phosphate binders were included. Those treated with cinacalcet for  $\geq 6$  months were compared to those who underwent parathyroidectomy without cinacalcet use or kidney transplantation. Propensity score matching (1:1) controlled for demographics, comorbidities, and cardiovascular therapies. Cox proportional hazards models estimated hazard ratios and 95% confidence intervals for mortality and cardiac outcomes. RESULTS: Among 11,581 patients, 1,478 (12.8%) underwent parathyroidectomy and 10,103 (87.2%) received cinacalcet. After matching, 1,227 patients were included in each group. Over a median follow-up of 4 years, parathyroidectomy was associated with lower risks of mortality (hazard ratio 0.68, 95% confidence interval 0.58-0.80) and composite cardiac events (0.75, 0.64-0.87). It was also associated with lower risks of ischemic heart disease, heart failure, and arrhythmias. Among patients with parathyroid hormone  $\leq 585$  pg/mL, parathyroidectomy remained associated with lower mortality (hazard ratio 0.73, 95% confidence interval 0.59-0.90) and cardiac risk (0.62, 0.50-0.77). CONCLUSIONS: Parathyroidectomy may provide superior long-term survival and cardiovascular outcomes compared to cinacalcet, even in patients with moderately elevated parathyroid hormone.

PubMed-ID: [41238436](#)

DOI: [10.1016/j.surg.2025.109851](#)

PMCID: PMC12626385

**Improving Intraoperative Parathyroid Hormone Monitoring with a Multidisciplinary Checklist: A Quality Improvement Initiative.**

*Otolaryngol Head Neck Surg*, 174(2):561-9.

A. R. Swisher, J. M. Hintze, C. H. Stucky, P. A. Cronin, P. Entezami, M. L. Hinni and B. A. Chang. 2026.

OBJECTIVE: Intraoperative parathyroid hormone (ioPTH) monitoring is crucial during parathyroid surgery to ensure chemical cure. However, delays in processing can prolong operative times. This study evaluates the effectiveness of a checklist to expedite ioPTH assay processes. METHODS: A multidisciplinary checklist was developed to standardize ioPTH collection and workflow. Thirty patients treated with use of the checklist were prospectively studied, while 30 patients treated without use of the checklist were retrospectively reviewed. Time intervals for post-15-minute ioPTH assay results were compared. RESULTS: Thirty age- and sex-matched patients were included in each group ( $n = 60$ ) involving 5 surgeons. The intervention and control group had a mean baseline PTH of 140.9 and 130.3 pg/mL and a post-15-minute ioPTH of 69.6 and 52.0 pg/mL, respectively. The mean time from sample collection to the post-15-minute ioPTH assay result was significantly reduced in the intervention as compared to the control group (22.2 vs 33.3 minutes;  $P < .01$ ). The proportional operative time spent awaiting ioPTH assay results was also reduced (24.4 vs 34.1%;  $P < .01$ ). In subgroup analysis, a significant difference in the total operative time was found in adenomatous disease (68.0 vs 92.2 minutes,  $P < .05$ ) but not four-gland hyperplasia (119.3 vs 142.3 minutes). DISCUSSION: The implementation of a simple intraoperative checklist effectively reduces the overall ioPTH assay processing time, creating a more efficient surgical workflow. It is low-cost and requires minimal additional resources. IMPLICATIONS FOR PRACTICE: This quality improvement intervention holds promise for broader adoption in parathyroid surgery to reduce delays and optimize patient care.

PubMed-ID: [41451691](#)

DOI: [10.1002/ohn.70081](#)

**Acute effects of parathyroidectomy on homocysteine levels in patients on dialysis.**

*J Visc Surg*, 163(2):103-8.

C. C. Tsai, C. Y. Kuo, Y. C. Ho and S. P. Cheng. 2026.

BACKGROUND: Elevated homocysteine levels are a known biomarker for cardiovascular disease. Previous studies have

reported inconsistent effects of parathyroidectomy on homocysteine levels. This study aimed to investigate the acute effects of parathyroidectomy on homocysteine levels. **METHODS:** A total of 357 dialysis patients who underwent parathyroidectomy for uncontrolled secondary hyperparathyroidism between 2011 and 2022 were included in the analysis. Baseline and postoperative plasma homocysteine levels were assessed. **RESULTS:** The median baseline homocysteine level was 19.2μmol/L, decreasing to 16.1μmol/L in the early postoperative period ( $P<0.001$ ). Baseline homocysteine levels showed a positive correlation with phosphorus but not with parathyroid hormone levels. The median change in homocysteine levels before and after surgery was -3.0μmol/L, reflecting a decrease of 16% from baseline. In multivariate analysis, patients with a higher body mass index or a longer duration of dialysis were less likely to experience a drop of more than 20% in homocysteine levels following parathyroidectomy. **CONCLUSION:** Plasma homocysteine levels decrease rapidly after parathyroidectomy. Further research is needed to clarify the relationship between this decrease and the benefits of surgical management.

PubMed-ID: [41807224](#)

DOI: [10.1016/j.jviscsurg.2025.11.001](#)

### **Ectopic parathyroid adenomas in primary hyperparathyroidism: anatomical classifications, localization strategies, and case series.**

*Int J Surg*, 112(4):9958-74.

R. Zhu, N. Yue, Y. Hong, Q. Ye, Z. Han, Z. Luo, C. Xie, H. Yan and X. Yu. 2026.

**BACKGROUND:** Ectopic parathyroid adenomas (EPAs) pose significant challenges in the diagnosis and management of primary hyperparathyroidism (PHPT) due to their atypical locations. This study aims to categorize EPAs based on their anatomical locations, describe the associated diagnostic strategies, and present case studies to illustrate clinical management. **METHODS:** EPAs were retrospectively reviewed based on cases from published literature and our institutional experience. Relevant studies were identified through a systematic search of PubMed and Embase. A comprehensive anatomical classification system was developed, categorizing EPAs into pharyngocranial, cervical, and mediastinal regions. **RESULTS:** From a total of 1278 screened publications, 137 studies encompassing 875 EPAs were identified and included. Combined with 13 original cases from our institute, these cases were comprehensively analyzed to develop an anatomically based classification system. EPAs were categorized into four types based on anatomical location: Type I (pharyngocranial), Type II (cervical, adjacent to the thyroid), Type III (cervical, distant from the thyroid), and Type IV (mediastinal). A combination of imaging modalities, including ultrasonography, CT, MRI, sestamibi scintigraphy, and SPECT, proved effective for preoperative localization. Case studies highlight clinical outcomes and challenges associated with each type. **CONCLUSION:** A comprehensive anatomical classification system for EPAs, integrated with advanced imaging modalities and correlated with biochemical profiles, improves preoperative identification and guides targeted treatment strategies.

PubMed-ID: [41417934](#)

DOI: [10.1097/JS9.0000000000004578](#)

PMCID: PMC13105754

### **Subjective health status, life performance and complications in chronic hypoparathyroidism - a German multicenter survey.**

*Front Endocrinol (Lausanne)*, 17:1723640.

C. T. Fuss, S. Engbers, N. Reisch, A. Hannemann, H. Volzke, H. J. Grabe, M. Nauck, M. Droste, H. S. Willenberg, N. Rayes, M. Fassnacht, M. Quinkler and S. Hahner. 2026.

**BACKGROUND:** There is mounting evidence that conventional replacement strategies with calcium and vitamin D are insufficient to fully prevent complications of chronic hypoparathyroidism (HypoPT) in all patients. **METHODS:** To investigate the disease burden of chronic HypoPT, we performed a survey in 205 HypoPT patients (159 females; median age 55 years; median disease duration 16 years). Patients received a disease-specific questionnaire asking for subjective health status, comorbidities, disease-related emergencies and interference of HypoPT with daily and work life. Patients were further assessed by the SF-36 questionnaire. Data was compared to sex- and age-matched subjects from the Study of Health in Pomerania SHIP-START, the German Health Interview and Examination Survey for Adults (DEGS1) and to 214 patients with adrenal insufficiency. **RESULTS:** Clinical symptoms associated with HypoPT during the past 12 months were reported by 92% of patients, requiring medical intervention in 32%. Since primary diagnosis of HypoPT, 36% of patients had presented at least once at an emergency department due to severe hypocalcemia (14.7 events per 100 patient years). Trigger factors for hypocalcemic symptoms were reported by 76% of patients (e.g. physical activity, infections, hot weather). In comparison to population-based controls, patients with HypoPT showed a higher prevalence of renal insufficiency (11% vs. 2%,  $p<0.001$ ) and more frequently received antihypertensive (44% vs. 34%;  $p=0.003$ ) and

antiepileptic drugs (5% vs. 2%,  $p=0.01$ ). Lifetime prevalence of both depression (22% vs. 15%,  $p=0.003$ ) and anxiety (21% vs. 6%,  $p<0.001$ ) were increased in HypoPT. SF-36 values indicated significantly reduced subjective health status in HypoPT patients compared to controls as well as patients with adrenal insufficiency. **CONCLUSION:** Despite established treatment, chronic HypoPT is associated with a variety of symptoms with a significant impact on daily life and work life. **TRIAL REGISTRATION:** <https://ClinicalTrials.gov/NCT03437174>.

PubMed-ID: [41987889](#)

DOI: [10.3389/fendo.2026.1723640](https://doi.org/10.3389/fendo.2026.1723640)

PMCID: PMC13076148

## Adrenals

### Meta-Analyses

#### **Evaluating the impact of adrenalectomy and mineralocorticoid receptor antagonists for primary aldosteronism on left ventricular remodeling: a systematic review and meta-analysis.**

*Eur J Endocrinol*, 194(1):S1-S13.

Y. C. Chang, U. L. Chen, C. S. Hung, Z. W. Chen, C. W. Liao, J. M. Brown, A. Vaidya, V. C. Wu, C. H. Tsai and Y. H. Lin. 2026. **BACKGROUND:** Primary aldosteronism (PA) is characterized by autonomous aldosterone production, which leads to left ventricular (LV) remodeling and adverse cardiovascular outcomes. This meta-analysis aimed to compare the effects of two treatment strategies, mineralocorticoid receptor antagonists (MRAs) and adrenalectomy, on the regression of LV remodeling in patients with PA. **METHODS:** Embase, PubMed, and Cochrane Library were searched for studies reporting the effect of adrenalectomy or medical therapy on reversing LV mass index (LVMI) in patients with PA. The outcome of interest was the reduction in LVMI after treatment. **RESULTS:** A total of 1197 patients with PA from 10 studies were included in the analysis. The meta-analysis demonstrated that both adrenalectomy and MRAs improved LVMI in patients with PA (adrenalectomy: standardized mean difference [SMD] = -0.49, 95% CI = -0.65 to -0.33; MRAs: SMD = -0.35, 95% CI = -0.48 to -0.22). The reduction in LVMI was greater following adrenalectomy in direct comparison analyses (difference-in-differences SMD = -0.15, 95% CI = -0.26 to -0.03). However, the effect size was small, and the impact of MRA optimization could not be assessed. In studies focusing specifically on unilateral PA, adrenalectomy demonstrated greater LVMI reduction than MRAs. **CONCLUSIONS:** This meta-analysis suggests that both adrenalectomy and MRAs improve LV remodeling. Although adrenalectomy was generally associated with slightly greater LVMI reductions than MRAs, the impact of optimized MRA therapy on LVMI reduction remains uncertain. When focusing specifically on patients with unilateral PA, adrenalectomy was associated with more pronounced regression of LV remodeling compared with MRA therapy.

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DOI: [10.1093/ajendo/lvaf271](https://doi.org/10.1093/ajendo/lvaf271)

PMCID: PMC12816874

#### **Cardiometabolic Risk Parameters in "Nonfunctioning" Adrenal Incidentalomas: A Systematic Review and Meta-analysis.**

*J Clin Endocrinol Metab*, 111(2):e619-e29.

V. Favero, D. Bernasconi, A. Maloberti, C. Parazzoli, A. Musolino, R. Chilton, A. P. Heaney, C. Eller-Vainicher, A. Scillitani and I. Chiodini. 2026.

**OBJECTIVE:** Several studies have investigated whether patients with nonfunctioning adrenal incidentalomas (NFAI) have an increased cardiometabolic risk, based on surrogate parameters such as the augmentation index (Aix), carotid intima-media thickness (cIMT), flow-mediated dilation (FMD), insulin resistance (IR), left ventricular mass index (LVMI), and pulse wave velocity (PWV), compared to patients without adrenal incidentalomas (AI). We sought to analyze the available literature to evaluate Aix, cIMT, FMD, IR, LVMI, and PWV in patients with NFAI as compared to patients without AI. **DESIGN:** Systematic review and meta-analysis. **METHODS:** We included studies that evaluated the cIMT and IR (primary outcomes) and Aix, FMD, LVMI, and PWV (secondary outcomes) in patients with NFAI vs matched subjects without AI. A random-effects model (DerSimonian and Laird) was used to calculate the standardized mean difference and 95% CI for

each outcome. RESULTS: Among the 24 available studies, 21 studies provided the necessary data (2228 subjects, mean age 53.3 +/- 2.9 years, 35% males). Data on cIMT, IR, AIX, FMD, LVMI, and PWV were reported in 12 (1063 subjects), 15 (1745 subjects), 2 (140 subjects), 3 (198 subjects), 3 (201 subjects), and 2 (140 subjects) studies, respectively. Compared with patients without AI, patients with NFAI showed statistically significant differences in cIMT, IR, AIX, FMD, LVMI, and PWV (standardized mean difference and 95% CI: 1.22, 0.87-1.58; 0.51, 0.32-0.69; 0.94, 0.38-1.50; -1.24, -1.84- -0.65; 0.41, 0.04-0.78; 1.03, 0.16-1.89, respectively). CONCLUSION: Based on cIMT, IR, AIX, FMD, LVMI, and PWV levels, patients with NFAI may be at increased cardiovascular risk.

PubMed-ID: [41165151](#)

DOI: [10.1210/clinem/dgaf597](#)

PMCID: PMC12819864

### **Transabdominal versus retroperitoneal laparoscopic adrenalectomy: A systematic review and meta-analysis.**

*Surgery*, 190:109817.

L. Gan, J. Wu, Z. Li, H. Cao, H. Wang, Y. Li, Z. Sun and W. Wang. 2026.

OBJECTIVE: To compare the safety and effectiveness of transabdominal laparoscopic adrenalectomy with retroperitoneal laparoscopic adrenalectomy. METHODS: We conducted a systematic review and meta-analysis of the main findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Assessing the Methodological Quality of Systematic Reviews Guidelines. Four databases were searched, including PubMed, Cochrane Library, Medline, and Scopus, and the time frame for the search was set from the creation of the databases to February 2025. RESULTS: There were 52 studies including 9,218 patients. The results showed that retroperitoneal laparoscopic adrenalectomy was superior to transabdominal laparoscopic adrenalectomy in terms of operative time (weighted mean difference, 8.58; 95% confidence interval, 1.49-15.66;  $P < .05$ ), length of stay (weighted mean difference, 0.90, 95% confidence interval, 0.64-1.17),  $P < .01$ ], estimated blood loss (weighted mean difference, 28.14; 95% confidence interval, 17.90-38.38,  $P < .01$ ), food intake time (weighted mean difference, 0.31; 95% confidence interval, 0.24-0.37,  $P < .01$ ), transfusion (odds ratio, 2.18; 95% confidence interval, 1.02-4.64,  $P < .05$ ), total complications (odds ratio, 21.32; 95% confidence interval, 1.07-1.63;  $P < .01$ ), and Clavien-Dindo grade  $\geq$  II complications (odds ratio, 21.87; 95% confidence interval, 1.17-3.00;  $P < .01$ ). There was no statistically significant difference between the 2 surgical groups in terms of time to ambulation, conversion, and Clavien-Dindo grade I-II complications. For large adrenal tumors ( $>5$  cm), retroperitoneal laparoscopic adrenalectomy was superior to transabdominal laparoscopic adrenalectomy in operative time (weighted mean difference, 21.40; 95% confidence interval, 1.20-41.60;  $P < .05$ ), length of stay (weighted mean difference, 0.96; 95% confidence interval, 0.57-1.36,  $P < .01$ ), estimated blood loss (weighted mean difference, 90.72; 95% confidence interval, 20.77-160.67;  $P < .05$ ), food intake time (weighted mean difference, 0.68; 95% confidence interval, 0.16-1.20,  $P < .05$ ), and total complications (odds ratio, 2.01; 95% confidence interval, 1.13-3.59;  $P < .05$ ). The difference in conversion was not statistically significant. For pheochromocytomas, retroperitoneal laparoscopic adrenalectomy was superior to transabdominal laparoscopic adrenalectomy in operative time (weighted mean difference, 26.9; 95% confidence interval, 13.13-40.69;  $P < .01$ ), length of stay (weighted mean difference, 1.38; 95% confidence interval, 0.82-1.94;  $P < .01$ ), estimated blood loss (weighted mean difference, 125.46; 95% confidence interval, 54.18-196.74;  $P < .01$ ), and food intake time (weighted mean difference, 0.84; 95% confidence interval, 0.42-1.27;  $P < .01$ ). The differences in conversion, transfusion, total complications, and intraoperative hemodynamic instability were not statistically significant. For large pheochromocytomas ( $>5$  cm), retroperitoneal laparoscopic adrenalectomy was superior to transabdominal laparoscopic adrenalectomy in terms of length of stay (weighted mean difference, 1.01, 95% confidence interval, 0.76-1.27;  $P < .01$ ) and estimated blood loss (weighted mean difference, 177.42; 95% confidence interval, 17.65-337.20;  $P < .05$ ). There was no statistically significant difference in terms of operative time, conversion, total complications, and intraoperative hemodynamic instability. CONCLUSION: In conclusion, this meta-analysis suggests that retroperitoneal laparoscopic adrenalectomy is a superior option to transabdominal laparoscopic adrenalectomy for the treatment of adrenal tumors and pheochromocytomas. For large adrenal tumors and pheochromocytoma ( $>5$  cm), retroperitoneal laparoscopic adrenalectomy remains a preferable option, but for larger ( $>7$  cm) and more complex adrenal tumors, transabdominal laparoscopic adrenalectomy should be given priority consideration. There is still a need for multicenter randomized controlled studies with larger sample sizes to support this conclusion.

PubMed-ID: [41151495](#)

DOI: [10.1016/j.surg.2025.109817](#)

### **Impact of diagnosis and targeted interventions on the quality of life and neuropsychiatric outcomes of patients with adrenal tumours: a systematic review.**

*Eur J Endocrinol*, 194(5):S41-S55.

B. Ruggiero, G. Zhu, L. Swan, O. Suntornlohanakul, M. Xu, C. L. Ronchi, Y. S. Elhassan, D. Yates and A. Prete. 2026.  
**OBJECTIVE:** To systematically evaluate the impact of adrenal tumour diagnosis and targeted interventions on health-related quality of life (HRQoL) and neuropsychiatric outcomes across tumour subtypes. **DESIGN:** Systematic review. **METHODS:** A literature search of MEDLINE, Embase, Cochrane Library, and CINAHL (January 1990-March 2026) identified studies reporting HRQoL and neuropsychiatric outcomes in adults with adrenal tumours, including non-functioning adrenal tumours (NFAT), mild autonomous cortisol secretion (MACS), adrenal Cushing's syndrome (CS), primary aldosteronism (PA), pheochromocytoma/paraganglioma (PPGL), and adrenocortical carcinoma (ACC). Study quality was assessed using CONSORT-PRO and Newcastle-Ottawa criteria. Due to methodological heterogeneity, findings were synthesized narratively. **RESULTS:** A total of 117 studies involving 35 361 patients were included. CONSORT-PRO quality was good but heterogeneous, whereas observational study quality was mostly moderate or low. Across tumour subtypes, adrenal tumours were consistently associated with impaired HRQoL and neuropsychiatric outcomes. A gradient of burden was evident, with mild impairment in NFAT, intermediate impairment in MACS and PA, and the most pronounced and persistent deficits in adrenal CS, PPGL, and ACC. Targeted interventions were often associated with improved patient-reported outcomes, though the magnitude and consistency of benefit varied across tumour subtypes and study design. Recovery was frequently incomplete. Most studies relied on generic HRQoL instruments, and no disease-specific neuropsychiatric tools were identified. **CONCLUSIONS:** Adrenal tumours are associated with substantial and often persistent impairment in patient well-being across tumour subtypes. Although treatment generally improves outcomes, residual symptoms are common, underscoring the need for long-term, patient-centred care and for the development of adrenal tumour-specific patient-reported outcome measures.

PubMed-ID: [42011921](#)

DOI: [10.1093/ejendo/lvag072](#)

### **Metastatic Disease in Pheochromocytomas and Paragangliomas in Various Genotypes-A Systematic Review and Meta-analysis.**

*J Clin Endocrinol Metab*, 111(2):580-90.

L. K. Svendsen, A. K. Rasmussen, M. C. Klose, J. Krogh and U. Feldt-Rasmussen. 2026.

**BACKGROUND:** Paragangliomas and pheochromocytomas (PPGLs) are rare neuroendocrine tumours with 10% to 20% of patients developing metastatic disease. The tumors exhibit a high degree of heritability, and pathogenic genetic variants have been associated with metastases. **OBJECTIVE:** We aimed to investigate the association between the genotype of PPGL patients and their risk of metastatic disease, adjusting for time. **METHODS:** A systematic search was conducted in PubMed and Embase. The primary outcome was the rate of metastatic disease per 100 followed patient-years analyzed through meta-analyses. **RESULTS:** A significantly increased rate of metastatic disease per 100 followed patient-years was observed in all pathogenic germline variants included in the analyses, compared to the group with no identified variant. The group with no variant had a rate of 1.55 per 100 patient-years. SDHA, SDHC, SDHD, VHL, RET, NF1, and MAX had rates of 13.73, 6.27, 2.03, 2.34, 1.91, 4.11, and 9.66, respectively. The rate of SDHB is not presented as statistical heterogeneity exceeded 75%. The pathogenic somatic variant EPAS1 showed a rate of 3.82. Cluster-divided meta-analyses resulted in rates of 4.41 and 3.0 for cluster 1 and cluster 2, respectively. Meta-regression analysis revealed a 2.3-fold higher rate for the SDHB variant compared to the other cluster 1 variants. **CONCLUSION:** We present associations between genotype and metastatic disease in PPGL patients. Our results indicate that patients harboring a pathogenic genetic variant have a higher rate of metastases compared to patients with no identified variant. High heterogeneity in several analyses suggests that further large cohort studies are needed.

PubMed-ID: [41183483](#)

DOI: [10.1210/clinem/dgaf584](#)

PMCID: PMC12819860

## **Randomized controlled trials**

### **Laparoscopic Versus Robotic Adrenalectomy: A Randomized Clinical Trial.**

*Ann Surg Oncol*, 33(2):1319-28.

E. Berber, A. Ibrahimli, E. Memisoglu, E. Akgun and R. Perez-Soto. 2026.

**BACKGROUND:** This study aimed to compare perioperative outcomes between laparoscopic and robotic transabdominal lateral adrenalectomies. **BACKGROUND:** Despite growing interest in robotic adrenalectomy (RA), its benefits compared

with those for laparoscopic adrenalectomy (LA) need to be identified. Two previously published randomized studies used out-of-date technologies and included only pheochromocytoma patients, respectively. **METHODS:** A prospective randomized clinical trial was conducted by a single surgeon between May 2024 and February 2025. Patients with adrenal tumors eligible for minimally invasive lateral transabdominal adrenalectomy were randomized to LA or RA. The trial was powered to detect a 30-min difference in operative time. The secondary outcomes were perioperative outcomes, cost, and ergonomics, measured by the NASA Task Load Index (NASA-TLX) and the Rapid Upper Limb Assessment (RULA). **RESULTS:** In the study, 27 patients were randomized to each group. The groups were similar in demographics, clinical characteristics, and operative indications. The operative times and secondary outcomes were similar between the groups except that the RA group had a lower median operating surgeon NASA-TLX score (16 vs 48;  $P \leq 0.001$ ) and a lower overall RULA score (14 vs 17;  $P = 0.001$ ) than the LA group. Operation room, hospital, and total costs were similar between the groups. Although all the procedures were completed as planned in the RA group, the LA group had four conversions from the original minimally invasive plan (conversion to open, hand-assisted procedure, and partial adrenalectomy and abortion of the procedure in one patient each). **CONCLUSIONS:** Perioperative outcomes, including cost, were similar between LA and RA, with better ergonomics and fewer conversions from the original minimally invasive surgical plan in the RA group.

PubMed-ID: [41139182](#)

DOI: [10.1245/s10434-025-18567-0](#)

PMCID: PMC12765717

## Consensus Statements/Guidelines

- None -

## Other Articles

### **Can virtual noncontrast computed tomography improve the diagnostic uncertainty of adrenal incidentalomas?**

*Surgery*, 191:110038.

L. Arthurs, M. Schumm, P. Curcio, Z. Gajic, R. Petrocelli, M. Taffel, R. Raghunathan, O. McAllister-Nevins, C. Chan, K. Patel, R. Liou, J. Prescott, J. Allendorf and I. Suh. 2026.

**BACKGROUND:** Although most adrenal incidentalomas are benign, many are identified by single-phase contrast-enhanced computed tomography, which is unreliable for excluding malignancy. Virtual noncontrast computed tomography is a newer modality with the potential to better characterize adrenal nodules. **METHODS:** Virtual noncontrast computed tomography of adrenal nodules with available reference standard of true noncontrast computed tomography were identified (2016-2024). Images were evaluated for nodule characteristics including Hounsfield unit attenuation and variability. Nodules were classified as benign ( $\leq 10$  Hounsfield units) or indeterminate/suspicious ( $> 10$  Hounsfield units) by true noncontrast computed tomography. Hounsfield units were compared between virtual noncontrast computed tomography and true noncontrast computed tomography. Variability in attenuation measurements was compared by evaluating Hounsfield unit differences 1 slice up and down from the chosen mid-depth image. Receiver operating characteristic analysis was used to define optimal virtual noncontrast computed tomography accuracy thresholds. **RESULTS:** After excluding 5 adrenal nodules due to suboptimal imaging, 67 nodules were identified. Based on true noncontrast computed tomography Hounsfield units, 23 nodules (34.3%) were benign, and 44 (65.7%) were indeterminate/suspicious. Hounsfield unit measurements for each nodule exhibited wide variability by both virtual noncontrast computed tomography and true noncontrast computed tomography. Virtual noncontrast computed tomography and true noncontrast computed tomography were significantly correlated with moderate effect size (Pearson coefficient 0.69,  $P < .001$ ). Conflicting impressions occurred for 6 nodules (9.0%). Overall, virtual noncontrast computed tomography exhibited outstanding discrimination between benign and indeterminate/suspicious nodules (area under the curve 0.94). Maintaining a threshold of  $\leq 10$  Hounsfield units achieved 93% sensitivity, 76% specificity, and 84% negative predictive value, whereas  $\leq 7$  Hounsfield units achieved 100% negative predictive value. The functional utility of virtual noncontrast computed tomography as a rule-out test applied to 16% of nodules. **CONCLUSION:** Despite wide variability in Hounsfield unit measurements, adrenal nodules are well defined by both virtual noncontrast computed tomography and true noncontrast computed tomography. Well-reconstructed virtual noncontrast computed tomography images can accurately rule out malignancy in selected patients, potentially obviating the need for additional imaging.

PubMed-ID: [41500073](#)

DOI: [10.1016/j.surg.2025.110038](#)

#### **Adrenal histologic and genetic characteristics of primary aldosteronism in late adulthood.**

*Eur J Endocrinol*, 194(2):208-16.

A. R. Blinder, D. Sapiro, J. E. Baker, Z. Qin, I. Bancos, M. L. Lyden, W. F. Young, H. Wachtel, D. L. Cohen, L. Kurzinger, M. Fassnacht, J. M. Luther, T. A. Williams, M. Reincke, A. F. Turcu, T. Else, T. J. Giordano, A. M. Udager, W. E. Rainey and K. Nanba. 2026.

OBJECTIVE: Recent studies suggest a unique disease profile in elderly patients with primary aldosteronism (PA), who have a high prevalence of comorbidities and low clinical cure rate post-adrenalectomy. This study aims to investigate histopathology and genetic characteristics of PA in late adulthood. METHODS: Formalin-fixed, paraffin-embedded adrenal tissue sections from 114 patients with PA who underwent unilateral adrenalectomy at age 60 or older were used.

Aldosterone synthase (CYP11B2) immunohistochemistry (IHC) was performed for histopathologic analysis. Somatic DNA variants were identified in aldosterone-producing tissue following CYP11B2 IHC-guided sequencing. RESULTS:

Histopathologic analysis revealed that 56 adrenals contained an aldosterone-producing nodule (APN) (49%), 44 contained an aldosterone-producing adenoma (APA) (39%), 7 contained multiple APN (6%), and 7 contained only non-functioning adenomas [NFA, of which 6 had at least one aldosterone-producing micronodule (APM) in the adjacent tissue] (6%). NFAs were also identified alongside APN/APA in 24 cases. An APN was the most common histologic subtype in men (51/88, 58%), while APA was predominant in women (18/26, 69%). Of 67 APNs with successful sequencing, the majority had variants in CACNA1D (40/67, 60%). KCNJ5 variants were the most common alteration in APA (14/44, 32%). CONCLUSIONS: Older individuals with lateralized PA exhibit distinct genetic and histologic causes of disease with sex differences in mutation prevalence and adrenal histopathology. In APN, the most frequently altered gene is CACNA1D, while KCNJ5 variants are most common in APA. Unlike young patients with PA, the presence of NFA is a frequent observation in late adulthood individuals with PA.

PubMed-ID: [41618603](#)

DOI: [10.1093/ejendo/lvag022](#)

PMCID: PMC13276716

#### **Case Report: Peritoneal disease from adrenal cortical carcinoma with hepatic metastases managed with cytoreductive surgery and multiple HIPEC sessions, resulting in survival beyond 13 years.**

*Front Surg*, 13:1725272.

A. Camarasa Perez, R. Wijayawardana, N. Ahmadi and D. L. Morris. 2026.

Adrenocortical carcinoma (ACC) is a rare and highly aggressive malignancy with limited therapeutic options and poor long-term survival, particularly in advanced stages. Complete surgical resection remains the cornerstone of treatment, although recurrence is common and management of metastatic disease is challenging. Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has shown survival benefits in other intraperitoneal malignancies, but its role in ACC remains uncertain due to the rarity of the disease and the scarcity of evidence. We present the case of a 46-year-old woman diagnosed with left-sided ACC in 2012, initially treated with laparoscopic adrenalectomy and adjuvant radiotherapy. Over the following years, she developed multiple peritoneal and hepatic recurrences, managed with repeated cytoreductive surgeries and systemic therapies, including mitotane-based chemotherapy. From 2014 to 2025, the patient underwent four cytoreductive surgeries combined with HIPEC using different intraperitoneal chemotherapy agents, including cisplatin, doxorubicin, and mitomycin C, each achieving complete cytoreduction. The intervals between procedures reached up to three years of disease-free survival, and the patient tolerated all treatments with minimal morbidity. Thirteen years after the initial diagnosis, she remains alive and functionally well following her most recent cytoreductive surgery and HIPEC for bladder and ileocecal recurrence. This case highlights the potential role of iterative cytoreductive surgery combined with HIPEC in achieving long-term survival and disease control in selected patients with recurrent or metastatic ACC. Although limited evidence precludes definitive conclusions, our findings suggest that the integration of HIPEC with surgical management may represent a valuable therapeutic option warranting further investigation in this rare and aggressive malignancy.

PubMed-ID: [41993797](#)

DOI: [10.3389/fsurg.2026.1725272](#)

PMCID: PMC13079003

**Duration of adrenal insufficiency after surgical treatment of endogenous hypercortisolism: a prospective cohort study.**  
*Eur J Endocrinol*, 194(1):1-12.

S. R. Chacko, S. Ahmadian, S. S. Sharma, J. Saini, V. Fell, S. J. Achenbach, E. J. Atkinson, J. J. Van Gompel, W. F. Young, Jr. and I. Bancos. 2026.

**OBJECTIVE:** Evidence on the duration of post-operative adrenal insufficiency (AI) in patients with endogenous hypercortisolism is scarce. We sought to determine the duration of post-operative AI and to identify factors associated with the duration of AI in patients undergoing surgery for endogenous hypercortisolism. **METHODS:** We conducted a single-center prospective cohort study, 2019-2025, of patients with endogenous hypercortisolism [Cushing syndrome (CS) or mild autonomous cortisol secretion (MACS)] treated with surgery. Associations of demographics, body mass index (BMI), clinical, and biochemical hypercortisolism severity, subtype of hypercortisolism, pre-surgical hypercortisolism duration, glucocorticoid type, and nadir cortisol in relation to duration of AI were investigated. **RESULTS:** The 242 patients [41% MACS, 46% pituitary CS, 12% adrenal CS, 1% ectopic CS, median age 50 years (IQR: 40-60), 85% women] who developed postsurgical AI were followed for a median duration of 13.7 months (IQR 7.2-26.3). The median time to recovery of AI was shorter in MACS vs. overt CS (3.9 months (95% CI: 3.3-6.2) vs. 13.5 months (95% CI 11.3-18.3),  $P$  value < .001). On multivariable analysis adjusting for age, sex, BMI, and glucocorticoid type, moderate to severe biochemical severity score ( $\beta$  = 11,  $P$  value < .001) and moderate to severe clinical severity score ( $\beta$  = 8.7,  $P$  < .001), were associated with a longer duration of AI. **CONCLUSIONS:** Baseline clinical and biochemical hypercortisolism severity scores may inform individualized counseling on post-operative AI duration in patients treated for CS and MACS.

PubMed-ID: [41424030](#)

DOI: [10.1093/ajeendo/lvaf264](#)

PMCID: PMC12772629

**A Global Approach to the Long-Term Follow-Up of 17 Families With Bilateral Macronodular Adrenal Disease.**

*J Clin Endocrinol Metab*, 111(3):e917-e26.

H. L. S. Charchar, G. A. Alencar, B. M. de Paula Mariani, A. W. Kuhn, J. T. de Camargo Silva, L. Bouys, P. Vaduva, M. Y. Nishi, F. L. Ledesma, M. Q. Almeida, V. Srougi, F. Y. Tanno, J. L. Chambo, A. C. Latronico, M. A. A. Pereira, J. Bertherat, B. B. Mendonca and M. C. B. Villares Frago. 2026.

**CONTEXT:** Bilateral macronodular adrenocortical disease (BMAD) is a rare and often underdiagnosed cause of adrenal Cushing syndrome (CS), with manifestations ranging from mild autonomous cortisol secretion (MACS) to overt CS. ARMC5 and KDM1A are the most frequently implicated genes in familial BMAD; however, long-term follow-up data on affected patients remain limited. **OBJECTIVE:** This retrospective study assessed the clinical and hormonal variability, genetic profiles, treatment approaches, and outcomes of 17 familial and 9 sporadic BMAD cases over a follow-up period ranging from 8 to 410 months at a Brazilian tertiary center. **METHODS:** A total of 250 individuals (50 index cases and 200 relatives) were included. Clinical, hormonal, and imaging data, along with histological and genetic analyses of ARMC5 and KDM1A, were evaluated. **RESULTS:** Among 250 individuals, 104 (26 index and 78 relatives) carried germline pathogenic/likely pathogenic ARMC5 variants. No KDM1A (likely) pathogenic variants were identified in ARMC5-wild-type patients. ARMC5-positive index cases exhibited severe clinical manifestations, evidenced by elevated cortisol levels (urinary, salivary, and post-dexamethasone suppression test) and reduced ACTH and DHEAS levels ( $P$  = .005,  $P$  = .042,  $P$  = .005,  $P$  = .041, and  $P$  = .007, respectively). Index cases had larger adrenal nodules ( $P$  < .0001). Adrenal-sparing surgery achieved 100% remission vs a 40% remission rate for unilateral adrenalectomy. Central nervous system meningiomas were observed in BMAD patients independent of ARMC5 status. Interestingly, malignant neoplasms were notably prevalent among ARMC5-altered individuals. **CONCLUSION:** The proposed management flowchart highlights the importance of genetic screening and continuous monitoring to mitigate the adrenal insufficiency, MACS recurrence, and tumor risk, while underscoring the need for tailored therapeutic strategies in BMAD, adapted to genetic alterations and ARMC5 status.

PubMed-ID: [40810200](#)

DOI: [10.1210/clinem/dgaf465](#)

**Objective assessment of vascular dysfunction in pheochromocytoma and paraganglioma patients and reversal following curative surgery: Results from prospective PheoCard study.**

*Surgery*, 189:109704.

S. Dariya, R. S. Ahada, R. Khanna, K. M. M. Vishvak Chanthar, S. Mayilvaganan, G. Chand, A. Mishra, A. Kapoor and G. Agarwal. 2026.

**BACKGROUND:** Hypertension and cardiovascular changes are hallmarks of pheochromocytoma/paraganglioma. Endothelium-dependent flow-mediated vasodilatory response and endothelium-independent nitroglycerin-mediated vasodilatory response, which are linked to cardiovascular mortality, have not been studied in

pheochromocytoma/paraganglioma. This study evaluated extent of vascular changes and impaired vasodilatory responses in patients with pheochromocytoma/paraganglioma and their reversal following curative surgery. **METHODS:** This prospective cohort study evaluated flow mediated vasodilatory response and nitroglycerin-mediated vasodilatory response in 40 patients with pheochromocytoma/paraganglioma (at diagnosis; after alpha blockade; 7 days, 3 months, and 6 months postsurgery) and in matched control subjects (at baseline), normalized for confounding factors affecting vasodilatory response. Patients underwent curative open/minimally invasive surgery. Significance of linear changes in vascular indices over time was calculated using appropriate statistical methods. **RESULTS:** Mean age of patients with pheochromocytoma/paraganglioma (10 normotensive, 6 paraganglioma, 25 male) was 35.4 +/- 15.5 years. No patients had persistent hypercatecholaminism; 42.5% remained hypertensive postsurgery. Flow-mediated vasodilatory response and nitroglycerin-mediated vasodilatory response exhibited less vasodilation in study group compared with normotensive and essential hypertensive control subjects. Mean flow-mediated vasodilatory response (%) in pheochromocytoma/paraganglioma cohort increased from 3.4 +/- 1.2 at baseline to 5.1 +/- 1.8 after alpha blockade and 7.2 +/- 1.8, 8.0 +/- 2.7, and 9.4 +/- 2.9 at 7 days, 3 months, and 6 months postsurgery, respectively, with 6-month values approaching those of healthy control subjects (9.1 +/- 4.5,  $P < .001$ ). Mean nitroglycerin-mediated vasodilatory response (%) improved from 8.0 +/- 2.4 (baseline) to 10.7 +/- 2.7 after alpha blockade and 13.6 +/- 3.3, 16.1 +/- 5.2, and 17.0 +/- 4.5 (near-normal) at 7 days, 3 months, and 6 months postsurgery, respectively ( $P < .001$ ). **CONCLUSIONS:** In this first-of-its-kind study performed using objective noninvasive vascular assessment methodology, patients with pheochromocytoma/paraganglioma were found to have impaired endothelium-dependent and endothelium-independent vasodilatory responses. The stunted vasodilatory responses are reversed and normalized following curative resection of catecholamine-secreting tumors.

PubMed-ID: [41058329](#)

DOI: [10.1016/j.surg.2025.109704](#)

#### **Long-term cardiac effects of adrenalectomy versus surveillance in mild cortisol excess: 5-year results from the prospective ITACA study.**

*Eur J Endocrinol*, 194(2):170-84.

D. De Alcubierre, D. Ferrari, A. Tomaselli, F. Moscucci, I. Bonaventura, A. Francia, E. Voza, I. Lospinuso, E. Ettore, V. Hasenmajer, M. Minnetti, E. Sbardella, M. Tenuta, S. Morelli, A. M. Paganini, A. M. Isidori and R. Pofi. 2026.

**OBJECTIVE:** To determine whether cardiac remodelling associated with mild autonomous cortisol secretion (MACS) is reversible after treatment and how trajectories compare with non-functioning adrenal incidentalomas (NFAI). **DESIGN:** Five-year prospective cohort study (ITACA; NCT04127552). **METHODS:** Sixty patients (35 MACS, 25 NFAI) underwent clinical, biochemical, and echocardiographic evaluations at baseline and after 1 and 5 years. MACS was managed with either active surveillance (AS,  $n = 22$ ) or unilateral adrenalectomy (ADRX,  $n = 13$ ). Longitudinal changes were analysed with linear mixed-effects models. **RESULTS:** At baseline, MACS had a higher prevalence of left-ventricular (LV) hypertrophy (46% vs 16%,  $P = .013$ ) and diastolic dysfunction (34% vs 12%,  $P = .050$ ), and greater LV mass index (LVMI) (median 100 vs 85 g/m<sup>2</sup>,  $P = .011$ ). Over time, the change in LVMI differed between NFAI, MACS-AS and MACS-ADRX ( $P = .004$ ). At 1 year, LVMI fell by -14.8 g/m<sup>2</sup> (95%CI -28.7 to -0.9) after ADRX and rose by 13.7 g/m<sup>2</sup> (0.8 to 26.5) under AS. By 5 years, LVMI returned to baseline in both MACS subgroups, whereas NFAI increased by 22.4 g/m<sup>2</sup> (12.3 to 32.5;  $P < .001$ ). Right-ventricular systolic excursion (TAPSE) improved only in AS (3.6 mm, 1.8 to 5.4;  $P = .001$ ). Global LV systolic and diastolic indices deteriorated similarly across groups. Major adverse cardiac events occurred in 13.3% of MACS-AS, 12.5% of ADRX, and 5.6% of NFAI patients. **CONCLUSIONS:** MACS is associated with early concentric LV remodelling that regresses after adrenalectomy but rebounds within 5 years, leaving surgical and surveillance patients with comparable cardiac geometry. Under AS, remodelling stabilizes, whereas NFAI continue a slow, progressive hypertrophic course. These findings support serial echocardiographic monitoring and underscore the need to test other cortisol-lowering therapies, alone or in combination with surgery, for durable cardioprotection.

PubMed-ID: [41572809](#)

DOI: [10.1093/ajendo/lvag018](#)

#### **Adrenal tumors in the elderly.**

*Endocr Relat Cancer*, 33(1)

A. Decmann, P. I. Turai, P. Perge and P. Igaz. 2026.

**ABSTRACT:** The incidence of adrenal tumors rises with age, but the link between adrenal aging and tumorigenesis is still not well defined. This mini-review summarizes age-related changes in both the adrenal cortex and medulla, including structural remodeling, altered steroidogenesis, and shifts in immune and cellular homeostasis. We then examine adrenocortical carcinoma (ACC), where clinical outcomes are poorer in older patients and where senescence,

inflammation, and sex-specific immune differences may shape disease behavior. Limited information is available for other adrenocortical tumors, while pheochromocytomas in the elderly are described mainly in case reports, often with diagnostic and perioperative difficulties. For other rare adrenal neoplasms, data are fragmentary. Much of the mechanistic evidence summarized here derives from preclinical models, and robust clinical validation remains limited; accordingly, translational inferences should be regarded as provisional. The evidence suggests that aging influences both the biology and clinical course of adrenal tumors, but systematic studies are lacking. This review brings together what is currently known and highlights many open questions. We hope this will serve as a starting point for further work on how aging affects adrenal function and tumor development and how this knowledge might be used to improve care of older patients.

PubMed-ID: [41532570](#)

DOI: [10.1530/ERC-25-0150](#)

### **Hair cortisol outperforms urinary free cortisol in diagnosing Cushing's syndrome: a cross-sectional study.**

*Hormones (Athens),*

H. Y. Deryol, S. Tek, E. Akpinar, B. Erkan, U. Keskin, M. Tuna, M. Niyazoglu and E. S. Hatipoglu. 2026.

**PURPOSE:** Hair cortisol concentration (HCC) is effective in the identification of Cushing's syndrome (CS), yet current guidelines have not incorporated its utilization. The limited use of HCC is a significant factor here, underscoring the need for additional data to validate the test. Earlier studies on HCC did not compare it with urinary free cortisol (UFC) and late-night salivary cortisol (LNSC) in cases with CS. We aimed to evaluate HCC's effectiveness in identifying hypercortisolemia in patients with endogenous Cushing's syndrome, comparing it to UFC and LNSC. **METHODS:** The study involved 23 individuals with active endogenous CS and 21 age- and gender-matched participants with non-functioning pituitary adenomas (NFA). HCC was evaluated through the ECLIA method. Cortisol and ACTH levels, dexamethasone suppression tests (DST), bedtime serum cortisol (BSC), UFC, and LNSC, all related to the hair collection period, were also included. **RESULTS:** Cases with CS had increased HCC relative to the control cases (24.2[IQR: 8.3-48.8] vs. 2.2[IQR: 0.7-5.7]ng/gr,  $p < 0.001$ ). The optimal HCC cut-off value, 6.15 ng/g, had 87% sensitivity and 91% specificity. In cases with CS, HCC was correlated with BSC, LNSC, and 1 mg-DST results ( $\rho = 0.5$ ,  $p = 0.03$ ;  $\rho = 0.5$ ,  $p = 0.01$ ; and  $\rho = 0.5$ ,  $p = 0.03$ ). In cases with CS, the false negative rates were 13% with HCC, 24% with LNSC, and 54.5% with UFC (HCC vs. LNSC,  $p = 0.4$ ; HCC vs. UFC,  $p = 0.01$ ). **CONCLUSION:** HCC demonstrated high diagnostic accuracy in patients with Cushing's syndrome and showed superior performance compared to urinary-free cortisol. Given its non-invasive nature and ability to reflect long-term cortisol exposure, HCC offers meaningful clinical implications as a complementary diagnostic tool, particularly in patients with discordant or borderline biochemical test results.

PubMed-ID: [41540319](#)

DOI: [10.1007/s42000-025-00750-3](#)

### **3D versus 2D laparoscopy for adrenal surgery: an international multicentric retrospective cohort study.**

*Int J Surg*, 112(2):4191-9.

G. Di Buono, A. Territo, J. I. Rodriguez-Hermosa, L. Cornejo, M. Rodriguez-Mane, G. Mantica, C. Terrone, N. Crisan, I. Andras, F. Esperto, R. M. Scarpa, A. Breda, M. Casadevall, R. Citarrella, G. Amato, G. Romano, M. Lodico, D. Matranga and A. Agrusa. 2026.

**BACKGROUND:** Laparoscopy is currently considered the standard of treatment for adrenal lesions but remains a challenging procedure. This retrospective cohort study aims to compare the use of 3D technology with traditional 2D laparoscopy for adrenalectomy through a large, multicentric, international patients' enrollment. **MATERIALS AND METHODS:** Data of this retrospective cohort study were collected from six high-volume European centers between January 2003 and December 2023. Eligible participants were adults between 18 and 85 years, candidates for laparoscopic adrenal surgery, stratified into two groups: those who underwent three-dimensional laparoscopic adrenalectomy (3D group) versus traditional two-dimensional vision system laparoscopic adrenal surgery (2D group). The incidence of overall complications was estimated and compared between two groups (main endpoint), in addition to comfort vision, surgical depth perception, and surgical strain of the surgical team (secondary endpoint). Other pre-, intra-, and postoperative data were reported as well. **RESULTS:** We included 356 patients: 108 (30.34%) underwent traditional laparoscopic surgery, and 248 (69.66%) underwent 3D laparoscopic surgery. The operative time was significantly shorter ( $P < 0.001$ ), with an average of 100 minutes for the 3D technique compared to 125.4 minutes for traditional laparoscopy. The conversion rate was 2% in the 3D group versus 7.4% in the 2D group ( $P = 0.026$ ). Blood loss was higher in the group treated with traditional laparoscopy (100.7 cc vs. 71.7 cc,  $P < 0.001$ ), as well as the use of postoperative drainage (68.5% vs. 33.5%,  $P < 0.001$ ). The postoperative hospital stay was longer for patients treated with the traditional technique, with an average of 4 days (SD = 2.7), compared to an average of 2.8 days (SD = 1.7) for patients treated with the 3D technique ( $P < 0.001$ ). Postoperative overall complications were lower in the 3D group, with a 14.1% cumulative incidence of patients

experiencing complications, compared to 16% in the traditional laparoscopy group, but not significantly ( $P = 0.615$ ). Grade 3b complications, to the Clavien-Dindo classification, were negligible in both the 3D laparoscopic group (0.4%) and the traditional laparoscopic group (0.9%), without any statistically significant difference between the two groups. Based on the subjective assessment of the two techniques, we observed significantly better scores in the 3D procedure versus traditional laparoscopic surgery ( $P < 0.001$ ). **CONCLUSION:** The obtained results reinforced the safety and efficacy of the 3D approach. Furthermore, surgeons' positive opinion of 3D laparoscopy is evidence of increased operator comfort and justifies its use in training and clinical practice.

PubMed-ID: [41247879](#)

DOI: [10.1097/J59.0000000000003964](#)

#### **More liberal use of bilateral adrenalectomy for bilateral adrenal tumours with cortisol excess.**

*Lancet Diabetes Endocrinol*, 14(3):188-9.

Q. Y. Duh and M. B. Mulder. 2026.

PubMed-ID: [41579870](#)

DOI: [10.1016/S2213-8587\(25\)00354-7](#)

#### **Tailored surgery for large adrenal tumors: the minimally invasive to open (hybrid) approach.**

*Updates Surg*, 78(1):385-95.

A. Dukaczewska, K. Ilgner, C. A. Kunze, J. Sladek, E. M. Dobrindt, P. E. Goretzki, J. Pratschke, M. T. Mogl and F. Butz. 2026. Conversion from minimally invasive techniques to open surgery has mostly been considered as an undesirable event associated with intraoperative complications or poor preoperative planning. However, the impact of conversion to open surgery during adrenalectomy for large adrenal tumours remains unclear. This study investigates the outcomes of conversion from minimally invasive to open surgery for adrenal masses  $\geq 60$  mm with an additional focus on the identification of survival predictors in patients with large adrenocortical carcinoma (ACC). We retrospectively analyzed 97 patients who underwent unilateral adrenalectomy for tumours  $\geq 60$  mm. Patient characteristics, tumour features, surgical approaches, and outcomes were compared. Survival outcomes in ACC patients ( $n = 34$ ) were assessed using Kaplan-Meier analysis, with prognostic factors evaluated via univariate Cox regression and Ridge Regression modeling. Of 97 patients, 41 (42%) underwent minimally invasive adrenalectomy (MIA), 40 (41%) open adrenalectomy (OA), and 16 (17%) required conversion to open surgery (hybrid adrenalectomy, HA). HA had a longer operative time (median 226.5 vs. 108.5 min;  $p < 0.001$ ) and hospital stay (median 9 vs. 4 days;  $p < 0.001$ ) compared to MIA but not OA (median 188 min;  $p = 0.102$ ; 10 days;  $p = 0.519$ , respectively). Overall, complications were more frequent in HA (43.7%) than MIA (7.3%;  $p = 0.003$ ) but similar to OA (37.5%;  $p = 0.897$ ). Minor complications were more common in HA than MIA (31 vs. 7%;  $p = 0.032$ ), while major complications were comparable (12.5 vs. 7.5%;  $p = 0.617$ ). Tumours in HA cases more often showed vascular infiltration ( $p = 0.001$ ) and required multivisceral resection ( $p = 0.002$ ). ENSAT tumour stage (OS: HR = 4.66,  $p = 0.041$ ; PFS: HR = 2.52,  $p = 0.005$ ) and the S-GRAS score (OS: HR = 6.00; PFS: HR = 1.50) were significant survival predictors in ACC, whereas the operative technique was not. Conversion to open surgery increases minor complications compared to MIA but not OA. ENSAT tumour stage and S-GRAS score predict survival in ACC, while the surgical approach does not. Timely conversion should be performed to ensure oncological safety when needed.

PubMed-ID: [40879871](#)

DOI: [10.1007/s13304-025-02388-7](#)

PMCID: PMC12909437

#### **Adrenal axis integrity after IV methylprednisolone therapy for thyroid eye disease: a retrospective cohort study.**

*Eur J Endocrinol*, 194(5):653-62.

G. Effraimidis, A. Kasotas and A. Bargiota. 2026.

**OBJECTIVE:** Only 5 prior studies, each involving 12 to 32 patients, have evaluated the impact of high-dose intravenous methylprednisolone (IVMP) on hypothalamic-pituitary-adrenal (HPA) axis function in patients with active moderate-to-severe thyroid eye disease (TED). Due to their small sample sizes and methodological limitations, uncertainty remains regarding the risk of adrenal suppression following this regimen. **METHODS:** We conducted a retrospective observational study of 127 adults with active moderate-to-severe TED treated with the standard IVMP protocol (cumulative dose: 4.5 g over 12 weeks) at the Department of Endocrinology and Metabolic Diseases, University General Hospital of Larissa, Greece. HPA axis integrity was assessed 7-10 days after the final IVMP dose using the 250-mug ACTH(1-24) stimulation test. Serum cortisol was measured at baseline, 30-, and 60-min post-ACTH. A peak cortisol level  $\geq 18.1$  mug/dL ( $\geq 500$  nmol/L) was considered indicative of adrenal sufficiency. **RESULTS:** Twelve patients were excluded due to unavailability of testing or contraindications. Among the 115 patients tested, 15 (13%) had baseline cortisol  $\geq 18.1$  mug/dL. At 30 min,

93% achieved adequate cortisol response, and at 60 min, 100% met the sufficiency threshold. All patients with baseline cortisol <5 mug/dL (150 nmol/L) demonstrated intact adrenal function on dynamic testing. CONCLUSIONS: In this cohort, adrenal responsiveness to the 250 mug ACTH test 7-10 days after completion of IVMP was preserved in all patients, suggesting that early post-treatment secondary adrenal insufficiency is uncommon. Although reassuring, these results should be interpreted cautiously, and clinicians should continue to rely on clinical judgment, supported by biochemical testing when indicated.

PubMed-ID: [42139516](#)

DOI: [10.1093/ejendo/lvag077](#)

#### **Quality of life in patients with pheochromocytoma and paraganglioma: influence of tumor type, genetics and surgical resection.**

*Eur J Endocrinol*, 194(2):80-90.

A. Fischer, H. Remde, C. Pamporaki, A. Prinzi, O. Kimpel, S. Kuppers, C. Hantel, K. Pacak, A. B. Grossman, F. Beuschlein, M. Fassnacht and S. Nolting. 2026.

CONTEXT: Pheochromocytomas and paragangliomas (PPGL) are rare endocrine tumors with high heritability. Carriers of pathogenic variants (PVs) in susceptibility genes face a lifelong risk of recurrence or metastatic disease. Quality of life (QoL) in patients with PPGL, a history of PPGL and PV carriers, remains insufficiently studied. METHODS: We assessed patient-reported QoL in patients with PPGL before and after surgery and in carriers of susceptibility PVs for the development of PPGLs within the prospective ProsPheo study. QoL was evaluated using standardized questionnaires (SF-12, PHQ-D, and GAD-7). RESULTS: A total of 202 participants were analyzed. SF-12 physical component summary scores (PCS) differed significantly across subgroups ( $P = .006$ ), with the lowest PCS scores in patients with metastatic PPGL (40.3) and unresected head and neck paragangliomas (HNPG) (40.0), compared with PV carriers after curative PPGL resection (50.2). Within metastatic disease, hormonally active tumors showed lower PCS scores than inactive tumors (36.9 vs 46.2;  $P = .03$ ). Perceived physical health in carriers of a PV without history of a PPGL was significantly lower compared to the age-matched general population. Mental health was not significantly impaired across all subgroups. Clinically relevant anxiety was reported in 15.2% of PV carriers and 21.7% of patients with unresected HNPGs, compared with about 5.9% in the general population. CONCLUSIONS: Patient-reported physical health was reduced in patients with metastatic PPGLs, unresected HNPGs, and PV carriers without prior PPGL, whereas patients after curative PPGL resection reported QoL comparable to the general population, regardless of PV status, suggesting that annual follow-up has minimal impact on QoL.

PubMed-ID: [41525330](#)

DOI: [10.1093/ejendo/lvag003](#)

#### **Correction to: Can the size of adrenal tumor impact hormonal secretion? A retrospective analysis of 170 adrenalectomies in a single center.**

*Langenbecks Arch Surg*, 411(1)

R. Frey, A. Posabella, S. Hosner, A. Fiore, A. Wilhelm, S. Eschlbock, R. Droeser, T. Delko and Lazaridis, II. 2026.

PubMed-ID: [41880028](#)

DOI: [10.1007/s00423-026-04025-2](#)

PMCID: PMC13017989

#### **Can the size of adrenal tumor impact hormonal secretion? A retrospective analysis of 170 adrenalectomies in a single center.**

*Langenbecks Arch Surg*, 411(1)

R. Frey, A. Posabella, S. Hosner, A. Fiore, A. Wilhelm, S. Eschlbock, R. Droeser, T. Delko and Lazaridis, II. 2026.

PURPOSE: Adrenal tumors are a heterogeneous group of neoplasms that may be hormonally active or inactive. Tumor size is a key factor in evaluating and managing these lesions. Understanding how size impacts hormonal activity, surgical outcomes, and complications can help guide treatment and follow-up. This study investigates the relationship between tumor size, hormonal secretion, and clinical outcomes in adrenal tumors. METHODS: We retrospectively analyzed data from patients who underwent adrenalectomy between 2007 and 2023 at the University Hospital of Basel. Tumors were categorized by pathology and stratified into three size groups based on histology results. RESULTS: A total of 170 patients who underwent adrenalectomy for adrenal tumors were analyzed. The most common adrenal pathologies were Conn's syndrome followed by pheochromocytoma, Cushing syndrome and incidentalomas. Hormone-producing tumors were present in 61.2% of cases. Larger tumors (> 4 cm) were associated with longer operative times ( $p = 0.03$ ). When tumor size was analyzed in relation to hormone production, small functional tumors (< 2 cm) were most commonly linked to Conn's

syndrome. Cushing syndrome was most prevalent among patients with tumors measuring between 2.1 and 4 cm. There were no significant differences in perioperative complication rates across the tumor size groups. **CONCLUSION:** Our results showed that tumor size was associated with both operative complexity and functional status. Larger tumors were linked to longer operative times. Smaller tumors were predominantly associated with Conn's syndrome, while tumors of intermediate size were most often related to Cushing syndrome. These findings highlight the relevance of tumor size in preoperative planning and functional assessment.

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DOI: [10.1007/s00423-026-04009-2](https://doi.org/10.1007/s00423-026-04009-2)

PMCID: PMC12975794

#### **Incidence and hospital outcomes of acute adrenal crisis in a Swiss-wide cohort study.**

*Eur J Endocrinol*, 194(4):441-53.

S. Gafner, K. Leitner, P. Schuetz, B. Mueller, R. Laager, T. Struja and A. Kutz. 2026.

**BACKGROUND:** Adrenal crises (AC) are life-threatening emergencies for which epidemiological data remain scarce, particularly in older adults. We analyzed nationwide data on AC-related hospitalizations in Switzerland between 2012 and 2022 to determine incidence, clinical outcomes, and predictors of adverse events, emphasizing differences across age groups and etiologies of adrenal insufficiency. **METHODS:** We conducted a nationwide retrospective cohort study using hospital discharge data linked to the national death registry. The primary outcome was the incidence of AC hospitalizations; secondary outcomes were a composite endpoint of in-hospital mortality, intensive care unit (ICU) admission, and 30-day rehospitalization. We also assessed 1-year mortality and duration of hospital and ICU stay. **RESULTS:** We identified 2302 AC-related hospitalizations with incidence increasing over time, peaking in patients >80 years, with the steepest rise in those with central adrenal insufficiency. Compared with matched controls, AC was associated with higher odds of the secondary composite outcome (IRR 1.60; 95% confidence interval [CI] 1.48-1.73), primarily driven by ICU admissions (IRR 1.99; 95% CI 1.8-2.21). Patients with unspecified etiology of adrenal insufficiency had the highest odds for in-hospital mortality (IRR 1.8; 95% CI 1.48-2.19) and 1-year all-cause mortality (IRR 1.41; 95% CI 1.23-1.62). Key predictors of adverse outcomes included unspecified etiology of adrenal insufficiency, advanced age, male sex, arginine vasopressin deficiency, sepsis, and cancer. **CONCLUSION:** In Switzerland, AC-related hospitalizations have increased over the past decade, primarily driven by an increase in central adrenal insufficiency, likely linked to expanding glucocorticoid and immunotherapy use. Older adults remain disproportionately vulnerable to adverse outcomes.

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DOI: [10.1093/ejendo/lvag056](https://doi.org/10.1093/ejendo/lvag056)

#### **Editorial: Enhancing adrenal tumor diagnostics: biomarkers and molecular mechanisms.**

*Front Endocrinol (Lausanne)*, 17:1843915.

P. Glinicki and H. Falhammar. 2026.

PubMed-ID: [42064775](#)

DOI: [10.3389/fendo.2026.1843915](https://doi.org/10.3389/fendo.2026.1843915)

PMCID: PMC13124580

#### **Mineralocorticoid Receptor Antagonist Pre-Adrenalectomy in Primary Aldosteronism.**

*J Clin Endocrinol Metab*, 111(4):e1153-e63.

J. Goi, M. Paja Fano, A. Rizo Gellida, M. Gonzalez-Boillos, P. Martin Rojas-Marcos, L. Caja Guayerbas, A. M. Garcia Cano, J. G. Ruiz-Sanchez, A. Vicente, E. Gomez-Hoyos, M. Recasens, R. Barahona San Millan, M. J. Picon Cesar, P. Diaz Guardiola, C. M. Perdomo, L. Manjon-Miguel, A. Rebollo Roman, C. Robles Lazaro, J. M. Recio-Cordova, M. Calatayud, N. Jimenez Lopez, M. Sampedro Nunez, E. Mena Ribas, A. Sanmartin Sanchez, C. Gonzalvo Diaz, C. Lamas, J. Serrano, T. Michalopoulou, S. Tenes Rodrigo, E. Pascual-Corrales, F. Jaen Aguila, N. Munoz Rivas, E. M. Moya Mateo, S. Gutierrez-Medina, F. A. Hanzu, P. Parra Ramirez and M. Araujo-Castro. 2026.

**CONTEXT:** Perioperative use of mineralocorticoid receptor antagonists (MRA) in patients with unilateral primary aldosteronism (PA) awaiting surgery is not well standardized. **OBJECTIVE:** The aim of this study was to compare the risk of postoperative complications and surgical outcomes between PA patients treated with MRA prior to adrenalectomy and those not pretreated. **METHODS:** Adrenalectomized patients for unilateral PA from the SPAIN-ALDO registry, with clinical, hormonal, and treatment information before and after adrenalectomy, were analyzed. **RESULTS:** A total of 355 surgically treated patients were included; 76.9% (n = 273) received presurgical treatment with MRA (spironolactone [64.5%], eplerenone [35.5%]). Adrenalectomy was guided by lateralization at adrenal venous sampling in 33.5% of the overall cohort, and by imaging in all the other cases. Patients pretreated with MRA had longer duration of hypertension, higher

prevalence of hypokalemia, and greater aldosterone concentrations than those not pretreated (n = 82). No differences in the rate of postsurgical hyperkalemia, hypoaldosteronism, renal function impairment, blood pressure changes, and biochemical outcomes were detected between groups in the immediate ( $\leq 30$  days) and short-term ( $\leq 90$  days) follow-up evaluations after surgery. At long-term follow-up ( $\geq 6$  months), patients pretreated with MRA exhibited better postsurgical biochemical outcomes (81.7% had complete biochemical response vs 57.1% of non-pretreated patients;  $P = .004$ ). In the multivariable analysis, the use of MRA prior to adrenalectomy was independently associated with a successful postsurgical biochemical response. **CONCLUSION:** Preoperative MRA therapy can be safely introduced to control blood pressure and potassium levels in patients with PA awaiting surgery, without increasing the risk of postoperative hyperkalemia, hypoaldosteronism, renal impairment, or hypotension.

PubMed-ID: [41045519](#)

DOI: [10.1210/clinem/dgaf545](#)

PMCID: PMC13017670

### **Robotic Adrenalectomy Is Associated With Shortened Hospital Stay and in Large Tumors ( $\geq 6$ cm) May Reduce Complications.**

*World J Surg*, 50(2):451-60.

N. Grunberg, N. Michot, D. Dussard, O. Saint-Marc, H. Guillerrou, E. Salame, M. Ouaisi and H. Najah. 2026.

**BACKGROUND:** Robotic adrenalectomy (RA) is increasingly adopted, but its clinical value compared with laparoscopic adrenalectomy (LA) remains unclear. We assessed perioperative outcomes and the learning curve of RA. **METHODS:** A bicentric retrospective study included 228 patients who underwent adrenalectomy between 2013 and 2023 (97 RA, 131 LA). Primary outcomes were intra- and postoperative complications (Clavien-Dindo, Comprehensive Complication Index, CCI). Secondary outcomes included operative time and length of stay (LOS). Subgroup analysis evaluated tumors  $\geq 6$  cm. RA learning curve was assessed with cumulative sum (CUSUM) analysis. **RESULTS:** Patients in the RA group had higher ASA scores, more prior abdominal surgery, and larger tumors. Overall complication rates were similar (RA 18.6% vs. LA 17.6%,  $p = 0.846$ ). RA was independently associated with shorter LOS (OR 0.48; 95% CI 0.26-0.84;  $p = 0.012$ ). In tumors  $\geq 6$  cm, RA reduced postoperative complications (5.3% vs. 35.3%,  $p = 0.037$ ). CUSUM analysis showed earlier improvements in operative time (after 25 cases) and later reductions in morbidity (after approximately 45 cases). **CONCLUSIONS:** RA is a safe alternative to LA even in complex patients. It shortens LOS overall and improves outcomes in large adrenal tumors. CUSUM analysis highlights a progressive but safe learning curve, supporting the integration of RA into endocrine surgical practice.

PubMed-ID: [41495380](#)

DOI: [10.1002/wjs.70221](#)

### **RET Lys666Asn has a low rate of MEN2-related tumors but may be associated with pheochromocytoma.**

*Hormones (Athens)*,

R. Halperin, N. Peshes-Yaloz, A. Tirosh and O. Twito. 2026.

**PURPOSE:** Multiple endocrine neoplasia type 2 (MEN2) is caused by germline pathogenic variants (PVs) in the RET proto-oncogene, leading to medullary thyroid carcinoma (MTC), pheochromocytoma, and primary hyperparathyroidism (PHPT). RET p.Lys666Asn is a rare PV, but its clinical significance remains incompletely understood. The purpose of this study is to expand the clinical understanding of the RET Lys666Asn variant. **METHODS:** Index patients carrying the RET Lys666Asn variant were identified through clinical genetic testing in two referral medical centers. Comprehensive clinical evaluation, biochemical screening, and imaging studies were performed to assess the presence of MTC, pheochromocytoma, and PHPT of the index patients and carrier family members. We performed a literature search on Lys666Asn carriers and their clinical manifestations. **RESULTS:** Ten individuals from five families were identified as carriers of the RET Lys666Asn variant. The median age at diagnosis was 43.7 years (range 2-75 years). Only one individual presented with pheochromocytoma, diagnosed at age 54. The rate of MTC, pheochromocytoma, and PHPT was 0 (0-0.26), 0.1 (0.01-0.39), and 0 (0-0.26), respectively. In a pooled analysis of cases reported in the literature, MTC, pheochromocytoma, and PHPT rate are 0.42 (0.28-0.57), 0.11 (0.04-0.22), and 0.03 (0-0.12), respectively. MTC had a wide age range at presentation (20-70 years). **CONCLUSION:** The RET Lys666Asn variant is associated with lower event rate of MEN2-related tumors compared to classical MEN2 variants, particularly MTC and pheochromocytoma. Despite its rarity, pheochromocytoma cannot be excluded in carriers, underscoring the need for individualized screening protocols based on specific RET variants.

PubMed-ID: [41857338](#)

DOI: [10.1007/s42000-026-00759-2](#)

**Pseudohypoxia and family history are key predictors of severe outcomes in hereditary pheochromocytoma and paraganglioma syndromes.**

*Eur J Endocrinol*, 194(3):367-80.

R. Halperin, G. Reznick-Levi, A. Khalaileh, R. Svirsky-Frayden, O. Reish, M. Sheikh-Ahmad, L. Saiegh, N. Saba Khazen, R. Bernstein-Molho, K. Weiss, N. Peshes Yaloz, G. Shlomei and A. Tirosh. 2026.

OBJECTIVE: Pheochromocytoma and paraganglioma (PPGL) have high genetic predisposition rates. In this multicenter study, we aimed to identify risk-modulating factors for disease development and aggressiveness in patients carrying pathogenic variants (PPGLgPV) related to PPGL genes. METHODS: Observational prospective study including patients with PPGL, family history of PPGL, or suspected PPGL-related hereditary syndrome. Patients underwent clinical and germline PPGLgPV evaluation. Machine-learning analyses were conducted to predict a patient's risk of carrying PPGLgPV, developing PPGL, and developing metastatic or multifocal disease. RESULTS: Of 221 patients (age 33.5 +/- 19.9 years, 45.2% males), 143 (64.7%) patients harbored PPGLgPV, and 91 (41.2%) developed PPGL (46 pheochromocytoma, 45 paraganglioma/both, 29 multifocal/metastatic PPGL). Age at diagnosis of <41 years with a positive family history showed a 100% positive predictive value (PPV) for carrying PPGLgPV, compared to an 86% negative predictive value (NPV) when diagnosed at age >40 years with a solitary PPGL. Pseudohypoxia (PH)-related PPGLgPV carriers were younger at PPGL diagnosis and had an increased risk of multifocal/metastatic disease. Elevated catecholamine metabolites and PH-related PPGLgPV had 80% PPV for metastatic/multifocal disease, vs high NPV for non-elevated catecholamine metabolites with negative family history (100%) or non-PH gene alterations (91%). Patients with PV found incidentally had a lower PPGL risk compared with carriers screened due to a family member with PPGL (P = .026). CONCLUSIONS: Machine learning identified combined clinical and genetic characteristics for predicting hereditary PPGL syndromes, and multifocal/metastatic PPGL. This enables personalized risk stratification to guide genetic testing and surveillance in patients with PPGL and their relatives.

PubMed-ID: [41783997](#)

DOI: [10.1093/ajendo/lvag042](#)

**Cortisol Testing to Diagnose Adrenal Insufficiency Following Adrenalectomy for Mild Autonomous Cortisol Secretion.**

*J Clin Endocrinol Metab*, 111(3):665-78.

O. Hamidi, B. Salama, T. Wang, J. W. Findling, C. D. Zhang, T. Carroll, S. Dream, A. Sada, V. Balderrama-Brondani, P. Dogra, A. Dackiw, S. Mirfakhraee, A. Mehta, S. Oltmann, T. McKenzie, T. Foster and I. Bancos. 2026.

CONTEXT: Patients with mild autonomous cortisol secretion (MACS) can develop adrenal insufficiency after unilateral adrenalectomy. OBJECTIVE: This work aimed to determine the prevalence, duration, and predictors of adrenal insufficiency, and compare postoperative basal cortisol and cosyntropin stimulation test (CST). METHODS: In this multicenter retrospective study of patients with MACS, adrenal insufficiency was diagnosed when postoperative basal cortisol was less than 10 microg/dL and/or CST < 18 microg/dL. The results were concordant when both tests met cutoffs. Biochemical (BSS) and clinical severity scores (CSS) were calculated. RESULTS: Among 281 patients with MACS (80% women), postoperative adrenal insufficiency was diagnosed in 153 (54.5%) patients. Adrenal insufficiency inversely correlated with age (odds ratio [OR] 0.67 per 10 years; 95% CI, 0.53-0.84). Low basal cortisol and CST were associated with younger age (OR 0.64 per 10 years for both) and higher BSS (OR 1.17 and 1.22, respectively). Basal cortisol and CST were discordant in 22% of patients, and the discordance rate was more common in patients with bilateral nodules (32% vs 19%; P < .001). The median time to adrenal insufficiency recovery was 3.9 months (IQR, 3-5.9 months), with longer duration associated with higher BSS and CSS: 3 months for mild, 4 to 5 months for moderate, and 12 to 14 months for severe BSS and CSS. CONCLUSION: Approximately half of patients with MACS developed postoperative adrenal insufficiency, with 50% recovering by 3.9 months after surgery. BSS correlated with basal cortisol, CST, and duration of adrenal insufficiency. As discordant results were noted in 22%, performing both basal cortisol and CST postoperatively should be considered.

PubMed-ID: [40966719](#)

DOI: [10.1210/clinem/dgaf515](#)

PMCID: PMC13056330

**Machine learning-based models for intraoperative blood loss of retroperitoneal laparoscopic adrenalectomy.**

*Surg Endosc*, 40(4):3140-50.

J. He, J. Zhao, Y. Luo, M. Li, Y. Han, D. Wei, Y. Wang and Z. Hou. 2026.

OBJECTIVE: Intraoperative blood loss (IBL) is a critical precipitating factor of intraoperative and postoperative complications. This study aims to identify risk factors and employ machine learning (ML) techniques to develop models for predicting IBL in patients undergo retroperitoneal laparoscopic adrenalectomy (RLA). METHODS: A retrospective study was performed with data from patients who underwent unilateral RLA at Beijing Anzhen Hospital from 2014 to 2021. The

data were randomly divided into training and validation sets. A volume  $\geq 100$  ml was defined as high IBL. Model training incorporated feature selection with least absolute shrinkage and selection operator (LASSO) and algorithms including logistic regression (LR), random forest (RF), neural network (NN), K-nearest neighbor (KNN), support vector machine (SVM) and AdaBoost. Various indicators were utilized to evaluate model performance. RESULTS: A total of 530 RLA cases were included. LASSO regression identified gender, surgeons' experience, disease type, lesion diameter and lesion location as predictive factors. Six ML models were derived and evaluated. Among which, LR, RF and NN models exhibited exceptional discriminatory power. The area under the curve (AUC) of the three models were 0.775, 0.769, 0.729 in the validation set, respectively. A nomogram and a online calculator were created. The calibration curve, decision curve analysis and clinical impact curve revealed its excellent clinical utility. CONCLUSION: This study presented and compared the use of various ML models for predicting IBL in RLA, which could assist in assessing surgical risks and tailored treatments without additional examination, and providing insights for the clinical application of ML.

PubMed-ID: [41591513](#)

DOI: [10.1007/s00464-026-12576-0](#)

### **Steroid replacement after adrenalectomy for mild autonomous cortisol secretion: Clinical predictors and a practical algorithm.**

*Surgery*, 191:109967.

A. Ibrahimli, E. Memisoglu, R. Perez-Soto, P. Rao, R. Correa, D. Li, R. Veeramachaneni, S. R. Bendaram and E. Berber. 2026. BACKGROUND: Mild autonomous cortisol secretion is identified in up to 50% of patients with adrenal nodules after a low-dose dexamethasone-suppression test. Although steroids are routinely started in patients with Cushing syndrome after adrenalectomy, there is confusion about postoperative steroid replacement in patients with mild autonomous cortisol secretion. The aim of this study was to investigate the frequency and clinical predictors of postoperative steroid replacement in patients with mild autonomous cortisol secretion undergoing unilateral adrenalectomy. METHODS: This was an institutional review board approved retrospective study. Mild autonomous cortisol secretion was defined as preoperative serum cortisol level of  $>1.8$   $\mu\text{g/dL}$  after low-dose dexamethasone suppression without signs and symptoms of overt Cushing syndrome. In patients who underwent unilateral adrenalectomy between 2000 and 2024 for mild autonomous cortisol secretion, a decision for postoperative steroid replacement was made based on a combination of parameters, including postoperative day 1 cortisol levels, adrenocorticotrophic hormone stimulation test results and clinical evidence of adrenal insufficiency. Univariate and multivariate logistic regression models were used to identify predictors of steroid replacement. Continuous data are expressed as medians (interquartile ranges). RESULTS: There was a total of 139 patients with mild autonomous cortisol secretion who underwent minimally invasive adrenalectomy. All patients had am cortisol levels, and 85 patients had adrenocorticotrophic hormone stimulation tests done on postoperative day 1. Postoperative steroid replacement was done on 32 patients on the basis of postoperative day 1 cortisol level  $<5$   $\mu\text{g/dL}$  ( $n = 15$ ), postoperative day 1 cortisol level  $<10$   $\mu\text{g/dL}$  and failed adrenocorticotrophic hormone stimulation test ( $n = 15$ ), and or symptoms of adrenal insufficiency ( $n = 2$ ). Independent predictors of postoperative steroid replacement therapy included preoperative plasma adrenocorticotrophic hormone  $<7.0$   $\text{pg/mL}$  ( $P = .02$ ) and cortisol  $>4.2$   $\mu\text{g/dL}$  on low-dose dexamethasone test ( $P = .008$ ). Patients were followed up for a median of 15 months (interquartile range, 5-38 months) with no evidence of adrenal insufficiency with this management. Steroids were weaned off within a median of 78 days (interquartile range, 35-251 days). CONCLUSION: To the best of our knowledge, this is the largest study to date on postoperative steroid management of patients with mild autonomous cortisol secretion. A safe algorithm was described to select patients for steroid replacement. In contrast to previous reports in the literature, a minority (23%) of the patients with mild autonomous cortisol secretion needed postoperative steroid replacement in this cohort with the algorithm used.

PubMed-ID: [41407599](#)

DOI: [10.1016/j.surg.2025.109967](#)

### **Phaeochromocytomas and paragangliomas harbour tumour-initiating SOX2+ stem cells.**

*Endocr Relat Cancer*, 33(5)

Y. Kemkem, M. Quinn, B. Kover, A. Santambrogio, J. Kaufman-Cook, O. Sherwin, L. D. Scriba, D. Brempou, M. V. Segoviano, D. Cameron, I. Berger, W. Ng, D. Nonaka, M. Theodoropoulou, C. Pamporaki, P. V. Carroll, L. Izatt, J. P. Chapple, S. R. Bornstein, N. Bechmann, C. Steenblock, R. J. Oakey and C. L. Andoniadou. 2026.

Phaeochromocytomas (PCCs) and paragangliomas (PGLs) are rare neuroendocrine tumours that arise in the neural crest (NC)-derived adrenal medulla and the paraganglia, respectively. Approximately 10-15% of patients with PCCs and 35-40% with PGLs go on to develop metastatic disease, leading to a reported median overall survival of 7 years. The development of prognostic markers and subsequent personal therapeutic strategies are hindered by a lack of understanding of

tumourigenesis. In other organs, cells with stem-like properties are at the root of tumour initiation and maintenance, due to their ability to self-renew and give rise to differentiated cells. We have recently shown that, in the human adrenal, a subset of sustentacular cells, endowed with a support role, are in fact SOX2+ postnatal adrenomedullary stem cells that are specified along the NC migratory route. In this study, we intended to determine if SOX2+ cells in PCCs and PGLs can behave as tumour-initiating stem cells. Using expression and transcriptomic studies, we demonstrate the presence of SOX2/SOX2-expressing cells across a broad range of PCCs and PGLs, irrespective of tumour aggressiveness, location, and causative mutation. In silico analyses reveal the co-expression of SOX2 and chromaffin cell markers in the tumour and reveal the active proliferation of these double-positive cells. Isolation of these cells in vitro in stem cell-promoting media, and their xenotransplantation on chicken chorioallantoic membranes, demonstrates that they have the potential to expand and metastasise in ovo, supporting their potential as tumour-initiating cells.

PubMed-ID: [42023823](#)

DOI: [10.1530/ERC-25-0242](#)

PMCID: PMC13188188

### **Psychosocial burden in adrenocortical carcinoma patients.**

*Eur J Endocrinol*, 194(1):13-21.

O. Kimpel, S. Kiermeier, E. Stahl, B. Altieri, M. Fassnacht and I. Maatouk. 2026.

OBJECTIVE: Distress, fear of progression (FOP), and depression are common in cancer patients and negatively impact patients' health-related quality of life (HRQOL). However, no studies have explored these aspects in adrenocortical carcinoma (ACC), yet. METHODS: We conducted a single-centre observational study in adults ( $\geq 18$  years) with ACC. We analysed questionnaires addressing FOP, distress (National Comprehensive Cancer Network distress thermometer), depression (patient health questionnaire, PHQ-9), and HRQOL (EORTC-QLQ-C30). Potentially influencing factors were evaluated. Multiple linear regression on HRQOL subscales was performed to identify associated psychosomatic correlations. RESULTS: Within 12 months, 105 patients were included (56.2% female; median age 49 years, 14.3% newly diagnosed, 46.7% tumour-free, 39.0% metastatic). The majority experienced an elevated level of distress (62%) and of FOP (59%). PHQ-9 results suggested major depression in 41%. Of note, these results were neither influenced significantly by tumour burden, hormone excess nor by cancer treatment. Patients reported moderate functioning scores (median 62.2) and moderate symptom burden (median 33.3) in the EORTC-QLQ-C30. Fatigue and insomnia were prominent symptoms. Tumour burden and treatment affected functioning and symptoms, with significant differences in appetite loss, diarrhoea, nausea, vomiting, and financial difficulties. Hormone excess showed no significant impact on these measures. Our questionnaires indicated a need for psychosomatic counselling in 80% of patients. CONCLUSIONS: Patients with ACC show high values for distress, FOP, and depression, which can only partly be explained by clinical characteristics. Our study suggests that psychosomatic support should be offered to all patients with ACC.

PubMed-ID: [41504709](#)

DOI: [10.1093/ejendo/lvaf259](#)

### **Incidence of Adrenal Masses Eventually Discovered in Patients Screened for Primary Aldosteronism.**

*J Clin Endocrinol Metab*, 111(2):e535-e40.

G. A. Kline, J. Low, J. J. Burkart, X. Y. Hu, K. Mellor, S. Przybojewski, J. King and A. A. Leung. 2026.

CONTEXT: Biochemical screening for endocrine hypertension may be complex; the known presence of an adrenal mass markedly increases the pretest probability for adrenal hypertension and may inform diagnostic efforts. OBJECTIVE: Model the potential incidence of adrenal masses that may be detected by routine adrenal imaging in patients with suspected endocrine hypertension. DESIGN: Retrospective cohort study. SETTING: Provincial administrative and clinical databases for radiology and biochemistry, Alberta, Canada. PARTICIPANTS: Patients with hypertension and any measurement of aldosterone-renin ratio (ARR), 2012 to 2019. MAIN MEASURES: Radiology report of any computed tomography or magnetic resonance imaging abdomen performed for any reason 0 to 12 years following ARR. Patients with any pre-ARR imaging data between 2002 and 2024 were excluded. The presence of adrenal mass, size, and density were recorded and stratified by imaging indication. RESULTS: Of 6942 unique hypertension patients with ARR, 1462 (21%) had imaging done at some point after ARR, 912 (62.4%) for indications unrelated to hypertension/adrenal and at a median 771 days (69-1577) post ARR. The incidence rate estimate was 7.2% (5.6-9.2%) of scans showed adrenal mass, median 1.4 cm (1.1-2.3), a rate well above the modern series of adrenal incidentaloma prevalence in unselected adults. The number needed to screen in this population was 14 (11-18) to detect an adrenal mass without a priori indication for adrenal imaging. CONCLUSION: Among patients screened for PA but without prior or subsequent directed adrenal imaging, 1 in 14 were later found to have an adrenal mass on imaging done for other indications. Given the impact on pretest probability for endocrine hypertension and further investigation steps, routine adrenal imaging might be considered whenever PA

suspicion is high.

PubMed-ID: [40581375](#)

DOI: [10.1210/clinem/dgaf371](#)

PMCID: PMC12819846

**Determinants of false-positive plasma free metanephrines and methoxytyramine: the role of medications and chronic disease.**

*Endocr Relat Cancer*, 33(5)

L. M. Knigge, K. Potthoff, G. Constantinescu, S. Fuld, K. Zawadzka, E. Tahirukaj, S. Bornstein, J. W. M. Lenders, G. Eisenhofer and C. Pamporaki. 2026.

Measurements of plasma free metanephrines provide a highly sensitive test for the diagnosis of pheochromocytoma/paraganglioma (PPGL). However, false-positive results remain common, posing a diagnostic dilemma for clinicians. The aim of this study was to determine whether chronic illness and commonly prescribed drugs can falsely elevate plasma free metanephrines. This retrospective study included 460 patients without PPGL. Disease exclusion was based on negative imaging or histopathological findings, or negative biochemistry at follow-up. Sex, age, plasma free normetanephrine, metanephrine, and methoxytyramine, the presence or absence of cardiometabolic comorbidities and/or chronic illness (CCI), and all prescribed medications at study inclusion were reported. In four patients under treatment with norepinephrine reuptake blockers (NRBs), metanephrines were measured at baseline and after short-term discontinuation of the drug. Among the 460 patients without PPGL, 88% (407/460) were receiving at least one medication. In this cohort, false-positive elevations of plasma free metanephrines were rare (7%). Multivariable analysis identified NRBs as the only drugs independently associated with increased plasma free normetanephrine levels ( $P < 0.001$ ), in a dose-dependent manner. Importantly, plasma free methoxytyramine concentrations were independently influenced by NRBs, antipsychotics, and nicotine use ( $P < 0.001$ ). Paired analyses in a subset of four patients before and after short-term NRB withdrawal showed normalization of plasma free normetanephrine concentrations. Plasma free metanephrines show high diagnostic reliability with minimal interference from CCI or commonly used medications. However, NRBs can increase normetanephrine and methoxytyramine concentrations, particularly at higher doses, and thus, their use requires cautious interpretation of plasma free metanephrine measurements.

PubMed-ID: [42007997](#)

DOI: [10.1530/ERC-25-0549](#)

PMCID: PMC13188186

**The effect of adrenalectomy on the patients with Mild Autonomous Cortisol Secretion.**

*Am J Surg*, 256:116922.

M. Kostek, R. Roy, A. Gillis, H. Chen and B. Lindeman. 2026.

BACKGROUND: Mild Autonomous Cortisol Secretion (MACS) is associated with cardiometabolic comorbidities, but the benefit of adrenalectomy remains controversial. METHODS: We retrospectively reviewed patients undergoing adrenalectomy between October 2019 and October 2024. MACS was defined as post-1 mg dexamethasone suppression test cortisol 1.8-5.0  $\mu\text{g}/\text{dL}$  without overt Cushing's syndrome. Pre- and postoperative clinical and biochemical outcomes were analyzed. RESULTS: Thirty-eight patients met inclusion criteria (median age 64 years; 60.5% female). Median post-DST cortisol was 2.9  $\mu\text{g}/\text{dL}$ , with a median follow-up of 258 days. Significant postoperative improvements were observed in systolic ( $p = 0.001$ ) and diastolic ( $p = 0.004$ ) blood pressure, HbA1c ( $p = 0.013$ ), and antihypertensive medication burden ( $p = 0.009$ ). General health status, HbA1c and number of antihypertensive medications improved in 76.3%, 58.4% and 52.8% of the patients, respectively. Clinical outcomes did not differ between patients with cortisol levels  $<2.5$  vs.  $\geq 2.5$   $\mu\text{g}/\text{dL}$ . CONCLUSION: Adrenalectomy in selected MACS patients is associated with improvements in blood pressure, glycemic control, and overall health, independent of preoperative cortisol levels.

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DOI: [10.1016/j.amjsurg.2026.116922](#)

**The impact of adrenalectomy on metabolic outcomes of patients with mild autonomous cortisol secretion defined by low-dose dexamethasone suppression testing.**

*Surgery*, 189:109775.

A. L. Kumar, S. Dream, T. Shaik, K. Doffek, R. Conrardy, J. W. Findling, T. B. Carroll, C. D. Zhang, D. B. Evans and T. S. Wang. 2026.

BACKGROUND: Up to 50% of patients with adrenal incidentalomas have mild autonomous cortisol secretion, which may increase their cardiometabolic morbidity, compared with patients with nonfunctional adrenal tumors. Studies evaluating

cardiometabolic outcomes of patients with mild autonomous cortisol secretion defined by 1-mg dexamethasone suppression testing (cortisol 1.8-5 mug/dL) have demonstrated mixed results. The aim of this study was to assess the metabolic outcomes of patients with mild autonomous cortisol secretion, defined by the 1-mg dexamethasone suppression testing criterion, compared with patients with nonfunctional adrenal tumors who underwent adrenalectomy. **METHODS:** We conducted a single-institution retrospective cohort study comparing adult patients who underwent unilateral adrenalectomy from November 30, 2011, to August 19, 2023, for mild autonomous cortisol secretion (1-mg dexamethasone suppression testing cortisol 1.8-5 mug/dL) or nonfunctional adrenal tumors (1-mg dexamethasone suppression testing cortisol <1.8 mug/dL). Preoperative prevalences and postoperative changes in diabetes mellitus, hypertension, dyslipidemia, and elevated body mass index ( $\geq 25$ ) were assessed. Patients were followed from the time of surgery until their last outpatient visit. Multivariable logistic regression was pursued for outcomes that varied between cohorts. **RESULTS:** A total of 65 patients (53 mild autonomous cortisol secretion and 12 nonfunctional adrenal tumors) were analyzed. Patients with mild autonomous cortisol secretion were older and more likely to have diabetes mellitus than patients with nonfunctional adrenal tumors (odds ratio: 7.81, 95% confidence interval [0.94, 64.96],  $P = .04$ ). Patients were followed for a median of 28.1 months [11.1, 55.3 months]. Patients with mild autonomous cortisol secretion were more likely to have postoperative weight improvement (odds ratio: 8.31, [0.97, 71.14],  $P = .03$ ). After adjusting for clinically relevant variables, the 1-mg dexamethasone suppression testing cortisol was predictive of postoperative weight improvement (odds ratio: 1.88, [1.1, 3.65],  $P = .04$ ). **CONCLUSION:** Weight loss should be considered as a potential benefit of adrenalectomy in patients with mild autonomous cortisol secretion.

PubMed-ID: [41046235](#)

DOI: [10.1016/j.surg.2025.109775](#)

#### **The impact of body mass and posterior adiposity indices in robotic adrenalectomy.**

*Surg Endosc*, 40(2):1488-96.

A. L. Kumar, A. Sanchez, K. Doffek, G. Taylor, T. W. F. Yen, T. S. Wang and S. Y. Dream. 2026.

**BACKGROUND:** Robotic adrenalectomy is performed via transabdominal (TA) or retroperitoneoscopic (RP) approaches, but the impact of body mass index (BMI) on robotic adrenalectomy outcomes in either approach is unclear. Posterior Adiposity Index (PAI), predictive of operative time in RP adrenalectomy, remains unevaluated with the robotic platform. This study assessed the impact of patient BMI and PAI on surgical outcomes in patients undergoing either TA or RP robotic adrenalectomy. **METHODS:** This was a single-institution retrospective cohort study of adult patients who underwent robotic adrenalectomy from 5/1/2018 to 6/17/2024. Patients were analyzed by approach and BMI. The primary outcome was operative time. Secondary outcomes included estimated blood loss (EBL), length of stay (LOS), and complications within 30 days. The correlation of operative time to PAI, BMI, and patient characteristics was assessed. **RESULTS:** 149 patients (age 55 yrs. [IQR:42,66], 70% female) underwent 98 TA and 51 RP robotic adrenalectomies. Patients who underwent TA robotic adrenalectomies had larger nodules, higher BMI, and greater EBL; operative time, LOS, and complications were similar. Patients with elevated BMI (BMI  $\geq 25$ ) had similar preoperative characteristics to those with normal BMI (BMI < 25); they had longer operative times (129 min [107, 156] vs. 118 [90, 134],  $p = 0.045$ ) and LOS (1 [1,1] vs 1 [1,1]  $p = 0.015$ ) including two patients with 8-day LOS, but similar EBL (5 [5,10] vs. 10 [5,23],  $p = 0.828$ ) and complication rates (15% vs 5%,  $p = 0.477$ ). Among TA, but not RP, patients, BMI weakly correlated with operative time ( $\rho = 0.320$ ,  $p < 0.005$ ). PAI did not correlate with operative time. **CONCLUSION:** This retrospective cohort study evaluating the impact of BMI and PAI on surgical outcomes in patients undergoing robotic adrenalectomy demonstrated that while elevated BMI (BMI  $\geq 25$ ) appears to prolong TA robotic adrenalectomy, PAI is not predictive of operative time in RP robotic adrenalectomy.

PubMed-ID: [41291330](#)

DOI: [10.1007/s00464-025-12416-7](#)

PMCID: PMC12881112

#### **Chemo-immunotherapy with cisplatin and nivolumab as second-line approach in metastatic adrenocortical carcinoma.**

*Eur J Endocrinol*, 194(2):199-207.

M. Lagana, S. Rodella, D. L. Bettini, A. Esposito, A. Abate, R. Ambrosini, M. Tamburello, F. Consoli, R. Tinti, S. Calza, G. Casole, G. A. M. Tiberio, S. Sigala, A. Berruti, S. Grisanti and D. Cosentini. 2026.

**CONTEXT:** No effective therapies are available for patients with advanced adrenocortical carcinoma (ACC) progressing after standard therapy: EDP (etoposide, adriamycin, and cisplatin) and mitotane (EDP-M regimen). These patients have poor prognosis with a median life expectancy of 6-7 months. Immunotherapy in this setting is promising. Concomitant chemotherapy administration can enhance the efficacy of immunotherapy, as demonstrated in other malignancies.

**OBJECTIVE:** This retrospective study aims to explore the activity of a combination of cisplatin and nivolumab administered

to patients with ACC who have previously undergone chemotherapy and mitotane treatment. **PATIENTS AND METHODS:** Cisplatin, 25 mg/m<sup>2</sup> on day 1, and nivolumab, 240 mg on day 2, every 2 weeks, were administered to advanced/metastatic ACC with disease progression to EDP-M regimen plus/minus other chemotherapeutic regimens. The primary endpoint was the disease response according to RECIST. Secondary endpoints were clinical benefit, disease control rate (DCR), overall survival (OS), progression-free survival (PFS), and safety. **RESULTS:** Twenty-three patients were enrolled between January 2023 and March 2025. The median follow-up was 15.1 months. Eight patients [34.8% (95% CI, 15.3%-54.2%)] obtained a partial response and 4 patients (17.3%) a stable disease; therefore, 12 patients (52.2%) obtained a clinical benefit. The DCR after 6 months was obtained in 39.1% [95% CI, 19.7%-61.5%] of patients. The median PFS was 4.3 months [95% CI, 3.9-13.0], and the median OS was 18.9 months [95% CI, 15.8-not reached]. Chemo-immunotherapy combination was well tolerated, and most toxicities were limited to grade G1-2 according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) criteria. One patient discontinued treatment after 1 cycle, due to grade 3 immune-related hepatitis. **CONCLUSION:** The combination of cisplatin and nivolumab is an active regimen in advanced, previously treated, ACC patients. The long survival achieved in this patient population with a poor prognosis is promising.

PubMed-ID: [41531268](#)

DOI: [10.1093/ejendo/lvag008](#)

### **Adiposity rebound and height velocity in patients with congenital adrenal hyperplasia.**

*Eur J Endocrinol*, 194(4):467-81.

N. R. Lawrence, I. Bacila, J. Tonge, C. Balagamage, J. Dawson, G. S. Collins, Z. Q. Lang, J. Bryce, M. Alimussina, M. Chen, S. R. Ali, N. Amin, N. H. Amr, F. A. Anverdeen, T. Bachega, M. Banaszak-Ziemska, F. Baronio, N. H. Birkebaek, W. Bonfig, M. Clemente-Leon, M. Cools, J. H. Davies, L. de Vries, C. de Bruin, H. Elsedfy, C. E. Fluck, A. Fu, G. Gazdag, A. German, E. Gevers, E. Globa, A. Guven, S. E. Hannema, V. Iotova, D. Janus, H. El Kaddouri, H. J. van der Kamp, R. Krone, N. Lenherr-Taube, O. Marginean, R. Markosyan, I. Mazen, H. Miles, M. C. de Miranda, K. L. Mohnike, C. Morris, A. Natarajan, U. Neumann, M. Niedziela, R. Ortolano, A. F. Perez, S. Poyrazoglu, U. Probst-Scheidegger, T. Randell, D. A. Rees, G. Russo, M. Salerno, L. De Sanctis, V. S. Luscher, S. N. Seneviratne, S. Shenoy, M. Shnorhavorian, M. R. Stancampiano, R. Tadokoro-Cuccaro, A. Thankamony, A. Utari, A. Vieites, M. Wasniewska, D. Yeste, J. W. Tomlinson, S. F. Ahmed and N. Krone. 2026. **OBJECTIVE:** Adiposity rebound is the first rise in BMI that occurs after the initial decrease during infancy. Early adiposity rebound, before age 5, is a risk factor for later obesity and metabolic problems. We investigated adiposity rebound in children with Congenital Adrenal Hyperplasia due to 21-hydroxylase deficiency (CAH). **DESIGN:** Longitudinal observational registry study. **METHODS:** Height, weight, and BMI from patients younger than 20 years in the I-CAH Registry was described by non-linear mixed-effects models. Covariates of glucocorticoid dose, mineralocorticoid dose, 17-Hydroxyprogesterone were assessed on growth and bone age. **RESULTS:** A total of 10 261 visits within 573 patients (43.6% male) showed significant variation in age at latest peak height velocity [8.4 years (SD = 3.0) in boys; 9.0 years (SD = 1.6) in girls]. Peak height velocity was more blunted in boys [7.7 cm/year (SD = 1.4)] than girls [7.4 cm/year (SD = 1.3)] in comparison to normative values. Adiposity rebound occurred earlier than age 5 years in 82% of the cohort, mean age 3.7 years (SD = 1.3) in boys and 3.9 years (SD = 0.9) in girls. Girls prescribed higher doses of glucocorticoid were associated with heavier weight in adolescence and earlier adiposity rebound. Bone age was increasingly advanced in those prescribed higher doses in both sexes. **CONCLUSIONS:** There is a large variation in the timing of adiposity rebound and SITAR-estimated latest peak height velocity in children with CAH. In addition to identifying individuals with CAH who may be at risk of adverse cardiometabolic outcomes these metrics may serve as early surrogate outcomes in future research investigating early-life treatment strategies.

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DOI: [10.1093/ejendo/lvag050](#)

### **Recurrent CACNA1HE282K is a gain-of-function mutation associated with primary hyperaldosteronism.**

*Eur J Endocrinol*, 194(1):22-34.

R. Li, Y. Jiang, Q. Chen, Y. Zhao, K. Lu, A. Nie, C. Zhang, T. Su, L. Jiang, W. Zhou, X. Zhong, L. Wu, R. Han, L. Ye and W. Wang. 2026.

**CONTEXT:** Germline CACNA1H mutations have been associated with primary aldosteronism (PA). Here, we described 3 newly discovered CACNA1H variants and explored the possible pathogenic mechanisms as well as therapeutic strategies. **DESIGN:** Targeted next-generation sequencing of 10 PA causative genes was performed in 305 PA patients. Variants with possible clinical significance in CACNA1H were identified. Functional analysis was performed in vitro including electrophysiology, steroid hormone production, and transcriptome. Responses to mibefradil and nifedipine were evaluated. **RESULTS:** We described 3 heterozygous germline CACNA1H variants (E282K, V213M, and S1249R) in 4 independent cases of PA. Recurrent E282K mutation was identified in 1 patient with severe early-onset PA and 1 patient

with bilateral adrenal hyperplasia (BAH). Electrophysiological analysis of mutant Cav3.2 channels revealed significant gain-of-function changes in the voltage-dependent activation and Ca<sup>2+</sup> current properties for Cav3.2E282K, while ambiguous for Cav3.2S1249R and Cav3.2V213M. Moreover, stable expression of the 3 CACNA1H variants in H295R cells led to increased aldosterone production and upregulated expression of genes involved in steroidogenic enzymes, both basally and after K<sup>+</sup> treatment. T-type calcium channel blocker showed more significant inhibition of aldosterone production in mutant Cav3.2 cells compared to L-type calcium channel blocker. CONCLUSIONS: Our study suggests that Cav3.2E282K is a gain-of-function mutation and T-type calcium channel blockers may be efficient in controlling aldosterone levels for PA patients carrying mutant Cav3.2.

PubMed-ID: [41403024](#)

DOI: [10.1093/ejendo/lvaf253](#)

### **Systemic therapy for advanced pheochromocytoma and paraganglioma: real-world evidence from a single-center cohort.**

*Endocr Relat Cancer*, 33(2)

Y. Liang, J. Xu, D. Huang, W. Tang, Z. Sun, L. Chen and J. Chen. 2026.

Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine neoplasms characterized by heterogeneous clinical and genetic profiles. Evidence regarding the efficacy of systemic therapies in this population remains limited. We retrospectively reviewed 157 PPGL patients treated at our center between 2021 and 2024. Clinical, pathological, genetic, and treatment data were collected. Outcomes of targeted therapy, chemotherapy, and somatostatin analogs (SSAs) were analyzed, including progression-free survival (PFS). We found that among the 113 patients who underwent next-generation sequencing, 47.8% harbored pathogenic variant, with SDHB being the most frequent. In the overall cohort, median PFS for targeted therapy, chemotherapy, and SSAs was 8.02, 5.06, and 16.03 months, respectively. For the most frequently used agents in each category - surufatinib, temozolomide-based chemotherapy, and lanreotide - median PFS was 13.08, 10.05, and 19.02 months, respectively ( $P = 0.46$ ). In the first-line setting, targeted therapy and SSAs demonstrated superior efficacy compared with chemotherapy (median PFS 20.01 and 15.05 vs 4.07 months;  $P < 0.05$ ), with no significant difference observed between surufatinib and lanreotide. In patients with SDHx pathogenic variant versus SDHx normal patient, the mPFS with lanreotide was 15.05 vs 22.05 months and, with temozolomide chemotherapy, was 11.01 vs 7.04 months; neither comparison showed a statistically significant difference. In the first-line setting, targeted therapy and SSAs were associated with longer PFS than chemotherapy, with surufatinib and lanreotide showing favorable disease control. SDHx pathogenic variant status did not show a clear association with response to TKIs or temozolomide, underscoring the need for validation in larger cohorts.

PubMed-ID: [41543031](#)

DOI: [10.1530/ERC-25-0437](#)

### **Natural history of large adrenal tumors.**

*Front Endocrinol (Lausanne)*, 17:1774131.

M. Macech, M. Stepień, J. Podgórska, S. Toutounchi, L. Koperski, J. Barankiewicz, M. Bobrowicz, A. Kondracka and U. Ambroziak. 2026.

OBJECTIVE: The aim of this study was to characterize large adrenal tumors (LATs), assess the diagnostic accuracy of imaging modalities in detecting malignant LATs, and determine whether further follow-up of seemingly benign LATs is necessary. PATIENTS AND METHODS: We retrospectively analyzed the clinical, biochemical, and imaging characteristics at presentation and during follow-up in a single-center cohort of patients with adrenal tumors  $\geq 4$  cm in diameter evaluated between June 2013 and June 2023. RESULTS: Of 1,473 patients with adrenal tumors, 269 (18.3%) had lesions measuring  $\geq 4$  cm in diameter, of whom 220 were included in the study. Among LATs, 34.6% were adrenocortical adenomas, 27.3% other benign adrenal tumors, 17.3% adrenocortical carcinomas, 11.4% other malignant tumors, and 9.6% pheochromocytomas. Overall, 44.7% of tumors were non-functioning, while 37.8% secreted corticosteroids. Sensitivity of unenhanced computed tomography attenuation values in detecting malignancy was 100% using the threshold  $>10$  Hounsfield units (HU) and 89.5% for  $>20$  HU (with specificity 66.1% and 81.4%, respectively). Magnetic resonance with chemical shift analysis demonstrated high sensitivity (94.4%) but low specificity (56.8%). (18)F-fluorodeoxyglucose-positron emission tomography integrated with computed tomography showed 100% sensitivity using an adrenal liver ratio  $> 1$ . When the maximum standardized uptake value  $>5$  cutoff was applied, sensitivity remained 100%, while specificity improved (100% vs. 82.1%). Eighty-seven tumors were managed with follow-up, with a mean duration of 30.1 months. Significant tumor growth occurred in four cases (4.6%): three myelolipomas and one indeterminate lesion in a patient with extra-adrenal malignancy. Adrenalectomy was performed in six patients (6.9%). Although these tumors were initially classified as adrenocortical adenomas, histopathology revealed benign lesions in five

cases and adrenocortical carcinoma in one. The risk of developing mild autonomous cortisol secretion among non-functioning tumors was 6.7%. No progression to overt Cushing's syndrome was observed. **CONCLUSION:** Although the risk of malignancy increases with tumor size, most LATs are benign. Imaging modalities demonstrate high sensitivity for detecting malignancy in LATs. No malignancies were identified in homogeneous lesions with attenuation <10 HU. LATs that do not meet these benign imaging criteria should undergo multidisciplinary evaluation and continued follow-up.

PubMed-ID: [41788772](#)

DOI: [10.3389/fendo.2026.1774131](#)

PMCID: PMC12957193

#### **More on Osilodrostat for Bilateral Adrenal Hypercortisolism in Primary Aldosteronism.**

*N Engl J Med*, 394(8):830-1.

Y. Mamoojee and R. Quinton. 2026.

PubMed-ID: [41707165](#)

DOI: [10.1056/NEJMc2518967](#)

#### **Clinical predictors of outcome in advanced adrenocortical carcinoma: a multicenter international ENSAT study.**

*Eur J Endocrinol*, 194(3):381-92.

A. Mangone, B. Altieri, E. Ferrante, I. Bancos, M. Luconi, B. Ziolkowska, A. B. Nekic, R. Libe, F. Ceccato, J. F. H. Pittaway, M. Lagana, G. Di Dalmazi, E. Peverelli, O. Kimpel, B. B. Fard, L. Canu, A. Kotecka-Blicharz, D. Kastelan, L. Bouys, I. Tizianel, G. Bennett, M. P. Schauer, Y. S. Elhassan, M. Detomas, L. Zanatta, M. Sadiq, G. Mantovani and C. L. Ronchi. 2026.

**OBJECTIVE:** Advanced adrenocortical carcinoma (ACC) is treated with mitotane alone or combined with cytotoxic chemotherapy, yet outcomes remain poor and prognostic models in this setting are lacking. This study aimed to evaluate the prognostic value of clinical parameters in a large cohort of patients with advanced ACC undergoing systemic therapy. **METHODS:** Multicenter, international cohort study investigating 418 patients with advanced ACC (61.5% = women, median age = 52 years) from 11 centers. Patients received mitotane monotherapy (n = 161), etoposide + doxorubicin + cisplatin +/- mitotane (n = 178), or second-line regimens (gemcitabine + capecitabine +/- mitotane or temozolomide + mitotane, n = 79). Variables included age, cortisol excess, performance status (ECOG-PS), tumor burden, and neutrophil-to-lymphocyte ratio (NLR) at start of therapy. Outcomes were overall survival (OS), time to progression (TTP), and best objective response. **RESULTS:** Tumor burden, cortisol excess, ECOG-PS, and NLR  $\geq 5$  independently predicted shorter OS (hazard ratio [HR] 1.55-2.68). We developed an integrated ENSAT Risk Score for Advanced ACC combining these variables: tumor burden (0-2), cortisol excess (0/1), ECOG-PS (0-2), and NLR (0/1). A score  $\geq 2$  (poor-risk) was significantly associated with worse OS and TTP across all treatment groups (HRs for OS: 3.05-3.96; TTP: 2.53-3.08). It also predicted poorer response to mitotane (P < .01) and second-line therapies (P = .04). **CONCLUSIONS:** The ENSAT Risk Score for Advanced ACC is a practical, prognostic tool for patients with advanced ACC receiving systemic therapy. Based on accessible clinical and biochemical markers, it can support treatment decisions and facilitate informed discussions in routine care.

PubMed-ID: [41790725](#)

DOI: [10.1093/ajeendo/lvag046](#)

#### **Indocyanine green (ICG) fluorescence in laparoscopic adrenalectomy: categorization of adrenal tumors relative to normal adrenal gland.**

*Updates Surg*, 78(1):397-403.

P. Metaxas, N. Dafnios, M. Konstantoulakis, C. Nastos, E. Mavrodimitraki, C. Polyzoos, M. Psarologos, M. Sotiropoulou, V. Drakopoulos and S. Kapiris. 2026.

ICG-fluorescent guided laparoscopic adrenalectomy (LA) has recently been adopted by endocrine surgeons but is still in its infancy. Consequentially, the optimal use of it in imaging different tumors is yet to be defined. All patients undergoing ICG-fluorescent guided LA in our department, from June 2020 until May 2024, were included in this study. Administration of 5mg of ICG was executed in 2 stages, before and after dissection of the anatomic plane of the adrenal gland. Adrenal tumors were categorized according to their fluorescent properties when compared to normal adrenal gland as "hyperfluorescent" or "hypofluorescent". Patient demographics, indication for surgery, tumor size, operative time and intraoperative complications were measured. This study included 61 patients undergoing LA, 31 being left LA and 30 right LA. Indications for surgery included aldosteronoma, pheochromocytoma, cushing syndrome, non-secreting adrenal tumors, myelolipoma, metastasis and possible carcinoma. Mean operative time was 124 +/- 24 min, mean dose of ICG injected was 10 mg (range 10-15 mg). Adrenal tumors were categorized as hyperfluorescent in 24 (39.4%) and hypofluorescent in 37 (60.6%) cases when compared to normal adrenal gland. Pheochromocytomas appeared hypofluorescent in 12/15 (80%) of cases while tumors of cortical origin were hypofluorescent in 21/38 (55%) of cases

compared to normal adrenal gland. Adrenal tumors exhibit different levels of fluorescent intensity according to their origin. Pheochromocytomas appear hypofluorescent in 80% of the cases, a finding that may assist surgeons when performing cortical sparing LAs addressing pheochromocytomas.

PubMed-ID: [41264218](#)

DOI: [10.1007/s13304-025-02450-4](#)

#### **Which bot is best? Accuracy and readability of generative artificial intelligence assistant responses on adrenal nodules.**

*Am J Surg*, 254:116859.

N. A. Moreno, A. Dixon, S. Y. Dream, A. H. Hamrahian, E. K. Fishman, S. M. Chen Cardenas, A. V. Rudin, A. Mathur and L. F. Morris-Wiseman. 2026.

INTRODUCTION: Patients increasingly use generative artificial intelligence assistants (chatbots) for medical information. We examined surgeon-perceived accuracy, reliability, and readability of chatbot responses to adrenal nodule queries.

METHODS: Six commonly asked adrenal nodule questions were input into five chatbots. Blinded answers were reviewed by 10 endocrine surgeons for correctness and reliability (6-point Likert scale) and content structure (3-point Likert scale).

One-way ANOVAs and Tukey adjusted post hoc analyses tested differences. Inter-rater reliability across surgeon ratings was assessed by two-way intraclass correlation coefficient. Reading grade levels were assessed using Lexile Text Analyzer (MetaMetrics, Inc). RESULTS: Correctness, reliability, and jargon use differed significantly ( $p \leq 0.05$ ). Perplexity scored highest for correctness, reliability, and thoroughness but used the most jargon. Gemini scored lowest on all domains, but used the least jargon. Mean Lexile reading level was 8th-10th grade. CONCLUSION: Chatbot responses about adrenal nodules vary significantly. More accurate, reliable, and thorough answers contained excess jargon, but all responses exceeded recommended patient education levels.

PubMed-ID: [41691948](#)

DOI: [10.1016/j.amjsurg.2026.116859](#)

#### **Subtype- and treatment-based analysis of calcium dynamics in primary aldosteronism.**

*Eur J Endocrinol*, 194(2):275-84.

T. Nakamura, I. Kurihara, Y. Mizutani, K. Kinouchi, S. Kobayashi and K. Hayashi. 2026.

OBJECTIVE: Primary aldosteronism (PA) adversely affects cardiovascular and renal health and has been linked to increased urinary calcium excretion, elevated parathyroid hormone (PTH) levels, and reduced bone mineral density. Although adrenalectomy and mineralocorticoid receptor antagonists (MRAs) are established treatments, their differential effects on calcium dynamics across PA subtypes remain unclear. DESIGN: We conducted a retrospective observational study, analyzing a large, well-characterized cohort on calcium metabolism in PA. A total of 352 patients with PA and 57 controls were evaluated. METHODS: Clinical and biochemical parameters, including intact PTH (iPTH) and urinary electrolyte levels, were retrospectively assessed. Comparative analyses were performed before and after treatment in 43 patients with unilateral PA (UPA) and 131 patients with bilateral PA (BPA), with a direct comparison of adrenalectomy and MRAs in UPA. RESULTS: Patients with PA had higher urinary fractional excretion of calcium (FECa) (1.28% vs 1.04%,  $P < .001$ ) and iPTH (60.0 vs 57.0 pg/mL,  $P = .047$ ) than controls, with more pronounced abnormalities in UPA (FECa, 1.50%, iPTH 73.1 pg/mL). Both treatments reduced FECa and iPTH levels, but adrenalectomy resulted in greater improvement than MRAs in the UPA (FECa, 0.68% post-MRA vs 0.36% post-adrenalectomy). In the BPA group, MRAs decreased FECa, irrespective of disease severity. CONCLUSION: Adrenalectomy was associated with greater improvements in calcium abnormalities than MRAs in patients with UPA, consistent with its cardiovascular benefits. These findings underscore the importance of subtype-specific strategies and suggest that adrenalectomy may offer additional benefits beyond cardiovascular outcomes.

PubMed-ID: [41719273](#)

DOI: [10.1093/ajendo/lvag035](#)

#### **National trends in ambulatory and inpatient minimally invasive adrenalectomy in the United States.**

*Surgery*, 190:109929.

S. H. Nguyen, C. B. Jensen, C. Larrain, Z. D. Leslie, J. V. Harmon and S. Ikramuddin. 2026.

BACKGROUND: The use of minimally invasive adrenalectomy has expanded. Although ambulatory minimally invasive adrenalectomy has demonstrated safety and feasibility in select settings, trends in utilization, surgical indication, and outcomes remain limited. This study aimed to evaluate national trends in the adoption and incidence of inpatient and ambulatory minimally invasive adrenalectomy in the United States from 2016 to 2022. METHODS: We conducted a retrospective cross-sectional study using the Nationwide Ambulatory Surgery Sample and National Inpatient Sample to identify adults aged  $\geq 20$  years who underwent elective minimally invasive adrenalectomy. Surgical indication, laterality, patient demographics, and hospital characteristics were assessed. Outcomes included charge, discharge disposition, and

mortality. Age- and sex-adjusted incidence was reported per 100,000 adults. RESULTS: Among a weighted total of 35,242 minimally invasive adrenalectomies, 8,917 (25.3%) were ambulatory. Ambulatory incidence rose from 0.22 to 0.59 per 100,000 adults (incidence rate ratio: 2.75, 95% confidence interval: 2.34-3.24), whereas inpatient incidence increased at a lower rate (incidence rate ratio: 1.24, 95% confidence interval: 1.07-1.43). Benign adrenal neoplasm was the most common indication in both settings. Ambulatory incidence increased for all indications except primary malignant neoplasms. Both left- and right-sided ambulatory adrenalectomies increased, with left-sided procedures being more common. Charges were lower in ambulatory settings. Overall, non-home discharge and mortality were rare. CONCLUSION: Incidence of ambulatory adrenalectomy has nearly tripled in less than a decade, primarily driven by benign adrenal neoplasms and outpacing increases in inpatient adrenalectomy. Given the substantial rise, societal guidelines and further evaluation of adrenalectomy-specific outcomes are needed to identify patients who may benefit from ambulatory adrenalectomy.

PubMed-ID: [41371192](#)

DOI: [10.1016/j.surg.2025.109929](#)

### **Effect of surgical versus conservative management on cardiovascular outcomes in patients with bilateral adrenal tumours and cortisol excess: an international, retrospective cohort study.**

*Lancet Diabetes Endocrinol*, 14(3):202-15.

E. Nowak, C. L. Vietor, R. A. Feelders, J. Hofland, M. Araujo-Castro, C. M. Ojeda, E. Pascual-Corrales, B. Salama, I. Bancos, R. Sandooja, M. Fassnacht, B. Altieri, M. Detomas, M. Bobrowicz, U. Ambroziak, A. Gladka, R. Giordano, F. Bioletto, M. Parasiliti-Caprino, E. M. Torre, D. Rivas-Otero, T. Gonzalez-Vidal, F. Ceccato, I. Tizianel, M. Torchio, S. Palmieri, A. Mangone, G. Mantovani, I. Chiodini, V. Favero, A. Prete, O. Suntornlohanakul, V. Morelli, M. Chiodaroli, M. Trofimiuk-Muldner, A. Hubalewska-Dydejczyk, S. Puglisi, G. Reimondo, K. I. Alexandraki, A. Spyroglou, H. Falhammar, P. Klosowski, A. Chrisoulidou, A. Tabarin, P. Loli, A. Angelousi, D. Pignatelli, F. Hanzu, S. Fuld, C. Pamporaki, S. Athimulam, M. Quinkler, A. Markou, T. Puar, T. Deutschbein, V. S. Hoffmann and M. Reincke. 2026.

BACKGROUND: Treatment for patients with bilateral adrenal tumours and cortisol excess is not standardised and poses a therapeutic dilemma. Untreated cortisol excess is associated with cardiometabolic morbidity and mortality, but bilateral adrenalectomy causes adrenal insufficiency and possibly life-threatening adrenal crises. Data on cardiovascular outcomes by treatment modality are scarce. In this study we aimed to evaluate mid-term and long-term clinical and biochemical outcomes in patients with bilateral adrenal tumours and cortisol excess by treatment strategy and diagnosis. METHODS: This retrospective, international cohort study (in 30 centres across 10 countries in Europe plus Singapore and the USA) included patients with bilateral adrenal tumours of 10 mm or larger, post-dexamethasone serum cortisol concentration of 50 nmol/L or higher, and at least 36 months of follow-up, with data collection between Feb 2, 2024, and Jan 31, 2025. Patients were excluded if they had adrenocorticotropin hormone (ACTH)-dependent cortisol excess, ACTH-dependent nodular adrenal hyperplasia, partial glucocorticoid resistance syndrome, a diagnosis inconsistent with benign adrenocortical lesions, or received systemic oral or intravenous glucocorticoids other than replacement therapy following adrenalectomy. Primary endpoints were all-cause mortality and clinical and biochemical remission rates. Secondary endpoints were the incidence of cardiovascular events, prevalence of vascular and metabolic comorbidities, and incidence of adrenal crises. FINDINGS: Of 629 patients who were diagnosed between Jan 1, 2000, and Jan 31, 2022, 105 (17%) had Cushing's syndrome and 524 (83%) had mild autonomous cortisol secretion (MACS), median age was 62 years (IQR 54.0-68.0), and 426 (68%) were female. 85 (81%) of 105 patients with Cushing's syndrome underwent surgery, and 384 (73%) of 524 patients with MACS received non-specific symptomatic treatment (ie, never underwent adrenalectomy or received steroidogenesis inhibitors). Over a median follow-up of 6.8 years, biochemical remission was achieved in 46 (45%) of 102 patients with Cushing's syndrome and in 67 (13%) of 517 patients with MACS. In both groups, 7% of patients died (Cushing's syndrome: seven of 105; MACS: 38 of 524) and 12% (13 of 105) of patients with Cushing's syndrome and 16% (82 of 524) of those with MACS had at least one cardiovascular event, without substantial differences across treatments. Smoking emerged as key modifiable mortality and cardiovascular risk factor in all patients, and in patients with MACS who only received non-specific symptomatic therapy, post-dexamethasone cortisol was also associated with increased mortality. Bilateral adrenalectomy led to full biochemical remission, few non-fatal adrenal crises, and improved arterial hypertension. Unilateral adrenalectomy and steroidogenesis inhibitors yielded heterogeneous biochemical outcomes and no substantial comorbidity improvement. Non-specific symptomatic treatment in MACS was associated with worsening of all investigated comorbidities. INTERPRETATION: Although mortality and cardiovascular event rates were similar across treatments, surgery led to better biochemical control and more favourable comorbidity outcomes. FUNDING: None.

PubMed-ID: [41579871](#)

DOI: [10.1016/S2213-8587\(25\)00302-X](#)

### **Development of an experimental model for vascularized adrenal gland transplantation in rats.**

*Front Surg*, 12:1749069.

C. Ozcan, S. M. Hazinedaroglu and T. Tug. 2025.

AIM: The adrenal gland is a vital endocrine organ responsible for maintaining physiological homeostasis. Bilateral adrenalectomy results in adrenal insufficiency, requiring lifelong hormone replacement therapy. This study aimed to establish a reproducible experimental model for vascularized adrenal gland transplantation in rats. MATERIALS AND METHODS: Twenty male Wistar Albino rats (180-220 g) were randomly assigned into two equal groups (n = 10 each): control and transplantation. The control group underwent bilateral total adrenalectomy. In the transplantation group, vascularized adrenal grafts-including the adrenal artery and vein with attached aortic and inferior vena cava segments-were anastomosed end-to-side to the recipient's femoral artery and vein using 10-0 nylon sutures under general anesthesia. On postoperative day 15, all recipients underwent bilateral adrenalectomy. On day 100, animals were sacrificed for macroscopic and histopathological evaluation of graft viability. RESULTS: All control rats died within 15 days, whereas all transplanted rats survived throughout the 100-day observation period. Macroscopic inspection revealed viable grafts without vascular compromise. Histopathological analysis demonstrated preserved cortical and medullary architecture, confirming the long-term viability of the transplanted adrenal glands. CONCLUSION: This study presents a technically feasible and reproducible model for vascularized adrenal gland transplantation in rats. The model provides a reliable experimental platform for future research on adrenal physiology and transplantation surgery.

PubMed-ID: [41602923](#)

DOI: [10.3389/fsurg.2025.1749069](#)

PMCID: PMC12833046

### **Adrenal tumour imaging: clinical, molecular, and radiomics perspectives.**

*Lancet Diabetes Endocrinol*, 14(1):62-81.

K. Pacak, M. A. Blake, A. T. Sweeney, A. Jha, A. Imperiale, H. Zaidi, M. Raffaelli, Z. Tudos, H. Timmers, A. Grossman, S. Nolting and D. Taieb. 2026.

Adrenal tumours have become a common incidental finding in the radiological evaluation of patients. Estimates suggest that 1-10% of the general population currently harbours an adrenal tumour, peaking in prevalence in the seventh and eighth decades of life. Advances in CT and MR have contributed to improved characterisation of adrenal masses, and novel radiopharmaceuticals are being developed for molecular characterisation and disease subtyping. As a result, the imaging and management of adrenal tumours have been important subjects of many guidelines and consensus statements. New radiomics approaches, together with machine learning, are now being introduced and are quickly shaping the way that imaging data are analysed and interpreted. Furthermore, the development of theranostics links the molecular biology of functioning tumours to targeted treatment options. In this Review, we summarise up-to-date imaging and follow-up approaches for adrenal tumours to provide patients with the most accurate diagnosis, thereby avoiding unnecessary additional tests or surgery.

PubMed-ID: [41265468](#)

DOI: [10.1016/S2213-8587\(25\)00300-6](#)

### **Reoperative adrenalectomy: Indications and outcomes.**

*Am J Surg*, 255:116740.

E. Pace, K. M. Ramonell, E. B. Habermann, K. L. McCoy, S. E. Carty, P. K. Fazeli, L. Yip and A. Sada. 2026.

BACKGROUND: Reoperative adrenalectomy, defined as subsequent ipsilateral adrenal resection, has been incompletely characterized. Utilizing a multi-institutional database, we investigated the outcomes of reoperative compared to primary adrenalectomy. METHODS: Using The Collaborative Endocrine Surgery Quality Improvement Program (CESQIP), patients undergoing primary and reoperative adrenalectomy were identified. 30-day outcomes were compared using Chi square and Wilcoxon sum tests. RESULTS: Out of 3558 patients, 3469 (97 %) had primary and 89 (3 %) reoperative adrenalectomy. Indications for adrenalectomy varied between groups,  $p < 0.01$ . Reoperative adrenalectomy was associated with longer operative time and length of stay, and higher rates of intra-operative complications and readmission. There was no difference in the 30-day mortality rate between the groups. CONCLUSIONS: Reoperative adrenalectomy is uncommon and is associated with increased morbidity. Patients should be counseled regarding possible operative complications. Although reoperation is associated with an extended length of stay and higher likelihood of readmission, there was no detriment to 30-day mortality.

PubMed-ID: [41318340](#)

DOI: [10.1016/j.amjsurg.2025.116740](#)

### **Presentation of a missense MDH2 variant in a Greek patient with pheochromocytoma.**

*Hormones (Athens)*, 25(1):289-96.

L. Papanastasiou, E. Kakargia, A. Sertedaki, D. P. Bouklas, M. Tampourlou, C. Kanaka-Gantenbein, A. Fountas and A. Markou. 2026.

**PURPOSE:** Approximately 40% of pheochromocytomas and paragangliomas (PPGLs) are caused by germline mutations. MDH2 encodes the mitochondrial malate dehydrogenase, a Krebs cycle enzyme, which is essential for the conversion of malate to oxaloacetate and which has recently been added to the list of potential PPGL susceptibility genes. In this report, we present a MDH2 germline variant in a Greek patient with pheochromocytoma. **CASE PRESENTATION:** A 66-year-old male patient presented for investigation of a 5.4 cm right adrenal incidentaloma, with imaging features not indicative of adenoma. During hospitalization, he experienced daily episodes of paroxysmal hypertension, tachycardia, headache, and pallor lasting approximately 10-20 min. Hormonal evaluation revealed significantly increased 24-h urine metanephrine and normetanephrine levels, leading to a diagnosis of pheochromocytoma. After alpha-blockers preparation, an uncomplicated laparoscopic right adrenalectomy was performed. Histology revealed a pheochromocytoma (PASS score 7) with a Ki-67 index of 6%. EpsilonXome sequencing identified the missense MDH2 variant, c.478G > A, resulting in replacement of valine by methionine at codon 160, p.Val160Met, of the MDH2 protein. Although this variant is considered to be of uncertain significance, recent in silico analysis showed that it results in protein three-dimensional structure destabilization and impairment of MDH2 molecular function, classifying it as likely pathogenic. Twelve months after adrenalectomy, the patient is asymptomatic with no evidence of disease recurrence. **CONCLUSIONS:** To our knowledge, this is the second reported case with the germline c.478G > A MDH2 variant and a pheochromocytoma. Further genetic studies are needed to determine the role of this variant in the PPGLs pathogenesis.

PubMed-ID: [41085877](#)

DOI: [10.1007/s42000-025-00730-7](#)

### **Plasma proteomic profiling identifies apolipoprotein A4 as a downregulated biomarker of adrenocortical carcinoma: a multi-platform discovery and validation study.**

*Eur J Endocrinol*, 194(5):641-52.

S. S. Park, H. Seo, S. J. Moon, H. N. Jang, S. H. Lee, S. J. Kim, K. E. Lee, D. Han and J. H. Kim. 2026.

**OBJECTIVES:** Adrenocortical carcinoma (ACC) is a rare, aggressive malignancy associated with heterogeneous prognosis. Preoperative differentiation from adrenocortical adenoma (ACA) remains challenging, and no serum tumor marker has been established. We aimed to identify circulating protein biomarkers that distinguish ACC from ACA using a stepwise, multiplatform proteomics strategy. **METHODS:** We assembled discovery (ACC = 10, ACA = 67) and verification (ACC = 7, ACA = 11) cohorts from a tertiary center and profiled fasting plasma using liquid chromatography-mass spectrometry (LC-MS/MS) with data-independent acquisition. Differentially expressed proteins (DEPs) were defined by t-tests with  $P < .05$  and  $|\text{fold-change}| > 1.2$ ; DEPs common to both cohorts were prioritized. Targeted validation by parallel reaction monitoring (PRM) used an expanded, two-center cohort including additional cases from Asan Medical Center (ACC = 31; ACA = 78). Orthogonal validation employed the Olink Explore 384 Inflammation II panel in an independent set (ACC = 15; ACA = 24). **RESULTS:** The discovery cohort yielded 67 DEPs (22 upregulated and 45 downregulated in ACC), and the verification cohort identified 17 DEPs. Three proteins, CD44, proteoglycan 4, and apolipoprotein A4 (APOA4), were common to both analyses and were underexpressed in ACC compared with ACA. In PRM, CD44 and APOA4 showed directionally concordant, significant decreases in ACC, prioritizing these markers for further evaluation. In the Olink analysis, 40 proteins differed between ACC and ACA after false discovery rate correction; APOA4 remained significantly lower in ACC. **CONCLUSION:** Across discovery, targeted, and orthogonal platforms, APOA4 consistently exhibited lower circulating levels in ACC, supporting its potential as a serum biomarker for the preoperative differentiation of ACC from ACA. External, multiethnic validation and clinically deployable assays, alone or within multimarker panels, are warranted.

PubMed-ID: [42097574](#)

DOI: [10.1093/ejendo/lvag079](#)

### **Fewer Pills, Lower Bills: Antihypertensive and Cost Outcomes of Adrenalectomy in Primary Aldosteronism.**

*Ann Surg Oncol*, 33(6):5659-68.

J. E. Passman, L. Owei, C. Brensinger, T. Barrett, L. R. Kelz, J. Hwang, J. B. Cohen and H. Wachtel. 2026.

**BACKGROUND:** Primary aldosteronism (PA) can be treated surgically or medically depending on disease lateralization and surgical candidacy. There is a dearth of data directly comparing antihypertensive medication trajectories and costs between these strategies. **PATIENTS AND METHODS:** We performed a retrospective cohort study of patients with new PA diagnoses and adrenal vein sampling to assess antihypertensive medication outcomes and treatment costs using Optum's de-identified Clinformatics((R)) Data Mart Database (2004-2022). Patients were stratified by receipt of adrenalectomy

versus medical management alone. The index time point was defined as adrenal vein sampling (AVS) for medically managed and adrenalectomy for surgically managed patients. Outcomes were assessed using regression models. RESULTS: Of 911 patients, 52% underwent adrenalectomy and 48% medical therapy. Adrenalectomy patients were younger, with higher Elixhauser scores. Antihypertensive medication use (2.9 versus 2.8,  $p = 0.636$ ) and costs did not differ at index. After 1 year, adrenalectomy patients used fewer antihypertensive medications (1.5 +/- 1.4) than medically managed patients (2.5 +/- 1.5,  $p < 0.001$ ). On regression, age ( $\beta = 0.02$ ,  $p = 0.002$ ), male sex ( $\beta = 0.40$ ,  $p < 0.001$ ), and baseline antihypertensive medications ( $\beta = 0.43$ ,  $p < 0.001$ ) were associated with higher antihypertensive medication requirement. Adrenalectomy patients were prescribed 1.11 fewer antihypertensive medications at one year ( $p < 0.001$ ). In the resistant hypertension subcohort, adrenalectomy reduced antihypertensive medications by 1.35 ( $p < 0.001$ ). Adrenalectomy was associated with US \$908 lower antihypertensive medication prescription costs ( $p < 0.001$ ) and 87% lower odds of potassium supplementation ( $p < 0.001$ ). CONCLUSIONS: Patients with PA who undergo adrenalectomy demonstrate a significant reduction in antihypertensive medications compared with medically managed patients. While there is significant upfront cost to surgical intervention, reduced long-term prescription costs are realized.

PubMed-ID: [41781764](#)

DOI: [10.1245/s10434-026-19347-0](#)

PMCID: PMC13179191

### **Predictive model for the diagnosis of ectopic Cushing syndrome.**

*Endocr Relat Cancer*, 33(6)

W. A. Rivera-Martinez, C. E. Builes-Montano, N. Aristizabal Henao, S. Cruz Calderon, N. A. Diaz Posada, M. J. Ramirez Castano, C. A. Builes Barrera, C. M. Gomez Serna, A. Roman-Gonzalez, A. Abreu Lomba, A. F. Garcia Ramos, D. Vernaza, A. Soto Moreno, A. Irigaray Echarri, M. D. Ollero Garcia-Agullo, M. D. Moure Rodriguez, A. Pinzon-Tovar, R. Garcia-Centeno, L. Gonzalez Fernandez, A. Cardona, B. Biagetti, F. Guerrero-Perez, L. Manzano Valero, A. Castro Luna, M. Paja, R. Camara, J. Gutierrez Restrepo, P. A. Castano Ceballos, N. Lopez Pompey, P. Iglesias, V. Alcazar, E. Menendez Torre, C. Lozano Aida, P. Candela, F. A. Hanzu and M. Araujo-Castro. 2026.

The purpose of our study was to develop and externally validate a multivariable diagnostic model to distinguish ectopic ACTH secretion (EAS) from Cushing's disease (CD) using routine clinical parameters. The model was derived from a Spanish multicenter retrospective cohort and externally validated in a Colombian cohort. Predictors were selected through a multivariable logistic regression model with penalized logistic regression (LASSO) using the Spanish cohort. Discriminative performance was assessed using the area under the ROC curve (AUC) and calibration using the slope, the origin, and the Brier score. The derivation cohort included 253 patients from Spain (199 with CD and 54 with EAS). The external validation cohort comprised 72 Colombian patients (53 with CD and 19 with EAS). In the derivation cohort, multivariable modeling identified four independent predictors: ACTH concentration, 24-h urinary free cortisol (UFC), serum potassium, and maximum pituitary tumor diameter. The final model demonstrated good discrimination in the derivation cohort (mean AUC of 0.987), with excellent calibration (calibration slope ranged from 0.998 to 5.22, intercept -0.2 to 0.99, Brier score 0.035). In external validation, model performance remained robust (AUC ranging from 0.9885 to 0.9890; Brier score 0.0381). The model achieved a sensitivity of 95.3%, specificity of 93.6%, positive predictive value of 82.3%, and negative predictive value of 98.7% for detecting EAS. Thus, the diagnostic model developed, based on routinely available clinical variables, shows high accuracy and calibration in differentiating between EAS and CD, supporting its potential use in diverse clinical settings and integration into diagnostic workflows.

PubMed-ID: [41989874](#)

DOI: [10.1530/ERC-25-0348](#)

### **A ten-year propensity score-matched comparison of lateral transabdominal and posterior retroperitoneoscopic approaches to adrenalectomy.**

*Surg Endosc*, 40(1):747-57.

L. Rossi, C. Becucci, A. De Palma, B. Gjelogshi, O. Della Posta, G. D'Amato, M. Paternoster, R. Morganti, C. E. Ambrosini and G. Materazzi. 2026.

BACKGROUND: Minimally invasive adrenalectomy (MIA) is mostly performed as lateral transabdominal adrenalectomy (LTA) or posterior retroperitoneoscopic adrenalectomy (PRA). This study aims to compare LTA and PRA in terms of perioperative outcomes. METHODS: A retrospective cohort study was conducted on 225 patients who underwent MIA from 2013 to 2023. Patients were divided into two groups: LTA ( $n = 182$ ) and PRA ( $n = 43$ ). Propensity score matching (PSM) was used for group balancing. RESULTS: PRA was associated with shorter operative times ( $p = 0.004$ ), shorter hospital stay ( $p < 0.001$ ), fewer drainage placements ( $p < 0.001$ ), shorter time to catheter removal ( $p = 0.028$ ), shorter time

to return to oral diet ( $p = 0.012$ ), and higher need for postoperative ICU stay ( $p = 0.001$ ). After PSM, PRA remained associated with shorter hospital stay ( $p = 0.019$ ) and lower rate of drainage placement ( $p < 0.001$ ). In multivariate analysis, no factors resulted in association with postoperative complications, while BMI resulted in association with a longer hospital stay ( $p = 0.016$ ). CONCLUSION: Both LTA and PRA demonstrated comparable safety profiles. PRA, however, was associated with a shorter hospital stay and reduced drain placement frequency.

PubMed-ID: [41361517](#)

DOI: [10.1007/s00464-025-12473-y](#)

### **Does Laterality Affect the Risk of Intraoperative Complications in Adrenalectomy?**

*J Surg Oncol*, 133(4):454-8.

L. Scheipner, S. Morra, A. Baudo, L. M. I. Jannello, C. Siech, M. de Angelis, J. A. Goyal, Z. Tian, F. Saad, S. F. Shariat, A. Briganti, F. K. H. Chun, N. Longo, L. Carmignani, O. De Cobelli, M. Seles, J. Mischinger, S. Ahyai and P. I. Karakiewicz. 2026. PURPOSE: To test the effect of laterality on the risk of intraoperative complications (ICs) in a contemporary cohort of adrenalectomy patients. METHODS: Within the Nationwide Inpatient Sample (NIS) database (2015-2019), we identified patients who underwent either minimal-invasive or open adrenalectomy. Multivariable logistic regression models tested for the association of laterality and IC. Additionally, this association was further tested in specific subgroups, namely patients with elevated body mass index (BMI)  $\geq 30$ , patients who underwent minimal-invasive adrenalectomy, and patients who underwent open adrenalectomy. RESULTS: Overall, we identified 4887 patients who underwent adrenalectomy. Of those, 2143 (44%) were right-sided, and 2744 (56%) left-sided. An IC was recorded in 90 (1.8%) patients. Right-sided adrenalectomy had significantly more IC compared to left-sided adrenalectomy (2.6% vs. 1.3%,  $p < 0.001$ ). After multivariable adjustment, right side emerged as an independent predictor for IC (OR 1.9,  $p = 0.007$ ). In subgroup analysis, right-side remained an independent predictor for IC in patients with BMI  $\geq 30$  (OR 4.08  $p = 0.003$ ) and minimal-invasive adrenalectomy (OR 2.3  $p = 0.01$ ) patients. CONCLUSION: ICs in adrenalectomy are rare, but are associated with high morbidity. Right-sided adrenalectomy carries an increased risk for IC. Conversely, surgeons should exercise particular caution when approaching the right adrenal gland to mitigate the associated risks and enhance patient outcomes.

PubMed-ID: [41723810](#)

DOI: [10.1002/jso.70195](#)

### **A novel 2D and 3D model for primary adrenocortical carcinoma of advanced and metastasized stage co-secreting cortisol, aldosterone, testosterone, 18-oxocortisol and 18-hydroxycortisol.**

*Endocr Relat Cancer*, 33(1)

I. Shapiro, C. Krauchi, E. Luca, S. Dettwiler, M. Peitzsch, W. Qi, A. Reul, F. Beuschlein, U. Maccio, S. Nolting, H. Debaix and C. Hantel. 2026.

Adrenocortical carcinoma (ACC) is a highly aggressive malignancy with poor survival rates and few treatment options. Preclinical models are indispensable to further strengthen our understanding of disease progression and development of novel therapeutic treatments. Here, we report the establishment of a new cell line named ZUC-1 originating from the resection of an advanced primary ACC and its characterization at the genomic, cellular and molecular level. ZUC-1 cells were successfully propagated as monolayer cultures and three-dimensional spheroids. LC-MS/MS analysis revealed for ZUC-1 cells co-secretion of cortisol, aldosterone and testosterone, and the model represented in direct comparison with other current ACC pre-clinical models furthermore significantly elevated expression of SF-1, CYP11B1 and CYP11B2 genes. Whole genome sequencing identified various mutations in genes linked to DNA repair/stress response, stemness, and also steroidogenesis. Interestingly, ZUC-1 represents genotypic and phenotypic variations that might be of interest beyond ACC, including congenital adrenal hyperplasia (CAH) and polycystic ovary syndrome (PCOS). Moreover, 18-oxocortisol and 18-hydroxycortisol release was detected in ZUC-1, conditions which are often linked to hyperaldosteronism, but forskolin, potassium and, at higher concentration, angiotensin II modulability of CYP11B2 for this model is retained. ZUC-1 spheroids exhibited furthermore an intra-spheroidal heterogeneous mix of canonical and non-canonical Wnt pathway activation. We conclude that due to its origin and unique geno- and phenotypes, ZUC-1 represents an intriguing model to further gain a basic understanding of adrenal function, the pathogenesis of ACC, but it might be also of interest in the context of CAH and PCOS.

PubMed-ID: [41528016](#)

DOI: [10.1530/ERC-25-0385](#)

### **Surgical management of metastatic adrenocortical carcinoma: Is there a role for multivisceral resection?**

*Surgery*, 189:109696.

O. A. Shariq, B. Kensing, J. P. Landry, C. D. Tzeng, M. A. Habra, M. T. Campbell, S. B. Fisher, N. D. Perrier, J. E. Lee and P. H. Graham. 2026.

**BACKGROUND:** Recent data suggest that cytoreductive surgery in metastatic adrenocortical carcinoma may improve survival. However, successful removal of locally invasive primary tumors in such patients may require complex en bloc and/or multivisceral resection, for which the survival benefits remain unclear. **METHODS:** We retrospectively analyzed 153 patients with metastatic adrenocortical carcinoma treated at our institution from 1998 to 2024. Patients were categorized into 3 groups based on treatment approach: multivisceral resection, adrenalectomy alone, and nonoperative management. Kaplan-Meier analysis and Cox proportional hazards models were used to evaluate overall survival across these groups. **RESULTS:** Among 153 patients (52% female; median age 49 years, interquartile range: 36-59 years), 24% underwent multivisceral resection, 18% had adrenalectomy alone, and 58% were managed nonoperatively. Overall, 68% of tumors were functional. The most frequent metastatic sites were the lung (71%) and liver (66%). The most frequent en bloc procedures included radical nephrectomy (64%) and partial hepatectomy (47%). The median overall survival was 33 months after multivisceral resection, 22 months after adrenalectomy alone, and 7 months with nonoperative management ( $P < .0001$ ). On multivariable analysis, multivisceral resection (hazards ratio = 0.31, 95% confidence interval: 0.18-0.50,  $P < .0001$ ) and adrenalectomy alone (hazards ratio = 0.50, 95% confidence interval: 0.28-0.88,  $P = .017$ ) were independently associated with longer overall survival compared with nonoperative management. **CONCLUSION:** Cytoreductive surgery, including multivisceral resection, may be associated with improved survival in metastatic adrenocortical carcinoma compared with nonoperative management. However, given the potential risks of these complex operations, they should be judiciously performed in select patients by experienced multidisciplinary teams.

PubMed-ID: [41006153](#)

DOI: [10.1016/j.surg.2025.109696](#)

### **Prevalence and clinical characteristics of Lynch syndrome-associated adrenocortical carcinoma.**

*Endocr Relat Cancer*, 33(1)

A. Sinha, K. I. Wolf, J. Osborne, E. A. Hesseltine, F. P. Worden, T. J. Giordano, G. D. Hammer and T. Else. 2026.

Lynch syndrome is the result of pathogenic variants in mismatch repair genes that increase the risk of cancer, including adrenocortical carcinoma. Little is known, however, about the clinical characteristics of patients with Lynch syndrome-associated adrenocortical carcinoma. In order to understand the clinical characteristics and prevalence of Lynch syndrome-associated adrenocortical carcinoma, we conducted a retrospective chart review of patients with adrenocortical carcinoma and germline genetic testing results, indicating pathogenic variants in mismatch repair genes consistent with Lynch syndrome at a single academic tertiary-care institution. In total, 21 patients with Lynch syndrome-associated adrenocortical carcinoma were identified from 2003 to 2024. Three patients met Amsterdam I criteria, and 12 patients met Amsterdam II criteria (including adrenocortical carcinoma as a Lynch syndrome-associated cancer). More than 90% of patients with available histopathology had high-grade tumors, suggesting a more aggressive nature. The prevalence of Lynch syndrome-associated adrenocortical carcinoma is estimated at 2.6%. This study further demonstrates that adrenocortical carcinoma is a Lynch syndrome-associated cancer and may be associated with a high-grade disease. Furthermore, our findings suggest that further research should be pursued to investigate the potential utility of immunotherapy for adrenocortical carcinoma, especially in the presence of microsatellite instability.

PubMed-ID: [41524568](#)

DOI: [10.1530/ERC-25-0389](#)

### **Potential mechanisms of the glucocorticoid withdrawal syndrome.**

*Eur J Endocrinol*, 194(4):R67-R81.

C. N. Snyder, E. D. Frontera, J. Meng, B. I. Wallace and J. L. Spencer-Segal. 2026.

Glucocorticoid withdrawal syndrome (GWS) is a frequent and clinically significant consequence of reducing chronic endogenous or exogenous glucocorticoid exposure. The syndrome presents with a range of symptoms involving musculoskeletal, gastrointestinal, neuropsychiatric, cardiovascular, and metabolic domains, which can closely resemble adrenal insufficiency or recurrence of an underlying autoimmune/inflammatory disease. As a result, the true prevalence, history, and clinical burden of GWS remain poorly defined, and recognition varies widely across clinical settings. The lack of treatment options for GWS contributes to detrimental exogenous glucocorticoid exposure in patients with rheumatologic, oncologic, and endocrine diseases. The underlying biological mechanisms of GWS remain incompletely understood, which represents a major barrier to the recognition and treatment of this syndrome. This review synthesizes current evidence on the epidemiology, clinical manifestations, and management challenges of GWS. We integrate

mechanistic insights from studies of chronic glucocorticoid excess, postoperative recovery of Cushing syndrome, and experimental models of glucocorticoid excess and deficiency. Glucocorticoid excess leads to central and peripheral adaptations involving the hypothalamic-pituitary-adrenal axis, glucocorticoid receptor signaling, circadian rhythms, immune and inflammatory pathways, metabolic and autonomic regulation, and glucocorticoid-sensitive neural circuits. We propose that GWS arises due to the confluence of these persisting adaptations with relative glucocorticoid deficiency and tissue- or cell-specific adaptations and recovery timelines. Thus, we provide a mechanistic framework for understanding the diverse manifestations of GWS and highlight key gaps that need to be addressed to improve mechanistic understanding, diagnosis, and clinical management.

PubMed-ID: [41988948](#)

DOI: [10.1093/ejendo/lvag062](#)

#### **Adrenal imaging features and associated pathologic diagnoses: A contemporary, longitudinal analysis.**

*Surgery*, 189:109693.

K. A. Stahl, A. Sada, Y. Baytar, A. K. Dasyam, J. K. Maranchie, P. K. Fazeli, R. S. Seethala, K. L. McCoy, L. Yip and K. M. Ramonell. 2026.

BACKGROUND: Imaging features are key in preoperative risk assessment of adrenal nodules, but current recommendations stem from low quality evidence. This study evaluates the performance of cross-sectional imaging features in predicting adrenal pathology. METHODS: All adult adrenalectomy cases (2015-2023) with preoperative cross-sectional imaging were retrospectively reviewed; pheochromocytomas and incidental adrenalectomies were excluded. Benign imaging features were defined as size  $\leq 4.0$  cm; Hounsfield units  $\leq 10$ , or Hounsfield units  $\leq 20$  on unenhanced computed tomography; absolute and relative contrast washout  $\geq 60\%$  and  $\geq 40\%$ , respectively, on adrenal protocol computed tomography; and loss of signal or homogeneity on T1-weighted magnetic resonance imaging. Performance of imaging features in identifying benign and malignant adrenal pathology were analyzed. RESULTS: Among the 250 adrenal specimens included, 21% were malignant, with 22 adrenocortical carcinomas and 30 other malignant lesions, whereas 79% were benign. Compared to benign, malignant lesions were larger (6.8 cm vs 4.4 cm,  $P = .002$ ) and none had densities of  $\leq 20$  Hounsfield units on unenhanced computed tomography scan or loss of signal on magnetic resonance imaging. Malignancy rate for lesions  $> 20$  Hounsfield units was 31%. Notably, 13.6% (3/22) of adrenocortical carcinomas and 63.3% (19/30) of other malignant lesions were  $< 4.0$  cm. Accuracy of imaging features in correctly identifying pathology was best (65%) using a density threshold of  $\leq 20$  Hounsfield units, and 48% of pathologically benign adrenal lesions were accurately identified as being benign on imaging. CONCLUSIONS: In this large, contemporary study, using adrenal lesion size  $> 4.0$  cm alone has low specificity (57%) in identifying malignant adrenal pathology and absolute contrast washout on adrenal protocol computed tomography can miss metastatic lesions. However, a density threshold of  $\leq 20$  Hounsfield units on unenhanced computed tomography reliably excludes malignancies, potentially avoiding adrenalectomy in 48% of patients.

PubMed-ID: [41033887](#)

DOI: [10.1016/j.surg.2025.109693](#)

#### **Adrenalectomy patients with mixed primary aldosteronism and hypercortisolism: An analysis of outcomes following surgery at a single institution.**

*Surgery*, 189:109855.

G. A. Taylor, M. Allen, A. Lisevick Kumar, K. Doffek, T. Shaik, T. B. Carroll, J. W. Findling, C. D. Zhang, D. B. Evans, T. S. Wang and S. Dream. 2026.

BACKGROUND: A subset of patients with primary aldosteronism have clinical and/or biochemical evidence of hypercortisolism, suggesting excess co-secretion of both aldosterone and cortisol (mixed primary aldosteronism/hypercortisolism). This study examined patients with mixed primary aldosteronism/hypercortisolism and compared their outcomes following adrenalectomy to those of patients with primary aldosteronism only. METHODS: This was a retrospective review of adults who underwent unilateral adrenalectomy at a single institution for primary aldosteronism. Patients were excluded if they did not undergo preoperative testing for hypercortisolism. Demographics, comorbidities, nodule size, adrenal venous sampling, laterality, and perioperative steroid usage were assessed to compare patients with mixed primary aldosteronism/hypercortisolism to those with primary aldosteronism only. The Primary Aldosteronism Surgical Outcome criteria were applied to assess clinical and biochemical success. RESULTS: Of 94 patients who underwent surgery, 28 (29.8%) had mixed primary aldosteronism/hypercortisolism. Patients with mixed primary aldosteronism/hypercortisolism tended to be older than those with primary aldosteronism only. Patients with mixed primary aldosteronism/hypercortisolism had larger adrenal glands on imaging (median 2.4 cm vs 1.3 cm,  $P = .002$ ) and had higher rates of discharge on glucocorticoid replacement therapy (35.7% vs 3.0%,  $P < .001$ ). On long-term follow-up, mixed

primary aldosteronism/hypercortisolism patients were more likely to remain hypertensive and/or on the same number of antihypertensive medications as before surgery (21.4% vs 3.0%,  $P = .014$ ). **CONCLUSION:** Patients with mixed primary aldosteronism/hypercortisolism were more likely to need postoperative glucocorticoid replacement and less likely to have a partial or complete clinical response to surgery. This highlights the importance of preoperative dexamethasone suppression test in all patients with primary aldosteronism to guide perioperative management, identify those at risk for postoperative adrenal insufficiency, and appropriately frame outcomes.

PubMed-ID: [41371823](#)

DOI: [10.1016/j.surg.2025.109855](#)

**Regional adrenalectomy completed by prophylactic hyperthermic intraperitoneal chemotherapy reduces the incidence of local and peritoneal recurrence after curative surgery for adrenocortical carcinoma.**

*Eur J Endocrinol*, 194(4):482-8.

G. A. M. Tiberio, G. Casole, D. Cosentini, M. Lagana, S. Sigala, S. Ministrini and A. Berruti. 2026.

**BACKGROUND:** Local and peritoneal recurrence (L/PR) after curative surgery for adrenocortical carcinoma has a high incidence and negatively affects the clinical course of the disease. We retrospectively reviewed our database to investigate the role of regional surgery and prophylactic HIPEC on oncologic outcome. **METHODS:** Fifty-eight patients with stage II and III adrenocortical carcinoma (ACC) who underwent curative surgery were grouped according to the therapeutic approach: 11 received regional adrenalectomy and HIPEC (REGHIPEC), 18 underwent regional adrenalectomy (REGIONAL), and 29 had simple adrenalectomy (SIMPLE). The primary outcome was local/peritoneal disease-free survival (L/PDFS); secondary outcomes included overall disease-free survival (ODFS) and disease-specific survival (DSS). **RESULTS:** HIPEC increased surgery duration by 80 minutes and hospital stay by 3 days. Major morbidity was 27.2% in the REGHIPEC group and 5.5% in the REGIONAL group. Median post-operative follow-up was 56 months for the entire cohort. L/PR was observed in 0%, 35%, and 82% of cases in the study groups, respectively. REGHIPEC and REGIONAL groups did not reach the median L/PDFS, while the SIMPLE group had a median L/PDFS of 23 months ( $P < .001$ ). Overall recurrence (including hematogenous metastases) was observed in 18%, 50%, and 86.2% of cases, respectively ( $P < .001$ ). Disease-specific mortality during follow-up was 18%, 33%, and 72.4% in the three groups, respectively. REGHIPEC and REGIONAL groups did not reach the median DSS, while the SIMPLE group had a median DSS of 63 months ( $P = .014$ ). **CONCLUSION:** HIPEC after regional adrenalectomy has decreases the incidence of local and peritoneal recurrence. If confirmed, this therapeutic strategy may change the surgical approach to stage II-III ACC.

PubMed-ID: [41894574](#)

DOI: [10.1093/ejendo/lvag057](#)

**Adrenocortical carcinoma as a manifestation of Birt-Hogg-Dube syndrome.**

*Endocr Relat Cancer*, 33(3)

K. I. Wolf, J. Osborne, A. M. Lerario, J. N. Vo, O. Hamidi, M. A. Habra, G. Hammer and T. Else. 2026.

Birt-Hogg-Dube syndrome (BHDS) is characterized by fibrofolliculomas, trichodiscomas, renal tumors, lung cysts, and spontaneous pneumothoraces. Other than renal cell carcinoma, no cancers have been confirmed as part of the BHDS tumor spectrum. Here, we set out to uncover if adrenocortical carcinoma (ACC) is associated with BHDS. A retrospective review at a single tertiary care center between 2010 and 2024 was performed using search terms describing the clinical manifestations of BHDS, adrenal tumors, and iterations thereof. The initial review identified 1,010 patients with ACC. Of these patients, 466 were evaluated by a genetic counselor, and 346 underwent genetic testing-seven of which were found to have either characteristic clinical features of BHDS or a confirmed diagnosis. The literature review over the same time period demonstrated five additional cases of malignant adrenal tumors in patients with BHDS. We observed BHDS, confirmed by a pathogenic FLCN variant in 0.7% of all ACC patients, or 1.5% of patients evaluated by a genetic counselor and 2.0% of all patients who underwent genetic testing. Testing for FLCN pathogenic variants should be considered during routine genetic evaluation of patients with ACC, and special attention should be paid to adrenal tumors in BHDS patients during surveillance for renal neoplasms as more than 50% of patients in this series developed metastatic disease.

PubMed-ID: [41838460](#)

DOI: [10.1530/ERC-25-0285](#)

PMCID: PMC13182339

**Prognostic impact of anatomic site in pheochromocytomas and paragangliomas: a population-based cohort study.**

*Eur J Endocrinol*, 194(5):684-93.

K. Wu, H. Bai, X. Liu, Y. Zhu, X. Li and Z. Liu. 2026.

**OBJECTIVE:** The prognostic importance of tumor location in pheochromocytomas and paragangliomas (PGLs) remains

controversial. This study aimed to assess whether anatomic site independently influences survival in PPGLs. DESIGN: Retrospective, population-based cohort using SEER 17 (2000-2022). METHODS: Patients with histologically confirmed PPGLs were categorized by the primary site as adrenal gland, head and neck, thorax, or abdomen. Overall and cancer-specific survival rates were analyzed using Kaplan-Meier and multivariable Cox models, including stage-stratified analyses. Propensity score matching (PSM) was performed to minimize confounding. RESULTS: Among 1468 patients, 55.9% had adrenal, 17.6% abdominal, 13.6% head and neck, and 12.8% thoracic tumors. Survival outcomes varied by site ( $P = .004$ ), with head and neck PGLs showing the most favorable prognosis. Multivariable and stage-stratified models revealed no independent impact of site in localized disease, but significant differences emerged in regional and metastatic stages: head and neck tumors demonstrated superior outcomes in regional disease, while adrenal pheochromocytomas exhibited the poorest prognosis in distant disease (HR 2.26, 95% CI 1.14-4.48). PSM analyses confirmed that survival equivalence between adrenal and head and neck tumors in early-stage disease diverged upon metastasis. CONCLUSIONS: The prognostic effect of anatomic site in PPGLs is stage-dependent. While location does not influence outcomes in localized disease, it becomes clinically meaningful with progression-favoring head and neck tumors and disadvantaging adrenal primaries in advanced stages. Incorporating site into stage-aware risk stratification and tailoring multimodal care for high-risk thoraco-abdominal/adrenal disease are warranted. Prospective, genotype-annotated registries should validate and refine these findings.

PubMed-ID: [42150003](#)

DOI: [10.1093/ejendo/lvag084](#)

#### **More on Osilodrostat for Bilateral Adrenal Hypercortisolism in Primary Aldosteronism. Reply.**

*N Engl J Med*, 394(8):831.

J. Young, C. Richa and A. Lacroix. 2026.

PubMed-ID: [41707166](#)

DOI: [10.1056/NEJMc2518967](#)

#### **The Role of Cortisol Secretion in Pheochromocytomas and Paragangliomas: Clinical and Perioperative Implications.**

*J Clin Endocrinol Metab*, 111(2):e541-e51.

K. Zawadzka, J. Calissendorff, E. Rzepka, M. Pedziwiatr, A. Hubalewska-Dydejczyk and H. Falhammar. 2026.

BACKGROUND: Pheochromocytomas and paragangliomas (PPGLs) are tumors marked by excessive catecholamine secretion. Patients with pheochromocytomas may have elevated plasma glucocorticosteroid concentrations. This study aimed to evaluate the prevalence, clinical implications, and perioperative outcomes of autonomous cortisol secretion in patients with PPGLs. DESIGN: This was a retrospective cohort study conducted across 2 tertiary endocrinology centers, including patients with PPGLs who underwent adrenalectomy or extra-adrenal surgery for paragangliomas. METHODS: Patients were divided based on the 1-mg dexamethasone suppression test (DST) results into suppressive and nonsuppressive groups (above or below 1.8 microg/dL [50 nmol/L]). Data on clinical characteristics, biochemical markers, tumor features, perioperative outcomes, and follow-up were analyzed. RESULTS: Among 106 patients, 24.5% exhibited nonsuppressive cortisol concentrations post-DST. These patients were older (median age: 66 vs 56 years,  $P < .001$ ), predominantly female (84.6% vs 48.8%,  $P = .001$ ), and presented with larger tumors (5.2 vs 4.0 cm,  $P < .05$ ). Diabetes was more common in the nonsuppressive group both before adrenalectomy/surgery (50.0% vs 26.8%,  $P < .05$ ) and after (33.3% vs 12.7%,  $P < .05$ ). The nonsuppressive group had higher urinary and plasma metanephrine concentrations, lower DHEAS concentrations, and more cardiovascular diseases. Perioperative complications, including blood loss, conversion to open surgery, and prolonged hospital stays, were more frequent in the nonsuppressive group ( $P < .05$ ). CONCLUSION: One-quarter of patients with PPGLs exhibit autonomous cortisol secretion, associated with larger tumors, higher diabetes prevalence, and increased perioperative risks. Routine DST screening may improve preoperative management and offer insights into the impact of cortisol on PPGLs outcomes.

PubMed-ID: [40578302](#)

DOI: [10.1210/clinem/dgaf361](#)

PMCID: PMC12819868

#### **Risk of recurrence after successful surgery for Cushing's disease and association with USP8 genotype and tumour size: an international, retrospective, longitudinal cohort study.**

*Lancet Diabetes Endocrinol*, 14(4):327-36.

Q. Zhang, Y. Cai, Y. Liu, B. Yao, P. Sharma, E. Ruoff, Z. Ma, S. Zopp, Y. Wu, A. P. Abreu, S. Zhang, M. A. Tichomirowa, Y. Wang, G. Stalla, N. Qiao, Z. Ye, F. A. Hanzu, H. Chen, M. Buchfelder, Z. Yao, J. Flitsch, Y. Li, J. Thorsteinsdottir, Y. Wang, I. Nasi-Kordhishti, H. Ye, J. Honegger, S. Sbiera, U. B. Kaiser, M. Fassnacht, Z. Zhang, M. Reincke, M. Theodoropoulou, Y. Zhao

and L. G. Perez-Rivas. 2026.

**BACKGROUND:** Recurrence after successful pituitary surgery remains a challenge in the management of patients with Cushing's disease, with no reliable predictors of long-term outcome. Pathogenic somatic USP8 variants are found in one third of cases and their association with recurrence is unclear. The aim of this study was to determine the association between USP8 status and postoperative outcome. **METHODS:** This international, retrospective, longitudinal study was done in eight tertiary centres in east Asia, Europe, and North America. We reviewed clinical records and genetic information of patients with clinically diagnosed and pathologically confirmed Cushing's disease who underwent first pituitary surgery in any of the participating centres between Jan 1, 1989, and April 1, 2024. Inclusion criteria were postoperative follow-up of at least 3 months after first pituitary surgery, known postsurgical outcome, and tissue availability or known USP8 status. The primary outcomes were recurrence and time to recurrence after first surgery. We assessed recurrence-free intervals and recurrence risk using survival analysis, multivariate logistic regression, and Cox proportional hazards models. **FINDINGS:** We retrospectively retrieved and examined clinical records from 558 patients, 123 of whom were excluded. 360 (83%) of 435 patients were female and 75 (17%) were male. We detected USP8 variants in 195 (45%) cases. Recurrence was recorded in 66 (18%) of 371 patients in immediate remission. Risk of recurrence depended on USP8 status and tumour size. Patients with USP8-variant microadenomas and USP8-variant macroadenomas had similar cumulative hazards for recurrence, so they were considered as a single risk group. 10-year recurrence rate was higher for USP8-variant tumours (36.8%, 95% CI 23.7-47.7) than for wildtype microadenomas (15.0%, 4.9-24.0; adjusted  $p=0.016$ ) but was lower than for wildtype macroadenomas (44.5%, 26.2-58.2; adjusted  $p=0.025$ ). Patients with USP8-variant tumours (hazard ratio 2.41, 95% CI 1.19-4.87;  $p=0.014$ ) or wildtype macroadenomas (4.48, 2.11-9.52;  $p<0.0001$ ) had significantly higher risk of recurrence than patients with wildtype microadenomas, even after adjusting for age, postoperative nadir serum cortisol, tumour invasion, and ethnicity or centre. **INTERPRETATION:** Combined USP8 genotype-tumour size identified patients at increased risk of recurrence, particularly in largely heterogeneous groups of patients with non-invasive tumours or low postoperative serum cortisol not considered high risk in standard care. Implementing this combined genetic-clinical stratification could provide more accurate risk assessment, indicate those at higher risk of recurrence, and ultimately personalise long-term follow-up in patients with Cushing's disease. **FUNDING:** Deutsche Forschungsgemeinschaft, National Natural Science Funds of China, and CAMS Innovation Fund for Medical Sciences.

PubMed-ID: [41785910](#)

DOI: [10.1016/S2213-8587\(25\)00396-1](#)

PMCID: PMC13179832

**CT Habitat-peritumoral fusion radiomics predicts aggressiveness and prognosis in pheochromocytomas and paragangliomas to inform intensified surgical strategies: A multicenter study.**

*Eur J Surg Oncol*, 52(6):111851.

Y. Zhou, Z. Zhang, K. Zhou, Y. Tan, J. Zhao, L. Zhong, X. Wei, J. Zhu, Z. Li, J. Du, L. Liu and L. Fang. 2026.

**BACKGROUND:** This study aimed to develop a dual-domain radiomics framework integrating probability-driven high-risk habitats and peritumoral microenvironmental features to accurately predict the aggressiveness of pheochromocytomas and paragangliomas (PPGLs). **METHODS:** This retrospective study included 356 patients with abdominal PPGLs from four institutions, who were divided into a training set ( $n = 182$ ) and two external test sets ( $n = 70$ ,  $n = 104$ ). Radiomic features were extracted from the whole-tumor and 1-mm peritumoral regions on contrast-enhanced CT images. Probability-driven habitat analysis utilizing a Support Vector Machine and K-means clustering was implemented to segment high-risk subregions. Following rigorous cascaded feature selection, a Random Forest-based fusion model was constructed to integrate key habitat and peritumoral features for predicting aggressiveness. Additionally, SHapley Additive exPlanations (SHAP) analysis was employed to evaluate feature importance and model interpretability. **RESULTS:** The habitat-peritumoral fusion model demonstrated superior predictive performance and robustness compared to traditional single-modality models, achieving area under the receiver operating characteristic curve values of 0.884 and 0.854 in external test sets 1 and 2, respectively. The model maintained excellent diagnostic efficacy across both  $>6$  cm and  $\leq 6$  cm tumor subgroups. Furthermore, the model-derived risk score successfully stratified metastasis-free survival in the overall cohort ( $P < 0.001$ ) and the clinically ambiguous  $\leq 6$  cm subgroup ( $P = 0.003$ ), serving as an independent prognostic factor ( $HR = 10.73$ ,  $P = 0.028$ ). **CONCLUSION:** The fusion model is a robust, non-invasive tool for preoperatively identifying high-risk PPGLs. Particularly for tumors  $\leq 6$  cm where decision-making is challenging, it provides objective evidence to individualize surgical strategies and stratify postoperative surveillance.

PubMed-ID: [42068698](#)

DOI: [10.1016/j.ejso.2026.111851](#)

### **Quality of life questionnaire development and validation for adrenocortical carcinoma patients.**

*Eur J Endocrinol*, 194(3):431-9.

M. Lagana, D. Cosentini, N. Farina, F. Consoli, C. Tagliaferro, F. Chiesi, B. Trevisan, V. Cremaschi, D. L. Bettini, A. Berruti and C. I. Ripamonti. 2026.

ACC patients' quality of life may be impacted by symptoms related to cancer or treatments, as well as emotional, spiritual, existential, social, economic, and sexual aspects. The aim was the development and psychometric validation of a new instrument (QoLACC) for measuring Patient-Reported Outcome in patients with ACC. The study was conducted from October 2024 to January 2025 at the Oncology Unit of Brescia's ASST. Fifteen patients and 15 physicians graded the comprehensibility/difficulty and relevance of the items of QoLACC whereas 37 consecutive patients assessed psychometric validity. Comprehensibility, difficulty and clinical relevance of the items to include in the QoLACC questionnaire were assessed by selected ACC patients and clinicians. Validated scales were co-administered to the developed QoLACC questionnaire to assess physical and psychological symptoms, and the test-retest reliability and construct validity psychometric validation were performed. The QoLACC items showed excellent content validity [0.93-1.00] and acceptable to excellent comprehensibility [0.80-1.00] and difficulty [0.80-1.00], with minor exceptions. Item analysis showed good discriminant capability and response variability. The total questionnaire has good reliability (the intraclass correlation coefficient (ICC) was 0.870 [95% CI: 0.734-0.937]) and construct validity proved by the moderate to strong correlations [0.39-0.62] between the QoLACC and the EORTC item 29 and item 30, the QoLACC financial section and the COST (0.47), and the QoLACC spiritual section and the JSWBS (0.60). We defined and validated the Italian questionnaire aiming to explore ACC patients' quality of life, to help the Health Care Professionals to manage and support these patients.

PubMed-ID: [41875393](#)

DOI: [10.1093/ejendo/lvag052](#)

### **Renal function after adrenalectomy in patients with primary aldosteronism.**

*Surgery*, 189:109761.

K. A. Stahl, K. M. Ramonell, A. Puli, P. K. Fazeli, K. L. McCoy, S. E. Carty, L. Yip and A. Sada. 2026.

BACKGROUND: Although adrenalectomy is recommended for unilateral primary aldosteronism, the postoperative effects on renal function remain poorly understood. We evaluated renal function after adrenalectomy and identified risk factors for function decline. METHODS: A single-institution retrospective study included adults undergoing adrenalectomy (2002-2024) for unilateral primary aldosteronism on the basis of adrenal venous sampling. Estimated glomerular filtration rate (eGFR)% change was defined as  $([\text{baseline eGFR} - \text{postoperative eGFR}]/\text{baseline eGFR}) \times 100$ . Univariate logistic regression assessed estimated glomerular filtration rate decline  $<60 \text{ mL/min/1.73 m}^2$  at 12 months. RESULTS: Of 107 patients, the median age was 55 years and 92 (86%) had baseline eGFR  $\geq 60 \text{ mL/min/1.73 m}^2$  before surgery. eGFR levels were available for 87 patients on postoperative day 1, 64 at 1 month, 43 at 6 months and 47 at 12 months, and eGFR declined from baseline in 37%, 58%, 74% and 66%, respectively. Median eGFR% decline was 13% on postoperative day 1, 18.2% at 1 month, 20.5% at 6 months and 20% at 12 months. One of 15 patients with baseline eGFR  $<60$  required dialysis 3 months postoperatively. Among 92 patients with baseline eGFR  $\geq 60$ , eGFR dropped  $<60$  in 26% and 32.5% at 1 and 12 months, respectively. After eGFR decline  $<60$  at 1 month, only 1 patient experienced recovery. Variables associated with eGFR decline  $<60$  at 12 months were older age, lateralization index  $>30$ , and 1 month eGFR decline  $<60$ . CONCLUSION: After adrenalectomy for unilateral primary aldosteronism, a significant decrease in estimated glomerular filtration rate was observed. Patients should be counseled on the high likelihood of unmasked renal impairment after adrenalectomy and estimated glomerular filtration rate monitoring is recommended for all patients.

PubMed-ID: [41046237](#)

DOI: [10.1016/j.surg.2025.109761](#)

## **NET**

### **Meta-Analyses**

-None-

## Randomized controlled trials

-None-

## Consensus Statements/Guidelines

### **NANETS Guidelines for the diagnosis and management of stage I-III rectal neuroendocrine tumors.**

*Endocr Relat Cancer*, 33(2)

H. Kennecke, E. Delpassand, S. Felder, F. Gleeson, J. Hallet, D. Horowitz, M. Hyrcza, B. W. Katona, M. Kiely, M. Kim, N. Mallak, V. Parkins, M. G. Varma and J. Pasieka. 2026.

Well-differentiated rectal neuroendocrine tumors (rNETs) are among the most common NETs and account for approximately 12-27% of all gastrointestinal NETs in North America. Significant discrepancies persist in the management of NETs regarding surveillance strategies, staging modalities, high-risk features, and criteria for surgical intervention. This guideline updates current practices of stage I-III rectal NETs with the utilization of GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology and Delphi method of consensus among leading experts in the North American region. We found that several technological advances, such as 68Ga- or 64Cu-DOTATATE SSTR PET/CT, and broad adoption of pelvic MRI have improved staging of rNETs, along with modified endoscopic mucosal and submucosal resection and full-thickness excision techniques that demonstrate efficacy and safety for resection. Pivotal long-term outcome studies provide insight into i) risk factors for regional lymph node metastasis, ii) the impact of R1 excision (endoscopic), iii) best practices for intermediate-sized rNETs (11-20 mm), and iv) risk in small rNETs ( $\leq 10$  mm). Recommendations were developed upon evidence-based conclusions from the GRADE review to define the role of baseline staging with MRI, advanced endoscopy, and transanal endoscopic surgical methods appropriate for T1 rNETs, the role of salvage therapy in cases of R1 resection, and the consideration of pathologic variables to direct definitive treatment and surveillance. We conclude that advances in screening programs and imaging allow for improved detection and staging of rNETs, while long-term outcome studies can better direct patients toward evidence-based treatment management and rectal organ preservation through less radical resection methods.

PubMed-ID: [41562331](#)

DOI: [10.1530/ERC-25-0303](#)

PMCID: PMC13138514

### **European Consensus Recommendations for Pediatric Neuroendocrine Tumor of the Appendix.**

*J Am Coll Surg*, 242(3):739-40.

C. Virgone and A. Redlich. 2026.

PubMed-ID: [41358633](#)

DOI: [10.1097/XCS.0000000000001718](#)

## Other Articles

### **Unravelling mesenteric fibrosis in small intestinal neuroendocrine tumours and implications for clinical management.**

*Endocr Relat Cancer*, 33(5)

M. Castanho Martins, E. van der Slik, J. Hofland, A. Blazevic, H. Hodgetts, D. Mandair, C. Toumpanakis, M. E. Caplin, L. J. Hofland, W. W. de Herder, K. Rombouts and R. A. Feelders. 2026.

Mesenteric fibrosis (MF) is an extensive fibrotic reaction common in small intestine neuroendocrine tumours (SI-NETs) and develops around mesenteric metastasis. While primary SI-NETs can remain asymptomatic for years, mesenteric metastasis (MM) and the resulting MF frequently leads to serious complications. Despite its clear impact on quality of life, MF pathophysiology remains poorly understood and treatment options are currently limited to surgical interventions. This review summarizes the literature on MF in SI-NET patients, emphasizing gaps in knowledge and potential research directions. Clinical research confirms that MF is a frequent complication, often causing severe morbidity, including mesenteric ischaemia and obstruction. Addressing these issues requires further research into MF pathogenesis and

contributory factors, such as elastic vascular sclerosis (EVS), which are currently underexplored. Advancing this field will necessitate collaboration, supported by clear definitions and standardized diagnostic and grading systems for MF linked to clinical data, which are presently lacking. While MF-directed translational research remains scarce, recent studies focusing on tumour microenvironment have begun to uncover possible pathways involved in MF. Serotonin, pro-fibrotic growth factors and cytokines may play a role in activating cancer-associated fibroblasts and immune cells within the tumour microenvironment, aggravating extracellular matrix protein deposition and possibly creating positive feedback loops that promote fibrosis. Recently classified as an organ, the mesentery may harbour unique properties for stimulating the establishment of MF. Emerging research is paving the way for new MF treatment options that are urgently needed.

PubMed-ID: [42007989](#)

DOI: [10.1530/ERC-25-0116](#)

PMCID: PMC13192698

#### **ASO Author Reflections: The Challenge of Peritoneal Metastases in Patients with Small Bowel Neuroendocrine Tumors.**

*Ann Surg Oncol*, 33(1):317-8.

J. Chang, L. C. Borbon, S. K. Sherman, P. H. Ear, A. M. Bellizzi, J. S. Dillon and J. R. Howe. 2026.

PubMed-ID: [41191303](#)

DOI: [10.1245/s10434-025-18587-w](#)

PMCID: PMC12689750

#### **Integrated local and global Ki67 profiling for prognostic stratification and therapeutic guidance in high-grade neuroendocrine neoplasms: a multicenter validation study.**

*Int J Surg*, 112(4):9987-99.

J. Chu, H. Gong, H. Gao, Z. Zhu, J. Shi, Y. Ma, Y. Ji, Q. Zhang, L. Cao, F. Tang, Y. Liang, J. Chen, W. Sheng, Q. Chen, X. Zhuang and D. Huang. 2025.

**BACKGROUND:** The distinction between high-grade neuroendocrine G3 tumors (G3 NETs) and carcinomas (NECs) is a critical diagnostic dilemma with profound therapeutic implications. Conventional Ki67 hotspot analysis often fails to provide robust risk stratification. We aimed to develop and validate a robust, interpretable digital pathology biomarker that overcomes these limitations to improve risk stratification and guide therapeutic decisions. **METHODS:** We developed the Integrated Local-Global Ki67 (IL-GKi67) score, which synergizes localized hotspot quantification with global intratumoral heterogeneity assessment from Ki67-stained whole-slide images. The score's prognostic and predictive performance was rigorously evaluated in a multicenter cohort (N = 349) with internal and external validation sets.

**RESULTS:** The IL-GKi67 score was a powerful and independent prognostic factor, where high scores correlated with drastically worse overall survival (multicenter validation: HR = 4.169, P = 0.009), remaining significant where the traditional hotspot method failed (P = 0.128). Most importantly, IL-GKi67 functioned as a definitive predictive biomarker. Patients with low IL-GKi67 scores derived a profound survival benefit from adjuvant chemotherapy (mOS: 45.0 months, at 50 months, the restricted mean survival time of chemo subset was 48.9 months (95% CI, 45.36 to 52.02); HR = 0.069, P = 0.002), an effect particularly pronounced in the aggressive NEC subgroup (HR = 0.061, P < 0.001). The score served as a powerful morphological surrogate for TP53 mutation status (P < 0.001) and refined the conventional G3 NET/NEC classification by re-stratifying a substantial portion of patients into more clinically relevant risk groups. **CONCLUSIONS:** IL-GKi67 is an interpretable and validated digital biomarker that overcomes the limitations of manual Ki67 assessment. By integrating local and global proliferation patterns, it improves risk stratification and provides a practical tool to guide personalized adjuvant chemotherapy decisions for patients with HGNETs.

PubMed-ID: [41417992](#)

DOI: [10.1097/JS9.0000000000004574](#)

PMCID: PMC13105724

#### **PRRT for well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP-NETs).**

*Endocr Relat Cancer*, 33(3)

V. Corbett, G. Gupta and A. Chauhan. 2026.

Neuroendocrine tumors (NETs) are rare, heterogeneous neoplasms with varying prognoses and management approaches. Peptide receptor radionuclide therapy (PRRT), targeting tumors expressing somatostatin receptors, delivers cytotoxic radiation to tumor cells. While PRRT has demonstrated efficacy in advanced, well-differentiated NETs, the optimal sequencing with other therapies remains an area of active research. This review explores PRRT's role in NET management, focusing on its mechanisms, clinical efficacy, safety profile, and integration into a multi-modal treatment strategy. We also examine evidence on the sequencing of PRRT with surgery, liver-directed therapy, chemotherapy, and targeted therapies

to optimize treatment outcomes. We conducted a comprehensive review of recent clinical trials, cohort studies, and expert consensus guidelines to assess PRRT's place in the treatment paradigm. Factors influencing treatment sequencing, such as tumor type, receptor expression, disease burden, and patient-specific characteristics, are also discussed. PRRT has proven effective for patients with advanced, somatostatin receptor-positive NETs, especially for inoperable tumors or those progressing after other therapies. While PRRT plays a vital role in management, its sequencing with other treatments remains complex, with evidence supporting its use both early and late in treatment based on individual patient factors. Optimizing its sequencing with other treatments requires further research but offers potential for improved outcomes. A personalized, multidisciplinary approach is essential for maximizing PRRT's benefits in NET management. This review article summarizes current evidence and describes patient-specific circumstances, enabling treatment provider to make informed PRRT sequencing decisions.

PubMed-ID: [41769977](#)

DOI: [10.1530/ERC-25-0495](#)

PMCID: PMC13126668

### **Surgical management of small intestinal neuroendocrine tumours.**

*Br J Surg*, 113(3)

J. Hallet, M. Falconi, S. Bennet, A. Frilling, A. Gangi, S. Gaujoux, R. Pommier, E. Bertani, G. A. Buerba, J. Chan, C. N. Clarke, S. Deguelte, J. Del Rivero, E. Nieveen van Dijkum, T. Dumitra, D. Eshmuminov, A. Engelsman, F. Fermi, S. Grozinsky-Glasberg, J. R. Howe, A. Lamarca, L. Meloche-Dumas, F. Mercier, S. Myrehaug, J. Perinel, C. De Ponthaud, V. Sallinen, Y. Song, H. Stuart, E. T. Janson, P. Tinguely, F. Tozzi, T. van Ginhoven, S. Warner, K. Soreide and S. Partelli. 2026.

PubMed-ID: [41777054](#)

DOI: [10.1093/bjs/znag016](#)

PMCID: PMC13036841

### **Surgical management of pancreatic neuroendocrine tumours.**

*Br J Surg*, 113(4)

J. Hallet, M. Falconi, G. A. Buerba, C. Clarke, J. Maxwell, H. Soares, S. Stattner, E. Nieveen van Dijkum, A. W. Acher, V. Andreasi, D. Bartsch, L. Bubis, D. Cavallucci, D. Chan, U. Clemente, M. Del Chiaro, K. Daskalakis, I. Dominguez-Rosado, T. Dumitra, K. Duncan, F. Fermi, G. K. Fusai, T. Hackert, J. R. Howe, I. Huivaniuk, D. Kaemmerer, L. Landoni, M. McNamara, A. Niessen, A. Pascher, A. Perren, R. Pommier, S. Sachdeva, S. Sadowski, A. Sauvanet, A. Singhi, H. Sorbye, E. Ward, A. Wei, L. Yen, K. Soreide and S. Partelli. 2026.

PubMed-ID: [41842405](#)

DOI: [10.1093/bjs/znag026](#)

### **Elevated vasoactive intestinal peptide concentrations poorly predict VIPoma.**

*Endocr Relat Cancer*, 33(1)

J. Korleski, L. E. Ospina Velasquez, J. Bornhorst, A. Algeciras-Schimnich, K. Ness, T. J. Hobday, R. Eiring, P. W. McGarrah, J. Starr, M. B. Sonbol, J. Hofland, R. Pearson and T. R. Halfdanarson. 2026.

VIPoma is a rare neuroendocrine tumor (NET) that is challenging to diagnose. While VIP concentrations are elevated in VIPoma, the optimal threshold for diagnostic purposes is not well defined. We aimed to study this in a single-institution population. We obtained results from vasoactive intestinal peptide (VIP) tests from 2011 to 2023 and reviewed the medical record of patients who had concentrations greater than our established assay-specific reference limit of 75 pg/mL. We compared plasma VIP concentrations between patient cohorts with and without VIPoma and determined the optimal threshold for VIP concentrations to predict a VIPoma in this population. Seventy-six patients met the selection criteria. Of these, nine cases of VIPoma were diagnosed. All patients had chronic diarrhea, and five patients had a previous diagnosis of a pancreatic neuroendocrine tumor (PNET). VIP concentrations drawn for acute/episodic diarrhea or flushing/diaphoresis did not lead to a diagnosis of a VIPoma. Mean VIP concentration was increased in patients with a VIPoma relative to those without, but the difference was not statistically significant (508 pg/mL vs 223 pg/mL,  $P = 0.31$ ). Using the threshold of 75 pg/mL, the positive predictive value for a VIPoma was 12%. The optimal VIP threshold was 442 pg/mL (OR: 11.96, 95% CI: 2.00-79.69,  $P = 0.01$ ), with statistically significant odds ratios starting at 200 pg/mL. Our findings suggest that elevated VIP concentrations are not predictive for a VIPoma and most patients with elevated VIP do not have a VIPoma. We recommend that VIP only be drawn in certain clinical scenarios to avoid unnecessary medical investigations.

PubMed-ID: [41498509](#)

DOI: [10.1530/ERC-25-0241](#)

### **EUS-Guided Radiofrequency Ablation as a Minimally Invasive Treatment for Insulinomas-A Single-Center Experience.**

*J Clin Endocrinol Metab*, 111(4):988-92.

B. Kovacevic, P. Vilmann, L. Brink, M. C. Klose, M. P. Sonne, U. Knigge and M. Andreassen. 2026.

CONTEXT: Insulinomas, although rare, are among the most common functional pancreatic neuroendocrine neoplasms (pNENs), causing debilitating and recurrent hypoglycemic episodes and severely affecting quality of life. OBJECTIVE: To evaluate endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) as a novel and minimally invasive treatment for insulinomas. PATIENTS: We retrospectively identified patients at a single tertiary care center between 2022 and 2025 with a suspicion of insulinomas (based on a positive fasting test and imaging) who underwent EUS-RFA. Lesions considered for RFA were biopsy-proven pNENs with a Ki-67 index <10%, and <25 mm in size. All patients were hospitalized for 24 hours and EUS-RFA was conducted under general anesthesia using a dedicated EUS-RFA needle and under direct ultrasound guidance. Mean follow-up duration was 15.5 months. The primary outcome measure was clinical success (symptom improvement with a documented increase in blood glucose) and safety. RESULTS: A total of 17 patients were identified and included. The mean age was 60.1 years and 53% were male. Normoglycemia was achieved after a single EUS-RFA session in 11 patients (64.7%), while 6 patients (35.3%) required a second EUS-RFA. The overall clinical success rate was 100% (n = 17/17; 95% CI: 80.4%-100.0%). A total of 4 adverse events were observed in 23 procedures (17.4%), 2 mild and 2 moderate (8.7%). CONCLUSION: EUS-RFA appears to provide complete symptom resolution and demonstrates a favorable safety profile compared to conventional surgery. However, the long-term efficacy of EUS-RFA remains to be determined.

PubMed-ID: [41120112](#)

DOI: [10.1210/clinem/dgaf571](#)

### **Evaluating the role of postoperative long-acting somatostatin analog therapy in patients with metastatic neuroendocrine tumors undergoing surgical debulking.**

*Surgery*, 189:109762.

T. Michelakos, J. Tobias, S. Abou Azar, B. Polite, J. M. Millis, C. Y. Liao and X. M. Keutgen. 2026.

BACKGROUND: The optimal timing of postoperative somatostatin analog resumption in patients with metastatic gastroenteropancreatic neuroendocrine tumors after surgical debulking is unknown and varies between institutions. We hypothesized that somatostatin analog resumption can be safely deferred after debulking in select patients. METHODS: We performed a retrospective cohort study of patients with well-differentiated gastroenteropancreatic neuroendocrine tumors with liver metastases who underwent liver debulking, synchronously or metachronously with primary tumor resection at an academic referral center (2019-2023). Clinicopathologic characteristics and progression-free survival were compared between patients who resumed somatostatin analog within 90 days of surgery and those who did not (never resumed or resumed >90 postoperative days). RESULTS: Of 83 patients, 56 (68%) had small bowel neuroendocrine tumors, whereas 27 (32%) had pancreatic neuroendocrine tumors. Twenty-seven (33%) resumed somatostatin analog within 90 days of debulking. The somatostatin analog resumption group had higher frequency of pancreatic neuroendocrine tumors (52% vs 23%, P = .01), extrahepatic metastases (70% vs 36%, P = .005), and higher Ki-67 index (median 4% vs 2%, P = .03). Somatostatin analog resumption was associated with worse progression-free survival (median 13 vs 21 months, P = .048). Pancreatic location (hazard ratio = 2.2, P = .003) and osseous metastases (hazard ratio = 2.0, P = .04) were independent predictors of shorter progression-free survival after debulking. Among patients who did not immediately resume somatostatin analog, small bowel neuroendocrine tumors had longer progression-free survival (median 34 vs 16 months, P = .02). CONCLUSION: Patients with small bowel neuroendocrine tumors without osseous metastases undergoing surgical debulking experience long progression-free survival and might therefore benefit from delaying postoperative somatostatin analog resumption. Our findings provide foundational data for a prospective trial.

PubMed-ID: [41073159](#)

DOI: [10.1016/j.surg.2025.109762](#)

### **Insulin-Dependence and Survival in Pancreatic Neuroendocrine Tumors: Results From the US-NTSG Group.**

*J Surg Oncol*, 133(2):153-60.

M. B. Mirza, J. J. Baechle, P. M. Smith, D. Ali, M. Dillhoff, G. Poultides, F. G. Rocha, C. S. Cho, E. R. Winslow, R. C. Fields, S. K. Maithel and K. Idrees. 2026.

INTRODUCTION: PNETs are rare pancreatic malignancies originating from islet cells and exhibit a strong co-occurrence with Diabetes Mellitus (DM), associated with worse survival outcomes. However, studies have yet to delineate the impact of insulin dependent (IDDM) and non-insulin dependent (NIDDM) on poor oncological outcomes. METHODS: Utilizing the U.S. Neuroendocrine Tumor Study Group database (1999-2016), we performed a retrospective cohort study of adult

patients who underwent primary surgical resection of PNETs. Patients were categorized based on preoperative diagnosis into non-DM, NIDDM, and IDDM cohorts. We used the Kaplan-Meier method and log-rank test to study cancer-specific survival (CSS). Cox proportional Hazards models were used to assess the impact of IDDM on CSS. RESULTS: Of the 1122 patients included in the analysis, 870 (77%) were non-DM, 168 (15%) were NIDDM, and 84 (8%) were IDDM. The groups were similar in tumor stage and grade. However, they differed in sex, BMI, age, ASA class, tumor location, preoperative HbA1c, and serum glucose ( $p$ -value  $< 0.05$ ). Patients with IDDM had significantly decreased 5-year CSS compared to patients without IDDM (CSS: IDDM 85%, NIDDM 94%, non-DM 93%, NIDDM + non-DM 93%;  $p < 0.01$ ). On multivariate analysis, IDDM was independently associated with worse CSS (HR 2.27, 95% Confidence Interval 1.15-4.45,  $p = 0.02$ ). CONCLUSION: Insulin dependence is associated with worse cancer-specific survival in PNET patients following surgical resection compared to PNET patients with NIDDM or without DM.

PubMed-ID: [41520322](#)

DOI: [10.1002/jso.70174](#)

PMCID: PMC12863235

### **Qualitative and Quantitative Analyses of Noninvasive Diagnosis of Insulinoma Using [18F]FB(ePEG12)12-Exendin-4 PET/CT.**

*J Clin Endocrinol Metab*, 111(1):209-17.

T. Murakami, H. Yoshida, K. Sakaki, D. Otani, K. Kawai Miyake, Y. Shimizu, H. Fujimoto, D. Yabe, Y. Nakamoto and N. Inagaki. 2025.

CONTEXT: This study represents the first interim report from a phase 2 clinical trial. Accurate localization of insulinomas remains a clinical challenge despite the availability of various imaging modalities. OBJECTIVE: The current study aimed to evaluate the efficacy of positron emission tomography/computed tomography (PET/CT) using [18F]FB(ePEG12)12-exendin-4 (18F-exendin-4), a novel 18F-labeled PEGylated glucagon-like peptide 1 (GLP-1) receptor-targeted imaging probe, for the noninvasive detection of insulinomas. METHODS: This prospective single-center study enrolled patients with biochemically confirmed hyperinsulinemic hypoglycemia suggestive of insulinoma. All patients underwent 18F-exendin-4 PET/CT, with scans performed at 60 and 120 minutes after injection. The findings of 18F-exendin-4 PET/CT were then compared with those of conventional imaging modalities performed before and after 18F-exendin-4 PET/CT in actual clinical settings, with all findings being verified through surgical and pathological findings. RESULTS: 18F-exendin-4 PET/CT successfully identified insulinomas in all 12 patients (100% sensitivity), showing significantly higher uptake in tumor tissues than in the surrounding pancreatic tissues and organs. The detection rate of 18F-exendin-4 PET/CT exceeded that of the conventional imaging modalities (CT, 83%; magnetic resonance imaging, 63%; endoscopic ultrasonography, 90%; selective arterial calcium stimulation, 89%). All identified lesions were surgically confirmed to be insulinomas, with complete clinical resolution of hypoglycemia after resection. CONCLUSION: 18F-exendin-4 PET/CT demonstrated effective sensitivity for noninvasive insulinoma detection, offering a reliable and practical diagnostic alternative to invasive procedures for precise and prompt preoperative localization with functional evaluation. This novel imaging approach may therefore improve the management of patients with suspected insulinomas.

PubMed-ID: [40391925](#)

DOI: [10.1210/clinem/dgaf253](#)

### **Metformin suppresses MEN1-associated pancreatic and pituitary neuroendocrine tumors: evidence from mouse models and clinical data.**

*Endocr Relat Cancer*, 33(2)

A. Nakano, Y. Huang, Y. Mistui, R. Shirai, Y. Chen, T. Tajima, Y. Sakaguchi, T. Moro, C. Hoshino, K. Terada, N. Sakata, A. Yokoyama, S. Hijioka, M. Ishiai, H. Kassai, Y. Tabata and R. Ohki. 2026.

Pancreatic neuroendocrine tumors (PanNETs) represent a rare subset of pancreatic cancers, comprising approximately 1-2% of all cases. Non-functioning PanNETs (NF-PanNETs), which account for the majority of PanNETs, can be difficult to treat as they show no hormone-related symptoms and are often not diagnosed until more advanced stages. Current therapeutic agents have limited efficacy, highlighting the need for novel treatment strategies. Multiple endocrine neoplasia type 1 is a hereditary syndrome strongly associated with PanNETs and pituitary neuroendocrine tumors (PitNETs), caused by germline mutations in the MEN1 gene. Using Men1 f/f-RipCre<sup>+</sup> mice, which develop both NF-PanNETs and PitNETs, we investigated whether long-term administration of metformin, a first-line anti-diabetic drug, could suppress tumor development and progression. Metformin significantly inhibited the elevation of blood glucose in Men1 f/f-RipCre<sup>+</sup> mice, and longer-term treatment attenuated PanNETs and restored normal insulin secretion. Metformin suppressed the proliferative pathways, including the PI3K/Akt/mTOR signaling pathway. In addition to its effects on PanNETs, metformin also attenuated PitNET development, elevated antiproliferative pathways, and suppressed

angiogenic pathways. Furthermore, clinical data revealed that NF-PanNET patients with prior metformin use exhibited improved prognosis. These findings demonstrate that blood glucose control through metformin represents a promising preventive and therapeutic strategy for NF-PanNETs and MEN1-associated neuroendocrine tumors.

PubMed-ID: [41568565](#)

DOI: [10.1530/ERC-25-0518](#)

PMCID: PMC12920065

**Localization of Benign Insulinomas With a Radionuclide Tracer Targeting the GLP-1 Receptor With Pegylated Exendin-4.**

*J Clin Endocrinol Metab*, 111(3):e957-e8.

M. A. Nauck and W. Uhl. 2026.

PubMed-ID: [40388377](#)

DOI: [10.1210/clinem/dgaf297](#)

**The Role of Primary Tumor Resection in Surgical Management of Asymptomatic Metastatic PNETs: A Retrospective Single-Center Study.**

*Ann Surg Oncol*, 33(4):3526-34.

V. Podrascanin, M. Ammann, H. Gudmundsdottir, Y. Dong, C. A. Thiels, S. G. Warner, M. J. Truty, M. L. Kendrick, R. L. Smoot, R. F. Pommier, K. Kozuma, T. R. Halfdanarson, D. M. Nagorney and P. P. Starlinger. 2026.

BACKGROUND: Cytoreductive hepatectomy has repeatedly been reported to improve prognosis in pancreatic neuroendocrine tumor liver metastasis (PNETLM). However, whether primary tumor resection impacts prognosis in asymptomatic synchronously metastasized pancreatic neuroendocrine tumors (PNETs) remains elusive. We aimed to evaluate the prognostic impact of primary tumor resection in patients undergoing cytoreductive hepatectomy for PNETLM. PATIENTS AND METHODS: This retrospective single-center study analyzed patients who underwent hepatectomy for pancreatic PNETLM between January 2000 and December 2020. Patients were categorized according to surgical approaches: cytoreductive hepatectomy without primary tumor resection at any time (non-PTR), cytoreductive hepatectomy and pancreaticoduodenectomy (PD), or cytoreductive hepatectomy and distal pancreatectomy (DP). Surgical outcomes and risk factors for overall survival (OS) were assessed. RESULTS: A total of 118 patients with asymptomatic PNETs and synchronous liver metastases were analyzed. The median OS was 10 years (95% CI: 6.5-12), with no significant differences across surgical approach regarding primary tumor resection (non-PTR: 10 years; PD: 8 years; DP: 9.5 years;  $p = 0.589$ ). Survival rates at 5 years were 66.7% in non-PTR, 62.3% in PD, and 65.8% in DP respectively. PFS was similar between groups ( $p = 0.301$ ). Extrahepatic disease and liver lesion count were significant predictors of progression-free survival in univariate analysis ( $p < 0.050$ ), while resection of the primary tumor had no significant impact ( $p = 0.749$ ). CONCLUSIONS: PNET primary tumor resection was not associated with improved long-term outcomes in PNETLM patients after cytoreductive hepatectomy. This should spark interest if refraining from primary resection might be an option in selected patients considering the risks associated with pancreatic surgery.

PubMed-ID: [41366165](#)

DOI: [10.1245/s10434-025-18835-z](#)

**Toward Consensus on the Management of Pediatric Neuroendocrine Tumor of the Appendix: In Reply to Virgone and Redlich.**

*J Am Coll Surg*, 242(3):740-1.

S. F. Polites. 2026.

PubMed-ID: [41358619](#)

DOI: [10.1097/XCS.0000000000001719](#)

**Reproductive and sexual sequelae of neuroendocrine tumour therapies: an under-recognised challenge.**

*Endocr Relat Cancer*, 33(4)

K. M. Shekhda, P. M. Shah, A. Biddanda, A. Grossman and M. Caplin. 2026.

Neuroendocrine tumours (NETs) are heterogeneous, biologically variable tumours arising from the diffuse neuroendocrine system. While more frequently seen in older patients, the incidence and prevalence of NETs in the younger population are increasing. In addition, because of their generally slow progression and favourable prognosis, coupled with widely available effective treatments, survival times even with metastatic tumours may often be prolonged. However, there is a paucity of data on the effect of treatment of NETs on men's and women's reproductive and sexual health. In this review, we have evaluated the effects of NET therapies, including somatostatin analogues (SSTAs), molecular targeted therapy (everolimus and sunitinib), peptide receptor radionuclide therapy (PRRT), and chemotherapy, on reproductive and sexual

function in patients with NETs. There is a lack of evidence on the detrimental effects of SSTAs on human fertility, and indeed, many patients have conceived successfully after many years of treatment with SSTAs. Even patients who have received SSTAs during pregnancy have generally shown positive maternal and fetal outcomes. While the effects of PRRT and molecular targeted therapy on fertility are as yet poorly defined, chemotherapy has a proven negative impact on fertility; thus, family and pregnancy planning are strongly recommended before the initiation of chemotherapy. Finally, data on the effects of NET treatment on sexual function are very limited; however, neuroendocrine tumours can express oestrogen receptors/progesterone receptors (ER/PR) or testosterone receptors (TR); thus, checking tumour tissue for ER/PR/TR status prior to considering hormonal therapy for sexual dysfunction should be considered but warrants additional studies.

PubMed-ID: [41921030](#)

DOI: [10.1530/ERC-25-0500](#)

PMCID: PMC13097117

### **Cabozantinib for advanced grade 3 neuroendocrine tumors: subgroup analysis of the phase 3 CABINET trial (Alliance A021602).**

*Endocr Relat Cancer*, 33(1)

J. R. Strosberg, T. Zemla, S. Geyer, S. Pulsipher, F. S. Ou, S. Behr, N. Raj, N. Vijayvergia, A. Dasari, E. M. O'Reilly, J. A. Meyerhardt, E. M. Wolin, T. R. Halfdanarson and J. A. Chan. 2026.

Well-differentiated grade 3 neuroendocrine tumors (NETs) have recently been described as a distinct category, and randomized data regarding efficacy of therapy for these patients are scarce. In the phase 3 CABINET trial, cabozantinib improved PFS compared with placebo in patients with advanced, previously treated, progressive extra-pancreatic NETs (epNETs) and pancreatic NETs (pNETs) of all grades. Here, we evaluate if these results remain consistent in a subgroup of patients with well-differentiated G3 NETs. Patients with locally advanced or metastatic epNETs or pNETs were randomized 2:1 in independent cohorts to receive cabozantinib 60 mg daily vs placebo. We analyzed outcomes of the subset of patients with G3 NETs (Ki-67 > 20%), combining patients in the pNET and epNET cohorts due to small sample sizes. Twenty-four patients had G3 NETs, 16 randomized to cabozantinib and 8 to placebo. Primary sites included pancreas (n = 12), GI tract (n = 7), unknown primary sites (n = 3), and lung/thymus (n = 2). Median PFS for patients with G3 NETs treated with cabozantinib was 7.9 vs 3 months with placebo (HR = 0.15, 95% CI: 0.04-0.57, 1-sided log-rank P = 0.0034). The confirmed overall radiographic response rate was 25% (4/16) with cabozantinib vs 0% (0/8) with placebo. Safety outcomes were consistent with published data for the trial as a whole. Subset analysis of the CABINET trial showed improved PFS associated with cabozantinib vs placebo for G3 NETs of pancreatic and extra-pancreatic origin. Despite limited numbers, these results suggest that cabozantinib can be an effective option for patients with advanced G3 NETs. ClinicalTrials.gov Identifier: NCT03375320.

PubMed-ID: [41524552](#)

DOI: [10.1530/ERC-25-0415](#)

PMCID: PMC12872296

### **Serotonin Expression and beta-Cell Phenotype Are Associated With Indolent Behavior in Pancreatic Neuroendocrine Tumors With Sclerosing Morphology.**

*J Surg Oncol*, 133(7):934-41.

A. L. Windon, F. Revetta, W. Chen and C. Shi. 2026.

BACKGROUND AND OBJECTIVES: ARX and PDX1 transcription factors have been considered indicators of the cell of origin for pancreatic neuroendocrine tumors (PanNETs). Some PanNETs show dense fibrosis (sclerosing morphology) and an association with serotonin expression. This study aimed to explore ARX and PDX1 expression in these tumors. METHODS: Pathology archives were searched from 2005 to 2019 for PanNETs with dense stromal fibrosis. Immunohistochemical stains for ARX, PDX1, and serotonin were performed and reviewed with pertinent clinical findings. RESULTS: Fifty-one PanNETs were evaluated. Serotonin expression was identified in 19 (37%) tumors. The mean tumor size was smaller in the serotonin-expressing group compared to the non-expressing group (1.7 +/- 1.1 vs. 2.5 +/- 1.2 cm, p = 0.03). Serotonin-expressing tumors demonstrated a beta-cell phenotype with absence of ARX expression in the majority of tumors (n = 16; 84.2%), while the non-expressing tumors demonstrated an alpha-cell phenotype with ARX expression (n = 24, 75%, p < 0.01). Synchronous/metachronous liver metastasis was more frequent in the serotonin non-expressing tumors (p = 0.020). Serotonin expression was associated with a better disease-free survival. CONCLUSIONS: Serotonin-expressing PanNETs more commonly showed a beta-cell phenotype, while non-expressing tumors favored an alpha-cell phenotype with more frequent liver metastasis. The expression of serotonin suggests more indolent behavior in this variant of PanNETs.

PubMed-ID: [41936041](#)  
DOI: [10.1002/jso.70247](#)  
PMCID: PMC13352224

**Comparison Between endoscopic submucosal dissection and laparoscopic endoscopic cooperative surgery for non-ampullary duodenal neuroendocrine tumors: a single-center retrospective cohort study.**

*Int J Surg*, 112(4):9086-92.

Z. L. Yang, Y. Liu, G. Chun-Guang, H. L. Ng, S. He, D. B. Zhao and G. Q. Wang. 2026.

BACKGROUND: Neuroendocrine tumors (NETs) are relatively rare in the duodenum. We aimed to compare the clinical outcomes of endoscopic submucosal dissection (ESD) and laparoscopic endoscopic cooperative surgery (LECS) for non-ampullary duodenal NETs. MATERIALS AND METHODS: This single-center retrospective study included patients with non-ampullary duodenal NETs treated with ESD or LECS between 2010 and 2024. Data on patient demographics, surgical outcomes, and short- and long-term prognoses were collected. RESULTS: We enrolled a total of 29 patients. No significant differences were observed between the ESD and LECS groups with regard to sex, age, height, weight, or tumor location. The median tumor diameter was significantly larger in the LECS group than in the ESD group (12.00 mm vs. 5.00 mm). The tumors in the LECS group were located deeper (submucosa or muscularis propria) than those in the ESD group. Both groups achieved high rates of en bloc resection (100% for ESD and 100% for LECS) and R0 resection (100% for ESD and 93.3% for LECS). There were no significant differences in postoperative complications, such as bleeding, stenosis, or abdominal infection between groups. The median duration of hospitalization was longer in the LECS group than in the ESD group (11.00 vs. 7.00 days). No recurrence or metastasis was observed in either group during follow-up. CONCLUSION: Both ESD and LECS demonstrated high en bloc resection rates and R0 resection rates, along with favorable short- and long-term prognoses for non-ampullary duodenal NETs. LECS appears to be a safe and effective treatment option with an efficacy comparable to that of ESD and may be suitable for larger or deeply infiltrating lesions, potentially helping avoid the need for more invasive surgical procedures.

PubMed-ID: [41427523](#)

DOI: [10.1097/JS9.00000000000004590](#)

PMCID: PMC13105492

**Characterization of small intestinal neuroendocrine tumorlets.**

*Endocr Relat Cancer*, 33(4)

A. Yogo, N. Akanuma, G. E. Kim, A. Paciorek, L. Zhang, P. Le, K. Hirose, C. U. Corvera, E. K. Bergsland and E. K. Nakakura. 2026.

Small intestine neuroendocrine tumors (SI-NETs) frequently present as multifocal primaries. We commonly observe microscopic lesions in the superficial layer of the small intestine of SI-NET patients. We aimed to define them as small intestinal neuroendocrine tumorlets (SINTs) and explore their clinical and biological significance. Twenty multifocal and twenty unifocal SI-NETs patients who received resection at a single institution were retrospectively reviewed. Four hundred and forty six archived pathological slides were examined for microscopic lesions located in the lamina propria, muscularis mucosa, and superficial submucosa. Clinicopathological associations and progression-free survival were analyzed. Previously published genomic data were re-analyzed. SINTs were identified in 50% of multifocal and 30% of unifocal SI-NET patients. Median SINT size was 95  $\mu$ m, with a median distance of 2.2 mm from the nearest mass. Compared to the 'true unifocal' group (unifocal without SINT), the 'multifocal-spectrum' group (multifocal or unifocal with SINT) had higher BMI (median: 27.6 vs 22.8,  $P = 0.0060$ ), higher rates of perineural invasion (OR: 5.5,  $P = 0.044$ ), larger mesenteric mass (median: 2.6 vs 1.6 cm,  $P = 0.034$ ), and more advanced pT stage (pT3 or pT4, OR: 7.2,  $P = 0.018$ ). Genomic re-analysis suggested that 13% of cells in multifocal primary tumors could share clonal origins, possibly indicating clonal spread via SINTs. SINTs may serve as a new biomarker for multifocal spectrum with local aggressiveness. The actual frequency of multifocal SI-NET may be higher than currently recognized in clinical practice. Further studies are needed to validate their prognostic and biological significance.

PubMed-ID: [41886547](#)

DOI: [10.1530/ERC-25-0425](#)

PMCID: PMC13097121

# General

## Meta-Analyses

-None-

## Randomized controlled trials

- None -

## Consensus Statements/Guidelines

- None -

## Other Articles

### **Risk Factors for Pituitary Adenoma Development in Multiple Endocrine Neoplasia Type 1: A Nationwide Study of 240 Cases.**

*J Clin Endocrinol Metab*, 111(3):e811-e20.

N. Valdes, A. R. Romero-Lluch, E. Diego, M. Calatayud, C. Lamas, M. Araujo-Castro, R. Martinez, J. Oriola, C. Alvarez-Escola, A. D. Perez, V. Alcazar, J. Sastre, M. I. Del Olmo, E. Boix, A. Vicente, R. Garcia-Centeno, S. Perez-Fernandez, M. D. Chiara and A. Casteras. 2026.

**OBJECTIVE:** Pituitary adenomas (PAs) are one of the three major lesions in Multiple Endocrine Neoplasia type 1 (MEN1), with a prevalence of 32% to 58%, yet their specific risk factors remain unidentified. This study aimed to identify predictors influencing PA occurrence in MEN1. **METHODS:** This nationwide, multicenter, retrospective cohort study involved 240 MEN1 patients, 55.8% female. The main variables were age-related penetrance, PA subtype and size, and MEN1 germline pathogenic variants (PVs). The primary outcome was PA development. Cox regression was applied first to the full cohort and then to a prospectively screened subgroup (n = 199) free of symptom-driven bias. **RESULTS:** PAs were detected in 112 (46.6%) patients at a mean age of 36.1 +/- 13.9 years; most (63.3%) were diagnosed through screening. Prolactinomas (49.1%) and microadenomas (62.5%) predominated. In the full cohort, the following independent factors were related to PA development: age (per additional year; HR 0.916, 95% CI 0.893-0.993; P < .001), prior primary hyperparathyroidism (HR: 3.090, 95% CI: 1.943-4.914, P < .001), non-missense MEN1 PVs (HR: 1.976, 95% CI: 1.125-3.468, P = .018), and female sex (HR: 1.706, 95% CI: 1.082-2.689, P = .022). The same factors remained significant in the screened subgroup.

**CONCLUSION:** Risk of PA in MEN1 clusters at younger ages and declines thereafter. Prior primary hyperparathyroidism, non-missense MEN1 PVs, and female sex further mark higher-risk profiles. These findings may help personalize PA follow-up-prioritizing closer imaging in early adulthood and allowing longer intervals when baseline imaging is normal and additional risk markers are absent-pending validation in larger multicenter studies.

PubMed-ID: [40921719](#)

DOI: [10.1210/clinem/dgaf497](#)

### **Endocrine Comorbidities in Fibromyalgia.**

*Clin Endocrinol (Oxf)*, 104(4):386-93.

E. Magen, L. Tolkin, S. Aamar, I. Magen, E. Merzon, I. Green, A. Golan-Cohen, S. Vinker and A. Israel. 2026.

**BACKGROUND:** Fibromyalgia (FM) is a chronic pain syndrome increasingly linked to immune and endocrine dysfunction. This study aimed to evaluate the prevalence of endocrine comorbidities in FM patients compared to matched controls using a large healthcare database. **METHODS:** A population-based case-control study was conducted using data from Leumit Health Services, Israel. The cohort included 9,232 adults diagnosed with FM according to ACR criteria, matched by age and sex to 46,160 control subjects. Endocrine disorders were identified via ICD-9 codes. Statistical analyses included Student's t-test or Mann-Whitney U test for continuous variables, Pearson's chi-squared or Fisher's exact test for

categorical variables, and multivariable logistic regression adjusting for age, sex, and BMI. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Both statistical significance and effect sizes are reported to facilitate assessment of clinical relevance. RESULTS: FM patients showed a significantly higher prevalence of endocrine comorbidities compared to controls. Thyroid disorders, including Hashimoto's thyroiditis (13.3% vs. 10.0%; OR = 1.38,  $p < 0.001$ ) and Graves' disease (4.1% vs. 3.0%; OR = 1.38,  $p < 0.001$ ), were more common. Diabetes mellitus type 1 (0.9% vs. 0.3%; OR = 3.64,  $p < 0.001$ ) and type 2 (23.5% vs. 18.6%; OR = 1.34,  $p < 0.001$ ), adrenal disorders such as Cushing's syndrome (OR = 5.01,  $p < 0.001$ ), prolactinoma (OR = 1.81,  $p = 0.014$ ), osteoporosis (19.1% vs. 11.6%; OR = 1.80,  $p < 0.001$ ), and vitamin D deficiency (39.9% vs. 30.3%; OR = 1.53,  $p < 0.001$ ) were also significantly associated. Less common conditions (e.g., thyroiditis subtypes and thyroid malignancy) also appeared more frequent among FM patients, though effect sizes varied and some associations did not reach robust significance. CONCLUSION: This is among the largest datasets to date to systematically examine a comprehensive spectrum of endocrine comorbidities in FM. Our findings suggest that FM and endocrine disorders may share overlapping pathophysiological mechanisms. Future studies should clarify causal pathways and assess the clinical utility of routine endocrine screening in FM patients.

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### **Magnesium as an endocrine modulator: physiological roles, clinical evidence, and therapeutic perspectives.**

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A. Palermo, A. M. Naciu, G. Zavatta, E. Sargentini, C. Menale, M. P. Yavropoulou, C. Cipriani, G. Tabacco and A. D. Anastasilakis. 2026.

CONTEXT: Magnesium deficiency is prevalent and increasingly recognized as an endocrine-relevant condition due to its involvement in hormone secretion, metabolic homeostasis, and cellular signaling. OBJECTIVE: To review current evidence on the role of magnesium in key endocrine systems and evaluate its clinical and therapeutic implications. EVIDENCE SYNTHESIS: Magnesium influences glucose metabolism, bone health, thyroid function, reproduction, cardiometabolic regulation, and HPA axis activity. Clinical evidence shows strong associations between magnesium status and several endocrine diseases. CONCLUSIONS: Magnesium plays a multifaceted endocrine role with clinically significant implications. Improved diagnostic approaches and further interventional studies are warranted.

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