EUROPEAN SOCIETY OF ENDOCRINE SURGEONS

ESES Review of Recently Published Literature

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

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

blue underline: Hyperlink to PubMed entry or web site of publisher. Clicking on hyperlink opens the corresponding web site in browser (in Vista: CTRL-click).

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Journal names are links to the journal's homepage!,

Thyroid

Meta-Analyses

Clinical prognostic risk assessment of different pathological subtypes of papillary thyroid cancer: a systematic review and network meta-analysis.
Langenbecks Arch Surg, 410(1):251.
J. Zhao, W. Zhang, D. Lu, C. Shao, Y. Chen, X. Huang, Y. Zhang and J. Xu. 2025.
There are multiple pathologic subtypes of papillary thyroid carcinoma (PTC), each with distinct clinical prognoses. However, the available data on the clinicopathologic risks associated with several common PTC subtypes are controversial and require more comprehensive evaluation. To address this, we conducted a systematic search of English-language databases, including PubMed, EMbase, Cochrane Library, and Web of Science, for studies on six PTC subtypes, including classic papillary thyroid carcinoma (CPTC), papillary thyroid microcarcinoma (PTMC), follicular variant of papillary thyroid carcinoma (FVPTC), tall cell variant of papillary thyroid carcinoma (TCVPTC), diffuse sclerosing variant of papillary thyroid carcinoma (DSVPTC), and columnar cell papillary thyroid carcinoma (CCVPTC). Our case-control study of clinicopathological prognostic analyses of six subtypes, with a search date of January 2000 to May 2024. Two researchers independently screened the literature, extracted data, and assessed quality and risk of bias according to set criteria. R software gemtc package, Stata 15.1 software were applied to perform reticulated Meta-analysis methods were applied to compare the clinicopathological features and prognostic assessment of classic papillary thyroid carcinoma and the other five subtypes in all the studies.The risk of distant metastasis was higher in patients with CCVPTC, TCVPTC, and DSVPTC than in CPTC.FVPTC and PTMC exhibit a lower risk of in situ tumor relapse compared to CPTC. The tumour size of TCVPTC was significantly larger than that of CPTC, while there was no significant difference in the tumour size of CCV, DSV, FVPTC, CPTC and PTMC. DSVPTC was significantly more multifocal than the other subtypes. This network meta-analysis confirms the aggressive biological behavior and poor prognosis associated with TCVPTC, DSVPTC, and CCVPTC. Therefore, these subtypes should be managed aggressively with total thyroidectomy and lymph node dissection if diagnosed preoperatively. In contrast, FVPTC and PTMC are less aggressive and have a better prognosis, suggesting that treatment and follow-up strategies for PTC should be tailored according to the histopathological subtype.
PubMed-ID: 40853492
DOI: 10.1007/s00423-025-03841-2
PMCID: PMC12378718

Association between vitamin D serum levels and thyroid cancer: a meta-analysis.
Front Endocrinol (Lausanne), 16:1602844.
L. Yang, P. Yun and F. Li. 2025.
BACKGROUND: Thyroid cancer (TC) has shown a rising prevalence worldwide. While numerous studies have explored the relationship between vitamin D levels and TC risk, their conclusions remain inconsistent. OBJECTIVE: This meta-analysis aims to evaluate the association between serum vitamin D levels, vitamin D deficiency, and TC based on existing evidence. METHODS: We systematically searched the Embase, Web of Science, and PubMed databases for human studies investigating the relationship between vitamin D and TC including a control group. A random-effects model with forest plots was employed to calculate the mean difference (MD) in serum vitamin D levels, the odds ratio (OR) for vitamin D deficiency, and the risk difference (RD) between TC cases and controls. Meta-regressions and subgroup analyses were conducted based on the season of serum 25(OH)D sampling, source of controls, timing of measurement, study type, and testing methods of 25(OH)D. A p-value <0.05 was considered statistically significant. RESULTS: A total of 23 studies were included. The meta-analysis revealed that TC patients had significantly lower serum vitamin D compared to the controls [SMD = -0.38 (95% CI: -0.62 to -0.14)].Additionally, vitamin D deficiency was significantly more prevalent among TC patients (OR = 1.33, 95% CI: 1.02 to 1.73, P < 0.05). The subgroup analyses demonstrated significant differences across most subgroups, except for post-operative measurements. Seasonal variation in 25(OH)D sampling was identified as a key source of heterogeneity. CONCLUSIONS: The meta-analysis suggests that lower serum vitamin D levels and vitamin D deficiency are significantly associated with an increased risk of TC. However, further studies with standardized protocols for seasonal sampling of vitamin D, source of control, measurement timing, study type, and testing methods of 25(OH)D are needed to clarify this relationship and its underlying mechanisms.
PubMed-ID: 40778274

DOI: 10.3389/fendo.2025.1602844
PMCID: PMC12328179

Precision of predictive nomograms for lymph node metastasis of thyroid cancer from Chinese real-world study: a systematic review and meta-analysis.
Front Endocrinol (Lausanne), 16:1617563.
Y. Wu, Y. Su, Y. Zhao, N. Mourdi and Z. Wang. 2025.
BACKGROUND: Current guidelines lack nomograms to predict lymph node metastasis (LNM) in thyroid carcinoma (TC) in China. Nomograms are simple, accurate tools to estimate the probability of specific events and have been extensively developed to predict LNM in TC. However, few effective nomograms have been validated in clinical practice. METHODS: The recommendations of the Cochrane Prognosis Methods Group were implemented in this systematic review. We conducted searches in PubMed, Web of Science, and Scopus for published research. The nomogram was categorized based on outcomes. We summarized the key characteristics and effectiveness of the nomogram and assessed the overall risk of bias (ROB). We employed random-effects and bivariate mixed-effects models to estimate the efficacy of the nomogram group and its predictive reliability. RESULTS: The systematic review identified 57 nomogram models from China, of which only 14 had external validation cohorts. While the applicability was acceptable, the heterogeneity among the included nomograms was substantial, leading to a high overall risk of bias (ROB). Ultrasound information was utilized in nearly all studies. Size, extrathyroidal extension (ETE), tumor consistency index (TCI), and multifocality are commonly employed independent risk factors. Both outcome models showed good to excellent predictive efficacy. However, the performance of models that integrate radiomics with clinical features was inferior to those using ultrasound alone. CONCLUSIONS: The feature-combined model offers several potential outcomes and advantages for clinical practice in China. Additionally, the systematic review serves as a reference tool for physicians to select appropriate nomograms based on individual clinical needs. Future research should focus on external validation and evaluation to minimize limitations in clinical utility.
PubMed-ID: 40704150
DOI: 10.3389/fendo.2025.1617563
PMCID: PMC12283272

Ultrasound-based artificial intelligence for predicting cervical lymph node metastasis in papillary thyroid cancer: a systematic review and meta-analysis.
Front Endocrinol (Lausanne), 16:1570811.
X. Wang, Y. Qi, X. Zhang, F. Liu and J. Li. 2025.
OBJECTIVE: This meta-analysis aims to evaluate the diagnostic performance of ultrasound (US)-based artificial intelligence (AI) in assessing cervical lymph node metastasis (CLNM) in patients with papillary thyroid carcinoma (PTC). METHODS: A comprehensive literature search was conducted in PubMed, Embase, Web of Science, and the Cochrane Library to identify relevant studies published up to November 19, 2024. Studies focused on the diagnostic performance of AI in the detection of CLNM of PTC were included. A bivariate random-effects model was used to calculate the pooled sensitivity and specificity, both with 95% confidence intervals (CI). The I(2) statistic was used to assess heterogeneity among studies. RESULTS: Among the 593 studies identified, 27 studies were included (involving over 23,170 patients or images). For the internal validation set, the pooled sensitivity, specificity, and AUC for detecting CLNM of PTC were 0.80 (95% CI: 0.75-0.84), 0.83 (95% CI: 0.80-0.87), and 0.89 (95% CI: 0.86-0.91), respectively. For the external validation set, the pooled sensitivity, specificity, and AUC were 0.77 (95% CI: 0.49-0.92), 0.82 (95% CI: 0.75-0.88), and 0.86 (95% CI: 0.83-0.89), respectively. For US physicians, the overall sensitivity, specificity, and AUC for detecting CLNM were 0.51 (95% CI: 0.38-0.64), 0.84 (95% CI: 0.76-0.89), and 0.77 (95% CI: 0.73-0.81), respectively. CONCLUSION: US-based AI demonstrates higher diagnostic performance than US physicians. However, the high heterogeneity among studies and the limited number of externally validated studies constrain the generalizability of these findings, and further research on external validation datasets is needed to confirm the results and assess their practical clinical value. SYSTEMATIC REVIEW REGISTRATION: https://www.crd.york.ac.uk/PROSPERO/view/CRD42024625725, identifier CRD42024625725.
PubMed-ID: 40556829
DOI: 10.3389/fendo.2025.1570811
PMCID: PMC12185295

Implications of five endoscopic and conventional open surgery on lateral neck dissection outcomes in patients with papillary thyroid carcinoma: a network meta-analysis and systematic review.
Surg Endosc, 39(7):4047-59.
Y. Tong, P. Li, W. Liu, S. Tan, X. Wang, Y. Zhang, Y. Ran, Y. Fang, Y. Fan, T. Wei and W. Zhao. 2025.
OBJECTIVES: The efficacy and safety of different surgical approaches to thyroidectomy with lateral neck dissection remain unclear. This study aims to evaluate five endoscopic and open techniques for thyroidectomy with lateral neck dissection and identify the most effective method. METHODS: A systematic search was conducted in PubMed, Web of Science, Embase, and the Cochrane Library for studies comparing different surgical approaches across multiple outcome indicators. The risk of bias was analyzed, and publication bias was assessed using funnel plot asymmetry tests. Both global and local inconsistency tests were performed to evaluate the agreement between direct and indirect comparisons. Pairwise and network meta-analyses were conducted for each outcome, with approaches ranked using Surface Under the Cumulative Ranking (SUCRA) values and curves. RESULTS: A total of 1251 patients across 13 clinical studies were included in the analysis. No significant statistical differences were found among the approaches for lymph node dissection and postoperative recurrence rates. The bilateral axillary breast approach yielded the highest number of lymph nodes (SUCRA value: 0.762). The suprasternal fossa approach had the lowest postoperative recurrence rate (SUCRA: 0.657) and performed well in metastatic lymph node dissection (SUCRA: 0.679). The bilateral axillary breast approach significantly reduced postoperative complication rates compared to the open and transaxillary approaches (mean differences: - 1.88 and - 0.23; 95% confidence intervals: - 3.87 to - 0.46 and - 0.62 to 0.29, respectively) and was the most effective in minimizing complications (SUCRA: 0.910). Open surgery demonstrated a significantly shorter operative duration. CONCLUSION: Endoscopic approaches are viable and safe alternatives to open surgery, with fewer postoperative complications, albeit at the cost of longer operative durations.
PubMed-ID: 39915312
DOI: 10.1007/s00464-025-11568-w

Quality of life in patients with overt hypothyroidism: a systematic review.
Eur J Endocrinol, 193(3):S26-S35.
M. Thvilum, S. M. Lind, E. Ebbehoj, S. Gregersen and D. Grove-Laugesen. 2025.
OBJECTIVE: Persistent symptoms and impaired quality of life (QoL) in hypothyroidism despite treatment with levothyroxine (LT4) receive increasing attention. We aimed at reviewing QoL in long-term treated hypothyroidism. DESIGN: This is a systematic review and meta-analysis. METHODS: The systematic literature search "hypothyroidism AND quality of life" was conducted in PubMed and Embase. We considered studies on QoL in adults with Hashimoto's thyroiditis (HT) or congenital hypothyroidism (CH), treated with levothyroxine for 6 months. Seven hundred and ninety-seven articles were screened for title-abstract, and 52 were assessed by full-text evaluation. Seventeen articles met eligibility criteria and were included. We summarize study finding within the domains mental well-being, physical well-being, and social role supported by meta-analyses. Studies were evaluated using Newcastle-Ottawa Scale. Two meta-analyses were performed using random effects model. RESULTS: Fourteen studies included patients with HT, and 3 evaluated QoL in CH. Mental and physical well-being was impaired in 10 studies, and social role impairments were detected in 7 studies. Study design was to some degree flawed in 13 studies, potentially hampering conclusions. The most frequent methodological issues were incomparable groups or lack of information on potential confounders like body mass index or comorbidity. However, when focusing on the methodologically most robust studies, conclusions remained and were supported by meta-analyses. CONCLUSION: Based on this systematic review and meta-analysis, despite methodological concerns in the available literature, QoL in patients with hypothyroidism is impaired. Future studies should address potential residual bias displayed and explore the impact of disease etiology, duration, and timing of diagnosis in relation to comorbidity, to reveal groups of patients susceptible to inadequate treatment response and guide our way to improve QoL in hypothyroidism.
PubMed-ID: 40911397
DOI: 10.1093/ejendo/lvaf179

Efficacy and safety of RET-kinase inhibitors in RET-altered thyroid cancers: a systematic review and single-arm meta-analysis.
Endocr Relat Cancer, 32(6)
I. J. Riya, I. J. Piya, J. N. Priantti, C. L. Lee, L. Barman and A. Altobi. 2025.
The RET proto-oncogene, which encodes a receptor tyrosine kinase, is an important factor in the pathogenesis of medullary and papillary thyroid cancers. Selpercatinib and pralsetinib, both specific RET-kinase inhibitors, are the only FDA-approved drugs for treating RET-altered thyroid cancer. We wanted to evaluate the safety and efficacy of

selpercatinib and pralsetinib in RET-altered thyroid cancers. We searched the PubMed, Embase, Cochrane, and Clinicaltrials.gov databases for randomized controlled trials and observational studies published up to March 30, 2024, and included those that reported any of the desired endpoints. The primary endpoints were 1-year progression-free survival (PFS), objective response rate (ORR), and disease control rate (DCR). Quantitative analyses were performed using the R programming language. We included four studies with 560 patients, 510 with RET-mutant and 50 with RET-fusion thyroid cancer. The 1-year PFS was 84% (95% CI, 79-88, I 2 = 43%), ORR was 69% (95% CI, 65-73, I 2 = 0) and DCR was 93% (95% CI, 89-96, I 2 = 44%). Some important grade >/=3 adverse events were hypertension (16%; 95% CI, 11-22; I 2 = 43%), diarrhea (3%; 95% CI, 2-5; I 2 = 0), increased ALT (11%; 95% CI, 8-14; I 2 = 0) and increased AST (6%; 95% CI, 4-10; I 2 = 0). In conclusion, these findings suggest that selpercatinib and pralsetinib are efficacious and safe for use in patients with RET-altered thyroid cancer.
PubMed-ID: 40331677
DOI: 10.1530/ERC-24-0219

Threshold-dependent risk of postoperative hypocalcemia in vitamin D-deficient patients undergoing total thyroidectomy: A meta-analysis.
Surgery, 182:109333.
K. Lopera and A. Sanabria. 2025.
BACKGROUND: Vitamin D deficiency is common and asymptomatic in many populations, and research reveals an association between vitamin D levels and postoperative hypocalcemia after total thyroidectomy. However, the definition of vitamin D deficiency has varied, and the threshold used might have a major impact on clinical results. The purpose of this study was to investigate the threshold effect in the relationship between vitamin D deficiency and the incidence of postoperative hypocalcemia. METHODS: A meta-analysis was done following Preferred Reporting Items for Systematic reviews and Meta-Analyses recommendations. Studies that examined preoperative vitamin D levels and assessed postoperative hypocalcemia in total thyroidectomy patients were included. The investigation explored 3 vitamin D insufficiency thresholds: 15, 20, and 30 ng/mL. Odds ratios for biochemical and clinical hypocalcemia were determined, and sensitivity analyses were conducted to ensure the findings were robust. The methodologic quality was assessed using the Quality In Prognosis Studies technique. RESULTS: Twenty-eight studies were included, with 4,944 patients, 80.4% of whom were female. The risk of having postoperative biochemical hypocalcemia was highest at the 15 ng/mL threshold (odds ratio 3.22, 95% confidence interval 1.69-6.12), and reduced as the threshold increased to 20 ng/mL (odds ratio 1.69, 95% confidence interval 1.17-2.45) and 30 ng/mL (odds ratio 1.87, 95% confidence interval 1.20-2.91). Similar patterns were seen in clinical hypocalcemia. CONCLUSION: This investigation demonstrates the existence of a threshold effect in the relationship between vitamin D deficiency and postoperative hypocalcemia after total thyroidectomy. The classification of vitamin D deficiency has a substantial impact on clinical outcomes, highlighting the significance of standardizing criteria to enhance preoperative treatment and patient care.
PubMed-ID: 40107090
DOI: 10.1016/j.surg.2025.109333

Systematic review and meta-analysis of diagnostic accuracy of one-step nucleic acid amplification for lymph node metastases of papillary thyroid carcinoma.
Langenbecks Arch Surg, 410(1):184.
M. M. Llompart-Coll, P. Dominguez-Garijo, M. Manyalich-Blasi, G. Domenech-Gomez, I. Perales-Galan, D. Saavedra-Perez, M. T. Rodrigo, S. Vidal-Sicart, M. Pera-Roman and O. Vidal-Perez. 2025.
PURPOSE: To evaluate the diagnostic accuracy and detection rate of lymph node metastases (LNM) in Papillary Thyroid Carcinoma (PTC) using the One-Step Nucleic Acid Amplification (OSNA) technique compared to conventional pathological methods. METHODS: A systematic search was conducted in PubMed, The Cochrane Library, Scopus, and Web of Science from May 1, 2023, to June 30, 2023, for studies published from January 1, 2005, to April 30, 2023. Observational studies assessing OSNA for LNM in PTC patients were included. Two independent reviewers performed study selection, record screening, data extraction, and quality assessment using QUADAS-2. Meta-analysis was conducted with Posit software (RStudio). RESULTS: Seven studies (2014-2021) involving 1,424 lymph nodes from 207 PTC patients were analyzed. The pooled sensitivity, specificity, and AUC of OSNA for detecting LNM were 0.905 (95% CI 0.838-0.946), 0.884 (95% CI 0.834-0.921), and 0.848, respectively. DISCUSSION: OSNA shows promising diagnostic accuracy compared to conventional pathological methods, with the potential to improve real-time lymphatic staging and aid intraoperative decision-making. Limitations include study heterogeneity and a lack of randomized controlled trials, affecting generalizability. Further research is needed to validate the long-term benefits of OSNA in clinical practice.
PubMed-ID: 40498173

DOI: 10.1007/s00423-025-03742-4
PMCID: PMC12158847

Preoperative Vitamin D Supplementation to Reduce Hypocalcemia Following Total Thyroidectomy: Systematic Review and Meta-Analysis of Randomized Clinical Trials.
Head Neck, 47(9):2541-51.
L. Canali, G. M. Pace, M. D. Russell, F. Gaino, L. Malvezzi, G. Mazziotti, A. Lania, G. Spriano, M. Mannstadt, G. W. Randolph and G. Mercante. 2025.
OBJECTIVE: This study aims to determine whether preoperative supplementation of vitamin D reduces the incidence of hypocalcemia following total thyroidectomy. METHODS: Conducted in conformity with the PRISMA statement, a systematic review and meta-analysis of randomized clinical trials (RCT) was performed assessing postoperative hypocalcemia and postoperative symptomatic hypocalcemia. RESULTS: The search strategy yielded 3808 potentially relevant publications, with eight RCTs ultimately included. These eight trials included a total of 902 patients (22.73% male, n = 205/902), with a median age of 48.9 years (95% CI, 43.5-53.5). Four trials administered only vitamin D in the interventional arm, three trials administered both calcium and vitamin D in the interventional arm, and one trial administered vitamin D in the interventional arm and calcium in both arms. Pooled results from the eight included trials showed a reduced risk of postoperative hypocalcemia in the intervention arm (RR, 0.77; 95% CI, 0.62-0.96; p = 0.02). When excluding the studies that administered calcium supplements in addition to vitamin D, the pooled results showed a similar reduced risk of postoperative hypocalcemia (RR, 0.74; 95% CI, 0.57-0.96; p = 0.03). Analysis of six trials reporting the incidence of postoperative symptomatic hypocalcemia (n = 564) showed a reduced risk in the vitamin D arm, with or without calcium, compared to the control arm (RR, 0.56; 95% CI, 0.34-0.93; p = 0.023). CONCLUSIONS: Our findings suggest that preoperative vitamin D administration, with or without calcium carbonate, significantly reduces the risk of postoperative hypocalcemia and symptomatic hypocalcemia in patients undergoing total thyroidectomy.
PubMed-ID: 40264388
DOI: 10.1002/hed.28174

Financial Toxicity Across the Thyroid Cancer Care Continuum: A Systematic Review.
Otolaryngol Head Neck Surg, 173(1):1-16.
M. Armache, R. Stemme, W. Najjar, N. L. Samaha, M. Hearn, S. Lazieh, E. Joseph, K. Frazier, D. Ball, J. O. Russell, C. Fakhry, L. A. Gharzai and L. J. Mady. 2025.
OBJECTIVE: To describe the financial toxicity (FT) associated with thyroid cancer (TC) across the care continuum and elucidate factors contributing to FT in this patient population. DATA SOURCES: PubMed, Embase, Cochrane, Web of Science, and Scopus. REVIEW METHODS: A systematic review was conducted of peer-reviewed studies on FT in patients with a history of TC, between 1995 and 2024, using search terms "thyroid cancer," "financial toxicity," and their relevant synonyms. Full-text, English-language studies reporting subjective (self-reported FT) and objective (out-of-pocket [OOP], employment changes, and bankruptcy) FT outcomes were included. RESULTS: A total of 927 studies were identified, with 13 meeting the inclusion criteria. Nine studies addressed subjective FT, with prevalence rates ranging from 16% to 47%. Younger age, lack of health insurance, belonging to a racial minority, and having a lower annual household income were significantly associated with increased FT. Patients with TC had higher OOP costs and bankruptcy rates compared to other cancer types or matched controls. CONCLUSION: Despite a generally favorable prognosis, patients with TC experience significant FT, particularly among vulnerable groups such as younger individuals, the uninsured, and racial/ethnic minorities. In the setting of the rising incidence of TC, it is essential to identify and address FT in this population. Addressing FT requires a multifaceted approach, which includes incorporating financial counseling and cost discussions in routine care, ensuring comprehensive insurance coverage, and implementing employer-level protections to mitigate income and insurance loss. Further research is needed to understand the potential financial implications of different care pathways in the treatment of TC.
PubMed-ID: 40277140
DOI: 10.1002/ohn.1241

Randomized controlled trials

Thyroidectomy with or without postoperative radioiodine for patients with low-risk differentiated thyroid cancer in the UK (IoN): a randomised, multicentre, non-inferiority trial.
Lancet, 406(10498):52-62.
U. Mallick, K. Newbold, M. Beasley, K. Garcez, J. Wadsley, S. J. Johnson, T. Stephenson, M. Gaze, A. Goodman, S. Jefferies, S. Sivabalasingham, N. Slevin, D. P. Wilkinson, E. Macias-Fernandez, D. Power, T. Roques, L. Speed, C. Nutting, G. Mochloulis, G. Gerrard, C. Candish, S. Morgan, D. Tripathi, P. Truran, C. Arthur, A. Wieczorek, K. Madhavan, J. Maclean, D. Boote, D. Kim, A. Pascoe, G. Pitiyage, S. Forsyth, E. Ambrose, E. Chang, K. Farnell and A. Hackshaw. 2025.
BACKGROUND: Patients with differentiated thyroid cancer can often be treated with postoperative radioiodine (also called radioiodine ablation) after total thyroidectomy. The IoN trial was designed to assess whether recurrence-free survival was non-inferior after no ablation compared with ablation in patients with low-risk differentiated thyroid cancer. METHODS: IoN was a multicentre, non-inferiority, phase 3 randomised trial conducted at 33 UK cancer centres. Eligible patients had complete (R0) resection following total thyroidectomy; stage pT1, pT2, pT3 (according to Tumour, Node, Metastasis staging version 7 [TNM7]), or pT3a (according to TNM8) disease; and N0, Nx, or N1a disease. Participants were randomly assigned (1:1) by minimisation, using a central electronic system, to have either 1.1 GBq ablation or no ablation, following thyroidectomy. Stratification factors were centre, age, T stage, and nodal status. Patients had annual neck ultrasound scans and 6-monthly serum thyroglobulin measurements. The primary endpoint was 5-year recurrence-free survival, defined by the absence of locoregional recurrent or persistent structural disease, distant metastases, or death from thyroid cancer. Non-inferiority was assessed with a margin of 5 percentage points. Per-protocol and intention-to-treat (ITT) analyses were done for the primary endpoint, and safety was analysed in the per-protocol population. The trial is registered with ClinicalTrials.gov (NCT01398085), ISRCTN (ISRCTN80416929), and EUDRACT (2011-000144-21), and is still in active follow-up. FINDINGS: We recruited 504 patients (including 390 [77%] female patients and 114 [23%] male patients) between June 26, 2012 and March 18, 2020 and randomly assigned 251 to receive no ablation and 253 to receive ablation (ITT population). 249 patients in the no ablation group did not have ablation and 231 in the ablation group had ablation (per-protocol population). Median follow-up was 6.8 years (IQR 5.6-8.6) in the no ablation group and 6.6 years (4.8-8.5) in the ablation group; 17 recurrences (eight in the no ablation group and nine in the ablation group; ITT population) occurred during follow-up. 5-year recurrence-free rates were 97.9% (95% CI 96.1-99.7) in the no ablation group versus 96.3% (93.9-98.7) in the ablation group in the ITT analysis, and 97.9% (96.1-99.7) versus 96.9% (94.7-99.1) in the per-protocol analysis. The 5-year absolute risk difference was 0.5 percentage points (95% CI -2.2 to 3.2, p(non-inferiority)=0.033; ITT analysis), showing that non-inferiority was reached. The observed recurrence rate was higher among patients with pT3 or pT3a tumours (four [9%] of 46 patients overall with pT3 or pT3a tumours vs 13 [3%] of 458 with pT1 or pT2 tumours), or N1a tumours (six [13%] of 47 with N1a vs 11 [2%] of 457 with N0 or Nx), but they were similar among those who did not receive ablation. Adverse events were similar between the groups, the most common being fatigue (63 [25%] of 249 in the no ablation group vs 65 [28%] of 231 in the ablation group), lethargy (34 [14%] vs 32 [14%]), and dry mouth (24 [10%] vs 21 [9%]), and there were no treatment-related deaths. INTERPRETATION: The IoN trial shows that ablation (or postoperative radioiodine) can be avoided for patients with pT1, pT2, and N0 or Nx tumours with no adverse features. Many patients with low-risk differentiated thyroid cancer worldwide can safely avoid postoperative radioiodine and its related hospitalisation and side-effects, which in turn results in lower health-care costs. FUNDING: Cancer Research UK.
PubMed-ID: 40543520
DOI: 10.1016/S0140-6736(25)00629-4

Clinical Validation of NerveTrend Versus NerveAssure Mode of Intraoperative Neuromonitoring in Prevention of Recurrent Laryngeal Nerve Injury During Thyroid Surgery: A Randomized Controlled Trial.
Ann Surg, 282(5):709-16.
M. Barczynski, M. Dworak, K. Krakowska, A. Pac and A. Konturek. 2025.
OBJECTIVE: To compare 2 modes of NIM Vital application in thyroid surgery: NerveTrend versus NerveAssure with respect to the prevalence of postoperative recurrent laryngeal nerve (RLN) injury. BACKGROUND: The use of NerveTrend compared with intermittent neuromonitoring (i-IONM) in thyroid surgery has recently been reported to result in a tendency toward reduced RLN injury on postoperative day 1 (POD1) and a significant decrease in the need for staged thyroidectomy. However, it remains unclear whether this technique is inferior to continuous neuromonitoring (NerveAssure). METHODS: Prospective, single-center, 2-arm randomized clinical trial. The primary outcome was the prevalence of RLN injury on POD1. In the NerveTrend group, the surgeon-operated i-IONM stimulation probe was used for trending amplitude and latency changes from the initial vagal electromyographic baseline (at pace based on surgical

judgment) to tailor the surgical strategy. In the NerveAssure group, it was performed using an Automatic Periodic Stimulation electrode placed on the vagus nerve. RESULTS: A total of 264 patients were randomized into the intervention group (NerveTrend) and the control group (NerveAssure), 132 patients, and 264 nerves at risk (NAR), each. RLN injury was found on POD1 in 3/264 (1.14%) versus 1/264 (0.38%) NAR, whereas staged thyroidectomy was not necessary in any of the patients in the study (P =0.624 and 1.0, respectively). CONCLUSIONS: NerveTrend mode was not inferior to the NerveAssure mode in thyroid surgery with respect to the risk of RLN injury, and both modes had the potential to abolish the need for staged thyroidectomy.
PubMed-ID: 40758439
DOI: 10.1097/SLA.0000000000006872
PMCID: PMC12513030

Consensus Statements/Guidelines

2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer.
Thyroid, 35(8):841-985.
M. D. Ringel, J. A. Sosa, Z. Baloch, L. Bischoff, G. Bloom, G. A. Brent, P. L. Brock, R. Chou, R. R. Flavell, W. Goldner, E. G. Grubbs, M. Haymart, S. M. Larson, A. M. Leung, J. Osborne, J. A. Ridge, B. Robinson, D. L. Steward, R. P. Tufano and L. J. Wirth. 2025.
Background: Differentiated thyroid cancer (DTC) is the most prevalent cancer of thyroid and is among the most frequently diagnosed cancers in the United States. The practice guidelines of the American Thyroid Association (ATA) for DTC management in adult patients (previously combined with thyroid nodules) were published initially in 1996, with subsequent revisions based on advances in the field. The goal of this update is to provide clinicians, patients, researchers, and those involved in health policy with rigorous, comprehensive, and contemporary guidelines to assist in the management of adult patients with DTC, emphasizing the patient journey beginning with a thyroid cancer diagnosis. Methods: The questions addressed were based, in part, on prior versions of the guidelines, with input from a larger, more diverse complement of stakeholders. The panel included members from multiple specialties involved in thyroid cancer care, including a patient advocate and an expert in systematic reviews/meta-analyses/guidelines who educated and supported task force members. The panel conducted systematic literature reviews to inform the recommendations and commissioned two additional systematic reviews. Published English-language articles were eligible for inclusion, with a final search date of July 1, 2024. A modified Grading of Recommendations Assessment, Development and Evaluation system was used for critical appraisal of evidence and determining the quality of data. The guidelines panel had editorial independence from the ATA. Competing interests of task force members were pre-vetted, regularly updated, communicated with task force members, and assessed and managed by ATA leadership and the Clinical Practice Guidelines and Statements Committee. Results: These revised guidelines begin with the initial cancer diagnosis and continue with recommendations for staging and risk assessment, initial treatment decisions, assessment of treatment responses, monitoring approaches, diagnostic testing, and subsequent therapies based on the strength of evidence for response and consideration of side effects and outcomes. Patient-reported outcomes and identified areas of need for additional high-quality research are highlighted. Conclusions: These revised evidence-based recommendations inform clinical decision-making in the management of DTC that reflect the changing science and optimize the evidence-based clinical care of patients throughout their journey with DTC. Critical areas of need for additional research are highlighted.
PubMed-ID: 40844370
DOI: 10.1177/10507256251363120

Other Articles

Heme-oxygenase-1: a key player in thyroid carcinoma development.
Endocr Relat Cancer, 32(8)
E. G. Alonso, M. Mascaro, K. Schweitzer, G. Giorgi, J. A. Carballido, A. Ibarra, V. Clemente, P. Pichel, S. Recio, L. Fernandez Chavez, G. P. Colo, E. N. Alonso, M. J. Ferronato, M. E. Fermento, M. M. Facchinetti and A. C. Curino. 2025.
ABSTRACT: Thyroid cancer is the most prevalent type of endocrine malignancy. Papillary thyroid carcinoma represents the majority of cases and is curable in approximately 90% of them, but it may also progress to anaplastic thyroid cancer, which

has a poor prognosis. Therefore, the identification of new therapeutic targets remains essential. In clinical practice, HO-1 mRNA is used as a biomarker to predict malignancy in thyroid nodules. However, its role in thyroid tumor progression remains understudied, as well as its potential as a therapeutic target. In this work, we confirmed that HO-1 protein is increased in human papillary thyroid cancer tissues and further demonstrated that high HO-1 mRNA is associated with progression to anaplastic thyroid cancer. Through pharmacological modulation of human papillary and anaplastic thyroid cells, and by genetically overexpressing HO-1 variants in papillary thyroid cells, we demonstrated that the overexpression of enzymatically active HO-1 enhances cell proliferation, migration, and cell cycle progression. Finally, we demonstrated that MEK/ERK signaling is partially involved in HO-1 effects. We concluded that HO-1 plays a relevant protumor role in thyroid cancer, and it may be a promising coadjuvant therapeutic target for papillary and anaplastic thyroid cancer.
PubMed-ID: 40742373
DOI: 10.1530/ERC-25-0177

Quality of Life and Management of Low-Risk Papillary Thyroid Cancer.
JAMA Surg, 160(10):1124.
R. C. Acker and R. R. Kelz. 2025.
PubMed-ID: 40833730
DOI: 10.1001/jamasurg.2025.2939

Medicaid expansion and thyroid cancer stage at presentation: A comparative study of two US states.
Am J Surg, 247:116447.
O. Akinyemi, T. Weldeslase, M. Fasokun, O. Eze, E. Odusanya, A. Yap, K. Limage, K. Hughes, E. Cornwell and A. Kalejaiye. 2025.
BACKGROUND: The Affordable Care Act (ACA) enabled states to expand Medicaid eligibility, extending coverage to millions, particularly in California. While Medicaid expansion has been linked to earlier diagnoses in several cancers, its impact on thyroid cancer-a slow-growing malignancy lacking formal screening-remains unclear. OBJECTIVE: To assess whether Medicaid expansion influenced thyroid cancer stage at presentation. METHODS: A retrospective cohort study using SEER data (2009-2020) compared adults aged 18-64 diagnosed with thyroid cancer in California (expansion) and Texas (non-expansion). Difference-in-differences logistic regression evaluated stage changes pre- (2009-2013) and post- (2016-2020) expansion, excluding a 2014-2015 washout period. RESULTS: Among 63,073 patients, no significant difference in stage at diagnosis was observed between states. Estimates for localized, regional, and distant disease changes ranged from -1.3 % to 1.1 % (all 95 % CIs included zero). CONCLUSION: Medicaid expansion was not associated with a significant shift in thyroid cancer stage at presentation.
PubMed-ID: 40505522
DOI: 10.1016/j.amjsurg.2025.116447

Evaluation of the Relationship Between Thyroid Hormone Levels and Bisphenol A in Children Aged 6-14 Years.
Clin Endocrinol (Oxf), 103(1):97-105.
P. Altun Yildirim, E. Nazlican, Z. Haytoglu, I. Turan, B. Kilincli, A. A. Aydin, E. Mengen and N. Daglioglu. 2025.
BACKGROUND: The incidence of hypothyroidism in childhood is increasing. This study aimed to investigate the potential role of exposure to bisphenol A, an environmental endocrine disruptor, and its substitutes in the development of hypothyroidism. To this end, thyroid hormone levels and urinary bisphenol concentrations were compared in newly diagnosed hypothyroid children and a healthy control group. METHODS: In this case-control study, 51 newly diagnosed hypothyroid children aged 6-14 years were matched with 51 healthy controls. The association between thyroid hormone levels and urinary bisphenol levels was investigated by measuring urinary bisphenol levels in both the case and control groups. RESULTS: There was no significant difference in age, sex or BMI percentile between the case and control groups. The groups were homogeneously distributed. When urinary bisphenol levels were examined, BPA, BPS, BPF and BPB were not detected in the control group. There was a significant difference between the groups in terms of urinary bisphenol BPS levels. The case group showed a mean total concentration of 16.5 ng/mL and a median of 5.8 ng/mL. Diagnosing hypothyroidism in the children can be considered by examining the bisphenol level. In the ROC analysis, if this level is over 1.3 and is considered positive for hypothyroidism, the sensitivity value is determined as 83.7% and the specificity value is 75%. CONCLUSION: This study demonstrated that at least 50% of the children in the case group had bisphenol concentrations exceeding the highest value recorded in the control group, suggesting that total BP levels could be used as a potential biomarker for hypothyroidism.
PubMed-ID: 40025791

DOI: 10.1111/cen.15221
PMCID: PMC12134418

Thyroid cancer quality of care indicators: A scoping review.
Am J Surg, 243:116223.
K. Ameri, M. Kwon, A. Watanabe and S. M. Wiseman. 2025.
BACKGROUND: Thyroid cancer, the most common endocrine malignancy, has highly variable practice patterns. This scoping review aimed to identify quantitative and qualitative quality of care indicators (QIs) essential for providing optimal care in thyroid cancer management. METHODS: A comprehensive search across MEDLINE, EMBASE, PubMed, and Web of Science identified QIs defining structures, processes, and outcomes in five care phases: pre-diagnosis, diagnosis, treatment, post-treatment surveillance, and end-of-life care. RESULTS: Of the 3,143 articles screened, 36 were included, yielding 135 unique QIs. Key diagnostic QIs were the use of a standardized ultrasound reporting system (n = 4), diagnostic fine needle aspiration biopsy (FNAB) (n = 3), and FNA cytology reporting with the Bethesda System (n = 3). Common treatment QIs included thyroidectomy by high-volume surgeons (>/=10-32 cases/year) (n = 7), preoperative voice assessment for high-risk patients (n = 4), and recurrent laryngeal nerve monitoring (n = 3). Serum thyroglobulin (Tg) monitoring was the primary post-treatment QI for recurrence (n = 2). CONCLUSIONS: Developing an evidence-based QI list can identify care gaps, direct targeted interventions, promote care standardization, and improve outcomes for thyroid cancer patients.
PubMed-ID: 39890473
DOI: 10.1016/j.amjsurg.2025.116223

Preoperative assessment of NIFTP clinicopathological characteristics and its impact on avoiding overtreatment.
Langenbecks Arch Surg, 410(1):204.
M. Andrade de Almeida, P. Canao, J. Capela, P. Sa Couto and S. Carneiro. 2025.
PURPOSE: Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a premalignant tumor formerly known as non-invasive encapsulated follicular variant of papillary thyroid carcinoma. The aim of this study was to investigate the clinicopathological traits of NIFTP to discern them from well-differentiated cancers and potentially avoid overtreatment. METHODS: We conducted a retrospective cohort study of NIFTP cases from July 2017 to November 2022 at our center. A review of demographic, clinical, sonographic, cytologic and surgical data was performed. RESULTS: During the study period 70 NIFTP cases were included. Among the cohort 74.3% (52/70) were women and the mean age was 55 years (range, 25-84). The majority of patients presented euthyroid (92.9%). Median NIFTP size was 2.5 cm (range, 1.0-10.8). Most nodules displayed low or intermediate risk on ultrasound being labeled EU-TIRADS 3 (46/70, 65.7%) and EU-TIRADS 4 (23/70, 32.9%). In cytology they were typically diagnosed as Bethesda III (15/70, 21.4%) or Bethesda IV (41/70, 58.6%). Regarding surgical procedures, 36 patients (51.4%) underwent lobo-isthmectomy and 34 patients (48.6%) received total thyroidectomy. Thirteen patients (18.6%) had coexisting microcarcinomas. No patients received radioiodine ablation. After a median follow-up of 27.5 months, no structural or biochemical recurrences were observed. CONCLUSION: Non-suspect thyroid nodules on preoperative ultrasound when combined with an indeterminate cytology and altered molecular profile should raise awareness towards the possibility of NIFTP. Even though neither FNAB nor CNB are definitive for NIFTP, CNB may be considered when additional architectural assessment is needed. Management with lobectomy seems to suffice unless total thyroidectomy is justified.
PubMed-ID: 40590978
DOI: 10.1007/s00423-025-03788-4
PMCID: PMC12213904

Metachronous metastasis of papillary thyroid carcinoma to the parotid gland: a case report and review of the literature.
Hormones (Athens), 24(2):367-75.
A. Antoniou, D. Tatsis, S. Papadopoulou, K. Pazaitou-Panayiotou and K. Vahtsevanos. 2025.
BACKGROUND: We present a case of metachronous metastasis of papillary thyroid carcinoma to the parotid gland, this being an extremely rare metastasis, and a literature review. CASE REPORT: A 56-year-old female patient presented with a history of a slowly growing mass on the left side of the neck. The patient reported a medical history of thyroidectomy due to papillary thyroid carcinoma 23 years previously and neck dissection for lymph node metastases 10 years previously, with additional therapy using radioactive iodine in both cases. Computed tomography (CT) of the neck revealed a single nodular solid mass in the tail of the left parotid gland which showed heterogeneous intake of contrast agent. FNA biopsy of the left parotid gland revealed cells typical of papillary thyroid carcinoma with positive immunochemistry for TTF-1. Due to this new metastasis, a total parotidectomy with preservation of the facial nerve was performed and additional therapy

with radioactive iodine was administered. CONCLUSION: Despite the fact that papillary thyroid carcinoma has a low incidence of regional and distant metastases, there are a few rare cases with distant metastases reported in the literature. Thus, awareness, especially among endocrinologists, and a multidisciplinary approach are crucial to ensure early detection and efficient treatment of these rare cases, distant metastases being the main cause of mortality and of reduction of overall survival rate among these patients.
PubMed-ID: 39648230
DOI: 10.1007/s42000-024-00619-x

Refining long-term surveillance requirements in patients with differentiated thyroid cancer.
Endocr Relat Cancer, 32(6)
S. Arman, M. Lyall and I. Nixon. 2025.
Differentiated thyroid cancer (DTC) has an excellent long-term prognosis following treatment. Despite this, post-treatment surveillance may last several years with no defined end-point. The aim of our study was to identify patients at the lowest risk of recurrence and suitable for early discharge. We conducted a retrospective analysis of a single centre database of all patients undergoing surgery for DTC between 2009 and 2022. We excluded patients with distant metastasis or those without a Tg level two years after complete thyroidectomy. Patients were grouped into hemithyroidectomy (H), total thyroidectomy (TT) and total thyroidectomy with radioactive ablation (TTR). TT and TTR groups were risk stratified using the Tg level at 2-year into undetectable/low (UL) (Tg < 0.2), medium (M) (0.2-1.0) and high (H) (>1.0). The 2015 American Thyroid Association (ATA) risk stratification system was used to further subdivide these groups. 481 patients were included in the study. The overall structural recurrence rate was 19/481 (3.9%) over a median follow-up period of 64 months (1-164). All recurrences occurred in the TTR group, with a median time to recurrence of 21 months. A higher Tg at 2-year (P < 0.00001) and a high ATA risk 2015 score (P = 0.007) were associated with higher rate of recurrence. Based on ATA guidelines, 100 patients were identified as low risk in the UL group, and there were no recurrences during the follow-up period. Our study suggests that individuals managed with hemithyroidectomy alone or with undetectable/low Tg levels within 2-year of treatment may be suitable for early discharge.
PubMed-ID: 40436035
DOI: 10.1530/ERC-25-0046

Combining Ultrasound Imaging and Molecular Testing in a Multimodal Deep Learning Model for Risk Stratification of Indeterminate Thyroid Nodules.
Thyroid, 35(5):590-4.
S. Athreya, A. Melehy, S. S. A. Suthahar, V. Ivezic, A. Radhachandran, V. R. Sant, C. Moleta, H. Zheng, M. Patel, R. Masamed, M. Livhits, M. Yeh, C. W. Arnold and W. Speier. 2025.
Objective: Indeterminate cytology (Bethesda III and IV) represents 15-30% of biopsied thyroid nodules and require additional diagnostic testing. Molecular testing (MT) is a commonly used diagnostic tool that evaluatesmalignancy risk through next generation sequencing of fine needle aspiration (FNA) samples. While MT achieves high sensitivity (97-100%) in ruling out malignancy, its specificity and positive predictive value (PPV) remain relatively low. This study proposes a multimodal deep learning model that integrates ultrasound (US) imaging with MT to improve risk stratification by enhancing PPV while maintaining high sensitivity. Combining these modalities leverages complementary information from both molecular and imaging data, addressing limitations in current approaches and offering a robust framework for evaluating indeterminate nodules. Methods: We retrospectively analyzed 333 patients with indeterminate thyroid nodules (259 benign, 74 malignant) at UCLA Medical Center between 2016 and 2022. We evaluated four configurations: whole frame US images, 256 x 256 patches, 128 x 128 patches, and an ensemble model combining the first three configurations. The clinical baseline consisted of Bethesda cytology and MT results. Models were assessed using five fold cross validation stratified by surgical outcomes. Results: The clinical baseline (Bethesda + MT) achieved an AUROC of 0.728 [0.68, 0.78] with sensitivity of 0.946 [0.88, 1.00], specificity of 0.664 [0.60, 0.73], and PPV of 0.448 [0.41, 0.48]. The proposed ensemble model demonstrated improved performance, achieving an AUROC of 0.831 [0.77, 0.89] with a sensitivity of 0.946 [0.88, 1.00], specificity of 0.703 [0.66, 0.75], and PPV of 0.477 [0.46, 0.50]. These improvements were statistically significant (p = 0.0008). Conclusion: Our multimodal model enhances MT performance by providing statistically significant improvements in PPV and specificity while maintaining high sensitivity. Our framework could be leveraged to reduce the number of benign thyroid resections in patients with indeterminate nodules. However, this study is limited by its single center dataset, lack of external validation, and the use of binarized MT outputs rather than granular malignancy risk probabilities. Future work should validate these findings across diverse populations and larger external datasets for more comprehensive risk stratification.

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DOI: 10.1089/thy.2024.0584

The use of thyroid cartilage needle electrodes during intra-operative nerve monitoring in thyroid surgery: A multi-center retrospective study.
Updates Surg, 77(4):1171-80.
K. Balci, Y. Turk, M. Ozdemir, P. Kuczma, C. Tresallet, C. W. Wu, T. Y. Huang, A. S. Muhammed, R. Muhammad, S. Suhaimi, N. Harlina, M. Buzejic, V. Zivaljevic, M. Jovanovic and O. Makay. 2025.
In previous studies, the use of thyroid cartilage needle electrodes (TCN) was defined as an inexpensive method for intra-operative nerve monitoring (IONM) in thyroid surgery. This multi-center retrospective study aims to determine the effectiveness and reliability of TCN in thyroid surgery. Patients operated on between January 2018 and August 2023 from five centers were included in this study. Demographic data, indications, type of surgery, IONM recording system, pre-post-resection vagus nerve (V1-V2), pre-post-resection recurrent laryngeal nerve (R1-R2) amplitudes and latency values, type of loss of signal (LOS), adverse event (AE), intra-operative injury mechanism, and post-operative vocal cord examination (VCE) were evaluated. Patients with abnormal preoperative vocal cord examination were excluded. A total of 2105 patients (3772 nerves at risk) were included [1626 (77%) female, 479 (23%) male]; within this study, 1112 patients (53%) received a diagnosis of malignancy, while 993 (47%) were diagnosed with benign conditions. The mean initial vagus amplitude was 1093.74 microV (+/- 861.39). LOS occurred in 63 patients [Type 1 (84%), Type 2 (16%)] and AE in 36. No false-positive LOS occurred. Forty-six (87%) of LOS type 1 patients and nine (90%) of LOS type 2 patients had vocal cord palsy (VCP) during VCE ($p < 0.05$). In AE patients, there were only two (5.5%) patients who had vocal cord palsy during VCE ($p < 0.05$). VCP occurred in 57(2.7%) patients, with 9 (0.42%) remaining permanent. TCN is an inexpensive and feasible alternative to endotracheal tube electrodes and a system with satisfying amplitudes. It can also precisely predict post-operative vocal cord functions.
PubMed-ID: 40266475
DOI: 10.1007/s13304-025-02178-1
PMCID: PMC12263753

Impact of Sternothyroid Muscle Division on Patient-Reported Swallowing Outcomes Following Thyroid Surgery: A Prospective Study.
Otolaryngol Head Neck Surg, 173(1):178-84.
J. Barlow, B. M. Laitman, J. Nogues, S. Chennareddy, C. Barron and R. L. Chai. 2025.
OBJECTIVE: Division of the sternothyroid muscle during thyroidectomy is a widely accepted surgical technique to provide improved exposure of the thyroid gland, superior pole vessels, and the external branch of the superior laryngeal nerve (EBSLN). Our group had previously shown no decrement in postoperative voice outcomes with this technique. However, given the known role of the strap muscles in swallowing function, this study aims to assess the impact of sternothyroid muscle division on patient-reported dysphagia. STUDY DESIGN: Prospective, consecutive cohort study. SETTING: Single institution urban tertiary health care system. METHODS: Adult patients who underwent total thyroidectomy or lobectomy with a single surgeon between November 2022 and July 2023 were enrolled. Patients with clinical evidence of significant preoperative dysphagia were excluded. Complete sternothyroid muscle division was performed in all cases. The integrity of the recurrent laryngeal nerve and EBSLN (when visualized) was confirmed through intraoperative nerve monitoring and postoperative flexible laryngoscopy. Differences between preoperative and postoperative patient-reported swallowing outcomes were assessed using the Eating Assessment Tool-10 (EAT-10). RESULTS: A total of 114 patients were included in the study. No statistically significant difference was found between mean preoperative and postoperative EAT-10 scores (0.63 vs 0.75, P = .677). These results remained consistent regardless of sex, history of reflux, unilateral or bilateral sternothyroid muscle division, performance of substernal resection of goiter, or final histologic diagnosis. CONCLUSION: Division of the sternothyroid muscle during thyroidectomy can be useful in the exposure of the thyroid gland without impact on patient-perceived swallowing disturbance.
PubMed-ID: 40226948
DOI: 10.1002/ohn.1253

Shared Decisionmaking in the Treatment of Hypothyroidism.
Clin Endocrinol (Oxf), 103(1):106-12.
A. C. Bianco. 2025.
BACKGROUND: Hypothyroidism, a condition characterized by an underactive thyroid gland, affects millions worldwide, leading to cognitive and metabolic slowdowns. It is most prevalent in women and older adults, with causes including

autoimmune thyroiditis, surgical thyroidectomy, and certain medications. STANDARD OF CARE AND LIMITATIONS: The standard treatment involves synthetic levothyroxine (LT4) monotherapy, which alleviates symptoms by converting to the active hormone, T3. However, some patients continue to experience symptoms such as fatigue, mood disturbances, and poor quality of life despite normalized TSH levels. This persistence of symptoms may stem from misdiagnosis, inadequate dosing, or incomplete normalization of thyroid hormone signaling. NEW FINDINGS: Research suggests that LT4 monotherapy may not fully restore T3 levels, leading to suboptimal symptom control. Consequently, combination therapy with LT4 and liothyronine (LT3) has been proposed as an alternative, aiming to balance T4 and T3 levels more effectively. Although randomized controlled trials have not identified significant differences in patient-reported outcomes between LT4 monotherapy and combination therapy, they indicate that patients may prefer the latter. CONCLUSION: Guidelines from leading endocrinology organizations now recommend considering combination therapy for patients with persistent symptoms despite adequate LT4 dosing. A patient-centered approach, emphasizing shared decision-making and individualized treatment plans, is essential for optimizing outcomes in hypothyroidism management. Further research is needed to refine dosing strategies and identify the patients who would benefit most from combination therapy.
PubMed-ID: 40077932
DOI: 10.1111/cen.15228

Reimagining the Therapeutic Approach for Anaplastic Thyroid Cancer: The Roadmap to a Cure.
Thyroid, 35(5):462-70.
M. E. Cabanillas, N. Akhave, V. Banuchi, N. Busaidy, R. Dadu, R. Ferrarotto, G. B. Gunn, S. Hamidi, M. C. Hofmann, S. M. Hosseini, P. C. Iyer, S. Y. Lai, A. Lee, A. Maniakas, M. S. Ning, M. Spiotto, J. R. Wang, M. D. Williams and M. Zafereo. 2025.
Background: Anaplastic thyroid cancer (ATC) is an aggressive cancer that leads to rapid death if left untreated. However, recent advances in ATC treatment have dramatically changed the prognosis in a select group of patients with BRAF(V600E) mutations. In these patients, BRAF/MEK inhibitors have been shown to dramatically and rapidly shrink tumors. Yet, these responses are short-lived unless additional treatment modalities are applied. In patients without a BRAF(V600E) mutation, the current available therapies are far less effective. Summary: In this article, we review the relevant literature and propose applying the "Total Therapy" approach used since the 1960s for another deadly but curable disease, acute lymphocytic leukemia, to ATC. We have adapted the concepts of Induction, Consolidation, and Maintenance, applying them to ATC. This regimen integrates the treatments we have found to be successful in ATC: combination systemic therapy using targeted therapy plus immunotherapy, surgery, radiation, and continuation of the systemic therapy for several years, thereby attempting to eradicate all residual ATC cells. Conclusions: There has been a renewed interest in understanding the genomics of ATC and treating these patients with urgency rather than just providing palliative care. This shift has led to significant improvements in the prognosis of ATC. With the right tools and a clear roadmap to guide us, we now aim to take on the challenge of curing these patients.
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DOI: 10.1089/thy.2025.0044
PMCID: PMC12491964

Adjuvant Pembrolizumab after Upfront Multimodal Therapy for Stage IVB Anaplastic Thyroid Cancer.
Thyroid, 35(7):763-70.
M. E. Cabanillas, N. L. Busaidy, G. B. Gunn, P. C. Iyer, R. Ferrarotto, M. Gule-Monroe, A. Maniakas, M. D. Williams, S. Liu, B. Fellman, M. Spiotto, S. Hamidi, N. Akhave, A. Lee, J. R. Wang, L. de Sousa, V. R. Marczyk, M. Zafereo and R. Dadu. 2025.
Background: Anaplastic thyroid cancer (ATC) has historically been almost uniformly fatal. In patients with the loco-regional disease (stage IVB), multimodal therapy (upfront surgery when feasible, radiation +/- concurrent chemotherapy) followed by observation is the current standard of care. Methods: Stage IVB ATC patients treated with multimodal therapy, followed by adjuvant pembrolizumab were studied. Data were combined from a prospective, phase 2 trial that closed early due to poor accrual, and a retrospective cohort of consecutive patients who received adjuvant pembrolizumab, mirroring the trial eligibility criteria. Patients received adjuvant pembrolizumab starting within 6 weeks after completion of radiation. An age and treatment-matched control arm treated with multimodal therapy without adjuvant pembrolizumab was selected for comparison. The primary objectives included median progression-free survival (PFS) and recurrence rate, and the secondary objective was median overall survival (OS). Results: Sixteen patients were included in each arm. The median age in both groups was 59 years. The median PDL1 score in the adjuvant pembrolizumab arm was 50% (range, 0-95%). The majority (88%) had upfront surgery in both groups. The median follow-up time was 24.3 months in the adjuvant arm and 56.7 months in the control arm. The median PFS in the adjuvant and control arm was not reached, and 5.4 months [CI: 2.04-16.20], respectively (p = 0.006; HR 0.24 [CI: 0.08, 0.73]). The median OS was not reached in the adjuvant pembrolizumab group. In the control group, the median OS was 31 months [CI: 13.9, NA] (p = 0.009; HR 0.11 [CI:

0.01, 0.83]). The 12-and 24-month survival rates were 80% [CI: 0.51-0.93] and 52% [CI: 0.25-0.74], respectively, in the control arm, whereas all patients in the adjuvant arm were still alive at 1- and 2-years. Conclusion: Adjuvant pembrolizumab appears to be a safe and effective strategy to prevent recurrences and prolong survival in stage IVB ATC patients following multimodal therapy. Confirmatory studies are needed.
PubMed-ID: 40609521
DOI: 10.1089/thy.2025.0194

All-cause mortality in patients with medullary thyroid carcinoma of different ages: an inverse L-curve analysis study.
Front Endocrinol (Lausanne), 16:1574985.
J. Chen, J. Chen, M. Zhang and Y. Hong. 2025.
BACKGROUND: Medullary thyroid carcinoma (MTC) is a malignancy with a high mortality rate and a wide age range. However, there are relatively few studies on the relationship between age and all-cause mortality in patients with MTC. As one of the important factors influencing cancer prognosis, the association between age and all-cause mortality in MTC patients needs to be further investigated. OBJECTIVE: The aim of this study was to investigate the relationship between age and all-cause mortality in MTC patients, especially whether there is an inverse L-shaped curve relationship, in order to provide new insights for clinical management and prognostic assessment. METHODS: A detailed retrospective cohort analysis of 1291 MTC patients diagnosed between 2000 and 2021 was included in this study using the Surveillance, Epidemiology, and End Results (SEER) database. Cox regression modelling, curve fitting, Kaplan-Meier (KM) survival curves and subgroup analyses were used to assess the association between age and all-cause mortality in MTC patients. Potential confounders, including patient sex, race, Summary stage, surgery, Lymph.node.dissection, tumour size and lymph node metastasis (LNM), were rigorously controlled. RESULTS: The risk of all-cause mortality in MTC patients increased by 6% per 1-year increase in age (hazard ratio HR=1.06, 95% confidence interval CI: 1.05-1.06, p<0.001). Further analysis revealed a significant inverse L-shaped relationship between age and all-cause mortality in MTC patients. Specifically, before the age of 50 years, the hazard ratio increased slowly with age (HR=1.024, 95% CI: 0.991-1.059) and the difference was not statistically significant (p=0.1616). After the age of 50 years, the hazard ratio accelerated with increasing age (HR=1.066, 95% CI: 1.051-1.081) and the difference was statistically significant (p<0.001). CONCLUSION: The results of this study confirm that there is an inverse L-shaped relationship between age and all-cause mortality in MTC patients. The risk of all-cause mortality in MTC patients increased significantly with age after age >50 years. This finding provides new insights into understanding the complex relationship between age and all-cause mortality in MTC, which may help inform clinical management and prognostic assessment.
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PMCID: PMC12185301

Long-Term Results of External Beam Radiation Therapy with or Without Concurrent Chemotherapy in Differentiated Thyroid Cancer.
Thyroid, 35(6):633-41.
J. Choi, E. Sherman, E. C. Dee, T. Treechairusame, K. Zakeri, J. J. Kang, Y. Yu, L. Chen, A. Shamseddine, S. M. McBride, N. Riaz, A. L. Ho, R. M. Tuttle, J. Fagin, M. Sabra, J. Cracchiolo, A. Shaha, R. J. Wong, R. Ghossein, N. Katabi and N. Y. Lee. 2025.
Background: A rare group of patients with differentiated thyroid cancers (DTCs) will have gross residual disease or recurrence following the standard primary therapies of surgical resection and radioactive iodine. In these patients with advanced DTC no longer amenable to further surgery, systemic, or radioactive iodine therapies, external beam radiation therapy (RT) is considered. Whether to add concurrent chemotherapy (CRT) to radiation for patients with advanced DTC remains unclear. We review the long-term follow-up of the largest single-institution experience on the use of RT alone versus CRT in advanced DTC. Methods: From 1989 to 2023, 327 patients with recurrent, gross residual, or unresected DTC were treated with RT alone or CRT. Patients with incomplete resection and/or unfavorable histology were preferentially treated with CRT. For this retrospective cohort study, locoregional control (LRC), distant metastasis-free survival (DMFS), and overall survival (OS) were evaluated using the Kaplan-Meier method. Results: CRT patients (n = 153) were 46% female and 61.6 +/- 11.7 years old versus RT alone (n = 174) were 48% female and 66.8 +/- 12.6 years old. Overall median follow-up was 109.7 months [confidence interval 100.3-123.5 months]. There were no differences in 4- and 10-year LRC, DMFS, or OS rates between groups (4-year LRC 89.0% RT alone vs. 86.6% CRT, p = 0.76; 4-year DMFS: 64.2% RT alone vs. 54.5% CRT, p = 0.08; 4-year OS: 58.5% RT alone vs. 56.9% CRT, p = 0.28). Worse grade 3+ acute dermatitis was reported with CRT (29% CRT vs. 10% RT alone, p < 0.0001). Eight patients developed a tracheoesophageal fistula (TEF), six of whom received CRT followed by tyrosine kinase inhibitor (TKI) therapy. TEF developed at a median of 7.3 months (range = 0.5-17.0

months) after TKI initiation. There were no differences in other acute toxicities, any late toxicities, rates of tracheostomy tube, percutaneous endoscopic gastrostomy (PEG) tube within 60 days of RT, or PEG tube persistence past one year. Conclusion: CRT did not demonstrate any benefit over RT alone in this retrospective study, although patients treated with CRT had worse disease. Late toxicities were similar, aside from greater TEF development after TKI therapy in CRT patients. Further research is necessary to elucidate who may benefit from CRT.
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PMCID: PMC12241838

Comparison of Progression-Free Survival in Familial Non-Medullary Thyroid Cancer and Sporadic Differentiated Thyroid Cancer Patients.
Thyroid, 35(6):642-51.
E. Chuki, N. Behairy, S. Auh, A. Makarewicz, C. N. Uttarkar Vikram, S. Kumari, P. Veeraraghavan, C. Cochran, S. Gubbi and J. Klubo-Gwiezdzinska. 2025.
Background: Familial non-medullary thyroid carcinoma (FNMTC) accounts for approximately 9% of differentiated thyroid cancer (DTC). There is conflicting data on the FNMTC aggressiveness compared with sporadic DTC (sDTC), leading to usually more extensive therapy applied for FNMTC, given its autosomal dominant genetic background. This study aimed to compare the progression-free survival (PFS) in patients with FNMTC and sDTC treated with standard therapy. Methods: This longitudinal retrospective cohort study included patients with FNMTC, defined as at least two first-degree relatives affected by DTC. FNMTC patients were matched with sDTC in a 1:3 ratio based on age, sex, American Thyroid Association recurrence risk stratification (ATA-R), extent of initial surgery, and diagnosis date. The primary outcome was PFS. Kaplan-Meier curves were used to compare PFS between the groups, and the Cox proportional hazards model was used to assess confounders. Results: From 95 affected FNMTC patients, 30 were excluded due to lack of follow-up data. The study population consisted of 65 FNMTC and 170 sDTC patients, with a median follow-up of 4.73 (2.87-10.27) years for FNMTC and 5.83 (2.33-10.79) years for sDTC ($p = 0.76$). There was 100% matching for ATA-R, sex, surgery type, and year of surgery and a satisfactory matching for age (43.12 +/- 15.11 vs. 42.76 +/- 12.46 years, $p = 0.85$). FNMTC exhibited a smaller tumor size (1.20 +/- 0.96 vs. 1.89 +/- 1.51 cm, $p < 0.01$) and fewer positive lymph nodes (range 0-13 vs. 0-38, $p = 0.009$) at presentation. The rate of repeated neck surgeries for persistent/recurrent disease was comparable between the groups: 13.8% (9/65) for FNMTC vs. 17.7% (30/170) for sDTC ($p = 0.48$). There was no difference in radioactive iodine (RAI) therapy dosage between the groups (104 [100-149] vs. 106 [76-160] mCi, $p = 0.82$). During follow-up, 15.4% of FNMTC and 18.2% of sDTC patients experienced disease progression ($p = 0.61$). PFS was non-different between groups ($p = 0.56$) and was associated with ATA-R (high vs. low hazard ratio [HR]: 9.2, confidence interval [CI]: 2.67-31.85, $p < 0.001$) and sex (male vs. female, HR: 2.5, CI: 1.11-5.6, $p = 0.026$). Conclusions: No difference in PFS between FNMTC and sDTC patients suggests comparable responsiveness to standard therapy. Therefore, the management of FNMTC should align with the standard of care for DTC to avoid overtreatment of FNMTC.
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PMCID: PMC12223381

Sexual dimorphism in thyroid cancer: evidence from preclinical studies.
Endocr Relat Cancer, 32(5)
F. Coperchini, A. Greco, P. Caccavale, I. Chiardi, L. Croce, M. Teliti, F. Magri and M. Rotondi. 2025.
Thyroid cancer (TC) exhibits strong sexual dimorphism, with higher incidence rates observed in females and more aggressive behavior in males. This disparity arises from complex interactions among genetic, hormonal and environmental factors. Data from preclinical studies evidenced a crucial role of sex hormones in driving TC prevalence and/or progression in males and females. In particular, estrogens would play a pro-tumorigenic role by directly activating estrogen receptor pathways and indirectly influencing tumorigenesis through mechanisms such as oxidative stress modulation, stimulation of thyroid stem cell proliferation, and alterations in the tumor microenvironment. Instead, androgens and androgen receptor (AR) signaling would exhibit dual roles in TC. AR downregulation in thyroid tissues is associated with increased tumor progression, whereas AR overexpression has demonstrated protective effects. These include inhibition of epithelial-to-mesenchymal transition, suppression of cell proliferation, downregulation of PD-L1 expression, and suppression of oncogenic microRNAs such as miR-146b. Conversely, androgens can promote tumor aggressiveness and metastasis in certain contexts, such as through VEGFC/VEGFR-3 signaling when a specific androgen-regulated gene is overexpressed. This review is aimed at summarizing the recent evidence coming from the literature data regarding both in vitro and in vivo studies on animal models investigating the multifaceted roles of sex hormones in TC, highlighting the critical need for

new prospective longitudinal studies, also in view of gender-affirming hormones therapy. Such research will enhance our understanding of hormonal influences across diverse populations and further explain the relationship between sexual dimorphism and TC pathogenesis.
PubMed-ID: 40197424
DOI: 10.1530/ERC-24-0348

Genetic origin of multifocal sporadic medullary thyroid cancer and C-cell hyperplasia.
Eur J Endocrinol, 192(6):737-43.
J. F. M. de Almeida, C. Romei, T. Ramone, R. Casalini, R. Ciampi, B. Fuochi, F. Signorini, C. Ugolini, V. Cappagli, L. S. Ward and R. Elisei. 2025.
OBJECTIVE: Sporadic medullary thyroid cancer (sMTC) mostly presents as a single lesion, but additional tumor foci may be present. The present study aimed to analyze the mutation profile of different tumor foci of multifocal sMTC to verify whether they represent an intra-organ metastatic dissemination or if they are independent tumors. Moreover, the genetics of C-cell hyperplasia (CCH) associated with sMTC was studied to verify whether CCH could be considered preneoplastic or reactive lesions. METHODS: Thirty-eight multifocal sMTCs and 15 sMTCs with associated CCH were included: A total of 106 tumor foci and 25 different CCH areas were studied. The mutational status was analyzed by Next-Generation Sequencing and/or droplet-digital PCR. RESULTS: Thirty-one/38 (81.6%) sMTCs had a somatic mutation in the main tumor, while 7/38 (18.4%) cases were negative. Thirty/31 (96.8%) mutated sMTCs had a single mutation, while 3 different mutations were detected in 1 case (3.2%). Twenty-eight/31 (90%) mutated sMTCs showed the same mutation profile in the main tumors and in all secondary foci, while 3 cases were discordant. Eleven/15 (73.4%) sMTC with CCH showed a somatic mutation in the main tumor, while 4 (26.6%) were negative. Only 1/11 (9%) mutated cases showed the same mutation in the main tumor and in the CCH. CONCLUSIONS: Our data demonstrate that multiple foci of sMTC share the same driver mutation as the main tumor and support the hypothesis that they are intrathyroidal metastases. Most of the CCH associated with sMTC should not be considered a preneoplastic lesion as they are negative for the mutation of the main sMTC.
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DOI: 10.1093/ejendo/lvaf109

Total thyroidectomy does not improve survival for all patients with unilateral papillary thyroid cancer exceeding 4 cm.
Am J Surg, 246:116395.
Y. Ding, Z. Feng and K. Cao. 2025.
BACKGROUND: Total thyroidectomy (TT) is recommended for papillary thyroid cancer (PTC) over 4 cm, but its universal benefit is uncertain. This study evaluates whether TT offers a significant advantage over lobectomy (LT) in improving overall survival (OS) and cancer-specific survival (CSS) for patients with unilateral PTC exceeding 4 cm. METHODS: The study included 8862 patients from the Surveillance, Epidemiology, and End Results (SEER) database (2004-2021) with unilateral PTC larger than 4 cm. The relationship between age and survival was assessed using the restricted cubic splines (RCS) model. The effects of LT and TT on OS and CSS across age groups were analyzed using Cox regression and Kaplan-Meier (KM) methods, with and without age stratification. Propensity score matching (PSM) and sensitivity analyses were conducted to assess the robustness of the results. RESULTS: TT did not improve OS (P = 0.888) or CSS (P = 0.907) compared to LT in the overall cohort. However, TT significantly improved OS (HR = 0.54, P = 0.004) and CSS (HR = 0.55, P = 0.018) in high-risk patients (T4, N1, or M1 stage), but not in low-risk patients. Age-stratified analysis showed TT benefited only young (18-55 years) high-risk patients, enhancing OS (HR = 0.29, P = 0.001) and CSS (HR = 0.35, P = 0.035). Older patients did not gain significant survival advantages from TT, regardless of risk status. These results were consistent in the PSM and sensitivity analyses. CONCLUSIONS: TT may not be the best approach for all unilateral PTC patients over 4 cm in terms of OS and CSS. It improves survival outcomes in young patients with advanced TNM stages but does not confer a significant OS or CSS advantage over LT for older or low-risk patients.
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DOI: 10.1016/j.amjsurg.2025.116395

Higher Distressed Communities Index is associated with more aggressive features in papillary thyroid cancer.
Am J Surg, 248:116520.
J. Z. Done, A. Helbing, R. Stemme, D. Foote, J. Weller, M. Xing, L. F. Morris-Wiseman and A. Mathur. 2025.
BACKGROUND: We sought to identify associations between living in an economically distressed community and the oncologic features and mutational status of papillary thyroid cancer (PTC). METHODS: Patients with PTC were identified retrospectively. Community distress was estimated using the Distressed Communities Index (DCI). Logistic regression was

used to assess associations between DCI, oncologic features, and tumor mutational status. RESULTS: Among 1062 patients, those from "at risk" (9.6%) or "distressed" (7.1%) communities were more likely to have tumors >4 cm (aOR 2.13, 95% CI 1.15-3.95), experience disease recurrence (aOR 1.84, 95% CI 1.16-2.91), and die due to thyroid cancer (aOR 3.56, 95% CI 1.26-10.05) compared to those in "prosperous" (41.6%) communities. No associations were found between DCI and tumor mutations or multifocality. CONCLUSIONS: Patients from "distressed" communities are diagnosed with more advanced thyroid cancer with higher rates of recurrence and death despite no differences in tumor mutational profile.
PubMed-ID: 40684641
DOI: 10.1016/j.amjsurg.2025.116520

Patients' obesity is linked to prolonged thyroidectomy operative time.
Langenbecks Arch Surg, 410(1):209.
B. Eliachar and O. Ronen. 2025.
PURPOSE: Obesity is a prevalent condition with potential implications for surgical outcomes, including thyroidectomy. This study investigated the relationship between body mass index (BMI) and the duration of thyroidectomy surgery and length of hospital stay. METHOD: A retrospective analysis of patient records. Data included patient age, sex, procedure type, surgery duration, length of hospital stay, histological results, and BMI. Statistical analysis methods (t-tests, ANOVA, Spearman/Pearson correlation, linear regression) were used. Patients were categorized into groups based on BMI. The primary outcome was the relationship between BMI and surgical outcomes. The research was conducted in a tertiary care academic medical center over 7 years (2016-2022). Included were patients who underwent a thyroidectomy performed by otolaryngology residents (N = 232). RESULTS: Surgery duration was significantly prolonged in obese patients, with an average increase of 1.3 min per BMI category (p-value < 0.01), resulting in a mean difference of approximately 10 min between normal weight and obese patients. Length of hospital stay was significantly extended for overweight and obese patients compared to the non-obese group (p-value < 0.01), with an average extension of 0.9 days between normal weight and obese groups. CONCLUSIONS: Obesity is associated with prolonged thyroidectomy surgery duration and length of hospital stay. Our findings highlight the importance of considering BMI in surgical planning and resource allocation. These results can inform preoperative counseling and perioperative management of obese patients undergoing thyroidectomy. Further research is needed to investigate specific factors contributing to prolonged surgery in obese patients.
PubMed-ID: 40601052
DOI: 10.1007/s00423-025-03789-3
PMCID: PMC12222316

Multigene Detection Analysis of Multifocal Papillary Thyroid Carcinoma.
Clin Endocrinol (Oxf), 103(2):251-9.
X. Fang, P. Luo, Z. Kai, P. Li, X. Chen and J. Huang. 2025.
OBJECTIVE: To analyze the relationship between clinical characteristics and pathogenic gene mutations in multifocal papillary thyroid carcinoma (MPTC) and to investigate the proportion of independent primary tumors (IP) versus intrathyroidal metastases (ITM) in MPTC. Additionally, to explore the correlation between specific gene mutations and clinical features such as multifocality, tumor size, and lymph node metastasis. METHODS: Patients with multifocal thyroid tumor meeting inclusion criteria were consecutively enrolled. Two lesions per case were selected for preoperative ultrasound-guided fine-needle aspiration biopsy (FNAB). All lesions were pathologically confirmed as papillary thyroid carcinoma postoperatively. FNAB samples were subjected to multi-gene panel testing and classified into three groups based on mutational profiles of 26 thyroid-related genes: (1) identical mutations in both lesions (intrathyroidal metastasis), (2) completely discordant mutations (independent primary tumors), and (3) shared mutations with an additional mutation in one lesion (uncertain origin). RESULTS: Among 58 initially enrolled MPTC patients, 8 were excluded due to noncompliant specimens. The final cohort included 50 patients (37 females, 13 males) with a mean age of 42.64 +/- 11.12 years. The median tumor diameter was 12.5 (IQR: 7.6, 20.0) mm, with 38.0% (19/50) classified as papillary thyroid microcarcinoma. A total of 128 mutations, 4 gene fusions, and 3 gene amplifications were detected across 100 qualified FNAB samples. BRAF V600E was the most prevalent mutation (84.0%, 84/100), followed by DICER1 (7.0%), PTEN (6.0%), and RET (4.0%). Identical mutational profiles (intrathyroidal metastasis) were observed in 64.0% (32/50) of cases, while 18.0% (9/50) exhibited completely discordant mutations (independent primary tumor). The remaining 18.0% (9/50) showed shared mutations with an additional mutation, predominantly in smaller lesions. The incidence of completely different mutations in ipsilateral lesions and bilateral lesions was different (p = 0.030). No significant correlation between BRAF V600E and clinical characteristics such as tumor size, multifocality, capsular invasion or lymph node metastasis (p > 0.05). CONCLUSION: Multi-gene panel testing of preoperative FNAB samples effectively discriminates clonal relationships in MPTC, revealing distinct molecular profiles between ITM and IP. The high prevalence of BRAF V600E mutations and

frequent clonal homogeneity underscore the necessity of comprehensive genetic profiling to guide personalized management. Routine multi-lesion sampling is advocated for optimizing risk stratification and surgical decision-making.
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DOI: 10.1111/cen.15251

Thyroid Diseases in Patients With Pituitary Neuroendocrine Tumours.
Clin Endocrinol (Oxf), 103(2):209-15.
N. Fengjuan, M. Chengzhi and Y. Shengyuan. 2025.
BACKGROUND: Due to the hypothalamic-pituitary-thyroid axis, thyroid disease is often associated with pituitary neuroendocrine tumours (PitNETs). However, the associations across different PitNETs subtypes remain underexplored. This study investigates the characteristics of thyroid disease in patients with different PitNETs subtypes and evaluates the impact of PitNETs treatment on thyroid disease. METHODS: A retrospective analysis was conducted on 168 patients with PitNETs who were categorised into 3 groups: GH (n = 53), PRL (n = 65) and NF (n = 50). All patients underwent thyroid ultrasonography, pituitary tests and thyroid function tests before treatment and 1 year after treatment. RESULTS: Thyroid volume was significantly larger in the GH group (30.78 +/- 7.87 mL, p < 0.01). The incidence of thyroid goitre and nodules was markedly higher in the GH group (73.58%, p < 0.01; 54.17%, p < 0.01), with a significantly higher proportion of multiple thyroid nodules in the GH group (79.31%, p < 0.01). Autoimmune thyroiditis was more common in PRL group (18.46%, p = 0.04), associated with elevated TPOAb (169.63 +/- 325.28 IU/mL, p = 0.02) and TGAb antibody levels (236.23 +/- 379.91 IU/mL, p = 0.02). One-year postoperative follow-up, the postoperative thyroid volume decreased from 23.45 +/- 8.99 mL to 20.42 +/- 6.48 mL (p < 0.01). The incidence of thyroid goiter decreased from 36.90% to 13.10% (p < 0.01). In patients with autoimmune thyroiditis, TPOAb and TGAb levels decreased significantly after treatment (p = 0.01, p < 0.01, respectively). CONCLUSION: Increased thyroid volume, goiter and multiple nodules are prevalent in GH-PitNETs patients, while autoimmune thyroiditis predominates in PRL-PitNETs. Treatment of PitNETs alleviates these thyroid manifestations. Routine thyroid ultrasound monitoring is recommended for PitNETs patients.
PubMed-ID: 40269579
DOI: 10.1111/cen.15256

Thyroid-stimulating immunoglobulin is not associated with aggressive clinicopathologic features in concomitant Graves' disease and papillary thyroid cancer.
Am J Surg, 247:116487.
B. M. Finnerty, T. Marshall, C. A. Annesi, R. Zarnegar, T. J. Fahey, 3rd, K. Long, F. T. Drake and T. Beninato. 2025.
BACKGROUND: Graves' disease has been associated with increased tumor aggressiveness in differentiated thyroid carcinoma, however, its correlation with thyroid stimulating immunoglobulin (TSI) remains unclear. METHODS: A tri-institutional retrospective review of 96 thyroidectomy patients with Graves' disease and papillary thyroid carcinoma (PTC) was performed (2002-2020). Clinicopathologic features and recurrence were compared based on TSI level. RESULTS: ATA risk stratification distribution was low (72.9 %), intermediate (14.6 %), and high (12.5 %). Recurrence rate was 11.5 % with median follow-up of 3.2 years. TSI was not associated with high-risk clinicopathologic features at its 50 % and 75 % quartiles. There was no difference in median TSI between patients with recurrence versus no recurrence [212 (IQR 98-361) vs. 327 (IQR 152-461), p = 0.148]. TSI was not associated with recurrence on univariable Cox regression, even when excluding microcarcinomas. CONCLUSIONS: In this majority low-risk PTC cohort with concomitant Graves' disease, TSI level is not associated with aggressive clinicopathologic features or recurrence.
PubMed-ID: 40544641
DOI: 10.1016/j.amjsurg.2025.116487

Response to Kakudo et al.: "High Rates of Unnecessary Surgery for Indeterminate Thyroid Nodules in the Absence of Molecular Test and the Cost-Effectiveness of Utilizing Molecular Test in an Asian Population: A Decision Analysis".
Thyroid, 35(5):597-8.
M. H. M. Fung, C. Tang, G. W. Kwok, T. H. Chan, Y. Luk, D. T. W. Lui, C. K. H. Wong and B. H. H. Lang. 2025.
PubMed-ID: 40296849
DOI: 10.1089/thy.2025.0150

Effectiveness of parathyroid autotransplantation during total thyroidectomy and functional recovery post-operation: A retrospective study.
Eur J Surg Oncol, 51(7):110007.
G. Ge, Y. Lu, H. Huang, Z. Kuang, H. Zhao, Y. Cao, Y. Xia and X. Li. 2025.

INTRODUCTION: Thyroid carcinoma is the most common endocrine malignancy, with total thyroidectomy being a standard treatment. However, this procedure carries a risk of hypoparathyroidism. Parathyroid autotransplantation (PAT) is recommended to prevent postoperative hypoparathyroidism, though its effectiveness and the recovery of parathyroid function remain poorly understood. METHODS: A retrospective study was conducted on patients who underwent total thyroidectomy with four-gland PAT at Peking Union Medical College Hospital between April 2012 and February 2024. Exclusion criteria included postoperative serum calcium levels >2.11 mmol/L without supplementation within 48 h and inadequate follow-up. Preoperative and postoperative serum calcium and parathyroid hormone (PTH) levels were analysed at multiple time points to assess parathyroid function recovery and the effectiveness of PAT. Patients were divided into an immediate transplantation group and a non-immediate transplantation group based on the timing of parathyroid gland transplantation. Serum calcium levels were compared between the groups at various time points. RESULTS: This study included 142 patients. Compared with preoperative levels, the mean of serum calcium and PTH levels significantly decreased at 24 h, 48 h and 1week postoperatively. From 1 month post-surgery serum calcium and PTH levels showed no significant difference compared with preoperative levels. The immediate transplantation group had higher serum calcium levels within the first month compared to the non-immediate group, but no significant difference was observed at later time points. Permanent hypoparathyroidism occurred in 1.4 % (2/142) of patients. CONCLUSION: PAT is effectively restores and maintains parathyroid function following total thyroidectomy. Functional recovery begins 1 week post-PAT and is complete in 1 month with stable function thereafter. Minimising in vitro parathyroid gland manipulation and performing PAT immediately can enhance early recovery of parathyroid function.
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DOI: 10.1016/j.ejso.2025.110007

Active Surveillance for Low-Risk Papillary Thyroid Microcarcinoma in China: A Prospective Study on Progression, Influencing Factors, and Cost-Effectiveness.
World J Surg, 49(5):1246-53.
Y. Ge, B. Zheng, C. Li, J. Zhou, J. Tong, L. Ye and Y. He. 2025.
BACKGROUND: The rising detection rate of papillary thyroid microcarcinoma (PTMC) necessitates effective management strategies to prevent overtreatment. Active surveillance (AS) has emerged as a potential solution; however, its applicability and cost-effectiveness within China's healthcare system need further investigation. This study aims to evaluate the feasibility and economic benefits of AS for Chinese patients with PTMC. METHODS: This prospective study enrolled 145 PTMC patients at Ruijin Hospital, Shanghai. We analyzed progression risk factors and compared 5-year medical costs between AS and immediate surgery (IS), employing SPSS 26 and R for Kaplan-Meier and COX survival analyses. RESULTS: Among the 145 participants, 105 completed the study. According to the Kaplan-Meier analysis, the cumulative progression rate in our study was 13% (95% CI: 0.05-0.20) over 35 months. Among these patients, 26 underwent surgery, and a higher lymph node metastasis rate was observed in patients with disease progression (61.5%) compared to those without progression (7.7%). Risk factors for PTMC progression included calcification, age, and tumor size. Economically, AS was theoretically more cost-effective than IS. The medical expense of IS with subsequent 5 years follow-up was approximately 6 times higher than that of a 5-year regimen of AS. CONCLUSIONS: AS is a cost-effective option for managing low-risk PTMC in China. High resolution ultrasonography allowed to detect disease progression. Patients younger than 40 years, the presence of initial tumor microcalcifications, and tumor size exceeding 7 mm were significantly associated with disease progression. Further validation of these findings is needed with larger sample sizes.
PubMed-ID: 40148245
DOI: 10.1002/wjs.12551

Tiered approach to molecular testing of thyroid fine needle aspiration samples may improve preoperative diagnosis.
Eur J Surg Oncol, 51(9):110082.
N. George, S. Chu, S. Manning, K. Z. Lim, M. Mond, E. Tay, B. Yellapu, K. Jones, A. Fellowes, B. Kumar, J. Serpell, S. Grodski, M. Shackleton, C. K. Yannakou and J. C. Lee. 2025.
BACKGROUND: Patients with indeterminate thyroid nodules continue to be a challenge to clinicians. Molecular testing on fine needle aspirates (FNA) is well established in the United States, but its access is limited elsewhere. We aimed to explore the utility of a pre-existing Next Generation Sequencing (NGS) platform, and the role of BRAF mutation in patient selection for preoperative molecular testing. METHODS: Patients were recruited from the Monash University Endocrine Surgery Database for BRAF immunohistochemistry status on histopathological samples; and prospectively for NGS testing of preoperative FNA samples, using the Archer DX VariantPlex (31 genes) and FusionPlex (40 genes) Comprehensive Thyroid and Lung panels. RESULTS: The mean age of 90 patients (103 nodules) for NGS testing was 53, with 58 % female. Most of the nodules (n = 72, 70 %) had indeterminate cytology. Histology showed malignancy in 52 (50 %) nodules; of

these, 45 had pathogenic DNA mutations and 3 had pathogenic RNA fusions on NGS testing of needle aspirates. The NGS panels were able to detect malignancy in indeterminate nodules with 75 % sensitivity, 85 % specificity, 80 % positive predictive value, and 81 % negative predictive value. 74 % of the papillary thyroid cancer population had BRAF mutations on immunohistochemistry, which showed 88 % concordance with the NGS results. CONCLUSION: This is the first Australian study to demonstrate that pre-existing, non-proprietary NGS mutation and fusion panels can achieve high diagnostic specificity and positive predictive value for malignancy in indeterminate thyroid nodules. Furthermore, we propose exploration of using BRAF V600E testing to select patients for full NGS analysis.
PubMed-ID: 40614342
DOI: 10.1016/j.ejso.2025.110082

A short review of current knowledge regarding long-term treatment of Graves' disease with antithyroid drugs.
Hormones (Athens), 24(2):347-58.
I. Giordani and G. P. Sykiotis. 2025.
Graves' disease is the most common form of hyperthyroidism, especially in younger people. Current European guidelines recommend antithyroid drugs as initial treatment for a period limited to 12-18 months. Definitive treatment such as surgery or radioactive iodine is proposed in the case of contraindication to antithyroid drugs or in the case of recurrence after medical treatment. However, more recent studies show that long-term antithyroid treatment is associated with reduced risk of recurrence without an increase in adverse effects. Such data support the option of long-term treatment of Graves' disease with antithyroid drugs and suggest the necessity for a change to long-standing practices in the field. Herein, after reviewing some general knowledge on Graves' disease treatment, we discuss the evidence regarding long-term treatment of Graves' disease with antithyroid drugs for endocrinologists, internists, and other specialists involved in the management of these patients. We consider the main studies in the field, outline their respective strengths and limitations, and, finally, present our opinion on when, in the light of this new evidence, endocrinologists should consider long-term treatment with antithyroid drugs.
PubMed-ID: 39636385
DOI: 10.1007/s42000-024-00618-y
PMCID: PMC12339586

Data-driven Thyroglobulin Cutoffs for Low- and Intermediate-risk Thyroid Cancer Follow-up: ITCO Real-world Analysis.
J Clin Endocrinol Metab, 110(5):e1377-e84.
G. Grani, S. D'Elia, E. Puxeddu, S. Morelli, E. Arvat, A. Nervo, G. Spiazzi, N. Rolli, M. C. Zatelli, M. R. Ambrosio, G. Ceresini, M. Marina, C. Mele, G. Aimaretti, M. G. Santaguida, C. Virili, A. Crescenzi, A. Palermo, R. Rossetto Giaccherino, L. Meomartino, M. G. Castagna, F. Maino, M. Trevisan, S. De Leo, M. G. Chiofalo, L. Pezzullo, C. Sparano, L. Petrone, G. Di Dalmazi, G. Napolitano, D. Tumino, U. Crocetti, F. Bertagna, M. Deandrea, A. Antonelli, C. Mian, A. Carbone, S. Monti, T. Porcelli, G. Brigante, D. Barbaro, M. Alfo, U. Ferraro Petrillo, S. Filetti and C. Durante. 2025.
CONTEXT: The utility of thyroglobulin (Tg) in the follow-up of patients with differentiated thyroid cancer has been well-documented. Although third-generation immunoassays have improved accuracy, limitations persist (interfering anti-Tg antibodies and measurement variability). Evolving treatment strategies require a reevaluation of Tg thresholds for optimal patient management. OBJECTIVE: To assess the performance of serum Tg testing in 2 populations: patients receiving total thyroidectomy and radioiodine remnant ablation (RRA) or treated with thyroidectomy alone. DESIGN: Prospective observational study. SETTING: Centers contributing to the Italian Thyroid Cancer Observatory database. PATIENTS: We included 540 patients with 5 years of follow-up and negative anti-Tg antibodies. INTERVENTIONS: Serum Tg levels assessed at 1-year follow-up visit. MAIN OUTCOME MEASURE: Detection of structural disease within 5 years of follow-up. RESULTS: After excluding 26 patients with structural disease detected at any time point, the median Tg did not differ between patients treated with or without radioiodine. Data-driven Tg thresholds were established based on the 97th percentile of Tg levels in disease-free individuals: 1.97 ng/mL for patients undergoing thyroidectomy alone (lower than proposed by the Memorial Sloan Kettering Cancer Center protocol and ESMO Guidelines, yet demonstrating good predictive ability, with a negative predictive value of 98% and 0.84 ng/mL for patients receiving postsurgical RRA. High sensitivity and negative predictive value supported the potential of these thresholds in excluding structural disease. CONCLUSION: This real-world study provides evidence for the continued reliability of 1-year serum Tg levels. The data-driven Tg thresholds proposed offer valuable insights for clinical decision-making in patients undergoing total thyroidectomy with or without RRA.
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PMCID: PMC12012673

Trends in incidence, mortality, and conditional survival of anaplastic thyroid cancer over the last two decades in the USA.

Front Endocrinol (Lausanne), 16:1585679.

H. Guo, J. Zhang, Y. Jia, Z. Liu, Y. Qi, C. Sun, Z. Cai and J. Wu. 2025.

BACKGROUND: Anaplastic thyroid carcinoma (ATC) is a highly aggressive malignancy, and there is currently a lack of up-to-date epidemiological data. Traditional survival analysis fails to capture the dynamic changes in prognosis for long-term survivors, while conditional survival (CS) analysis, a critical tool for adaptive risk stratification, remains underexplored in ATC. METHODS: Patients diagnosed with ATC between 2000 and 2021 were identified from the Surveillance, Epidemiology, and End Results (SEER) database. Temporal trends in age-adjusted incidence and incidence-based mortality were analyzed using Joinpoint regression to calculate annual percentage changes (APCs) with 95% confidence intervals (CIs). Overall survival (OS) was estimated using the Kaplan-Meier method. CS rates were calculated using the formula: CS(y/x) = OS(y+x)/OS(x). Prognostic factors were identified using Best Subset Regression (BSR), LASSO, and univariate and multivariate Cox regression analyses, and these factors were incorporated into a CS-nomogram model. The predictive performance of the model was validated using evaluation metrics, including the area under the receiver operating characteristic curve (AUC). Point values were assigned to the model's predictive factors, and a risk stratification system was developed based on the optimal threshold of the total score. RESULTS: From 2000 to 2021, the age-adjusted incidence of ATC increased from 0.066 to 0.077 per 100,000 (APC: 2.308%, 95% CI: 1.187-3.441), peaking at 0.119 in 2018. Mortality trends paralleled this rise, with age-adjusted mortality increasing from 0.037 to 0.051 per 100,000 (APC: 2.380%, 95% CI: 1.129-3.646). CS analysis demonstrated a progressive increase in survival rates over time, with the 24-month cumulative survival rate rising from 14.0% to 93.8%, with the most pronounced temporal changes observed in patients with distant disease. Prognostic factors identified through BSR, LASSO, and Cox regression included age, SEER stage, and treatment. A novel CS-nomogram was successfully developed and validated for dynamic real-time survival prediction, enabling identification of high- and low-risk patient groups. CONCLUSION: The incidence and incidence-based mortality of ATC have increased over the past few decades. The CS rates of ATC patients have dynamically improved over time. The CS-nomogram, integrating age, SEER stage, and treatment, provides clinicians with a personalized, dynamic, and real-time survival prediction tool that helps alleviate survivors' psychological distress, reduces anxiety, and optimizes precision follow-up strategies.

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A Deep Learning-Based Artificial Intelligence Model Assisting Thyroid Nodule Diagnosis and Management: Pilot Results for Evaluating Thyroid Malignancy in Pediatric Cohorts.

Thyroid, 35(6):652-61.

E. J. Ha, J. H. Lee, N. Mak, A. K. Duh, E. Tong, K. W. Yeom and K. D. Meister. 2025.

Purpose: Artificial intelligence (AI) models have shown promise in predicting malignant thyroid nodules in adults; however, research on deep learning (DL) for pediatric cases is limited. We evaluated the applicability of a DL-based model for assessing thyroid nodules in children. Methods: We retrospectively identified two pediatric cohorts (n = 128; mean age 15.5 +/- 2.4 years; 103 girls) who had thyroid nodule ultrasonography (US) with histological confirmation at two institutions. The AI-Thyroid DL model, originally trained on adult data, was tested on pediatric nodules in three scenarios axial US images, longitudinal US images, and both. We conducted a subgroup analysis based on the two pediatric cohorts and age groups (>/=14 years vs. < 14 years) and compared the model's performance with radiologist interpretations using the Thyroid Imaging Reporting and Data System (TIRADS). Results: Out of 156 nodules analyzed, 47 (30.1%) were malignant. AI-Thyroid demonstrated respective area under the receiver operating characteristic (AUROC), sensitivity, and specificity values of 0.913-0.929, 78.7-89.4%, and 79.8-91.7%, respectively. The AUROC values did not significantly differ across the image planes (all $p > 0.05$) and between the two pediatric cohorts ($p = 0.804$). No significant differences were observed between age groups in terms of sensitivity and specificity (all $p > 0.05$) while the AUROC values were higher for patients aged <14 years compared to those aged >/=14 years (all $p < 0.01$). AI-Thyroid yielded the highest AUROC values, followed by ACR-TIRADS and K-TIRADS ($p = 0.016$ and $p < 0.001$, respectively). Conclusion: AI-Thyroid demonstrated high performance in diagnosing pediatric thyroid cancer. Future research should focus on optimizing AI-Thyroid for pediatric use and exploring its role alongside tissue sampling in clinical practice.

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DOI: 10.1089/thy.2024.0627

Practice-changing evidence for low-risk differentiated thyroid cancer.
Lancet, 406(10498):5-6.
D. M. Hartl. 2025.
PubMed-ID: 40543517
DOI: 10.1016/S0140-6736(25)00781-0

Letter to editor: Clinical performance of a machine learning-based model for detecting lymph node metastasis in papillary thyroid carcinoma: a multicenter study.
Int J Surg,
D. He and S. Jie. 2025.
PubMed-ID: 40679989
DOI: 10.1097/JS9.0000000000002949

Limited value of genetic profiling in guiding radioiodine therapy for metastatic differentiated thyroid cancer.
Endocr Relat Cancer, 32(5)
Z. He, C. Wang, C. Liu, K. Zhang, J. Wang, X. Wang, Y. Zhang and L. Chen. 2025.
Assessing the 131I-avidity of metastatic differentiated thyroid cancer (mDTC) is pivotal to characterizing the nature of disease and optimizing the therapeutic strategy. In this prospective study, the predictive value of genetic profiling of 18 selected thyroid cancer-relevant genes for 131I-avidity and the response to radioiodine therapy (RT) was studied in comparison with those of diagnostic 131I scan. During univariate analysis, BRAF status (odds ratio, (OR) = 12.47, 95% confidence interval (CI): 5.03-30.89, P < 0.001) and TNM-M stage (P = 0.029) were found to be associated with 131I-avidity, but multivariate analysis identified BRAF V600E as the sole independent factor associated with the non-131I-avidity (OR = 12.98, 95% CI: 3.77-44.73, P < 0.001). The predictive values of BRAF wild-type for 131I-avidity and BRAF V600E for non-131I-avidity were 84.6 and 69.4%, respectively, both lower than those of diagnostic 131I scan (positive predictive value of 100%, P = 0.031; negative predictive value of 81.1%, P = 0.219). The predictive value of BRAF V600E for non-131I-avidity was not significantly improved when combined with TERT promoter mutation (76.9 vs 69.4%, P = 0.736). Moreover, the predictive value of BRAF V600E for biochemical non-response was 70.8% (17/24), while no correlation was found between BRAF status and structural response. In contrast, a negative diagnostic 131I scan was significantly associated with both biochemical and structural non-responses, with predictive values of 81 and 100%, respectively. The current study demonstrated that genetic profiling is of limited value in guiding RT for mDTC, while a diagnostic 131I scan proved superior in this respect.
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Thyroid volume-new reference values for defining thyroid enlargement.
Eur J Endocrinol, 192(6):728-36.
T. Ittermann, A. Angelow, J. F. Chenot, H. Volzke, M. Heier, B. Linkohr, A. Peters, C. Meisinger and S. Kiel. 2025.
OBJECTIVE: Upper reference values for thyroid volume are 25 mL for men and 18 mL for women. Thyroid volume alters with age, body weight, body height, and iodine status, which is not considered in the current limits. The aim was to develop reference equations, considering age, body weight, and height to calculate individual reference values for thyroid volume. DESIGN: This cross-sectional study used data from 3 independent cohorts (SHIP-START, SHIP-TREND, and KORA-F4) in Germany. SHIP-START-0, a population-based health survey, was carried out in Northern Germany, from 1997 to 2001. SHIP-TREND-0, a second independent sample of the same study region, was carried out between 2008 and 2012. KORA-F4, a population-based health survey, was conducted between 2006 and 2008 in Southern Germany. METHODS: A total of 11 549 individuals (51% women) were included in the data analysis. Eight thousand six-hundred and six individuals (45% women) were used as the thyroid-healthy reference population when developing equations. Sex-stratified quantile regression models for the 95th percentile using age, body weight, and height as explanatory variables were performed. RESULTS: The overall reference value was 38.7 mL for men and 28.6 mL for women. According to the established cut-offs, 34% of the overall population would have had goitre compared with 7% when using our equations. CONCLUSION: Upper reference values for thyroid volume are too low for an adult, previously iodine-deficient population and do not consider age, body weight, and height. Using individualised equations reduces the prevalence of thyroid enlargement substantially and can lead to a decrease in overdiagnoses and the use of medical resources.
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Shear wave elastography combined with high-frequency ultrasound for predicting the presence of occult carcinoma contralateral to unilateral papillary thyroid cancer.
Surg Oncol, 62:102267.
S. N. Jia, D. Wang, Z. X. Zhao and T. T. Xue. 2025.
OBJECTIVE: To investigate the correlation between high-frequency ultrasound (US) signs and shear wave elastography (SWE) parameters of papillary thyroid carcinoma (PTC) in a unilateral lobe and the contralateral lobe occult PTC, and to evaluate the value of SWE in combination with high-frequency US in predicting contralateral occult carcinoma of the thyroid gland preoperatively, to provide clinicians with assistance in the selection of preoperative surgical approaches. METHODS: We collected a total of 552 preoperatively diagnosed patients with unilateral thyroid carcinoma and postoperatively pathologically confirmed PTC. High-frequency US and SWE were performed before surgery. Based on the pathologic findings, they were divided into the contralateral occult PTC positive group and the negative group. To investigate the association between the ultrasonographic features of unilateral PTC and the presence of contralateral occult carcinoma by univariate and multivariate analyses, and comparing the accuracy of high-frequency US alone, SWE alone, and SWE combined with high-frequency US in predicting contralateral occult PTC. RESULTS: Univariate analysis showed that the differences between the two groups of extrathyroidal extension (ETE), ipsilateral multifocality, the combination of Hashimoto's thyroiditis (HT), the combination of lymph node metastasis, and Emax and Emean values of the primary tumors were statistically significant ($P < 0.05$). The multifactorial binary logistic regression model showed that the differences between the two groups of extrathyroidal extension, ipsilateral multifocality, lymph node metastasis, HT and high Emax value were all independent predictors of contralateral occult PTC. The ROC curve analysis showed no statistically significant difference between high-frequency ultrasound and SWE in predicting the AUC of contralateral occult PTC (0.739 vs 0.699,$P = 0.185$). The AUC for predicting contralateral occult PTC using high-frequency US combined with SWE was significantly higher than the AUC predicted using high-frequency US and SWE alone (0.794 vs 0.739, $P = 0.005$; 0.794 vs 0.699,$P < 0.001$) CONCLUSION: SWE combined with high-frequency US improves the prediction of contralateral occult PTC, and the presence of contralateral occult PTC is more likely in the presence of extrathyroidal extension of a unilateral lobe lesion of the thyroid gland, ipsilateral multifocality, metastasis to cervical lymph nodes, high Emax, and the combination of HT.
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DOI: 10.1016/j.suronc.2025.102267

Impact of positive lymph nodes and RAI therapy on survival in N1b papillary thyroid carcinoma.
Front Endocrinol (Lausanne), 16:1551075.
J. Jian, M. Wei, X. Li, Q. Xiong, J. Xiang, S. Zhao, Y. Peng and J. Huang. 2025.
BACKGROUND: Patients with N1b papillary thyroid carcinoma (PTC) was associated with a worse prognosis. The prognostic role of positive lymph nodes (PLN) and whether postoperative radioactive iodine (RAI) therapy conferred a survival benefit were debatable issues in these patients. METHODS: Data were drawn from the SEER database for PTC patients with clinical N1b disease diagnosed between 2004-2015. All patient underwent total thyroidectomy with or without RAI. Patients were categorized by age (>/=55 years and <55 years) and analyzed based on PLN. Propensity score matching (PSM) were used to balance characteristics between patients who did and did not receive RAI therapy. Overall survival (OS) was the primary outcome. Kaplan-Meier survival analysis and Cox analysis were performed. RESULTS: A total of 4343 N1b PTC patients were included, with 884 patients aged >/=55 years and 3459 patients aged <55 years. In patients aged >/=55 years, the optimal PLN cutoff for risk stratification was 8. Those with PLN >/=9 had significantly lower 5-year (83.7% vs. 90.1%), 10-year (67.4% vs. 78.8%) and 15-year (50.3% vs. 59.5%) OS rates. After adjusting, the hazard ratio for death in the PLN >/=9 group increased by 30%. After PSM, in subgroup of aged >/=55 years and PLN >/=9, the survival benefit was notable in those received RAI therapy. In contrast, for patients aged >/=55 years and PLN </=8 or aged <55 years, no survival difference was found between those received RAI and those not. CONCLUSIONS: In N1b PTC patients aged >/=55 years, PLN >/=9 predicted a poorer survival. Postoperative RAI therapy offered survival benefits for this subgroup.
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PMCID: PMC12137069

Global, regional, and national burden of thyroid cancer in women of child-bearing age, 1990 to 2021 and predictions to 2035: An analysis of the global burden of disease study 2021.
Front Endocrinol (Lausanne), 16:1555841.
T. Jiang, L. Bin, H. Liu, C. Gao and X. Liu. 2025.
BACKGROUND: Thyroid cancer has increased globally, particularly among young women, highlighting the need for

research on its epidemiological characteristics and disease burden in women of child-bearing age. This study aimed to analyze the global and regional burden of thyroid cancer from 1990 to 2021, focusing on women of child-bearing age, and to predict trends up to 2035. METHODS: This study analyzed the global and regional burden of thyroid cancer from 1990 to 2021, focusing on women of child-bearing age, using data from the Global Burden of Disease Study. Key indicators assessed included incidence, mortality, and disability-adjusted life years (DALYs) of thyroid cancer in different regions. Statistical analysis techniques were employed to compare the burden across regions and countries, examining the effects of age, sex, and socio-demographic index (SDI) on disease burden. The Bayesian Age-Period-Cohort model was used to predict the incidence, mortality, and DALYs of thyroid cancer from 2022 to 2035. RESULTS: Globally, in 2021, there were 67,558 new cases of thyroid cancer among women of child-bearing age, with 3,260 deaths and 206,508 DALYs. Compared to 1990, new cases increased by 156.86%, deaths increased by 52.33%, and DALYs increased by 61.72%. The age-standardized incidence rate (ASIR), mortality rate (ASMR), and DALYs rate (ASDR) per 100,000 population were 3.37, 0.16, and 10.38, respectively. The Estimated Annual Percentage Change (EAPC) for ASIR was 1.47, indicating an increasing trend, whereas the EAPCs for ASMR and ASDR were -0.35 and -0.05, showing decreasing trends. The burden of thyroid cancer among patients with women of child-bearing age exhibited a significant age-related trend, peaking in the 45-49 age group. There were significant regional and national variations in thyroid cancer burden, which are closely related to the SDI. By 2035, a notable increase in the incidence, mortality, and DALYs associated with thyroid cancer among women of child-bearing age has been predicted globally. CONCLUSION: Over the past 30 years, thyroid cancer incidence among women has significantly increased globally, with slightly declining mortality and DALYs rates. Significant regional and national variations are closely linked to the SDI. As the population ages and incidence continues to rise, targeted prevention and treatment strategies, particularly in low SDI regions, are crucial to effectively reduce mortality and DALYs.
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PMCID: PMC12245710

Who Is Diagnosing Pediatric Thyroid Nodules? A Tertiary Children's Hospital Review.
Otolaryngol Head Neck Surg, 173(1):251-9.
J. M. Justice, J. Sethurathnam, N. Nayak, H. Chen, K. Patel, S. Bartz, C. Baron, B. Patterson and R. H. Belcher. 2025.
OBJECTIVE: The incidence of pediatric thyroid cancer has increased. Little is documented about which providers are diagnosing pediatric thyroid nodules and how this impacts care. Our objective was to analyze how nodules are identified and how diagnosing provider type impacts nodule size and management. STUDY DESIGN: Retrospective chart review. SETTING: Tertiary care children's hospital. METHODS: Pediatric patients (aged 0-17) with at least one thyroid nodule diagnosed between 2006 and 2023 were reviewed. Diagnosing provider type, diagnostic method, nodule size, clinical management, and final diagnosis were analyzed. RESULTS: The study included 351 patients. Primary care providers diagnosed the largest proportion of nodules (43.0%), followed by incidental nodules by radiologists (24.2%). The proportion diagnosed by radiologists increased from 12% to 31% after 2017 (P < .001). Primary care providers were more likely to use physical exam than pediatric endocrinologists (65% vs 42%, P = .004), who more often used ultrasound (56% vs 37%, P = .02). Primary care providers diagnosed nodules with a median diameter of 1.50 cm, larger than that of pediatric endocrinologists and radiologists, both 0.8 cm (P = .01, P < .001). Compared to patients diagnosed by radiologists, patients diagnosed by primary care providers more often underwent biopsy (P = .02) or surgery (P < .001) and received a malignant diagnosis (P = .001). CONCLUSION: Primary care providers play a key role in detecting pediatric thyroid nodules, and a physical exam is vital in identifying significant pathology. Radiologic incidental nodules increased in frequency over our study timespan. Future research should consider the impact of socioeconomic status or geographic location on nodule size and management.
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DOI: 10.1002/ohn.1232
PMCID: PMC12207357

Letter: "High Rates of Unnecessary Surgery for Indeterminate Thyroid Nodules in the Absence of Molecular Test and the Cost-Effectiveness of Utilizing Molecular Test in an Asian Population: A Decision Analysis" by Fung et al.
Thyroid, 35(5):595-6.
K. Kakudo, A. Bychkov, J. F. Hang, M. Hirokawa, S. Keelawat, Z. Liu, R. Srinivasan and C. K. Jung. 2025.
PubMed-ID: 40130275
DOI: 10.1089/thy.2025.0072

Risk of Contralateral Central Compartment Recurrence Following Unilateral Therapeutic Neck Dissection for Papillary Thyroid Carcinoma.
J Surg Oncol, 132(4):633-9.
K. Kaminer, T. Rozenblat, I. Shavit, I. Finkel, L. Sasson, I. Shimon, D. Hirsch, G. Bachar and E. Robenshtok. 2025.
BACKGROUND AND OBJECTIVES: The utility of bilateral central compartment neck dissection (CCND) in patients with papillary thyroid carcinoma (PTC) and unilateral clinically node-positive disease remains debatable. Previous studies evaluated contralateral occult lymph-node metastases, which do not necessarily correlate with clinical recurrences. The objective of our study was to evaluate whether unilateral CCND is sufficient, specifically evaluating recurrence in the contralateral central neck. METHODS: Patients with PTC treated with total thyroidectomy and therapeutic unilateral CCND with at least 2 years of follow-up were included. RESULTS: A total of 118 patients had unilateral therapeutic CCND, 58% with lateral neck dissection, 63% female, mean age of 48.1 +/- 16.3 years. Mean follow-up was 6.2 +/- 3.9 years, tumor size 17.6 +/- 12 mm, 39% had minimal extrathyroidal extension (ETE) and 4% had gross ETE. A mean of 2.6 +/- 2.6 LN were involved in the central compartment (size 9.4 +/- 6.5 mm) and 4.4 +/- 4 involved in the lateral neck (size 24.9 +/- 14.3 mm). Recurrence on the ipsilateral side was detected in 6 patients (5%), while contralateral central compartment recurrence (the primary outcome) was detected in only 1 patient (1%). CONCLUSIONS: In patients with PTC and unilateral clinically node-positive central compartment disease, unilateral therapeutic CCND is sufficient, with only 1% risk of recurrence in the contralateral central compartment.
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DOI: 10.1002/jso.70063
PMCID: PMC12455540

Cytological Alterations of Benign Thyroid Nodules Following Radiofrequency Ablation.
Laryngoscope, 135(7):2638-44.
E. Kandil, M. H. Hussein, K. Sugumar, M. Patel, M. Russell, G. Randolph and E. A. Toraih. 2025.
BACKGROUND: Radiofrequency ablation (RFA) has emerged as a minimally invasive treatment for benign thyroid nodules. However, concerns exist about potential cytological progression following RFA. This study investigated the incidence of progression from benign (Bethesda II) to indeterminate (Bethesda III-IV) cytology and evaluated RFA's long-term efficacy and safety. METHODS: This prospective study included patients with benign thyroid nodules treated with RFA from July 2019 to December 2023. Pre- and post-ablation fine-needle aspiration (FNA) cytology results were analyzed. Treatment efficacy was assessed through nodular volume changes and thyroid function, while safety was evaluated through complication rates. RESULTS: Among 312 benign thyroid nodules treated with RFA, post-ablation FNA showed 12 cases (3.84%) progressed to Bethesda III, all confirmed benign by Afirma Gene Sequencing Classifier. Three patients underwent surgical resection due to inadequate volume reduction, with histopathology confirming benign nature. RFA achieved sustained nodular volume reduction, with a median reduction rate of 88% at 60 months. The overall complication rate was 3.2%, with no major complications requiring hospitalization. CONCLUSIONS: RFA demonstrates low risk of cytological progression and high efficacy in treating benign thyroid nodules. The significant volume reduction and favorable safety profile support RFA as a viable surgical alternative in selected patients. Future studies with larger cohorts and longer follow-up are needed to validate these findings and identify treatment success predictors.
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DOI: 10.1002/lary.32130
PMCID: PMC12230929

Communication of Voice-Related Complications in Thyroidectomy: A Qualitative Analysis.
Otolaryngol Head Neck Surg, 172(5):1560-9.
D. D. Kao, C. B. Jensen, E. Bacon, N. D. Hogikyan, B. R. Roman and S. C. Pitt. 2025.
OBJECTIVE: This study aims to characterize patient-surgeon discussions of voice-related complications during thyroidectomy for low-risk thyroid cancer. STUDY DESIGN: A qualitative study. SETTING: Three academic medical centers. METHODS: Pre-operative clinic visits between 14 surgeons (6 otolaryngologists and 8 endocrine surgeons) and 49 patients with low-risk (cT1-2, N0) thyroid cancer were audio-recorded and transcribed. Qualitative analysis was used to evaluate surgeon counseling strategies and patient concerns related to voice. RESULTS: Patients aged from 20 to 77 years old were predominantly female (77.6%) and white (89.9%). Surgeons presented risk with negative framing and numerical percentages (1%-4%) and/or qualified the risk as "low" or "small" for a lobectomy, but a "much bigger deal" for bilateral nerve injury in total thyroidectomy. At a minimum, surgeons referred to voice dysfunction as "voice change." Some further described "hoarseness" or the "inability to project voice." Other surgeons imitated what voice dysfunction would sound like. A few surgeons probed the importance of voice to a patient's life. One surgeon imparted that having a voice-

related complication "can be really emotional." Patients responded with varying degrees of concern about voice changes after surgery, from feeling "super concerned ... about losing [their] voice" to feeling "ok" with it "as long as [they're] around to deal with it." CONCLUSION: Significant variability exists in how surgeons describe and set expectations about voice-related complications. The degree to which patients value voice-related outcomes differed based on their occupation and hobbies, but this was tempered by their cancer diagnosis. Further research is needed to identify optimal disclosure of voice-related risks and expectations.
PubMed-ID: 39963871
DOI: 10.1002/ohn.1162
PMCID: PMC12035516

Hashimoto's thyroiditis- What's in a name?
Hormones (Athens), 24(2):389-94.
M. Khachaturov, D. G. Goulis and P. Perros. 2025.
Hashimoto's thyroiditis (HT) is the most common autoimmune endocrine disease worldwide with an annual incidence of 0.3-1.5 per 1000 people and a prevalence of 8% of the general population. At least nine terms appear in the literature denoting HT, which are used as synonyms or are terms describing disorders closely related to HT. Moreover, the definitions of HT vary, and the role of several parameters in making a diagnosis remains unclear. Furthermore, the term "thyroiditis" is often used among experts to describe the triphasic evolution in thyroid status (thyrotoxicosis, hypothyroidism, and euthyroidism) that can occur not only after some forms of HT but also in other causes of thyroid inflammation. The present work proposes novel approaches for the nomenclature problems. Firstly, we should abandon the eponym "Hashimoto" in keeping with recent trends. The void left can be replaced by the terms "autoimmune thyroiditis" or "autoimmune thyroid disease", which are already in use. In communicating among ourselves and with patients, it is imperative and good practice to provide, whenever possible, context to these terms by specifying whether they apply to thyroid status, presence or absence of goiter, thyroid autoantibodies, imaging, cytology/histology, epidemiology, or etiology. Secondly, the considerable potential harm associated with treating euthyroid people with thyroid hormones could be curtailed by avoiding testing for thyroid autoantibodies or performing thyroid imaging in asymptomatic euthyroid patients following the current guidelines and by discouraging the use of the word "disease" when the evidence is based only on results of investigations, such as positive antibodies, or imaging.
PubMed-ID: 40172784
DOI: 10.1007/s42000-025-00646-2

Subclinical Thyroid Dysfunction and Mortality in an Older, Community-Dwelling Population-Results of the PolSenior Study.
Clin Endocrinol (Oxf), 102(6):730-41.
P. Kocelak, A. J. Owczarek, M. Mossakowska, M. Puzianowska-Kuznicka, M. Bolanowski, M. Olszanecka-Glinianowicz and J. Chudek. 2025.
OBJECTIVE: There is limited data concerning the effect of untreated subclinical thyroid disorders on mortality in older adults. Therefore, this study aimed to analyze 5-year overall mortality among participants in the PolSenior study with treated and untreated subclinical thyroid dysfunction. DESIGN AND METHODS: The study group consisted of 407 participants with thyroid disorders (305 with hypothyroidism and 102 with hyperthyroidism) and 2776 euthyroid individuals aged 65 years and older. Overall mortality risk factors were assessed with Cox proportional hazard regression. Additionally, overall survival analyses were performed with Kaplan–Meier estimates stratified by sex and hypo-/hyperthyroidism status. RESULTS: In women, there was no difference in survival between the euthyroid and hypothyroid groups. Survival was significantly worse in patients with subclinical hyperthyroidism than in euthyroid and treated hyperthyroidism patients. In men, there were no differences in survival between the hyperthyroidism group and the subclinical hypothyroidism or euthyroid group. Notably, survival was better in the treated hypothyroidism group than in the euthyroid group. According to the multivariate models, subclinical hyperthyroidism appeared to be linked to a 30% reduction in survival among women (hazard ratio [HR] for mortality = 1.43; 95% CI = 0.98-2.07, p = 0.06) but not among men. CONCLUSIONS: Our study showed that women with subclinical hyperthyroidism had a higher mortality rate. At the same time, men with treated hypothyroidism had improved survival compared to those in the euthyroid group among participants aged 65 years and older during a 5-year follow-up period. Subclinical hypothyroidism did not influence the survival rates.
PubMed-ID: 39991800
DOI: 10.1111/cen.15220

Impact of microscopic margin involvement on recurrence of papillary thyroid carcinoma.
Eur J Surg Oncol, 51(9):110208.
H. Kwon, H. Kim, H. Hwang and B. I. Moon. 2025.
INTRODUCTION: A positive surgical margin (PSM) is identified in about 10 % of patients with thyroid cancer. Macroscopic PSM indicates overt residual cancer, which can cause remnant tumor regrowth or metastasis, leading to worse outcomes. However, most patients with PSM have only microscopic margin involvement, whose prognostic implications remain unclear. This study investigated the impact of microscopic PSM on recurrence in patients with papillary thyroid carcinoma (PTC). MATERIALS AND METHODS: Between 2009 and 2023, 1495 patients who underwent total thyroidectomy for PTC were enrolled. A 1:3 propensity score matching was performed to adjust for potential confounders. The primary outcome measure was 5-year recurrence-free survival. RESULTS: A microscopic PSM was found in 68 (4.5 %) patients and was associated with larger tumor size ($p = 0.003$), extrathyroidal extension ($p < 0.001$), multifocality ($p = 0.001$), and lymph node metastasis ($p = 0.016$). After a mean follow-up of 7.7 years, 37 patients experienced disease recurrence: 6 (9.2 %) in the microscopic-PSM group and 31 (2.2 %) in the clear-margin group. The 5-year recurrence-free survival rate was significantly worse in the microscopic-PSM group (90.1 % vs. 98.2 %; $p = 0.003$). A microscopic PSM increased the risk of recurrence by approximately fivefold (hazard ratio 4.958, 95 % confidence interval 1.996-12.31) compared with a clear margin. CONCLUSION: Microscopic margin involvement was associated with an increased risk of recurrence in patients with PTC. Patients with microscopic PSM require judicious treatment and follow-up strategies.
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DOI: 10.1016/j.ejso.2025.110208

FDG-avid thyroid nodules are at a significantly increased risk of malignancy.
Am J Surg, 248:116400.
B. D. Laurie, E. Thomas, H. Nguyen, S. Ryan and D. Leong. 2025.
BACKGROUND: FDG-avid thyroid incidentalomas pose a diagnostic challenge due to their potential for malignancy. This study evaluated the malignancy rates in FDG-avid thyroid nodules, stratified by fine needle aspiration (FNA) cytology results. METHODS: A retrospective cohort study was conducted on patients with FDG-avid thyroid incidentalomas who underwent surgical resection between 2012 and 2023. The primary outcome was malignancy rates stratified by pre-operative cytology results. Logistic regression was used to assess the utility of patient age, gender and nodule size for predicting malignancy in FDG-avid thyroid incidentaloma. RESULTS: Of 258 patients included, malignancy rates stratified by cytology were: Bethesda I (15.4 %), Bethesda II(11.1 %), Bethesda III(29.1 %), Bethesda IV(34 %), Bethesda V (83.3 %), and Bethesda VI (98.3 %). The overall malignancy rate was 48.1 %, predominantly papillary thyroid carcinoma. No significant differences in malignancy were observed concerning age, gender, or nodule size. CONCLUSION: FDG-avid thyroid nodules exhibit a significantly higher risk of malignancy, particularly in Bethesda categories III to VI.
PubMed-ID: 40425430
DOI: 10.1016/j.amjsurg.2025.116400

Redifferentiation therapy in unresectable or metastatic radioactive iodine refractory thyroid cancer: an International Thyroid Oncology Group statement.
Lancet Diabetes Endocrinol, 13(6):516-27.
S. Leboulleux, L. Boucai, N. Busaidy, C. Durante, J. A. Fagin, S. Fazeli, A. G. Gianoukakis, B. R. Haugen, H. Kang, B. Konda, T. W. Laetsch, L. Locati, M. Ryder, C. Spitzweg, F. P. Worden, L. Wirth and A. Ho. 2025.
In patients with follicular cell-derived thyroid cancer that have distant metastases and no iodine uptake, redifferentiation-ie, the restoration of tumoural (131)I uptake with systemic therapy-is now possible. The use of mitogen-activated protein kinase (MAPK) inhibitors for a short period of time before the administration of high activity (131)I shows promising results with iodine uptake restoration and tumour response. Redifferentiation has been used in patients with BRAF-mutated and RAS-mutated tumours in prospective trials and in the case of patients with RET or NTRK fusions. The iodine uptake restoration ranges from 33% to 95%, and tumour response rates from 11% to 80%. There is substantial variability between trials with regards to inclusion criteria, duration of redifferentiation drug therapy, activity of radioactive iodine, and use of dosimetry. Randomised studies are missing to clearly establish the effectiveness and applicability of redifferentiation. Thus, long-term studies are needed to establish the most effective redifferentiation protocols. The objectives of this Review are to: (1) provide a comprehensive review of the available results from prospective trials and case reports, including results regarding the restoration of radioiodine uptake and treatment efficacy (morphological and biological); (2) describe the differences in redifferentiation trial design between studies and discuss their potential impact on treatment efficacy; (3) describe the implications and limitations of dosimetry; and (4) outline the key questions to be addressed in future redifferentiation trials.

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Efficacy and safety of thermal ablation for Bethesda III/IV thyroid nodules: a retrospective study.
Front Endocrinol (Lausanne), 16:1572535.
S. Li, Y. Wei, Z. L. Zhao, L. L. Peng, Y. Li and M. A. Yu. 2025.
OBJECTIVES: To evaluate the efficacy and safety of thermal ablation (TA) for the treatment of Bethesda III and IV thyroid nodules. MATERIALS AND METHODS: A retrospective analysis was conducted on 154 patients with Bethesda III (n = 82) and IV (n = 72) thyroid nodules treated with microwave or radiofrequency ablation between December 2016 and October 2023. Patients were followed for a median of 19 months. Outcomes assessed included nodule volume reduction rate (VRR), complications, and disease progression. RESULTS: The median VRR at 12 months was 97% (Bethesda III) and 88% (Bethesda IV), increasing to 100% and 96% by 36 months, respectively, with no significant differences between groups. No major complications were encountered, minor complications occurred in 4 patients (4/154, 2.6%), including 3 cases of transient hoarseness and 1 case of neck pain, resolving spontaneously. Disease progression (3/154, 1.9%) occurred in both groups, with new tumor in each group, no other disease progression occurred. CONCLUSION: Thermal ablation could be a safe, effective, and minimally invasive alternative to surgery for Bethesda III/IV thyroid nodules, achieving substantial volume reduction with minimal complications.
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PMCID: PMC12081258

A machine learning-based model for predicting recurrence in intermediate- and high-risk differentiated thyroid cancer: insights from a retrospective single-center study of 2388 patients.
Front Endocrinol (Lausanne), 16:1552479.
Y. Li, Z. Tang, A. Ren, G. Tian, J. Zhang, Y. Wang, J. Liu and J. Ming. 2025.
PURPOSE: Current guidelines provide a recognized yet broad framework for stratifying recurrence risk in differentiated thyroid cancer (DTC) patients. More precise tools are needed for intermediate- and high-risk groups. This study aims to identify recurrence-associated risk factors and develop a machine learning-based predictive model. METHODS: In this retrospective analysis, 2,388 DTC patients were randomly assigned to a training group (1,910 cases) and a validation group (478 cases). Predictive factors were identified using univariate and multivariate analyses. Six machine learning models were trained and validated, with performance evaluated through accuracy, area under the curve, and clinical utility via decision curve analysis. RESULTS: Independent risk factors for recurrence included intraglandular dissemination, total tumor size, bilateral cervical lymph node involvement, and Hashimoto's thyroiditis, while normal/elevated TSH and multifocal nodules were protective. The random forest model demonstrated the best performance (training accuracy: 0.801; validation accuracy: 0.808). A random forest-based online calculator was developed to facilitate individualized risk assessment in clinical settings. CONCLUSIONS: The random forest model effectively predicts DTC recurrence, offering a practical tool for individualized risk assessment and aiding clinical decision-making.
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DOI: 10.3389/fendo.2025.1552479
PMCID: PMC12208848

Efficacy and Safety of Thermal Ablation for Indeterminate Thyroid Nodules: A Systematic Review of the Literature and Meta-Analysis.
Thyroid, 35(7):748-62.
H. Lim, S. J. Cho, Y. Jeong, S. Y. Jeong and J. H. Baek. 2025.
Background: The management of indeterminate thyroid nodules (ITNs), classified as Bethesda III and IV, is challenging due to biopsy limitations in distinguishing benign from malignant nodules. While diagnostic lobectomy is the standard, thermal ablation (TA) is increasingly considered for patients ineligible or unwilling to undergo surgery. This systematic review and meta-analysis therefore evaluate the efficacy and safety of TA for ITNs. Methods: A comprehensive search of MEDLINE, EMBASE, and COCHRANE databases was conducted through May 11, 2025, for studies on ITNs treated with TA, with >/=12 months of follow-up and reported clinical or safety outcomes. Case reports, abstracts, and reviews were excluded. Two radiologists independently performed data extraction and quality assessment. Outcomes included volume reduction rate (VRR), regrowth, delayed surgeries, malignancy detection, and complications. The Risk of Bias for Nonrandomized Studies (RoBANS) tool was used for quality assessment. A random-effects model synthesized pooled estimates, with heterogeneity quantified by Higgins' I(2). Results: A total of 15 studies with 1149 nodules were analyzed, showing

progressive VRR increase, plateauing at 48 months. The pooled 12-month VRR was 81.0% (confidence interval: 76.0-85.9%). Hydrodissection significantly improved VRR at 6 months (p = 0.03), while larger nodules were more prone to regrowth. Major complications occurred in 1.8% (21/1149), with no reported metastasis. Regrowth and delayed surgery occurred in 2.3% (26/1149) and 0.3% (4/1149), respectively, with three malignancies upon delayed surgery. Conclusions: TA may be considered a minimally invasive alternative for ITNs who are not candidates for or decline surgery, demonstrating favorable efficacy and safety. However, study limitations, short follow-up, and residual malignancy risk necessitate careful follow-up, particularly for larger nodules. Advanced TA techniques such as hydrodissection may enhance outcomes by increasing the likelihood of complete ablation. Long-term prospective studies and randomized trials are needed to confirm TA's role in clinical practice.
PubMed-ID: 40658618
DOI: 10.1089/thy.2024.0679

DNA-PKcs inhibition as a therapeutic approach for differentiated thyroid cancer.
Endocr Relat Cancer, 32(8)
S. F. Lin, W. Y. Chen, C. Hsueh, T. C. Chou and R. J. Wong. 2025.
DNA-dependent protein kinase catalytic subunit (DNA-PKcs) is a serine-threonine protein kinase that plays critical roles in cellular processes fundamental to cancer. DNA-PKcs may be a potential target for differentiated thyroid cancer (DTC) therapy. A DNA-PKcs inhibitor, M3814, was evaluated for its use in DTC therapy. M3814 caused cytotoxicity in a dose-response fashion in four DTC cell lines (TPC1, K1, FTC-133, and FTC-238). M3814 induced cell cycle arrest at the S phase in DTC cells. M3814 monotherapy was able to repress the growth of the K1 tumor model. M3814 in combination with lenvatinib demonstrated synergism in vitro, and this combination was more effective than any single therapy in an FTC-133 xenograft model. These results reveal that M3814 has significant potential in treating DTC, singly or in drug combination.
PubMed-ID: 40689425
DOI: 10.1530/ERC-25-0031

Genomic Differences in Thyroid Cancers From Primary Sites Versus Distant Metastases in Individual Patients: A Clinical Perspective and Preliminary Report.
Head Neck, 47(7):1907-27.
Y. B. Lin, H. W. Hu, A. K. Chung, J. Y. Lu, W. C. Wu, I. H. Chiu, I. Chu, C. C. Lin, J. H. Lee, F. J. Nien, K. Y. Chen, M. H. Wu, C. N. Chen, C. W. Wang, T. C. Kuo, C. H. Lin, M. F. Cheng, W. Y. Chiu, S. W. Kuo, W. H. Hsih, C. Y. Wang, W. S. Yang, P. L. Chen and S. R. Shih. 2025.
BACKGROUND: Distant metastasis is a leading cause of thyroid cancer (TC)-related deaths. Genetic profiling is typically limited to one sample per patient due to cost and sampling-risk concerns. Differences between samples from thyroid and distant metastasis within individual patients are unclear. METHODS: Patients with TC and distant metastasis were recruited for genetic analysis. RESULTS: Using a TC-specific NGS panel, 66 specimens from 29 patients were analyzed, identifying 16 mutations and 4 fusions, including two novel fusions (FGFR2-SHTN1 and RFTN1-BRAF). Genetic alterations differed between primary and metastatic sites in nine patients (31%), predominantly in additional oncogenic alterations (89%). More genetic alterations were found at the primary site in three patients and metastatic sites in four. Distinct mutations were found in two patients. A longer time interval between specimen acquisitions was significantly associated with genetic discrepancies (p = 0.032). CONCLUSION: Patterns of genetic discrepancies between primary and metastatic TC vary, offering valuable insights for clinical practice.
PubMed-ID: 39936351
DOI: 10.1002/hed.28100

A novel deep learning model based on multimodal contrast-enhanced ultrasound dynamic video for predicting occult lymph node metastasis in papillary thyroid carcinoma.
Front Endocrinol (Lausanne), 16:1634875.
R. Liu, F. Yuan, B. Wang, W. Chen, J. Ye and Y. He. 2025.
OBJECTIVE: This study aimed to evaluate the value of constructing a multimodal deep-learning video model based on 2D ultrasound and contrast-enhanced ultrasound (CEUS) dynamic video for the preoperative prediction of OLNM in papillary thyroid carcinoma (PTC) patients. METHODS: A retrospective analysis was conducted on 396 cases of clinically lymph node-negative PTC cases with ultrasound images collected between January and September 2023. Five representative deep learning architectures were pre-trained to construct deep learning static image models (DL_image), CEUS dynamic video models (DL_CEUSvideo), and combined models (DL_combined). The area under the receiver operating characteristic

curve (AUC) was used to evaluate model performance, with comparisons made using the Delong test. A P-value of less than 0.05 was considered statistically significant. RESULTS: The DL_CEUSvideo, DL_image, and DL_combined models were successfully developed and demonstrated. The AUC values were 0.826 (95% CI: 0.771-0.881), 0.759 (95% CI: 0.690-0.828), and 0.926 (95% CI: 0.891-0.962) in the training set, and 0.701 (95% CI: 0.589-0.813), 0.624 (95% CI: 0.502-0.745), and 0.734 (95% CI: 0.627-0.842) in the test set. Finally, sensitivity, specificity, and accuracy for the DL_CEUSvideo, DL_image, and DL_combined models were 0.836, 0.671, 0.704; 0.673, 0.716, 0.707; and 0.818, 0.902, 0.886 in the training set, and 0.556, 0.775, 0.724; 0.556, 0.674, 0.647; and 0.704, 0.663, 0.672 in the test set, respectively. CONCLUSION: These results demonstrated that the multimodal deep learning dynamic video model could preoperatively predict OLNM in PTC patients. The DL_CEUSvideo model outperformed the DL_image model, while the DL_combined model significantly enhanced sensitivity without compromising specificity.
PubMed-ID: 40778281
DOI: 10.3389/fendo.2025.1634875
PMCID: PMC12329689

Clinical performance of a machine learning-based model for detecting lymph node metastasis in papillary thyroid carcinoma: A multicenter study.
Int J Surg, 111(6):4062-7.
W. Liu, J. Zheng, L. Han, W. Qu, Q. Wu, Z. Yuan, G. Jia, X. Wang, L. Ye, J. Zhang, S. Zhang, X. Cao, Y. Liu and Z. Ai. 2025.
Papillary thyroid carcinoma (PTC) is a common endocrine malignancy with a generally favorable prognosis, but lymph node metastasis (LNM) complicates treatment and increases recurrence risk. Current preoperative methods like neck ultrasound often miss LNM, leading to unnecessary surgeries. This study developed a non-invasive, artificial intelligence (AI)-driven predictive model for LNM using gene expression data from 157 PTC patients and validated it with qRT-PCR across 807 participants from multiple centers. The model focused on three key genes - RPS4Y1, PKHD1L1, and CRABP1 - chosen for their predictive strength. A random forest algorithm achieved high accuracy, with an AUROC of 0.992 in training and 0.911-0.953 in external validation. RPS4Y1 emerged as a standout predictor, showing the strongest distinction between metastatic and non-metastatic cases. The study also identified immune-related pathways, such as TGF-beta signaling and cancer-associated fibroblast activation, as critical in metastasis. This gene expression-based model offers a non-invasive, cost-effective solution for predicting LNM, providing valuable insights to guide surgical decisions and reduce unnecessary procedures, ultimately improving patient outcomes.
PubMed-ID: 40265473
DOI: 10.1097/JS9.0000000000002400
PMCID: PMC12165525

Incidence and distribution of neck node metastases in hereditary vs. sporadic medullary thyroid cancer at basal calcitonin serum levels </=100 pg/ml: 30-year experience.
Eur J Surg Oncol, 51(7):109756.
A. Machens, K. Lorenz, F. Weber and H. Dralle. 2025.
BACKGROUND: The frequency and distribution of neck node metastases are ill-defined for the growing subset of patients with hereditary and sporadic medullary thyroid cancer (MTC) who present with preoperative basal calcitonin serum levels </=100 pg/ml. METHODS: This study, evaluating 30-year data from a tertiary surgical center, aimed to provide that information. RESULTS: Included were 256 previously untreated patients with basal calcitonin levels </=100 pg/ml: 125 patients with hereditary MTC, 9 (7.2 %) of whom harbored node metastases; and 131 patients with sporadic MTC, 17 (13.0 %) of whom revealed node metastases (P = 0.150). With basal calcitonin levels </=40 pg/ml, node metastases were less frequent (5 % [5 of 97 patients] for hereditary MTC; 9 % [6 of 69 patients] for sporadic MTC) than above that mark (14 % [4 of 28 patients] for hereditary MTC; and 18 % [11 of 62 patients] for sporadic MTC). Node metastases limited to the ipsilateral lateral neck, sparing the central neck, were found in 2 (22 %) of 9 node-positive patients with hereditary MTC and 5 (29 %) of 17 node-positive patients with sporadic MTC. The lowest basal calcitonin levels associated with nodal disease were 15.7 pg/ml in a 24-year-old male non-index patient with hereditary MTC, and 14.1 pg/ml and 14.3 pg/ml in two 46- and 68-year-old female patients with sporadic MTC. CONCLUSION: Central node dissection at the time of thyroidectomy may be beneficial in experienced hands at increased basal calcitonin levels </=100 pg/ml. When preoperatively increased calcitonin levels persist after central neck dissection, exploration of the ipsilateral lateral neck may be worthwhile.
PubMed-ID: 40101681
DOI: 10.1016/j.ejso.2025.109756

Deep Learning Discovers New Morphological Features while Predicting Genetic Alterations from Histopathology of Papillary Thyroid Carcinoma.
Thyroid, 35(7):771-80.
I. Marion, S. Schulz, C. Glasner, J. N. Kather, D. Truhn, M. Eckstein, C. Mueller, A. Fernandez, S. Marquard, M. Oliver Metzig, W. Roth, M. M. Gaida, S. Strobl, D. C. Wagner, A. Schad, M. Jesinghaus, N. Hartmann, T. J. Musholt, J. I. Staubitz-Vernazza and S. Foersch. 2025.
Background: Papillary thyroid carcinoma (PTC) is the most common malignant tumor of the endocrine system. BRAF mutations occur in 40-60%, panRAS mutations in 10-15%, and different gene fusion events such as RET fusions in 7-35% of these neoplasms. Artificial intelligence (AI) methods could be used to predict genetic changes from conventional histopathological slides. Methods: In this retrospective study, we used two independent cohorts of patients with PTC, totaling 662 cases for the establishment of our AI pipeline. The Cancer Genome Atlas cohort (496 cases) served as the developmental cohort, while the Mainz cohort (166 cases) served as an independent external test cohort. BRAF, panRAS, and fusion status was determined for all of these patients as target variables. Vision Transformer was trained on digitized annotated hematoxylin and eosin-stained slides for the presence of these alterations. Highest probability image tiles were used to identify new morphological criteria associated with the genetic changes. Results: The trained model resulted in an area under the receiver operating characteristic curve of 0.882 (confidence interval 0.829-0.931) for BRAF, 0.876 (0.822-0.927) for panRAS, and 0.858 (0.801-0.912) for gene fusions. Accuracy was 79.3% (72.7-85.8%) for BRAF, 89.3% (84.2-94.0%) for panRAS, and 84.7% (78.8-90.2%) for gene fusions. The performance on the validation set was almost identical to that on the test set. Analyzing the highest predictive tiles, novel morphological criteria for fusion-associated PTC could be discovered. Conclusions: Our study demonstrates that predicting genetic alterations in digitized histopathological slides using AI is feasible in patients with PTC. Our model showed high accuracy in predicting these changes, making it potentially suitable for pre-screening. Explainability approaches uncovered previously undescribed morphological patterns associated with certain genotypes. Providing pathologists with these AI-based features could improve their accuracy. Assuming further positive prospective validation, this discovery could contribute to a deeper understanding of PTC.
PubMed-ID: 40607934
DOI: 10.1089/thy.2024.0691

Is it possible to rule out level II and level VB dissection in patients with metastatic papillary thyroid cancer?
Front Endocrinol (Lausanne), 16:1520539.
T. Matlim Ozel, S. Akbulut, A. Celik, G. Yildiz, H. Y. Barut, F. M. Dogukan and S. Sari. 2025.
BACKGROUND: The completeness of surgical resection is a key factor influencing outcomes in patients with papillary thyroid carcinoma (PTC) and regional lymph node metastases. However, the optimal extent of therapeutic lateral neck dissection remains a matter of debate This study aimed to assess the diagnostic accuracy of preoperative ultrasonography (US) in detecting lateral lymph node metastasis (LLNM) in patients with PTC and to identify clinical and pathological factors predictive of metastases at levels II and V. METHODS: This retrospective study included consecutive patients with PTC who underwent comprehensive lateral neck dissection at a single tertiary center between June 2020 and July 2024. RESULTS: In 63 patients, a total of 78 comprehensive lateral neck dissections were performed. Of the patients, 41 (65%) were male and 22 (35%) were female, with a median age of 37 years (range, 24-49 years). Lymph node metastases were identified in 46 (58.9%), at level II, 561 (78.2%) at level III, 60 (76.9%) at level IV, and 9 (11.5%) at level Vb. Metastasis to level IIb was detected in 5 dissections. Among the 9 patients with level Vb metastases, 7 (77.8%) had involvement of four different cervical levels. The specificity of US in identifying metastatic disease was notably high at both level II (80%) and level Vb (87%). Independent predictors of metastatic involvement at level II and level Vb lymph nodes was associated with extrathyroidal extension [level II: odds ratio (OR) 7.88, p=0.03; level V: OR 6.91, p=0.043] and a largest metastatic lateral lymph node size above 2 cm [level II: OR 18.58, p=0.03; level V: OR 11.32, p=0.03]. CONCLUSION: Routine dissection of level IIa is recommended in N1b PTC due to high metastasis rates. However, level IIb dissection may be omitted in selected cases given its low metastasis rate and potential morbidity, with intraoperative frozen section serving as a useful guide. Similarly, level Vb dissection may be avoided when lateral lymph nodes are <2 cm, multilevel involvement is absent, and ultrasonographic findings are negative.
PubMed-ID: 40862116
DOI: 10.3389/fendo.2025.1520539
PMCID: PMC12375478

Exploring actionable targets to address disparities in thyroid cancer survival: A study of patients with aggressive variants of papillary thyroid cancer.
Am J Surg, 248:116428.

A. J. Monreal, A. N. Eze, S. M. Thomas, K. S. Johnson, R. P. Scheri and H. S. Kazaure. 2025.
BACKGROUND: Despite compromised survival, disparities studies on aggressive variants of papillary thyroid cancer (PTC) are sparse. METHODS: Using the NCDB (2004-20), adult Non-Hispanic Whites (NHW), Non-Hispanic Asians or Pacific Islanders (NHAPI), Hispanics, and Non-Hispanic Blacks (NHB) with aggressive variants were abstracted. Mortality risk was estimated using Hazard Ratios (HR). RESULTS: NHB patients had larger tumors ($p < 0.001$) but lower thyroidectomy rates ($p = 0.04$). For all patients, cancer stage posed the strongest mortality risk (HRs Stage II-IV vs. Stage I: 2.75, 4.18, 8.04, $p < 0.001$), however, this was substantially higher by stage for NHBs (HRs Stage II-IV: 4.78, 7.57, 10.49, $p < 0.001$). Age >/=55 years was the strongest risk factor for Hispanics ($p < 0.001$); non-private insurance was the strongest risk factor for NHAPI, NHBs, and NHWs. CONCLUSION: Beyond health insurance, actionable targets to improve PTC survival vary by race/ethnicity. For NHBs, higher clinical stage and worse survival by stage might indicate compromised access to optimal care. For Hispanics, improved follow-up, particularly for patients >/=55 years, may enhance survival.
PubMed-ID: 40435539
DOI: 10.1016/j.amjsurg.2025.116428

'Curiouser and curiouser' - an invited commentary regarding FDG-avid thyroid nodules.
Am J Surg, 248:116470.
E. C. Moore. 2025.
PubMed-ID: 40544027
DOI: 10.1016/j.amjsurg.2025.116470

Postoperative and permanent hypocalcemia after indocyanine green (ICG) angiography-guided total thyroidectomy and central neck dissection: A retrospective cohort study.
Surgery, 181:109142.
P. Moreno Llorente, M. Alberich Prats, A. Garcia Barrasa, M. Pascua Sole and J. L. Munoz de Nova. 2025.
BACKGROUND: This study aimed to compare the rates of postoperative and permanent hypocalcemia between postthyroidectomy indocyanine green angiography and indocyanine green angiography-guided thyroidectomy performed intraoperatively for identification and preservation of the parathyroids. METHODS: We undertook a retrospective study of 2 cohorts of patients with thyroid cancer undergoing total thyroidectomy and central neck dissection. The first cohort (control group) included patients who underwent postthyroidectomy indocyanine green angiography to predict parathyroid function by scoring the degree of fluorescence (0, black; nonvascularized; 1, gray/heterogeneous: partially vascularized; and 2, white: well vascularized), and the second cohort (angiography-guided thyroidectomy) included patients undergoing initially indocyanine green angiography-guided thyroidectomy to identify the feeding vessels of the parathyroid glands followed by postthyroidectomy indocyanine green angiography. RESULTS: There were 54 patients (97 sides) in the control group and 43 (71 sides) in the angiography-guided thyroidectomy group. The superior glands were significantly better preserved (indocyanine green score of 2) in the angiography-guided thyroidectomy group as compared with the control group (53.7% vs 34.5%, P = .026). The final parathyroids with an indocyanine green ICG score of 2 was greater in the angiography-guided thyroidectomy group than in the control group (47.8% vs 26.6%, P = .016). Postoperative hypocalcemia was significantly more common in the control group than in the angiography-guided thyroidectomy group (31.5% vs 7.0%, P = .007) as well as permanent hypocalcemia (11.1% vs 0%, P = .032). CONCLUSION: Indocyanine green angiography-guided thyroidectomy allowing identification of the vascular supply of the parathyroid glands contributes to preserve functioning glands and to prevent postsurgical hypocalcemia.
PubMed-ID: 39884218
DOI: 10.1016/j.surg.2024.109142

Low-Dose Versus High-Dose Lenvatinib in Radioiodine Refractory Differentiated Thyroid Cancer-A Real-World Safety and Efficacy Analysis.
Clin Endocrinol (Oxf), 102(6):721-9.
J. S. Moulika, K. R. Chandekar, S. G. Ravindra, B. P. G, S. Ballal, M. Tripathi, S. Satapathy and C. Bal. 2025.
OBJECTIVE: Lenvatinib, a tyrosine kinase inhibitor, is approved for the treatment of radioiodine refractory differentiated thyroid cancer (RR-DTC) at a dose of 24 mg/day. Given its significant toxicity profile, the present study aimed to compare the safety and efficacy of initial low-dose lenvatinib to that of higher starting doses in patients with RR-DTC. METHODS: This retrospective study included patients with RR-DTC who were classified as: Group-A: patients receiving 10mg/day, and Group-B: patients receiving >/= 14mg/day of lenvatinib as starting dose. Safety, radiological response (as per RECIST 1.1) and progression-free survival (PFS) outcomes were analysed and compared. RESULTS: A total of 105 patients with RR-DTC were included in this study (Group-A: 60, Group-B: 45). The study found that Group-B experienced significantly higher

rates of drug interruptions (68.9% vs 48.3%, p = 0.035) and dose reductions (60% vs 11.7%; p < 0.001) compared to Group-A. Adverse events such as hand-foot skin reaction (77.8% vs 58.3%), diarrhea (28.9% vs 11.7%), hepatotoxicity (33.3-40% vs 11.7-18.3%), and electrolyte imbalance (15.6% vs 3.3%) were also more frequent in Group-B (p-values < 0.05). However, both groups showed similar objective response rates (47.1% vs 46.3%; p = 0.936) and comparable PFS outcomes (restricted mean survival time at 24 months: 22.8 vs 21.4 months, p = 0.128). CONCLUSIONS: The study suggests that starting with lower doses of lenvatinib, followed by dose escalation if tolerated, may offer a safer approach with significantly lower rates of drug interruptions and dose reductions, with comparable efficacy in RR-DTC patients. Further validation by larger prospective trials is warranted.
PubMed-ID: 39901765
DOI: 10.1111/cen.15214

Targeting RET in medullary thyroid cancer.
Endocr Relat Cancer, 32(8)
K. Newbold and L. Cheng. 2025.
ABSTRACT: Medullary thyroid cancer (MTC) is a rare cancer, accounting for 2-3% of all thyroid cancers. Point mutations in the RET proto-oncogene can be detected in 25-65% of MTC. These mutations commonly occur in the cysteine-rich or tyrosine kinase domains, leading to constitutively active tyrosine kinase activity in RET. In the last decade, significant advancements have been made in treating MTC with the advent of tyrosine kinase inhibitors, especially in RET-mutated MTC. Multikinase inhibitors such as vandetanib and cabozantinib were the first few effective inhibitors, which have been shown to slow disease progression in the treatment of advanced MTC. In more recent years, these have been followed by highly selective RET inhibitors selpercatinib and pralsetinib, which have made their way into the clinic, demonstrating high efficacy and a more favourable side-effect profile due to their reduction in off-target effects. In spite of these successes, there remains a continued need to develop strategies to overcome treatment resistance.
PubMed-ID: 40742350
DOI: 10.1530/ERC-24-0291

Utility of prophylactic central dissection in papillary thyroid carcinoma with clinically apparent lymph node metastases isolated to the lateral neck.
Surgery, 181:109160.
S. Ngo, T. X. Hu, C. Y. Zhu, E. G. Hughes, Y. V. Mao, M. W. Yeh, M. J. Livhits and J. X. Wu. 2025.
BACKGROUND: The utility of prophylactic ipsilateral central neck dissection in papillary thyroid carcinoma presenting with clinically/sonographically apparent lymph node metastases isolated to the lateral neck is unclear. The study assessed whether prophylactic central neck dissection was associated with improved recurrence-free survival. METHODS: Single-center retrospective cohort study of patients undergoing thyroidectomy and lateral neck dissection for initial treatment of papillary thyroid carcinoma with clinically/sonographically apparent lymph node metastases isolated to the lateral neck from 2006 to 2022. We compared patients who underwent prophylactic central neck dissection with those who did not. Primary outcome was estimated recurrence-free probability, calculated using the Kaplan-Meier method and log-rank test. RESULTS: The study cohort comprised 65 patients, 53 (81.5%) of whom received prophylactic central neck dissection in addition to total thyroidectomy and lateral neck dissection. Clinicopathologic features in the 2 groups were similar. Median follow-up was 50.2 months. The estimated 10-year recurrence-free probability was 92.5% for patients who received prophylactic central neck dissection and 66.7% for those who did not receive prophylactic central neck dissection (P = .013). Two of the 6 structural recurrences in the non-prophylactic central neck dissection group were found in the central neck and could potentially have been prevented by prophylactic central neck dissection. Patients who received prophylactic central neck dissection had a higher likelihood of achieving excellent response to therapy compared to patients who did not (59% vs 25%, P = .05). The rate of permanent hypoparathyroidism was comparable among patients who underwent prophylactic central neck dissection versus those who did not (P = .3), and no vocal cord palsy was observed in either group. CONCLUSIONS: In patients initially presenting with clinically apparent nodal metastases of papillary thyroid carcinoma isolated to the lateral neck, prophylactic central neck dissection performed concurrently with total thyroidectomy and lateral neck dissection is associated with improved recurrence-free survival and greater likelihood of excellent response to therapy.
PubMed-ID: 39938126
DOI: 10.1016/j.surg.2025.109160

A Comparison of the Predictive Value of International Medullary Thyroid Carcinoma Grading System (IMTCGS) With That of Other Risk Factors in a Chinese Medullary Thyroid Carcinoma Cohort.

Clin Endocrinol (Oxf), 102(5):589-99.
J. Ni, X. Zhang, Y. Liu and Y. Ling. 2025.
BACKGROUND: The International Medullary Thyroid Carcinoma Grading System (IMTCGS) was recently introduced in medullary thyroid carcinoma (MTC). This study aimed to assess the predictive value of the IMTCGS for disease response and survival, and compare its predictive ability with that of other traditional risk factors in a Chinese MTC cohort. METHODS: The data of 137 MTC patients undergoing initial surgery between January 2004 and June 2023 were included for analysis. Histologic features were reviewed by two pathologists. Kaplan-Meier survival analysis and Cox proportional hazard model were performed to analyse the association between risk factors (including IMTCGS high vs low grade) and progression-free survival (PFS) and disease-specific survival (DSS). ROC analysis and Delong's test were used to compare the predictive ability of IMTCGS with that of other risk factors. RESULTS: Local recurrence, distant metastasis, and disease-specific death were observed in 14/134 (10.45%), 3/134 (2.24%), and 6/137 (4.38%) MTC patients, respectively. IMTCGS, TNM stage, postoperative calcitonin, postoperative CEA, and vascular invasion were associated with PFS in Kaplan-Meier survival analysis (all $p < 0.05$). Postoperative calcitonin was the only independent predictor for PFS in multivariate analysis (HR = 1.002, $p = 0.002$). ROC analysis and Delong's test showed that postoperative calcitonin had superior predictive value for structural recurrence than IMTCGS (AUC 0.90 vs. 0.64, $p = 0.002$). IMTCGS, TNM stage, and vascular invasion were associated with DSS in Kaplan-Meier survival analysis (both $p < 0.05$). In multivariate analysis, IMTCGS was the only independent predictor for DSS (HR = 11.23, $p = 0.05$). The AUC of IMTCGS was 0.81 ($p = 0.01$) for disease-specific death. CONCLUSION: In this Chinese MTC cohort, IMTCGS was a powerful predictor of disease-specific death, while postoperative calcitonin was a powerful predictor of structural recurrence.
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DOI: 10.1111/cen.15195

Long-Term Clinical Outcomes of Patients with Differentiated Thyroid Cancer Treated with Lenvatinib: Results from Real-World Practice in Japan.
Thyroid, 35(7):781-8.
R. Onaga, T. Enokida, N. Tanaka, Y. Hoshi, T. Kishida, R. Kuboki, M. Sato, N. Takeshita, H. Tanaka, T. Fujisawa, S. Okano, H. Nishino, M. Ito and M. Tahara. 2025.
Background: Although accumulated experience with lenvatinib in patients with differentiated thyroid cancer (DTC) and progressive radioactive iodine (RAI)-refractory disease has been used to improve management strategies for this disease, findings regarding the actual clinical picture and long-term observation data are insufficient. Methods: We conducted a retrospective cohort study of patients with DTC who received lenvatinib treatment from 2011 to 2022 at the National Cancer Center Hospital East, Japan. The patients were treated under the following treatment and management policies (1) starting dose at 24 mg/day, (2) schedule modification according to individual adverse events status (planned drug holidays), (3) dose escalation of lenvatinib, and (4) local therapy at disease progression, if applicable. This is a retrospective cohort study, although some patients were enrolled in a prospective clinical trial (NCT01321554 and UMIN000022243). Results: Of 91 patients, 59 (64.8%) had papillary carcinoma and 22 (24.2%) had follicular carcinoma. Best overall response in all patients was 60.4% (partial response in 55 and complete response in 0). With a median observation period of 2.9 years (range, 0.1-12.4; interquartile range, 1.7-4.6) under supportive management, including the planned drug holidays (n = 72, 79.1%), dose escalation of lenvatinib at systemic disease progression (n = 21, 23.1%), and local therapy for oligoprogressive disease (n = 11, 12.1%), median progression-free survival and overall survival were 2.4 years (95% confidence interval [CI] 1.9-3.3) and 5.1 years (95% CI 3.3-6.7), respectively. At the time of data cutoff, 19.8% had discontinued lenvatinib treatment due to adverse events, although no adverse event was grade 5. Conclusions: In patients with RAI-refractory DTC treated with lenvatinib, careful treatment optimization and management of adverse events contribute to a favorable, durable prognosis.
PubMed-ID: 40488639
DOI: 10.1089/thy.2025.0040

Prophylactic central neck dissection in clinically node-negative papillary thyroid carcinoma: 10-year impact on surgical and oncologic outcomes.
Surgery, 181:109258.
P. Papini, L. Rossi, A. Matrone, A. De Renzis, R. Morganti, L. Valerio, C. E. Ambrosini, G. Materazzi and R. Elisei. 2025.
BACKGROUND: The role of prophylactic central compartment lymph node dissection in clinically node-negative papillary thyroid carcinoma is debated. This study presents the findings from a 10-year follow-up of a single-institution randomized controlled trial assessing the role of prophylactic central compartment lymph node dissection in clinically node-negative papillary thyroid carcinoma. METHODS: Between 2008 and 2010, a total of 196 patients with clinically node-negative

papillary thyroid carcinoma were randomly assigned to 2 groups in a 1:1 ratio to undergo total thyroidectomy (group A) or total thyroidectomy with prophylactic central compartment lymph node dissection (group B). Patients received low-dose radioactive iodine treatment (30 mCi) postoperatively, with additional doses as needed. Monitoring included serum thyroglobulin, thyroglobulin antibodies, and neck ultrasound imaging. RESULTS: At the end of the follow-up, 151 patients were analyzed, after 28 from group A and 17 from group B were excluded. The 2 groups were similar in age at diagnosis (P = .643), sex distribution (P = .735), body mass index (P = .134), ultrasound-estimated thyroid volume (P = .650), and histologic tumor features. After >10 years (12.9 +/- 2 years), no significant differences were observed in surgical and oncologic outcomes. The mean thyroglobulin levels were 0.1 +/- 0.1 ng/mL in group A and 0.3 +/- 1.3 ng/mL in group B (P = .146). Both groups showed similar findings in the need for further surgery (P = .917), for additional radioactive iodine (P = .979), and mean radioactive iodine dosage (P = .822). No difference was documented in permanent recurrent laryngeal nerve palsy (P = .640), permanent hypocalcemia (P = .238), and serum calcium level (P = .181). The only observed distinction was more parathyroid removal in prophylactic central compartment lymph node dissection cases based on histologic examination (P = .005). CONCLUSION: Prophylactic central compartment lymph node dissection does not significantly affect surgical and oncologic outcomes in patients with clinically node-negative small papillary thyroid carcinoma after long-term follow-up.
PubMed-ID: 39983243
DOI: 10.1016/j.surg.2025.109258

Impact of tumor size on oncological and surgical outcomes in robot-assisted transaxillary surgery for papillary thyroid carcinoma.
Eur J Surg Oncol, 51(11):110422.
P. Papini, L. Rossi, L. Russo, C. Becucci, A. De Palma, C. E. Ambrosini, M. Puccini and G. Materazzi. 2025.
BACKGROUND: Robot-assisted transaxillary thyroidectomy (RATT) has emerged as a remote access approach for differentiated thyroid carcinoma (DTC), yet data on its oncological efficacy for tumors larger than 3 cm, particularly in European cohorts, remain scarce. This study aimed to evaluate surgical and oncological outcomes of RATT in patients with papillary thyroid carcinoma (PTC), stratified by tumor size. MATERIALS AND METHODS: We retrospectively reviewed 270 patients with histologically confirmed PTC who underwent RATT between July 2012 and August 2022 at a single tertiary center. Patients were categorized into two groups based on tumor size: Group A (<3 cm, n = 226) and Group B (>/=3 cm, n = 44). Surgical outcomes, complication rates, and oncological parameters-including serum thyroglobulin (Tg) levels, anti-thyroglobulin antibodies, and structural recurrence-were analyzed. Subgroup analysis was conducted based on radioiodine ablation (RAI) status. RESULTS: No significant differences were observed between groups in terms of operative time, hospital stay, or postoperative complications. Tg levels after RAI were comparable between Group A and Group B (p = 0.999), indicating similar biochemical response. Only one patient experienced structural recurrence during follow-up (mean: 48 +/- 31 months). Patients who underwent lobectomy alone showed no evidence of recurrence regardless of tumor size. No independent predictors of Tg levels were identified. CONCLUSIONS: RATT appears to be a safe and oncologically effective approach for PTC, even for tumors >/=3 cm. These findings support the broader use of RATT in selected patients, with outcomes comparable across tumor sizes. Further multicenter studies with longer follow-up are warranted to validate these results.
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DOI: 10.1016/j.ejso.2025.110422

AI-based multimodal prediction of lymph node metastasis and capsular invasion in cT1N0M0 papillary thyroid carcinoma.
Front Endocrinol (Lausanne), 16:1580885.
X. Peng, P. Wu, W. Li, T. Ou-Yang, S. C. Tang, S. Zhou, H. Li, X. Song and Y. Tang. 2025.
BACKGROUND: Accurate preoperative evaluation of cT1N0M0 papillary thyroid carcinoma (PTC) is essential for guiding appropriate treatment strategies. Although ultrasound is widely used for clinical staging, it has limitations in detecting lymph node metastasis (LNM) and capsular invasion (CI), which may lead to misclassification of high-risk patients. Such undetected risks pose safety concerns for those undergoing radiofrequency ablation. This study aimed to develop an artificial intelligence (AI)-assisted predictive model that integrates ultrasound radiomics and deep learning features to improve the identification of LNM and CI, thereby enhancing risk stratification and optimizing treatment strategies for cT1N0M0 PTC patients. METHODS: A total of 203 PTC patients were divided into high-risk (CI or LNM) and low-risk groups, with 142 assigned to the training set and 61 to the internal test set. Regions of interest delineation was performed using ITK-Snap. Radiomic features were extracted with PyRadiomics, and embedding features were obtained through the Vision Transformer (ViT) model. Risk-related features were selected using least absolute shrinkage and selection operator

(LASSO), variance thresholding, and recursive feature elimination (RFE). Single-modal and multimodal models were developed using feature-level and decision-level fusion. Feature importance was assessed using Shapley Additive exPlanations (SHAP). Model performance was evaluated using recall, accuracy, and area under curve (AUC). RESULTS: Among 1,001 radiomics features, 47 were selected via LASSO and RFE, and 15 relevant features from 768 ViT features. In the internal test set, NeuralNet models based on radiomics and 2D deep learning achieved AUCs of 0.756 and 0.708, respectively, and 0.829 and 0.840 in the training set. The multimodal RandomForest model outperformed single-modality models, with an AUC of 0.763 in the test set and 0.992 in the training set. Decision-level fusion models, such as DLRad_LF_Avg and DLRad_LF_Max, improved the external test set AUC to 0.843. SHAP analysis identified key features linked to tumor heterogeneity. CONCLUSION: The multimodal AI model effectively predicts high-risk cT1N0M0 PTC, outperforming single-modality models and aiding clinical decision-making.
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DOI: 10.3389/fendo.2025.1580885
PMCID: PMC12148903

Exploring the tumor suppressor role of RIN1 in familial thyroid carcinoma.
Endocr Relat Cancer, 32(5)
L. Picello, M. Dalle Nogare, D. Puggina, C. Salvoro, G. Pennelli, G. Gaudenzi, S. Carra, M. Oldani, D. Gentilini, L. Fugazzola, A. Faggiano, G. Vitale, G. Occhi and G. Vazza. 2025.
The genetic component is thought to play an important role in the development of familial non-medullary thyroid carcinoma (fNMTC), but the involved molecular mechanisms and genes are poorly understood. The MAPK kinase cascade, particularly involving RAS and BRAF, is crucial in cancer development, with RIN1 emerging as a notable gene due to its differential expression across various tumor types. We identified a frameshift mutation (c.798delC: p.V267Sfs*83) in the RIN1 gene in a family with non-medullary thyroid cancer (NMTC) through whole-exome sequencing. Paraffin-embedded tumor tissues were analyzed to investigate the mutation's characteristics and its potential implications within the thyroid cellular context. Functional assays and RNA sequencing using CRISPR/Cas9-edited Nthy-ori 3-1 thyroid cell line and xenograft zebrafish models confirmed the mutation effect and the putative RIN1 tumor suppressor role. The study revealed significant alterations in cellular behavior upon RIN1 knockout, including increased cell viability, proliferation and colony formation, alongside morphological changes indicative of epithelial-mesenchymal transition. Enhanced phosphorylation of ERK and AKT suggested MAPK pathway dysregulation following RIN1 depletion, supporting its potential tumor suppressive role. Phenotypic rescue experiments confirmed that reintroduction of wild-type RIN1 restored normal cellular behavior. RNA sequencing demonstrated differential gene expression between RIN1-/- and control cells, particularly affecting pathways associated with cancer progression, closely resembled signatures specific to NMTC. This study provides compelling evidence supporting RIN1 as a tumor suppressor gene within thyroid cells. In addition, the findings highlight its potential significance as novel gene involved in FNMTC pathogenesis.
PubMed-ID: 40116813
DOI: 10.1530/ERC-24-0344

Management of Adverse Events During Treatment for Advanced Thyroid Cancer.
Thyroid, 35(7):716-29.
T. J. Roberts and L. J. Wirth. 2025.
Background: The management of advanced thyroid cancer has rapidly evolved as several multikinase, and gene-specific inhibitors have substantially improved survival for patients with most types of thyroid cancer. Optimizing management of the treatment-related adverse events (TRAEs) from these medications is important to improve quality of life and outcomes for patients with thyroid cancer. This narrative review discusses common and clinically significant TRAEs of treatments for thyroid cancer and effective management approaches. Summary: Published literature was reviewed to summarize available information on the incidence of TRAEs with medications used to treat thyroid cancer and management approaches for these TRAEs. There are common TRAEs across many treatments for advanced thyroid cancer including fatigue, hypertension, gastrointestinal toxicities, rashes, and hand-foot syndrome. Additionally, several other TRAEs with thyroid cancer treatments are significant because of their frequency with specific medications (e.g., pyrexia syndrome) or their severity (e.g., thromboembolic events and cardiac impairment). Data from clinical trials and real-world data along with expert guidelines and insights from experienced clinicians can guide management approaches for many of these TRAEs. Conclusions: The toxicity profiles are well established for treatments for advanced thyroid cancer, there are evidence-based management approaches for many commonly encountered scenarios. Following these approaches to optimizing management of TRAEs can improve the quality of life and outcomes for patients with thyroid cancer.

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DOI: 10.1089/thy.2024.0755

Integrin-fibronectin interaction is a pivotal biological and clinical determinant in papillary thyroid carcinoma.
Endocr Relat Cancer, 32(6)
D. Rocco, A. Tortora, V. Marotta, A. M. Machado, H. S. Selistre-de-Araujo and M. Vitale. 2025.
Integrins influence tumor growth, metastasis, and angiogenesis, making them potential targets for therapeutic intervention. In this study, we analyzed the TCGA mRNA-seq dataset to assess the expression levels of fibronectin (FN1) and associated integrin subunits, evaluating their relationship with clinical features in papillary thyroid cancer (PTC). These findings were further validated in a cell model. FN1 mRNA levels in BRAFV600E-positive PTC were 80-fold compared to normal thyroid tissue (NT), whereas PTC with RAS mutations exhibited FN1 levels similar to NT. ITGAV, encoding the alphav integrin subunit, which pairs with beta3 to form a receptor for FN, was also overexpressed in PTC. Elevated FN1 expression, and to a lesser extent ITGAV, correlated positively with lymph node metastasis, advanced cancer stages, extrathyroidal extension, and poorer prognoses. Patients in the highest quartile of FN1 expression had an increased risk of disease recurrence (OR = 7.277, 95% CI: 2.019-26.191, P < 0.0024). A non-tumoral thyroid cell line and two PTC cell lines were used as models to validate the mRNA-seq results. The proliferation and migration of a FN1 knock-out PTC cell mutant were significantly reduced and proliferation was restored upon the addition of soluble FN. DisBa-01, a recombinant RGD-disintegrin derived from Bothrops alternatus snake venom, which acts as an antagonist to the FN/alphavbeta3 interaction, inhibited PTC cell proliferation and migration. These results demonstrate that FN expression is a hallmark of aggressiveness in PTC. FN/alphavbeta3 interaction plays a pivotal role in PTC, suggesting that the FN/alphavbeta3 signaling is a potential therapeutic target for disintegrins or other molecules with similar action.
PubMed-ID: 40423510
DOI: 10.1530/ERC-25-0101
PMCID: PMC12150248

DNA Methylation Dynamics and Prognostic Implications in Metastatic Differentiated Thyroid Cancer.
Thyroid, 35(5):494-507.
H. Rodriguez-Lloveras, C. Zafon, C. Iglesias, J. Marcos-Ruiz, J. Gil, A. Rueda-Pujol, L. Gonzalez, R. Mayor, E. N. Klein Hesselink, B. M. van Hemel, C. Carrato, C. Perello-Fabregat, J. Hernandez-Losa, R. Somoza, R. Pluvinet, J. F. Sanchez-Herrero, L. Sumoy, J. Seoane, G. Riesco-Eizaguirre, C. Montero-Conde, M. Robledo, J. Hernando, J. Capdevila, J. L. Reverter, M. Puig-Domingo, T. P. Links and M. Jorda. 2025.
Background: Distant metastases (DM) are the leading cause of thyroid cancer-related death in patients with differentiated thyroid cancer (DTC). Despite significant progress in understanding DNA methylation in DTC, the methylation landscape of metastatic primary tumors and DM remains unclear. Our primary objective was to investigate DNA methylation dynamics during DTC progression, with a secondary goal of assessing potential clinical implications. Materials and Methods: We conducted a multicenter retrospective study in patients with DTC who underwent surgery at five university hospitals. We profiled DNA methylation in a discovery series of 97 samples (15 normal tissues, 30 non-metastatic [non-mDTC], and 35 metastatic [mDTC] primary DTC, and 17 paired metastases [lymph nodes and DM]). Results were validated in an independent series of 17 non-mDTC and 13 mDTC. We used receiver operating characteristic curve analysis to evaluate the identified prognostic CpG-signature. Results: DNA methylation alterations, mostly hypomethylation, increased progressively from primary tumors to DM, both in papillary (PTC) and follicular (FTC) thyroid carcinomas. Compared with normal tissue, non-metastatic primary PTC (non-mPTC) exhibited more hypomethylated than hypermethylated CpGs in contrast to non-metastatic primary FTC (non-mFTC). However, metastatic tumors, both mPTC and mFTC, predominantly exhibited hypomethylated CpGs. The overlap of differentially methylated CpGs (DMe-CpGs) was low between non-mPTC and non-mFTC (14% non-mPTC DMe-CpGs present in non-mFTC) but significantly higher between mPTC and mFTC (60% mPTC DMe-CpGs present in mFTC), underscoring the convergence of epigenetic changes during metastatic progression. The presence of many de novo DMe-CpGs from metastatic primary tumors (83% from mPTC and 40% from mFTC) in DM, including metachronous DM, supports the hypothesis that DM originates from a major subclone of the primary tumor. We identified and validated a 156-CpG signature in primary tumors capable of distinguishing between non-mDTC and mDTC, offering potential prognostic value for DM development regardless of histology. Conclusions: These results show a progressive increase in DNA methylation alterations, mainly hypomethylation, during PTC and FTC metastatic progression, suggesting a linear model, though the DNA methylation dynamics differs between the two histological types. The analysis of the 156-CpG signature in primary tumors may help identify patients with DTC at high risk for DM, enhancing a more personalized treatment.

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DOI: 10.1089/thy.2024.0303

Levothyroxine therapy in thyroidectomized patients: ongoing challenges and controversies.
Front Endocrinol (Lausanne), 16:1582734.
L. Rossi, M. Paternoster, M. Cammarata, S. Bakkar and P. Miccoli. 2025.
This mini-review provides an update on the challenges and controversies surrounding levothyroxine therapy in thyroidectomized patients, following an extensive review on dosing strategies and available formulations. Despite efforts to establish an ideal dosage adjustment method, achieving optimal thyroid hormone replacement remains complex due to interindividual variations in the hypothalamic-pituitary-thyroid axis and the pharmacokinetic and pharmacodynamic limitations of exogenous levothyroxine. Additionally, this review highlights the importance of evaluating the risk-benefit ratio of levothyroxine therapy, particularly in the setting of TSH suppression, focusing on its effects on quality of life, bone metabolism, and cardiac rhythm. Levothyroxine-induced subclinical hyperthyroidism may contribute to an increased risk of atrial fibrillation and alterations in bone mineral density, with implications that remain a subject of debate. Given the incomplete replication of endogenous thyroid hormone action by levothyroxine monotherapy, a tailored therapeutic approach is crucial. Despite ongoing research, the optimal management of thyroidectomized patients continues to be an open issue.
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DOI: 10.3389/fendo.2025.1582734
PMCID: PMC12146200

Long-Term Durability of Active Surveillance of Small, Low-Risk Papillary Thyroid Cancer.
JAMA Surg, 160(10):1117-24.
A. M. Sawka, S. Ghai, L. Rotstein, J. C. Irish, J. D. Pasternak, E. Monteiro, J. Chung, J. Su, W. Xu, A. O. Esemezie, J. M. Jones, A. Gafni, N. N. Baxter, D. P. Goldstein and G. Canadian Thyroid Cancer Active Surveillance Study. 2025.
IMPORTANCE: In managing early-stage cancers, active surveillance (AS) may be preferentially favored by older individuals. In counseling patients, it is important to understand the durability of AS in the context of age. OBJECTIVE: To evaluate the durability of AS in patients with small, low-risk papillary thyroid cancer (PTC) according to age at the time of choosing AS. DESIGN, SETTING, AND PARTICIPANTS: This single-center, prospective, long-term follow-up cohort study was conducted at a tertiary care hospital in Toronto, Ontario, Canada. Adult patients with small, localized, low-risk PTC less than 2 cm in maximal diameter were enrolled between May 2016 and February 2021. The clinical outcome data were analyzed up to the time point of May 25, 2025, and final data analysis was performed in June 2025. EXPOSURE: All patients were offered the choice of AS or thyroid surgery. MAIN OUTCOMES AND MEASURES: The primary outcome was the overall rate of AS crossover to definitive treatment (treatment completed or recommended by an investigator) and the indications. Cumulative crossover incidence function curves were examined according to age, with death from other causes as the competing risk. RESULTS: A total of 200 patients (155 patients under AS and 45 who had immediate surgery) were followed up for a median (IQR) duration of 71 (59-84) months. Overall mean (SD) age was 52.0 (14.9) years, and 153 patients (76.5%) were female. There were no observed thyroid cancer-related deaths or any distant metastatic disease. The overall crossover rate from AS was 23.9% (37/155; 32 completed treatment, 3 declined surgery for disease progression, and 2 awaiting treatment). Crossover reasons included disease progression (56.8% [21/37]), patient preference (40.5% [15/37]), and ultrasound imaging limitations precluding accurate tumor measurement under active surveillance (tumor border not clearly distinguishable from heterogeneous echotexture of the thyroid parenchyma in a patient with Hashimoto thyroiditis; 2.6% [1/37]). The 5-year age-stratified cumulative overall crossover incidence rates were 41.5% (95% CI, 25.6%-56.8%) in patients younger than 45 years, 20.9% (95% CI, 12.3%-31.1%) in those aged 45 to 64 years, and 5.1% (95% CI, 0.9%-15.2%) in those aged 65 years and older (P < .001). CONCLUSION AND RELEVANCE: This single-center Canadian cohort study found that AS is a durable long-term management strategy for small, low -risk PTC, particularly in older individuals. Older individuals may be less likely to cross over to surgery after choosing AS.
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DOI: 10.1001/jamasurg.2025.2957
PMCID: PMC12368792

Prevalence and Management of Complications of Laser Ablation for Benign Thyroid Nodules.
J Clin Endocrinol Metab, 110(7):e2383-e96.
L. Scappaticcio, N. Di Martino, P. Ferrazzano, M. I. Maiorino, P. Caruso, A. Volatile, M. Longo, G. Docimo, E. Iervolino, P. Trimboli, K. Esposito and G. Bellastella. 2025.

CONTEXT: Percutaneous laser ablation (LA) is today regarded as a valuable therapy for symptomatic, benign solid (noncystic) thyroid nodules (STNs). OBJECTIVE: We assessed the prevalence of complications from LA for benign and STNs and their management. METHODS: We conducted a systematic review with meta-analysis of data from published studies on LA of STNs, in addition to author institutions. A random effects meta-analysis was performed on the prevalence rates. RESULTS: The literature search yielded 1351 studies, of which 38 studies were included, in addition to our institutional experience (4745 STNs in total). The overall quality of each included study was judged as fair. The prevalence of "overall" complications of LA was 23% ([CI, 17%-30%], I2 93.7%, 1208 of 4702 thyroid nodules [TNs]). The prevalence of "minor" complications of LA was 21% ([CI, 15%-27%], I2 93.7%, 1159 of 4702 TNs). The prevalence of "major" complications of LA was 2% ([CI, 1%-3%], I2 54.0%, 49 of 4745 TNs). Sensitivity analyses did not modify the results, except for dysphonia, whose pooled prevalence was higher when using local anesthesia (2%; CI, [1%-3%], I2 25.2; P = .010) or conscious sedation (2%; CI, [1%-4%], I2 27.2; P = .014). The pooled prevalence rate of local pain was 15% (CI, [12%-20%], I2 89.3). Local pain was transient and typically mild to moderate, sometimes severe, requiring analgesics for 1 to 5 days up to 1 month. The pooled prevalence rate of dysphonia was 2% (CI, [1%-2%], I2 30.3). All cases of dysphonia were transient except for one permanent case. CONCLUSION: LA for benign and noncystic STNs can be considered a generally safe technique. Major complications are rare.
PubMed-ID: 39973303
DOI: 10.1210/clinem/dgaf108

Detection of PTEN Mutations in Fine Needle Aspiration Biopsies of Indeterminate Thyroid Nodules: Impact on Diagnosis and Prognosis.
Head Neck, 47(8):2145-51.
L. E. Schlegel, M. Brill-Edwards, Z. X. Wang, C. McNair, S. Gargano and E. Cottrill. 2025.
BACKGROUND: Data connecting PTEN mutations with thyroid cancer risk for indeterminate nodules remain limited due to the rare nature of these mutations. The aim of this study was to determine the relationship between PTEN mutations identified in cytologically indeterminate nodules and final pathology and clinical outcomes. METHODS: This 8-year retrospective study includes adults with indeterminate thyroid nodules positive for a PTEN mutation and available correlative surgical histopathology. RESULTS: Twenty-three patients with 24 total nodules met the inclusion criteria. The cytology specimens were characterized as Bethesda III (n = 19) and Bethesda IV (n = 5). Specific PTEN mutations detected are described in detail. Final histopathology included the following: benign (n = 18, 75.0%), papillary thyroid carcinoma (n = 3, 12.5%), follicular thyroid carcinoma (n = 2, 8.3%), and poorly differentiated thyroid carcinoma (n = 1, 4.2%). CONCLUSIONS: Together, our data suggest that PTEN mutations in indeterminate thyroid nodules result in a 25.0% risk of malignancy (Bethesda III: 16.7% and Bethesda IV: 60%).
PubMed-ID: 40055996
DOI: 10.1002/hed.28127
PMCID: PMC12248271

Association of BRAF V600E Allele Frequency With Clinicopathologic Outcomes in Papillary Thyroid Cancer.
J Clin Endocrinol Metab, 110(8):2164-71.
M. A. Schumm, Y. E. Nikiforov, M. N. Nikiforova, A. I. Wald, C. H. Tseng, S. Smooke-Praw, J. X. Wu, M. W. Yeh and M. J. Livhits. 2025.
CONTEXT: BRAF V600E mutation is the most common genetic driver of papillary thyroid cancer (PTC), where it is found with various allele frequency (AF), reflecting the proportion of cells carrying the mutant and wild-type gene alleles. OBJECTIVE: To determine whether BRAF V600E AF can improve prognostication and inform initial surgical management of PTC. METHODS: This retrospective cohort study (2016-2019) at UCLA Health included consecutive patients with Bethesda V/VI nodules and isolated BRAF V600E mutation who underwent surgery with histopathology showing PTC. Blinded ThyroSeq v3 molecular analysis was conducted after completion of initial management and follow-up. The risk of aggressive histopathology and cancer persistence/recurrence were assessed. RESULTS: Of 73 patients, the median BRAF V600E AF was 25.5% (IQR, 16.7%-34.3%). Higher median AF was seen in patients classified as American Thyroid Association high-risk (37%) vs intermediate-risk (25.3%, P < .01) and low-risk (24.7%, P < .01), largely attributed to higher AF in patients with gross extrathyroidal extension (ETE) (40.1% vs 25.2% without gross ETE, P = .02). No differences in AF were observed on the basis of lymph node positivity or presence of aggressive variants of PTC. A higher BRAF V600E AF was also found in patients with tumors >/= 2 cm vs < 2 cm (median 32.0% vs 24.4%, P < .01). Over 4.1 years of follow-up, disease persistence/recurrence was found in 7 patients (9.4%) and was associated with higher median AF than those without recurrence (35.3% vs 25.2%, P = .02). Higher AF was associated with poorer recurrence-free survival (AF >/= 35%; HR 7.40; CI, 1.4-38.1). CONCLUSION: Higher AF was associated with gross ETE and increased recurrence risk. This may

inform initial management in patients with PTC harboring an isolated BRAF V600E mutation.
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DOI: 10.1210/clinem/dgae774

Limited Utility of Routine Surveillance Ultrasound in Differentiated Thyroid Cancer Patients With Undetectable Postoperative Thyroglobulin Levels.
Clin Endocrinol (Oxf), 102(5):600-6.
Y. J. Seo, R. Tiu, K. Stahl, E. Hughes, C. H. Tseng, M. Yeh, M. Livhits and J. X. Wu. 2025.
BACKGROUND: Neck ultrasound (US) and serum thyroglobulin (Tg) measurements are mainstays of long-term differentiated thyroid cancer (DTC) surveillance. Given the high sensitivity of serum Tg, we aimed to assess the utility of neck US in DTC patients who underwent total thyroidectomy and have undetectable serum Tg. METHODS: We performed a retrospective cohort analysis of DTC patients who underwent a total thyroidectomy at our institution (2010-2023) and received US-guided fine needle aspiration (FNA) during their surveillance. Patients were categorised into three lab categories based on serum Tg and Tg antibody (Tg Ab) status before the biopsy: (1) 'Negative Tg' if undetectable Tg (< 0.2 ng/dL) and Tg Ab, (2) 'Positive Tg' if detectable Tg and undetectable Tg Ab, and (3) 'Positive Tg Ab' if detectable Tg Ab. To calculate the positive predictive value (PPV) of neck US, we defined the 'true positive' of US as findings that prompted an FNA biopsy resulting with DTC, and 'false positive' findings prompting an FNA biopsy that did not result as DTC. RESULTS: A total of 118 patients were included, encompassing 146 FNA biopsies: 33 (23%) had Negative Tg, 84 (57%) had Positive Tg, and 29 (20%) had Positive Tg Ab lab results before their biopsies. The PPV of neck US in the setting of Negative Tg was 3% (one true positive, 32 false positives), while the PPV was 50% (42 true positives, 42 false positives) for Positive Tg, and 52% (15 true positives, 14 false positives) for Positive Tg Ab cohorts. Sub-analysis of the Positive Tg cohort using different serum Tg level cutoffs revealed a PPV of 29% at just detectable serum Tg of 0.2 ng/dL, and PPV of 38% for Tg < 1.0 ng/dL. The PPV stabilised at 58% for Tg levels >/= 1 ng/dL. CONCLUSION: With the low PPV of neck US, high cost of surveillance, and the advent of ultra-sensitive serum Tg measurements, future guidelines should consider reducing routine neck US surveillance in patients with undetectable serum Tg and only performing it when there is a rise in serum Tg levels.
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DOI: 10.1111/cen.15198

Noninvasive Deep Learning System for Preoperative Diagnosis of Follicular-Like Thyroid Neoplasms Using Ultrasound Images: A Multicenter, Retrospective Study.
Ann Surg,
H. Shen, Y. Huang, W. Yan, C. Zhang, T. Liang, D. Yang, X. Feng, S. Liu, Y. Wang, W. Cao, Y. Cheng, H. Chen, Q. Ni, F. Wang, J. You, Z. Jin, W. He, J. Sun, D. Yang, L. Liu, B. Cao, X. Zhang, Y. Li, S. Pei, S. Zhang and B. Zhang. 2025.
OBJECTIVE: To propose a deep learning (DL) system for the preoperative diagnosis of follicular-like thyroid neoplasms (FNs) using routine ultrasound images. SUMMARY BACKGROUND DATA: Preoperative diagnosis of malignancy in nodules suspicious for an FN remains challenging. Ultrasound, fine-needle aspiration cytology, and intraoperative frozen section pathology cannot unambiguously distinguish between benign and malignant FNs, leading to unnecessary biopsies and operations in benign nodules. METHODS: This multicenter, retrospective study included 3634 patients who underwent ultrasound and received a definite diagnosis of FN from 11 centers, comprising thyroid follicular adenoma (n=1748), follicular carcinoma (n=299), and follicular variant of papillary thyroid carcinoma (n=1587). Four DL models including Inception-v3, ResNet50, Inception-ResNet-v2, and DenseNet161 were constructed on a training set (n=2587, 6178 images) and were verified on an internal validation set (n=648, 1633 images) and an external validation set (n=399, 847 images). The diagnostic efficacy of the DL models was evaluated against the ACR TI-RADS regarding the area under the curve (AUC), sensitivity, specificity, and unnecessary biopsy rate. RESULTS: When externally validated, the four DL models yielded robust and comparable performance, with AUCs of 82.2%-85.2%, sensitivities of 69.6%-76.0%, and specificities of 84.1%-89.2%, which outperformed the ACR TI-RADS. Compared to ACR TI-RADS, the DL models showed a higher biopsy rate of malignancy (71.6% -79.9% vs 37.7%, P<0.001) and a significantly lower unnecessary FNAB rate (8.5% -12.8% vs 40.7%, P<0.001). CONCLUSION: This study provides a noninvasive DL tool for accurate preoperative diagnosis of FNs, showing better performance than ACR TI-RADS and reducing unnecessary invasive interventions.
PubMed-ID: 40689491
DOI: 10.1097/SLA.0000000000006841

From data to Diagnosis: How artificial intelligence is revolutionizing preoperative assessment of thyroid nodules and cancer.
Eur J Surg Oncol, 51(9):110191.

K. Shen, M. Tan, Y. Liu, X. Xu and S. Yang. 2025.
BACKGROUND: Thyroid nodules are frequently detected in the general population, raising concerns about the challenges of overdiagnosis and overtreatment. Artificial intelligence (AI) offers novel solutions for the preoperative evaluation of thyroid nodules. However, there has not yet been a comprehensive literature review on current applications. METHODS: We reviewed the preoperative assessment methodologies for thyroid nodules and delineated the latest advancements in the utilization of sophisticated AI within the preoperative evaluation framework. RESULTS: AI improves the accuracy of diagnostic procedures in preoperative evaluation of thyroid nodules by enhancing imaging, cytopathology diagnostics, and prognostic assessments. With its ability to automatically process large volumes of imaging and cytopathology data, AI minimizes reliance on clinical experience and reduces the occurrence of errors caused by subjective judgment. Furthermore, AI can integrate diverse data sources, providing a deeper understanding of the underlying value and interaction within the data, thereby enhancing comprehensive disease assessment and prognostic predictions. CONCLUSION: The AI-assisted preoperative assessment approach improves diagnostic accuracy and robust evidence for developing individualized treatment strategies.
PubMed-ID: 40543139
DOI: 10.1016/j.ejso.2025.110191

Letter to the Editor Regarding "Thyroid Radiofrequency Ablation- Thermal Effects on Recurrent Laryngeal Nerve Using Continuous Intraoperative Neuromonitoring Animal Model".
Otolaryngol Head Neck Surg, 172(5):1805-6.
C. F. Sinclair, V. Dhillon, S. Hodak, J. Kuo, K. Patel, J. Russell and R. P. Tufano. 2025.
PubMed-ID: 39791923
DOI: 10.1002/ohn.1130

Prevalence of thyroid cancer in Europe.
Br J Surg, 112(6)
A. V. Sterpetti and G. Sterpetti. 2025.
PubMed-ID: 40580060
DOI: 10.1093/bjs/znaf138

Clinicopathological features and outcomes in patients with concurrent medullary and papillary thyroid carcinoma.
Front Endocrinol (Lausanne), 16:1625989.
R. Sun, X. Liu, J. Liu, Z. Li and Y. Wang. 2025.
OBJECTIVE: The co-existence of medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC) is rare. The study analyzed the clinicopathological findings and prognosis of concomitant PTC in MTC patients. METHODS: Clinicopathological data and follow-up outcomes of 25 patients with concurrent medullary and papillary thyroid carcinoma (combination group) between January 2009 and May 2024 were collected and analyzed retrospectively. We compared clinicopathologic characteristics and follow-up outcomes between patients with concurrent MTC and PTC (combination group) and those with MTC alone (MTC group). RESULTS: The 25 patients with concurrent MTC and PTC comprised 19 females and 6 males. There were no statistically significant differences between the combination group and the MTC group in terms of age, gender, or pathological features such as the diameter of MTC lesions, multifocality, extra-thyroidal extension (ETE), number of lymph node (LN) resected, the number of LN metastasis, the maximum diameter of LN metastasis, and TNM staging. The recurrence rate was similar between the two groups. Univariate analysis showed that the max tumor diameter, capsule invasion, extracapsular invasion and recurrent nerve invasion were associated with the risk of biochemical/structural abnormalities in MTC group. Multivariate analysis showed that only the max tumor diameter and capsule invasion were significant independent prognostic factors for biochemical/structural abnormalities. CONCLUSION: The result of this comparative study between patients with MTC and PTC co-existence and those with MTC alone showed similar invasiveness and prognosis.
PubMed-ID: 40862114
DOI: 10.3389/fendo.2025.1625989
PMCID: PMC12375443

The role of AI in optimizing interventional ablative techniques for thyroid nodules: Paving the way for precision-driven endocrine surgery.
Am J Surg, 247:116317.
N. Swaminathan, I. Chaudhary and H. Chen. 2025.

PubMed-ID: 40157867
DOI: 10.1016/j.amjsurg.2025.116317

The evolving landscape of thyroid eye disease: present and future.
Eur J Endocrinol, 193(2):R15-R24.
D. Toro-Tobon and M. N. Stan. 2025.
Thyroid eye disease (TED) is a complex ocular autoimmune disorder primarily associated with Graves' disease. It leads to significant morbidity due to orbital inflammation, fibrosis, and tissue expansion. While corticosteroids have been the traditional mainstay of therapy, recent advancements in understanding TED pathophysiology have driven the development of targeted treatments. Notably, inhibition of the insulin-like growth factor-1 receptor with teprotumumab has revolutionized TED management, demonstrating efficacy in reducing proptosis and disease severity. Additional emerging therapies, including neonatal Fc receptor inhibitors, thyroid-stimulating hormone receptor blockers, and interleukin-6 receptor antagonists, offer promising alternatives for patients with active and refractory disease. Despite these advancements, challenges remain in disease classification and outcome assessment. As the landscape of TED management continues to evolve, this review provides a comprehensive overview of current and emerging therapies for TED, critically examines gaps in disease evaluation, and highlights the evolving paradigm of patient-centered care. Future efforts should focus on optimizing therapeutic algorithms, refining risk stratification models, guiding personalized treatment, and promoting a multidisciplinary approach, which remain essential in improving outcomes and quality of life for affected individuals.
PubMed-ID: 40794607
DOI: 10.1093/ejendo/lvaf156

The Landmark Series: Extent of Surgery for Low-Risk Differentiated Thyroid Cancer.
Ann Surg Oncol, 32(5):3119-25.
T. M. Ullmann and J. A. Sosa. 2025.
The management of patients with differentiated thyroid cancers (DTCs) at low risk for disease progression or relapse after treatment remains controversial. These patients have excellent disease-specific survival. Therefore, minimizing the impact of treatments on patients' quality of life is particularly important. For these reasons, the pendulum has swung in recent years to favor less extensive surgery toward lobectomy instead of total thyroidectomy, away from prophylactic (central compartment) lymphadenectomy, and even in some cases, omitting surgery altogether. This review discusses several of the influential studies from the past two decades that have had an impact on the management for these patients, including a shift toward more personalized care.
PubMed-ID: 40009309
DOI: 10.1245/s10434-025-17063-9
PMCID: PMC11976359

Thyroid Carcinoma in Birt-Hogg-Dube Syndrome: Case Series and Review of Literature.
Thyroid, 35(7):828-35.
S. Vaid, E. Chuki, P. Veeraraghavan, M. Jedlinski-Obrzut, K. Bukhari, J. Klubo-Gwiezdzinska and S. Gubbi. 2025.
Background: Thyroid cancer (TC) is infrequently encountered in Birt-Hogg-Dube (BHD) syndrome. We describe three BHD patients with TC and review the relevant literature. Patient Findings: Patient 1, a 55-year-old male with BHD, developed dedifferentiated oncocytic TC with distant metastases, requiring systemic therapy and radiation. Genetic testing revealed pathogenic variants (PVs) in FLCN, DAXX, and TP53. Patient 2, a 51-year-old female, and her 30-year-old daughter (patient 3) were diagnosed with papillary TC and treated with surgery and radioiodine. Tumor testing in patient 3 demonstrated PV in BRAF (V600E). Gene query analysis (n = 2285 patients) identified 2% FLCN PV prevalence in sporadic TCs, but the prevalence increased to 23% in anaplastic TCs. Literature review revealed 15 TC cases in BHD with diverse clinical presentations. Conclusions: TCs are rare in BHD. FLCN PVs may not be the sole molecular drivers in TCs but may have a substantial role in the development of aggressive TCs.
PubMed-ID: 40658617
DOI: 10.1089/thy.2024.0641
PMCID: PMC12281115

Lobectomy with ipsilateral central lymph node dissection might be an appropriate surgical method for select cases of isthmic papillary thyroid carcinoma: a retrospective study with propensity scores matching analysis.
Front Endocrinol (Lausanne), 16:1588323.

B. Wang, C. R. Zhu, H. Wen, Y. Fei, Z. J. Wu, H. Liu, X. M. Yao and J. Wu. 2025.
OBJECTIVE: The study aimed to ascertain the appropriate surgical method for isthmic papillary thyroid carcinoma (PTC). METHODS: We reviewed the records of patients who underwent thyroid surgery for PTC in our institution from July 2018 to June 2024. The isthmus was categorized into central isthmus and paracentral isthmus. Data were compared to explore the risk factors of contralateral paratracheal lymph node metastasis (LNM) and the presence of more than 5 metastatic lymph nodes between patients with paracentral isthmic PTC and those with lobar PTC, and between patients with paracentral isthmic PTC and those with central isthmic PTC. Propensity score matching was used to identify a cohort of patients with similar baseline characteristics among patients with paracentral isthmic PTC and lobar PTC to minimize discrepancies in the number between the two groups. RESULTS: Prelaryngeal and/or pretracheal LNM was confirmed to be an independent risk factor for contralateral paratracheal LNM (OR = 3.43; 95%CI 1.74 - 8.92; p = 0.013) and presence of more than 5 metastatic lymph nodes (OR = 4.55; 95%CI 1.46 - 14.15; p = 0.009) in patients with paracentral isthmic PTC and lobar PTC. While, the location in the paracentral isthmus did not exhibit a significant association with them in these patients. Conversely, being located in the central isthmus was confirmed to be a risk factor for contralateral paratracheal LNM (OR = 4.67; 95%CI 1.53 - 14.21; p = 0.007) and the presence of more than5 metastatic lymph nodes (OR = 4.55; 95%CI 1.46 - 14.15; p = 0.009) among patients with isthmic (central and paracentral) PTC. CONCLUSION: Lobectomy with ipsilateral central lymph node dissection might be appropriate for paracentral isthmic PTC without prelaryngeal and pretracheal LNM. Total thyroidectomy with bilateral central lymph node dissection might be necessary for central isthmic PTC.
PubMed-ID: 40708718
DOI: 10.3389/fendo.2025.1588323
PMCID: PMC12286821

Clinical outcome and influencing factors of differentiated thyroid cancer patients with radioiodine-refractory lung metastasis.
Front Endocrinol (Lausanne), 16:1622539.
C. Wang, Y. Li, G. Qin, J. Li, G. Wang, X. Liu and X. Wang. 2025.
PURPOSE: A subset of patients with differentiated thyroid cancer and lung metastases (DTC-LM) may progress to radioiodine-refractory (RAIR) disease, which is associated with a poor prognosis. This study aimed to investigate the clinical outcomes and potential risk factors associated with RAIR disease in DTC-LM patients. METHODS: 177 DTC-LM patients who underwent radioiodine (RAI) therapy at our center were retrospectively analyzed. Clinicopathological profiles were compared between the RAI-avid (RAIA) and RAIR groups. Univariate and multivariate regression analyses were conducted to identify risk factors for RAIR status and progressive disease (PD). RESULTS: Overall, 80 patients were included in the RAIR group, accounting for 45.2% of the total patients. Multivariate analysis revealed that older age and higher T stage were independent risk factors for RAIR disease. Age>/=55 years (HR: 2.975, 95% CI: 1.424 -6.218, P = 0.004), RAI-avid status (HR: 4.315, 95% CI: 1.753 - 10.622, P = 0.001) and the ps-Tg>/=528.5ng/mL (HR: 3.665, 95% CI: 1.656 - 8.107, P = 0.001)were identified as independent predictors of PD. Kaplan-Meier analysis revealed a lower progression-free survival (PFS) rate in the RAIR group than in the RAIA group (P< 0.001). CONCLUSION: RAIR disease is common among DTC-LM patients and is associated with adverse clinical outcomes. Age, RAI avidity status, and ps-Tg levels serve as important predictors of PD. Early risk stratification and individualized management strategies are crucial to improving outcomes in DTC-LM patients.
PubMed-ID: 40831949
DOI: 10.3389/fendo.2025.1622539
PMCID: PMC12358278

Comparison of the surgical outcomes of endoscopic thyroidectomy via a contralateral-axillo-bilateral-breast approach and open thyroidectomy.
Langenbecks Arch Surg, 410(1):201.
H. Weng, W. Qiu, T. Yan, Y. Tang, Z. Chen, B. Guo, X. Huang, Y. Fan and Z. Yang. 2025.
BACKGROUND: Endoscopic thyroidectomy via extracervical approaches has been developed to avoid anterior neck surgical scars. However, each approach has its own limitations. We developed a novel endoscopic thyroidectomy via the contralateral-axillo-bilateral-breast approach (CABBA-ET) and compared the surgical outcomes with those of open thyroidectomy (OT). METHODS: We retrospectively reviewed patients who underwent thyroidectomy by the same surgeon between January 2021 and December 2023 at our institution. The surgical outcomes and postoperative complications of CABBA-ET and OT were compared after propensity score matching (PSM) of the clinicopathologic characteristics. RESULTS: A total of 433 patients who underwent CABBA-ET or OT were enrolled in this study, of whom 83

underwent CABBA-ET, and the remaining 350 underwent OT. After PSM, 16 pairs of patients with benign thyroid nodules and 56 pairs of patients with differentiated thyroid carcinoma (DTC) were matched between the CABBA-ET and OT groups. Compared with the OT group, patients with benign nodules and DTC in the CABBA-ET group had a longer operation time (both P < 0.01) and a higher 24-h postoperative drainage volume (P = 0.03 and < 0.01). The length of hospitalization was comparable between the two groups, and there were no significant differences in postoperative complications. CONCLUSIONS: CABBA-ET is a viable cosmetic procedure and may represent an alternative for selective patients.
PubMed-ID: 40590963
DOI: 10.1007/s00423-025-03784-8
PMCID: PMC12214002

Development of a Nomogram to Integrate Molecular Testing and Clinical Variables to Improve Malignancy Risk Assessment Among Cytologically Indeterminate Thyroid Nodules.
Thyroid, 35(5):508-15.
J. Wu, P. Stewardson, M. Eszlinger, M. Khalil, S. Ghaznavi, E. Nohr, A. Box and R. Paschke. 2025.
Background: The introduction of molecular testing (MT) of cytologically indeterminate thyroid nodules (ITNs) alone has not impacted thyroidectomy rates. Due to this, we evaluated the incremental diagnostic value of various clinical variables in addition to MT results, in predicting the risk of malignancy (ROM) among ITNs. Methods: This prospective observational study included 1024 consecutive ITNs that underwent reflexive ThyroSPEC MT between Jul 30, 2020, and Oct 30, 2023. A multivariable logistic regression model was built to assess the relationship between histology outcomes and clinical variables, including nodule discovery by palpation, ultrasound risk categories, maximum nodule size, Bethesda category, Bethesda atypia, and ThyroSPEC categories. A total of 332 out of 1024 patients who underwent surgery and had complete data for all variables were included in the model. A nomogram was subsequently developed based on the model. Results: The model achieved a cross-validated AUC of 0.831 (95% confidence intervals: 0.787-0.874). Patients with high-risk mutations or malignant molecular markers exhibited significantly higher odds (152.79 times) of malignancy compared to those with mutation-negative or benign molecular marker results. Patients with maximum nodule size >5 cm have 4.34 times higher odds of malignancy than those 0-2 cm. The presence of nuclear atypia increased the odds of malignancy by 4.26 times, while ultrasound malignancy risk category 5 increased the odds of malignancy by 2.89 times compared to categories 1-3. Positive palpation discovery increased the odds by 1.83 times. The integrated ROM estimated from the regression model is significantly associated with the surgery type (p < 0.001). In the low (0-30%) and intermediate ROM (31-70%) categories, lobectomy alone is the most common surgery (61% and 70%, respectively), while in the high ROM (>70%) category, total thyroidectomy dominates (62%). Conclusions: Although MT alone played an important role in decision-making regarding surveillance versus surgery in our study population, integrating MT results with additional clinical variables improved the malignancy risk prediction for ITNs. Our results highlight the importance of contextualizing MT results within an integrated interdisciplinary thyroid nodule diagnostic pathway.
PubMed-ID: 40040545
DOI: 10.1089/thy.2024.0481

Complications after thermal ablation for thyroid nodules across countries.
Front Endocrinol (Lausanne), 16:1608164.
S. Wu, Y. Cai, X. Liu and C. Zhu. 2025.
OBJECTIVE: Thermal ablation is an effective treatment for thyroid nodules; however, the range of complications associated with thermal ablation is unclear. In this study, we analyzed the complications of thyroid nodule thermal ablation in our hospital in combination with data from different countries for further analysis to determine the complications. METHODS: 536 patients treated by thermal ablation at Shanghai Ninth People's Hospital from Jan 2021 to Dec 2023 were enrolled in this retrospective study. The types and numbers of complications were recorded. Studies reporting complications of thermal ablation for thyroid nodules were identified in the PubMed database from Jan 2004 to Mar 2024. The incidence rate and types of complications were analyzed. Finally, we compared our data with those studies. RESULTS: Twelve types of complications associated with thermal ablation occurred to patients in our hospital. The overall incidence was 10.82%. The top five complications were pain, edema, voice changes, hematoma, and vascular reactions. In addition, 21 kinds of complications were reported across 13 countries, and the average incidence rate was 12.61%. The top five complications were pain, vocal changes, edema, hematoma, and fever. The total incidence rate did not significantly differ between our hospital and other countries (P >/= 0.05), though the incidences of specific complications, including tracheal injury, vasovagal reaction, dyspnea, scarring, infection and fever, were significantly different (P < 0.05). CONCLUSIONS: The incidence of complications associated with thermal ablation of thyroid nodules is similar across countries. However, the proportions and types of complications vary regionally.

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PMCID: PMC12339322

Is prophylactic central neck dissection necessary for patients with clinically node-negative papillary thyroid microcarcinoma? A follow-up study of more than 10 years.
Front Endocrinol (Lausanne), 16:1597661.
Z. G. Wu, W. T. Zheng, L. J. Chen, F. S. Zhu, Z. S. Ma, F. L. Cao, B. B. Cui, B. J. Xie and X. Q. Yan. 2025.
BACKGROUND: Therapeutic central neck dissection (CND) is strongly recommended for patients with clinically node-positive (cN1) papillary thyroid carcinoma (PTC). However, the role of prophylactic central neck dissection (PCND) remains controversial for clinically node-negative (cN0) PTC, particularly in papillary thyroid microcarcinoma (PTMC). To better elucidate the benefits and disadvantages, we conducted a retrospective analysis with a follow-up of more than 10 years. METHODS: A total of 377 consecutive patients were enrolled in this study between April 2011 and March 2015. 146 patients underwent total thyroidectomy alone (TT group), while 231 patients underwent total thyroidectomy and prophylactic central compartment lymph node dissection (TT+PCND group). Considering the low risk of recurrence, all patients did not receive radioiodine treatment. Post-surgical pathological and preoperative clinical courses, local recurrence, postoperative complications, and follow-up data were all collected. RESULTS: In the TT+PCND group, 82 patients (35.3%) had occult lymph node metastasis and a higher risk of postoperative complications, including lymphatic leakage, recurrent laryngeal nerve injury, hypoparathyroidism, and accidental parathyroidectomy. Hypoparathyroidism and accidental parathyroidectomy showed a significantly increased risk ($p = 0.005$, $p = 0.049$). However, there were no differences in survival and recurrence rates between the two groups. CONCLUSIONS: Routine prophylactic central neck dissection is unnecessary for patients with clinically node-negative papillary thyroid microcarcinoma, as the postoperative complications are significant, while the benefits remain unclear.
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DOI: 10.3389/fendo.2025.1597661
PMCID: PMC12122332

Hashimoto's thyroiditis and its activity status influence the assessment of lymph node metastasis of thyroid cancer.
Front Endocrinol (Lausanne), 16:1567181.
C. Yan, Y. Zhao, Q. Zhang and X. He. 2025.
BACKGROUND AND PURPOSE: Hashimoto's thyroiditis plays a crucial role in the biological behavior of papillary thyroid carcinoma. The purpose of this study was to explore the impact of Hashimoto's thyroiditis on the preoperative evaluation of thyroid cancer. METHOD: Univariate and multivariate analyses were performed to explore the clinicopathological characteristics and the risk factors for lymph node metastasis (LNM) in 2,261 patients with papillary thyroid carcinoma. RESULTS: The clinical data showed that the clinicopathological characteristics varied in different states of Hashimoto's thyroiditis and levels of the thyroid peroxidase (TPO) antibody ($p < 0.05$). In cases without Hashimoto's thyroiditis, the multivariate analysis showed that male sex (OR = 1.991, 95%CI = 1.574-2.517, $p < 0.05$) was the independent risk factor for LNM, but not in the cases with concurrent Hashimoto's thyroiditis. The area under the receiver operating characteristic (ROC) curve of the non-Hashimoto's thyroiditis cases was 0.727 (95% CI = 0.703-0.752, $p < 0.05$), while that in cases with Hashimoto's thyroiditis was 0.632 (95% CI = 0.590-0.674, $p < 0.05$). Analysis of the differentially expressed genes in the different subgroups found that, in men, the differential genes among the different LNM statuses were mainly enriched in immune pathways, while in women and in younger patients, the genes were mainly enriched in cytokine and kinase pathways; in older patients, the genes were enriched in the extracellular matrix. CONCLUSION: Hashimoto's thyroiditis can affect the preoperative evaluation of thyroid cancer. In addition, sex might affect the biological behavior of papillary thyroid carcinoma, which may result from the different immune and cellular statuses among different sexes and ages.
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DOI: 10.3389/fendo.2025.1567181
PMCID: PMC12148851

A study on the diagnostic value of artificial intelligence combined with a contrast-enhanced ultrasound scoring system in partially cystic thyroid carcinoma.
Front Endocrinol (Lausanne), 16:1514185.
X. H. Yan, Q. Chen, Y. W. Xin, S. J. Yuan, J. J. Liu, H. Y. Jia, Y. Wen, Y. J. Zhang, W. W. Fan, Y. F. Zhao, P. Liang and L. P. Liu. 2025.
OBJECTIVES: The aim of this study was to investigate the diagnostic value of the contrast-enhanced ultrasound (CEUS)

scoring system, artificial intelligence (AI) and the American College of Radiology Thyroid Imaging and Reporting Data System when used by sonographers of different seniority levels individually and in combination for the diagnosis of partial cystic thyroid nodules (PCTNs). MATERIALS AND METHODS: A retrospective analysis of conventional ultrasound and CEUS images of enrolled patients was performed, and a CEUS scoring system was established. The sensitivity, specificity, and area under the curve (AUC) of CEUS and AI individually and in combination for diagnosis were compared among sonographers with different seniority levels. RESULTS: A total of 166 nodules (83 benign and 83 malignant) from 152 patients with PCTNs were analyzed in this study. Nine CEUS features of PCTNs were observed and summarized; eight of these features differed between the two groups (all $p < 0.05$) and were included in the CEUS scoring system. CEUS and AI used by junior and senior physicians effectively diagnosed PCTNs. AI improved the diagnostic efficacy of junior physicians. AI assistance combined with CEUS had the best diagnostic efficacy, with an AUC=0.985 for senior physicians and an AUC=0.967 for junior physicians, with no significant difference ($P>0.05$). CONCLUSIONS: The CEUS scoring system established in this study has high diagnostic value for PCTNs. The use of CEUS and AI can improve the diagnostic accuracy of sonographers and improve the prognosis of PCTN patients.
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DOI: 10.3389/fendo.2025.1514185
PMCID: PMC12263380

Next-generation sequencing of targetable gene fusions in radioiodine-refractory thyroid cancer: a multicenter study.
Endocr Relat Cancer, 32(7)
J. Yoo, M. Kim, H. K. Kim, D. Y. Shin, M. J. Jeon, B. H. Kim, H. C. Kang, J. Lee, D. J. Lim and W. G. Kim. 2025.
We aimed to determine the prevalence and clinical significance of targetable gene fusions in patients with radioiodine-refractory thyroid cancer. This multicenter retrospective cohort study enrolled 111 patients from five tertiary medical centers, with molecular profiling performed using targeted next-generation sequencing. The analysis revealed that 58 (52.3%) patients possessed BRAFV600E mutation, while 25 (22.5%) had RAS mutations. Among the 20 (18.0%) patients with gene fusions, 13 had RET fusions, three had NTRK fusions, one had a BRAF fusion, and three had nondriver gene fusions. The group with targetable gene fusions was significantly younger compared to those with BRAF or RAS mutations ($P < 0.001$) and predominantly had classic papillary thyroid carcinoma. Furthermore, targetable gene fusions were detected in 30.8% of patients with refractory thyroid cancer harboring wild-type BRAF. More than half of the patients received systemic tyrosine kinase inhibitor therapy and three patients with confirmed RET or NTRK fusions achieved meaningful clinical benefit with selective agents. These findings suggest that a stepwise molecular testing strategy - initiating with BRAF single gene analysis followed by next-generation sequencing for assessing targetable gene fusions - may be a rational approach, particularly for younger patients with papillary thyroid carcinoma, for identifying candidates for precision therapy. This supports the integration of molecular profiling into routine clinical practice for radioiodine-refractory thyroid cancer and emphasizes its utility in guiding personalized treatment decisions in this challenging disease subset.
PubMed-ID: 40569242
DOI: 10.1530/ERC-25-0089

Does one session suffice? Evaluation of single-session ethanol ablation for thyroid cysts of varying sizes.
Am J Surg, 248:116519.
W. S. Yu, P. H. Lai, H. L. Lee, Y. H. Wang, C. L. Su, Y. S. Lee and K. L. Cheng. 2025.
PubMed-ID: 40700913
DOI: 10.1016/j.amjsurg.2025.116519

Thyroid storm during the recovery phase after non-thyroid surgery in a hyperthyroid patient: a case report and literature review.
Front Surg, 12:1633314.
J. Zeng, T. Yang and L. Wu. 2025.
BACKGROUND: Thyroid storm is a life-threatening endocrine emergency characterized by an acute exacerbation of thyrotoxicosis, often triggered by stressors such as surgery or infection, with a mortality rate of 8%-25%. Although the risk is well-documented in thyroid surgeries, perioperative thyroid storm following non-thyroid procedures is exceedingly rare, posing diagnostic and therapeutic challenges. This case report and literature review aim to highlight the clinical features and management strategies for perioperative thyroid storm in non-thyroid surgical patients through a case analysis and literature review. CASE PRESENTATION: A 53-year-old Chinese male with a 20-year history of poorly controlled hyperthyroidism (irregular medication adherence) underwent closed reduction and intramedullary nailing for a right

femoral fracture. Preoperative evaluation revealed mildly elevated free triiodothyronine (FT3: 6.87 pmol/L) and profoundly suppressed thyroid-stimulating hormone (TSH: <0.01 mIU/L). Antithyroid medication was omitted on the day of surgery. Following surgery and transfer to the recovery room, the patient demonstrated delayed emergence from anesthesia, with a Burch-Wartofsky score of 45 and persistent tachycardia (heart rate 144 bpm), meeting Grade 1 thyroid storm criteria per Japan Thyroid Association guidelines, indicating a definitive thyroid storm. After about one hour, the patient was diagnosed with thyroid crisis. Intravenous hydrocortisone (100 mg) and continuous esmolol infusion were promptly initiated, leading to gradual heart rate stabilization at 120 bpm. Approximately 20 minutes later, the patient regained full consciousness and met criteria for discharge from the recovery room. The patient was discharged on postoperative day 10 without complications. CONCLUSIONS: This case underscores that non-thyroid surgery can precipitate thyroid storm in hyperthyroid patients, even with atypical presentations (e.g., absence of hyperpyrexia). Early recognition relies on vigilance toward tachycardia and altered mental status. Perioperative management should emphasize: (1) rigorous preoperative optimization of thyroid function to achieve euthyroidism; (2) vigilant postoperative monitoring for early signs of thyroid storm; and 3) prompt diagnosis using the Burch-Wartofsky scale and guideline-based criteria, followed by combined therapy with beta-blockers, corticosteroids, and antithyroid drugs. This case uniquely demonstrates that non-thyroid surgery can precipitate thyroid storm without classic hyperthermia, highlighting the need for standardized monitoring protocols in hyperthyroid surgical patients.
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DOI: 10.3389/fsurg.2025.1633314
PMCID: PMC12301401

Nomogram for predicting difficult transoral and submental thyroidectomy: a retrospective model development and validation study with large-scale population.
Surg Endosc, 39(5):3202-14.
L. Zhan, B. Guo, Z. Tao, X. Deng, Z. Ding, B. Wu, Z. Yang, M. Guo, X. Tao, X. Gu and Y. Fan. 2025.
OBJECTIVE: No prior studies have described or stratified the difficulty of transoral and submental thyroidectomy (TOaST). We aimed to investigate preoperative factors as indicators of difficult TOaSTs and to develop a predictive model accordingly. METHODS: This retrospective study included 255 eligible DTC patients who underwent total thyroidectomy and central neck dissection (CND) via transoral and submental endoscopic approach between February 2021 and April 2024. These patients were randomized into training and validation groups in a 7:3 ratio. Procedures were categorized into difficult and normal TOaST based on operation time, conversion to open and intraoperative injury. Univariate and multivariate logistic regression analyses were used to assess the association between surgical difficulty and factors regarding demographics, laboratory tests and ultrasound information. A nomogram was then developed and validated internally. Surgical and oncological profiles and follow-up data were also analyzed. RESULTS: Five independent risk factors for difficult TOaST were identified in multivariate analysis: age (OR 0.84, $p < 0.001$), male sex (OR 4.75, $p = 0.016$), thyromental distance (TMD) < 7 cm (OR 7.59, $p < 0.001$), presence of diffuse changes on ultrasound (OR 14.5, $p < 0.001$), and elevated anti-thyroid peroxidase antibody (TPO-Ab) level (OR 5.22, $p = 0.005$). The nomogram performed well on both the training and the validation datasets, achieving an area under curve (AUC) of 0.908 and 0.888, respectively. Calibration curves for both datasets also fit well. There was no significant difference in complication rates between the difficult and normal TOaST groups. CONCLUSION: The developed nomogram provides a reliable, straightforward prediction of difficult TOaST, thus supporting preoperative preparation and consultation, as well as optimizing training and promotion.
PubMed-ID: 40216625
DOI: 10.1007/s00464-025-11725-1
PMCID: PMC12041166

Comment on "The Surgical Management of Intracranial Metastasis Secondary to Follicular Cell-Derived Thyroid Carcinoma".
J Surg Oncol, 132(3):403-4.
H. Zhang, J. Xu and X. Zhu. 2025.
PubMed-ID: 40401363
DOI: 10.1002/jso.28131

Lobectomy vs total thyroidectomy for unilateral papillary thyroid carcinoma with ipsilateral cervical lymph node metastasis.
Front Endocrinol (Lausanne), 16:1564752.
S. Zhang, K. Zhou, J. Wang, M. Zhao, X. Mao, J. Shang and X. Lan. 2025.

OBJECTIVE: This study aimed to compare the prognosis of unilateral papillary thyroid carcinoma(PTC) patients with ipsilateral cervical lymph node metastasis(IC-LNM) under the treatment of unilateral lobectomy(uLT) vs total thyroidectomy(TT) in order to find out the optimal surgery for these patients without other clinical risk characteristics. METHODS: PTC patients at Zhejiang Cancer Hospital between 2012 and 2022 were retrospectively reviewed. Additionally, a propensity score matching(PSM) was performed on patients treated with uLT or TT. Recurrence-free survival(RFS), overall survival(OS), hospitalization costs, postoperative complications, and other clinical characteristics were analyzed between the two groups. RESULTS: Ultimately, 682 unilateral PTC patients with IC-LNM were available in the study. After PSM with possible prognostic factors(such as gender, age, primary tumor size, multifocality, extrathyroidal invasion, and T-stage), 225 pairs of patients were available. With a median of 81(5-154) months follow-up, 22 patients(9.8%) in the uLT and 12(5.3%) in the TT recurred. There were no significant differences in 5-year RFS and 5-year OS between uLT and TT groups. However, TT group was significantly correlated with higher risk of transient and permanent hypoparathyroidism, higher levothyroxine doses, longer hospital stays, and higher hospitalization costs than uLT group($p<0.05$). CONCLUSIONS: Our study indicated that there were no differences in recurrence and survival between unilateral PTC patients with IC-LNM treated with uLT or TT for the primary tumor. However, uLT group had a lower risk of postoperative complications and a lower hospitalization cost than TT group. Thus, for selected unilateral PTC patients with IC-LNM without other risk features, uLT could be recommended.
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DOI: 10.3389/fendo.2025.1564752
PMCID: PMC12328177

Machine learning-based quantification of overall and internal ultrasound characteristics for diagnosing malignant partially cystic thyroid nodules.
Front Endocrinol (Lausanne), 16:1635122.
Y. Zhang, J. Jiang, A. Chen, D. Zhang, L. Wang, X. Yuan, X. He, S. Yu, J. Wang and Q. Zhou. 2025.
INTRODUCTION: Partially cystic thyroid nodules (PCTNs) with malignant potential are frequently underestimated due to limited recognition of their sonographic characteristics. METHODS: This retrospective analysis included 486 PCTNs identified between March 2021 and September 2022. Machine learning (ML) was employed to quantitatively evaluate the overall ultrasound characteristics of the whole nodule as well as the internal ultrasound characteristics of its solid part. Three diagnostic models were constructed based on different sets of ultrasound data. The dataset was split into training and testing subsets at a 7:3 ratio. Key ultrasound characteristics such as marked hypoechogenicity, calcifications, solid component>/=50%, and unclear internal margins were emphasized. RESULTS: Among the models, the integrated one-incorporating both overall-nodule and internal solid-part characteristics-achieved superior diagnostic performance, with an area under the curve (AUC) of 0.96 (0.93-0.99) on the test data. The model demonstrated an accuracy of 0.91 (0.85-0.95), a sensitivity of 0.88 (0.73-0.97), a specificity of 0.92 (0.85-0.96), a negative predictive value of 0.96 (0.91-0.99), and a positive predictive value of 0.77 (0.61-0.89). This comprehensive model significantly outperformed the model utilizing only overall nodule characteristics (AUC = 0.85, P = 2.35e-6), and demonstrated comparable effectiveness to the model based solely on internal characteristics (AUC = 0.93, P = 1.01e-1). DISCUSSION: The results support the clinical utility of an ML-driven approach that integrates comprehensive ultrasound metrics for the reliable identification of malignant PCTNs.
PubMed-ID: 40842501
DOI: 10.3389/fendo.2025.1635122
PMCID: PMC12364630

Letter to the Editor: "Minimal access versus open approaches for thyroid cancer: analysis and recommendations".
Int J Surg, 111(8):5743-4.
Z. Zhang, Y. Zou and J. He. 2025.
PubMed-ID: 40497924
DOI: 10.1097/JS9.0000000000002622

Prognostic factors for progression free survival in patients with medullary thyroid cancer: a multicenter cohort study.
Updates Surg, 77(4):1153-60.
G. Zheng, J. Liu, H. Xu, C. Dong, X. Cao, Q. He, G. Zhang, W. Wang, L. Wang, X. Yang, J. Liu, M. Hao, K. Xue, G. Li, X. Liu, C. Ding, X. Wang and H. Zheng. 2025.
Many patients with medullary thyroid cancer (MTC) experience recurrent or persistent disease after surgery due to its aggressive nature. However, the prognostic factors for progression-free survival (PFS) have been poorly investigated. This study aimed to explore prognostic factors associated with PFS in patients with MTC. Patients with MTC were enrolled from

15 medical centers in Shandong Province, China, between January 2010 and December 2021. Univariate and multivariate Cox regression analyses were used to explore the prognostic factors for PFS in patients with MTC. Receiver operating characteristic curve analysis was performed to determine the optimal cutoff value of the metastatic lymph node ratio (LNR) in predicting PFS. Patients with MTC from the Surveillance, Epidemiology, and End Results (SEER) database were used to test the predictive value of the LNR cutoff for overall survival (OS) and disease-specific survival (DSS). In the Shandong cohort, extrathyroidal extension (HR, 1.622; 95% CI 1.022-2.575, P = 0.040), LNR (HR, 2.806; 95% CI 1.121-7.025, P = 0.028), and T3 stage (HR, 2.060; 95% CI 1.074-3.952, P = 0.030) were independent risk factors for PFS in patients with MTC. The optimal cutoff value of the LNR for predicting PFS was 0.19. Compared to patients with LNR < 0.19, those with LNR >/= 0.19 suffered worse PFS (Log-rank P < 0.0001) in the Shandong cohort, and worse OS (Log-rank P < 0.0001) and DSS (Log-rank P < 0.0001) in the SEER cohort. This study identified prognostic factors for PFS in patients with MTC. LNR >/= 0.19 could be used as an adverse prognostic factor for patients with MTC.
PubMed-ID: 40392415
DOI: 10.1007/s13304-025-02193-2

Predicting central lymph node metastasis in papillary thyroid microcarcinoma: a breakthrough with interpretable machine learning.
Front Endocrinol (Lausanne), 16:1537386.
W. Zhou, L. Li, X. Hao, L. Wu, L. Liu, B. Zheng, Y. Xia and Y. Liu. 2025.
OBJECTIVE: To develop and validate an interpretable machine learning (ML) model for the preoperative prediction of central lymph node metastasis (CLNM) in papillary thyroid microcarcinoma (PTMC). METHODS: From December 2016 to December 2023, we retrospectively analyzed 710 PTMC patients who underwent thyroidectomies. Feature selection was conducted using the least absolute shrinkage and selection operator (LASSO) regression method, alongside the Support Vector Machine-Recursive Feature Elimination (SVM-RFE) algorithm in conjunction with multivariate logistic regression. Eight ML algorithms, namely Decision Tree, Random Forest (RF), K-nearest neighbors, Support vector machine, Extreme Gradient Boosting, Naive Bayes, Logistic regression, and Light Gradient Boosting machine, were developed for the prediction of CLNM. The performance of these models was evaluated using area under the receiver operating characteristic curve (AUC), decision curve analysis (DCA), sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and F1 scores. Additionally, the Shapley Additive Explanation (SHAP) algorithm was utilized to clarify the results of the optimal ML model. RESULTS: The results indicated that 32.95% of the patients (234/710) presented with CLNM. Tumor diameter, multifocality, lymph nodes identified via ultrasound (US-LN), and extrathyroidal extension (ETE) were identified as independent predictors of CLNM. The RF model achieved the highest performance in the validation set with an AUC of 0.893(95%CI: 0.846-0.940), accuracy of 0.832, sensitivity of 0.764, specificity of 0.866, PPV of 0.743, NPV of 0.879, and F1-score of 0.753. Furthermore, the DCA demonstrated that the RF model exhibited a superior clinical net benefit. CONCLUSION: Our model predicted the risk of CLNM in PTMC patients with high accuracy preoperatively.
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DOI: 10.3389/fendo.2025.1537386
PMCID: PMC12104047

Patient-reported outcomes by individuals with differentiated thyroid cancer who underwent minimal-access versus conventional open thyroidectomy: a real-world propensity score-matching study.
Int J Surg, 111(6):3710-21.
Y. Zhou, H. Tian, G. Zhang, B. Hu, Y. Wang, W. Yan, X. Wu, K. Zhang, J. Deng, Y. Liang, X. Qi, L. Ren and Y. Zhang. 2025.
BACKGROUND: Minimal-access surgery has been widely used in differentiated thyroid cancer (DTC) management and its therapeutic effectiveness is well-proven. However, little is known about how minimal-access thyroidectomy affects patient-reported outcomes (PRO). MATERIALS AND METHODS: In this real-world cross-sectional study, 6221 patients with DTC who underwent minimal-access or conventional open thyroidectomy were included and required to fill out PRO questionnaires, including the Thyroid Cancer-Specific Quality of Life, the European Organisation for Research and Treatment of Cancer's Core Quality of Life Questionnaire, and Fear of Progression Questionnaire-Short Form. Of the 3586 patients who completed the questionnaires entirely, 915 and 2671 belonged to the minimal-access and open groups, respectively. To reduce bias and balance confounding factors, propensity score matching was performed, after which 1818 patients were equally divided between the two groups. RESULTS: Compared with the open group, the minimal-access group reported better PRO in terms of the THYCA-QOL summary score (P < 0.001), neuromuscular (P = 0.038), voice (P < 0.001), concentration (P = 0.044), sympathetic (P = 0.002), throat/mouth (P < 0.001), and scar (P < 0.001), feeling chilly (P < 0.001), and tingling hands/feet (P = 0.002). Subgroup analysis demonstrated that minimal-access thyroidectomy can

be optimal for most patients from the PRO perspective. Moreover, longitudinal PRO comparisons indicated that at </=6 months postoperatively, the open group experienced more problems in neuromuscular, voice, sympathetic, throat/mouth, scar, feeling chilly, tingling hands/feet, headache, and lower global health status scores (all P < 0.05). However, except for voice, scar and tingling hands/feet, nearly all the differences disappeared after 7 months postoperatively. Intergroup comparisons suggested that the minimal-access group required less time to recover to a stable state. CONCLUSIONS: The minimal-access group exhibited significantly superior postoperative PRO compared to the open group. Furthermore, the PRO trajectories of the two groups differed, with the minimal-access group demonstrating a considerably shorter recovery time. If better PRO is desired, minimal-access thyroidectomy may be preferred.
PubMed-ID: 40277385
DOI: 10.1097/JS9.0000000000002418
PMCID: PMC12165580

Thyroglobulin-to-tumor volume ratio combined with ultrasound features for diagnosing thyroid follicular neoplasms.
Front Endocrinol (Lausanne), 16:1626766.
X. Zhu, F. Liu, J. Liu, Z. Li and Y. Ma. 2025.
OBJECTIVE: Current preoperative diagnostics inadequately differentiate benign from malignant thyroid follicular neoplasms. This study evaluated the diagnostic utility of thyroid function markers and contrast-enhanced ultrasound (CEUS) features in differentiating follicular thyroid adenoma (FTA) from follicular thyroid carcinoma (FTC), focusing on a novel parameter: the thyroglobulin-to-tumor volume ratio (Tg/Vol ratio). METHODS: We retrospectively analyzed 432 resected thyroid follicular neoplasms. A comprehensive comparison was performed regarding baseline characteristics, thyroid function profiles, and CEUS features between FTA and FTC groups through univariate and multivariate binary logistic regression. Diagnostic performance was determined via receiver operating characteristic (ROC) curve analysis. The prevalence of FTC across serum marker subgroups was assessed, followed by the development of a multivariate diagnostic model integrating the Tg/Vol ratio with CEUS characteristics. RESULTS: Among 432 patients (352 females, 81.5%) with a median age of 47 years, multivariate logistic regression analysis revealed three independent predictors of FTC: capsular involvement (odds ratio [OR] = 9.958, 95% confidence interval [CI]: 2.453 - 40.424, p = 0.001), Tg/Vol ratio >7.412 (OR = 3.508, 95% CI: 1.388 - 8.868, p = 0.008), and male gender (OR = 3.474, CI: 1.751 - 6.891, p < 0.001). Subgroup analyses revealed higher FTC prevalence in patients with Tg > 409.18 mug/L (20.41%, p = 0.002) and Tg/Vol ratio > 20.68 (20.41%, p = 0.009). The combined diagnostic model incorporating Tg/Vol ratio and CEUS features demonstrated 69.4% sensitivity, 77.0% specificity, and the area under the curve(AUC) of 0.769. CONCLUSION: While elevated preoperative Tg correlates with malignant potential, but the Tg/Vol ratio emerges as a more robust preoperative discriminator. The combined diagnostic model incorporating Tg/Vol ratio and CEUS features significantly improves FTC detection accuracy.
PubMed-ID: 40708719
DOI: 10.3389/fendo.2025.1626766
PMCID: PMC12286834

Parathyroids

Meta-Analyses

Efficacy of Radiofrequency Ablation-Guided by Ultrasound in Primary Hyperparathyroidism: A Systematic Review and Meta-Analysis.
Head Neck, 47(5):1504-11.
A. Rodrigues, L. C. Pereira, T. D. D. Cabral, E. Pasqualotto, I. F. Scabello, M. P. B. Rocha, F. C. A. de Moraes, A. L. D. Araujo and L. P. Kowalski. 2025.
BACKGROUND: Radiofrequency ablation guided by ultrasound (RFA-USG) is an alternative treatment for primary hyperparathyroidism (PHPT) patients. Despite showing accurate precision and minimal invasion, its efficacy remains questionable. METHODS: We searched PubMed, Embase, Scopus, Cochrane Library, Portal Regional da Biblioteca Virtual em Saude (BVS), Web of Science databases for randomized controlled trials (RCTs) and observational studies evaluating RFA-USG in PHPT patients. Statistical analysis was performed with R software, version 4.4.3. RESULTS: Eight studies were included with 208 patients with PHPT undergoing RFA-USG treatment. After 3 months of treatment, parathyroid volume was 0.31 mL (0.16-0.61), Parathyroid hormone (PTH) level was 60.71 pg/mL (53.87-68.42), and calcium level was 5.43 mEq/L (2.63-11.23). The occurrence of hoarseness among the patients was 4.4% (1.64-11.02). CONCLUSION: RFA-USG is safe for PHPT patients, with associated parathyroid volume reduction and decrease in PTH. However, further study is needed to compare RFA-USG to the gold standard of surgery for PHPT.
PubMed-ID: 39823162
DOI: 10.1002/hed.28032

Randomized controlled trials

rhPTH(1-84) for hypoparathyroidism: a randomized study of patient-reported outcomes.
Eur J Endocrinol, 193(2):310-9.
M. L. Brandi, T. Vokes, N. M. Appelman-Dijkstra, O. Ayodele, B. Decallonne, R. de Jongh, M. Diaz-Curiel, W. Fraser, R. D. Finkelman, A. Heck, S. W. Ing, P. Kamenicky, A. A. Khan, C. S. Kovacs, B. Lapauw, G. Leese, G. Mantovani, G. Martinez Diaz-Guerra, L. Masi, M. Melo, A. Palermo, N. L. Reddy, L. Rejnmark, E. Tokareva, M. C. Vantyghem, S. Wang, M. Warren and B. Yan. 2025.
OBJECTIVE: To assess the impact of recombinant human parathyroid hormone (1-84) [rhPTH(1-84)] compared with placebo, in combination with conventional therapy with vitamin D and/or calcium supplements, on health-related quality of life (HRQoL) in patients with symptomatic chronic hypoparathyroidism (cHypoPT). DESIGN: Randomized, double-blind, placebo-controlled, phase 3b-4 study (ClinicalTrials.gov ID: NCT03324880). METHODS: Eligible patients with symptomatic cHypoPT were randomized to receive subcutaneous rhPTH(1-84) 25-100 microg/day or placebo. The primary endpoint was the change from baseline to week 26 in Hypoparathyroidism Symptom Diary (HypoPT-SD) symptom subscale score. Key secondary endpoints were changes from baseline to week 26 in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue and in 36-item Short Form Health Survey physical component summary (SF-36v2 PCS). RESULTS: In total, 93 patients were randomized to receive treatment: 45 received rhPTH(1-84) and 48 received placebo. Change from baseline to week 26 in HypoPT-SD symptom subscale score was significantly greater (improved) in the rhPTH(1-84) group than in the placebo group (difference in least-squares mean changes, -0.53; 95% confidence interval, -0.90 to -0.15, P = .003). Key secondary endpoints, changes between baseline and week 26 in the FACIT-Fatigue and SF-36v2 PCS scores were also significantly greater (improved) in the rhPTH(1-84) group than in the placebo group. The safety profile of rhPTH(1-84) was consistent with previous findings, and no new safety signals were identified. CONCLUSIONS: rhPTH(1-84) alongside conventional therapy improved symptom burden (as measured by the HypoPT-SD) and HRQoL to a greater extent than conventional therapy alone in patients with symptomatic cHypoPT.
PubMed-ID: 40711996
DOI: 10.1093/ejendo/lvaf148

Consensus Statements/Guidelines

- None -

Other Articles

Assessing the feasibility of near infrared autofluorescence imaging in minimally-invasive video assisted parathyroidectomy and the autofluorescence signature of parathyroid adenomas. A single center surgical case series.
Surg Endosc, 39(5):2964-72.
S. Bakkar, A. Chorti, T. Papavramidis, G. Donatini and P. Miccoli. 2025.
BACKGROUND: The role of near-infrared autofluorescence (NIRAF)-imaging in thyroid surgery is well-established. However, its role in hyperparathyroidism surgery is yet to be defined due to the lack of consensus regarding the autofluorescence (AF) pattern of parathyroid adenomas (PAs). Furthermore, its utility in minimally invasive video-assisted parathyroidectomy (MIVAP) has yet to be assessed. OBJECTIVE: To assess the feasibility of utilizing NIRAF-imaging via the limited-access of MIVAP and whether PAs demonstrate a unique AF signature allowing NIRAF-imaging to serve as an intraoperative diagnostic tool. METHODS: The clinical records of patients who underwent MIVAP for hyperparathyroidism between February and October 2024 were retrospectively reviewed. The primary endpoint was to assess the feasibility of NIRAF-imaging in MIVAP and whether PAs demonstrate a defining AF pattern. Secondary endpoints included whether certain AF patterns of PAs correlated with specific PA features including cell type, size, and/or location. Furthermore, operative-time and cost implications were assessed. RESULTS: 24 consecutive patients underwent MIVAP for hyperparathyroidism. NIRAF-imaging was feasible via the limited-access with no technical difficulties reported. AF patterns included high-intensity AF in 10 (38.5%), low-intensity AF in 10 (38.5%), and cap AF in 6 (23%). A new AF pattern was also described and referred to as "double cap AF". No significant differences in the patterns of AF were observed (p = 0.2). The pattern of AF did not considerably correlate with the predominant cell type, size or location of the PA. However, mediastinal PAs demonstrated a significantly higher tendency for cap AF. The additional time added to the procedure applying the technology was only a few minutes. However, it conferred a considerable additional cost. CONCLUSION: In experienced hands, a direct minimal-access did not preclude utilizing NIRAF-imaging. PAs seem to lack a uniform characteristic AF signature implying a limited diagnostic role of NIRAF-imaging in parathyroid surgery apart from confirming normal parathyroid tissue. The study has been registered in ClinicalTrials.gov; registration number: NCT06779760.
PubMed-ID: 40119064
DOI: 10.1007/s00464-025-11675-8

Patients with normocalcemic versus hypercalcemic hyperparathyroidism: What's really the difference?
Am J Surg, 244:116272.
S. Balachandra, R. Wang, R. Akhund, A. Allahwasaya, B. Lindeman, J. Fazendin, A. Gillis and H. Chen. 2025.
INTRODUCTION: Primary hyperparathyroidism (HPT) is typically characterized by elevated parathyroid hormone (PTH) and hypercalcemia; however, some patients develop normocalcemic hyperparathyroidism. Patients with normocalcemic HPT have an elevated PTH with normal calcium levels and no other secondary causes of elevated PTH, and therefore have a unique biochemical profile. The aim of this project is to compare the demographics, presentation, and outcomes for patients with normocalcemic HPT versus patients with hypercalcemic HPT undergoing parathyroidectomy. METHODS: A single institution, retrospective review was conducted between January 2016 and June 2022. Patients were classified as either having hypercalcemic (calcium >10.4 mg/dL) or normocalcemic (calcium </=10.4 mg/dL) HPT. Cure was defined as normal calcium for 6 months post-operatively in the hypercalcemic HPT group and normal PTH (<88 pg/mL) for 6 months post-operatively in the normocalcemic HPT group. RESULTS: Of the 701 patients included in the study, 566 (80.7 %) had hypercalcemic HPT and 135 (19.3 %) had normocalcemic HPT. The preoperative Ca was 11 +/- 0.7 mg/dL in the hypercalcemic group and 9.8 +/- 0.4 mg/dL in the normocalcemic group (p < 0.001). The preoperative PTH was 148.2 +/- 180 pg/dL in the hypercalcemic group and 117.4 +/- 105.3 pg/dL in the normocalcemic group (p = 0.06). The average age of normocalcemic patients was 56 +/- 15 years, compared to 59 +/- 15 years in the hypercalcemic group (p = 0.07). There was no significant difference in sex (p = 0.42). African American patients were more likely to present with hypercalcemic HPT (19.1 %) than with normocalcemic HPT (9.6 %, p = 0.01). Normocalcemic patients were more likely to report pre-operative symptoms of kidney stones compared to patients with hypercalcemia (53.3 % versus 30.4 %, p < 0.001). There was no significant difference in pre-operative symptoms of fatigue, bone pain, or fractures. Patients with hypercalcemic

HPT were more likely to present with adenoma (64.3 %); whereas patients with normocalcemic HPT were more likely to present with hyperplasia (43.3 %, p < 0.001). More patients with normocalcemic HPT underwent thymectomy compared to patients with hypercalcemia (39.3 % versus 20.8 % respectively, p < 0.001). 92.0 % of normocalcemic patients achieved cure post-operatively, which was significantly less than in the hypercalcemic group (97.0 %, p = 0.02). The 8.0 % of normocalcemic patients that did not achieve cure had a mean PTH level of 147.9 +/- 159 pg/mL at 6 months post-operative. Four patients with normocalcemic HPT had recurrence of disease (3 %), and three of the four patients underwent bilateral exploration. CONCLUSIONS: Patients with normocalcemic HPT present with different symptoms compared to patients with hypercalcemic HPT prior to surgery. Additionally, patients with normocalcemic HPT are less likely to achieve cure after surgery, which warrants further investigation.
PubMed-ID: 40022764
DOI: 10.1016/j.amjsurg.2025.116272
PMCID: PMC12276955

The Landmark Series: Management of Primary Hyperparathyroidism.
Ann Surg Oncol, 32(5):3126-34.
J. M. Broekhuis, D. L. Fraker and J. B. Liu. 2025.
Surgery is the only definitive treatment for primary hyperparathyroidism (PHPT). The surgical management of PHPT has evolved over the past several decades in response to the continually growing body of evidence supporting its effectiveness in both symptomatic and asymptomatic disease. As imaging modalities for localization, operative approach, and intraoperative adjuncts, such as intraoperative parathyroid hormone testing, have been optimized, careful evaluation of the timing of parathyroidectomy in relationship to the disease's natural history has been pursued to limit the detrimental end-organ effects of untreated PHPT. Herein, we review select studies examining key aspects of PHPT management fundamental to the practicing surgical oncologist and endocrine surgeon caring for patients with PHPT.
PubMed-ID: 40025363
DOI: 10.1245/s10434-025-17045-x

Correction: Ultrasound detection of normal parathyroid glands: detection rate, topographic anatomy and the role of underlying thyroid disease.
Front Endocrinol (Lausanne), 16:1664368.
I. Chiardi, P. Makovac, A. Leoncini, F. Forte, M. Rotondi and P. Trimboli. 2025.
[This corrects the article DOI: 10.3389/fendo.2025.1595940.].
PubMed-ID: 40873951
DOI: 10.3389/fendo.2025.1664368
PMCID: PMC12378866

Ultrasound detection of normal parathyroid glands: detection rate, topographic anatomy, and the role of underlying thyroid disease.
Front Endocrinol (Lausanne), 16:1595940.
I. Chiardi, P. Makovac, A. Leoncini, F. Forte, M. Rotondi and P. Trimboli. 2025.
INTRODUCTION: Visualizing normal parathyroid glands (PTGs) using ultrasound (US) has historically been challenging. This study aims to assess the detection rate of normal PTGs in thyroid patients and evaluate their echostructure, anatomical location and their relation with the underlying thyroid pathology. METHODS: A retrospective observational study was conducted over four weeks (September-October 2024) at the Thyroid Unit of Ente Ospedaliero Cantonale (EOC). Consecutive thyroid patients undergoing US for any thyroid indication were included, while those with a history of parathyroid disease, chronic kidney disease, or recent thyroid surgery were excluded. The primary outcome was the detection rate of normal PTGs. Secondary outcomes included PTG echostructure, anatomical location, and correlations with patient characteristics (age, gender, BMI, thyroid volume, and underlying thyroid pathology). RESULTS: Normal PTGs were identified in 45.1% of patients (n=51). Most PTGs were located near the lower pole of the thyroid lobes and appeared mildly hyperechoic. Thyroid volume was inversely associated with PTG detection (p=0.001), while underlying thyroid pathology (e.g., thyroiditis, nodular disease) had no significant impact on detection rates. CONCLUSION: Normal PTGs can be visualized using US, particularly near the lower thyroid poles. Detection rates decrease in patients with larger thyroid volumes or athyreotic status. These findings confirm and expand on recent studies, challenging the historical belief that normal PTGs are undetectable, with potential implications for endocrine imaging and surgical planning.
PubMed-ID: 40708724

DOI: 10.3389/fendo.2025.1595940
PMCID: PMC12286828

A retrospective analysis of the management of renal hyperparathyroidism; evaluating changes in practice and outcome in an era of calcimimetics.
Langenbecks Arch Surg, 410(1):172.
W. P. Duggan, R. Patterson, N. M. Smyth, N. Kyne, D. Synnott, N. McHugh, R. Y. Teo, R. Hill, U. Khan, S. Paul, D. Reddan, C. Wall, W. Plant, J. Kinsella, O. Young, A. Lowery, P. Redmond, P. Conlon and A. D. K. Hill. 2025.
PURPOSE: Hyperparathyroidism (HPT) is a common and significant complication of chronic kidney disease (CKD). Both parathyroidectomy and cinacalcet, are used routinely in an effort to manage this cohort. Unfortunately, there remains no guideline consensus on how best to combine these treatments into an effective strategy. We look to assess the efficacy of these interventions and identify factors predicting recurrence and the development of post-operative complications. We also examine changes in our practice nationally following the arrival of cinacalcet as an alternative or an abridge to definitive surgical management. METHODS: This was a nationwide study. We conducted a retrospective analysis of a prospectively maintained database. All patients who underwent a parathyroidectomy as management of secondary or tertiary HPT between 1999 and 2023 were included. A control group of patients managed with cinacalcet were also included. RESULTS: Our cohort included 155 patients managed with parathyroidectomy and 203 patients treated with cinacalcet. Pre-operative Alkaline phosphatase > 200 IU/L was predictive of hungry bone syndrome (HBS) on univariate (P = 0.003) and multivariate (P = 0.002) analysis, whilst a PTH > 1000 pg/ml (P = 0.012) was also predictive of HBS on univariate analysis. In an attempt to identify an optimal PTH cut off to trigger surgical referral we found mean serum PTH levels were significantly higher at 5 years in the cohort of patients who had a PTH > 1000 pg/ml prior to surgical intervention (39 +/- 32 Vs 374 +/- 544, P = 0.045). CONCLUSIONS: Our findings re-emphasise the efficacy and safety of parathyroid surgery in the management of renal HPT and suggest earlier surgical referral may improve the incidence of post-operative HBS and recurrent HPT.
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DOI: 10.1007/s00423-025-03744-2
PMCID: PMC12129844

Construction and validation of a predictive model for the serum phosphorus reduction after total parathyroidectomy in patients with secondary hyperparathyroidism.
Front Endocrinol (Lausanne), 16:1584602.
Y. Feng, Y. Zhou, X. Feng, Q. Sa, N. Zhang, W. Xie, B. Liu, F. Chen, G. Cheng and W. Zhang. 2025.
OBJECTIVE: We aimed to construct a predictive scoring model for the factors influencing serum phosphorus reduction following total parathyroidectomy (tPTX) in secondary hyperparathyroidism (SHPT) and provide a reference for identifying patients who can successfully correct hyperphosphatemia before surgery. METHODS: The clinical data of 529 patients with SHPT who underwent tPTX were retrospectively analyzed according to the inclusion and exclusion criteria. Univariate and multivariate analyses were conducted to determine the independent factors and establish a predictive scoring model. The receiver operating characteristic curve (ROC) was applied to verify the model in the training and validation groups, respectively. RESULTS: In the whole group, 315 patients had a significant decrease in serum phosphorus after tPTX. Univariate and multivariate analysis showed that preoperative alkaline phosphatase (AKP), intact parathyroid hormone (iPTH) and free triiodothyronine (FT3) were independent influencing factors to promote the decrease of serum phosphorus after tPTX; Serum phosphorus and bone pain were inhibitory factors (all P<0.05). According to the cut-off value, AKP>193.33 U/L, iPTH>1808 pg/mL, FT3>2.825 pg/mL, serum phosphorus>2.285 mmol/L and bone pain were used to establish the predictive scoring model for serum phosphorus decline. The results showed that the success rate of serum phosphorus reduction was 67.55% at 10~14 points and 95.35% at 15~24 points. The area under ROC curves (AUC) for the training and validation group were 0.818 (95% CI=0.775~0.861) and 0.840 (95% CI=0.780~0.901, both P<0.05). CONCLUSION: The established prediction score model for serum phosphorus decrease has a good prediction efficiency which is helpful for the early identification. The model provides important clinical guidance for the postoperative management and treatment of SHPT.
PubMed-ID: 40510469
DOI: 10.3389/fendo.2025.1584602
PMCID: PMC12158720

The Effect of Preoperative Biochemical Parameters on the Development of Hungry Bone Syndrome After Surgery for Primary Hyperparathyroidism.
Clin Endocrinol (Oxf), 103(3):311-6.
M. Hadi, A. Mansouri, S. Seyedyousefi and R. Salehidoost. 2025.
BACKGROUND: Hungry bone syndrome (HBS) characterised by prolonged hypocalcemia, occurs commonly following parathyroidectomy in patients with primary hyperparathyroidism (PHPT). Although this complication is common, research in this field is very scarce. This study aimed to determine the incidence, characteristics of patients with HBS, and the effect of preoperative biochemical parameters on HBS. METHODS: In this retrospective study we enroled 144 patients with PHPT who underwent successful parathyroidectomy from January 2010 to January 2020. Preoperative and postoperative laboratory parameters were assessed. Logistic regression analysis was used to identify factors affecting the incidence of HBS. RESULTS: One hundred six patients (73.6%) were women and the female-to-male ratio was 2.8-1. The median (IQR) age of all patients was 54 (19) years. HBS developed in 25 (17.36%) patients (5 men and 20 women, p = 0.425). Total calcium and parathyroid hormone preoperatively were significantly higher in patients with HBS, while serum phosphorus and magnesium levels did not differ statistically between the two groups. The resected parathyroid gland volume was higher in those with HBS compared to those without. Postoperatively, patients with HBS had longer hospital stays and lower serum phosphorus levels. However, these variables could not predict the occurrence of HBS after surgery in the performed regression model. CONCLUSION: The patients with HBS had higher levels of calcium and parathyroid hormone preoperatively, along with larger resected parathyroid glands. Nevertheless, preoperative parameters were unable to predict HBS. Therefore, biochemical monitoring after surgery seems necessary to detect HBS and protect patients from severe hypocalcemia.
PubMed-ID: 40351002
DOI: 10.1111/cen.15268

Identifying the missing parathyroid: Remember to explore the carotid sheath.
Am J Surg, 248:116430.
M. He and S. M. Wiseman. 2025.
PubMed-ID: 40425431
DOI: 10.1016/j.amjsurg.2025.116430

Germline mutations of GCM2 cause a novel variant of hereditary primary hyperparathyroidism.
Updates Surg, 77(4):1191-200.
M. Iacobone, S. Watutantrige-Fernando, S. Zovato, S. Tognazzo, S. Dughiero, V. Augenti, V. Camozzi, C. Mian, F. Torresan, C. Nomine-Criqui and L. Brunaud. 2025.
Primary hyperparathyroidism (pHPT) occurs as hereditary disease in approximately 10% of cases. GCM2 germline mutations have been recently described as responsible for the development of a novel variant of hereditary pHPT. This study aimed to determine the features of GCM2-related pHPT. Demographics, laboratory, and surgical data were assessed in a series of 17 index cases carrying GCM2 mutations undergoing surgery for pHPT. The GCM2 germline pathogenic variant c.1181 A>C p.(Tyr394Ser) was detected in 59% of cases. GCM2-related pHPT was diagnosed at a median age of 57 years (range 32-82) with a Female/Male ratio 1.8. Preoperative median calcemia was 2.89 mmol/L (range 2.69-3.8). Family history of pHPT was absent in 65% of cases. Complete clinical, surgical and follow-up data were available for 13 patients. At initial surgery, bilateral neck exploration with subtotal parathyroidectomy was performed in 46% of patients; achieving cure in all cases at a median follow-up of 51 months (range 7-60). In the remaining cases undergoing selective parathyroidectomy, a persistent pHPT occurred in 3 cases; recurrent pHPT in 1 patient (after a disease-free interval of 4 years) while 3 are disease free at a mean follow-up of 21 months. Thus, at an overall prolonged follow-up (median 48 months, range 7-216), multiglandular involvement occurred in 77% of cases. GCM2 germline mutations may cause hereditary pHPT, even if it may mimic sporadic variant due to the absence of familial history and late onset. The main feature is multiglandular involvement, needing bilateral neck exploration and subtotal parathyroidectomy to achieve long-term cure.
PubMed-ID: 40329145
DOI: 10.1007/s13304-025-02179-0
PMCID: PMC12263790

An exceptionally rare case of a giant parathyroid adenoma with carcinoma-like presentation.
Hormones (Athens), 24(2):575-80.
P. Kazakou, D. Vrachnis, S. A. Paschou, K. Nastos, H. Sarlani, K. Kantreva, K. Stefanaki, T. Psaltopoulou, G. Kyriakopoulos, P. Korkolopoulou and K. Saltiki. 2025.
Giant parathyroid adenoma (GPA) is an extremely rare cause of primary hyperparathyroidism (PHPT) and may sometimes mimic parathyroid carcinoma (PC). Parathyroid carcinoma is also a very rare entity. Both preoperative and postoperative diagnosis of the two conditions remains a challenge. The purpose of this article is to present the diagnostic and therapeutic approach used for a 76-year-old female patient with a GPA measuring 5.4 x 2.3 cm, mimicking PC. The patient was referred to our clinic for the management of severe hypercalcemia revealed during the neurological evaluation of psychiatric and cognitive symptoms, confusion, weakness, and bone pain. PHPT was confirmed based on the patient's biochemical profile, which showed extremely high levels of serum calcium and parathyroid hormone (PTH). Wholebody computed tomography revealed a large nodule below the inferior pole of the right lobe of the thyroid gland and no further pathology in other organs. En bloc resection of the tumor with removal of the ipsilateral hemithyroid and other involved tissues was performed. Histopathological evaluation was diagnostic for a GPA. Post-surgery hungry bone syndrome (HBS) developed and was treated. However, the patient succumbed 3 weeks later due to septic shock. GPA is an exceptionally rare endocrine tumor that should be suspected along with PC in patients with significantly elevated levels of PTH and calcium, and/or palpable neck mass. In our case, diagnosis was based principally on histopathological examination together with clinical presentation, biochemical profile, and imaging studies. Resection of the tumor remains the treatment of choice.
PubMed-ID: 39831932
DOI: 10.1007/s42000-025-00627-5
PMCID: PMC12339605

Percutaneous ethanol and calcitriol injection therapy for hyperparathyroidism - a single-centre experience.
Front Endocrinol (Lausanne), 16:1562493.
E. K. F. Leong, R. M. See, Z. Lin, M. C. S. Chin, J. W. Y. Chew, K. Y. Ngiam and J. W. K. Lee. 2025.
BACKGROUND: The purpose of this study is to evaluate the use of percutaneous ethanol and calcitriol injection therapy for hyperparathyroidism (HPT), while taking into account the efficacy, safety and feasibility as an ambulatory procedure alternative to surgical parathyroidectomy. METHODS: We included nine patients who underwent percutaneous injection therapy for HPT from January 2018 to December 2021 in our institution. They were followed up from date of first percutaneous injection until death or October 2022 (mean duration of 9.0 months). RESULTS: Four patients underwent percutaneous ethanol injection therapy (PEIT) (mean age 61.0 [31-89] years old), while the remaining five underwent percutaneous calcitriol therapy (PCIT) (mean age 62.6 [35-91] years old). The analyzed parameters are age, BMI, serum turn over markers as iPTH, Ca, alkaline phosphatase and vitamin D. Two out of the four patients undergoing PEIT had a successful outcome, although one needed to continue cinacalcet due to persistent serum calcium levels. Three out of five PCIT patients in our series had successful procedure, although one subsequently developed refractory disease. CONCLUSION: PEIT and PCIT are feasible and safe therapeutic alternatives to surgical parathyroidectomy in HPT refractory to medical treatment, with postulated benefits of decreased costs and being an outpatient procedure. However, further studies are necessary to evaluate the efficacy and cost-effectiveness with these techniques prior to widespread adoption.
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DOI: 10.3389/fendo.2025.1562493
PMCID: PMC12173880

An explainable radiomics-based machine learning model for preoperative differentiation of parathyroid carcinoma and atypical tumors on ultrasound: a retrospective diagnostic study.
Front Endocrinol (Lausanne), 16:1617032.
C. Liu, W. Li, B. Wen, H. Xue, Y. Zhang, S. Wei, J. Gong, L. Huang, J. He, J. Yao and Z. Zhou. 2025.
BACKGROUND: Parathyroid carcinoma (PC) and atypical parathyroid tumors (APT), constituting rare endocrine malignancies, demonstrate overlapping clinical-radiological presentations with benign adenomas. This study aimed to investigate the predictive performance of three radiomics-based machine learning models for the identification of PC/APT from solitary parathyroid lesions using ultrasound. METHODS: This retrospective diagnostic study analyzed 913 surgically-confirmed parathyroid neoplasms (mean age 54.2 +/- 13.7 years; 694 females, 219 male) from Nanjing Drum Tower Hospital (n = 730) and Jinling Hospital (n = 183). The cohort comprised 90 malignant lesions and 823 benign adenomas, divided into training (Hospital I) and external test cohort (Hospital II). A radiomic signature derived from 544 quantitative ultrasound features was developed using three machine learning classifiers: Random Forest (RF), Support Vector Machine

(SVM), and Logistic Regression (LR). The performance of the predictive models was evaluated based on the pathological diagnosis. RESULTS: The RF-based radiomics model showed excellent diagnostic performance. The AUC of this model (0.933) was higher than that of SVM (0.900, P < 0.05) and LR (0.901, P < 0.05). The accuracy, precision, recall, and F1-score of RF model in distinguishing PA from APT/PC were 0.940, 0.683, 0.638 and 0.660. The explainable bar chart, heatmap and Shapley Additive exPlanations (SHAP) values were used to explain and visualize the main predictors of the optimal model. CONCLUSION: This radiomics framework provides a promising tool to support doctors in the clinical management of parathyroid lesions.
PubMed-ID: 40862115
DOI: 10.3389/fendo.2025.1617032
PMCID: PMC12375457

Parathyroidectomy and Risk of Incident Diabetes in Patients With Primary Hyperparathyroidism.
JAMA Surg, 160(10):1125-32.
X. Liu, D. T. W. Lui, X. Xiong, L. Li, Y. Luk, C. H. Wong, C. H. Lee, C. K. H. Wong, M. M. H. Fung and B. H. H. Lang. 2025.
IMPORTANCE: Primary hyperparathyroidism (PHPT) is linked to insulin resistance, glucose intolerance, and diabetes. Whether parathyroidectomy is associated with lower risk of diabetes has not been evaluated in a large cohort. OBJECTIVE: To examine the independent association between parathyroidectomy and the risk of incident diabetes in patients with PHPT. DESIGN, SETTING, AND PARTICIPANTS: Patients diagnosed with PHPT between January 2006 and December 2023 were identified from a territorywide electronic health database in Hong Kong and classified into surgical and nonsurgical groups based on presence of subsequent parathyroidectomy. They were followed up with from the index date (first diagnosis of PHPT), until the outcome of interest (incident diabetes), death, or end of the study period (December 2023), whichever came first. EXPOSURE: Parathyroidectomy vs nonsurgical management. MAIN OUTCOMES AND MEASURES: The primary outcome of this study was incident diabetes. Inverse probability of treatment weighting was used to balance all baseline characteristics. Cox proportional hazards regression was used to evaluate the hazard of incident diabetes associated with parathyroidectomy. RESULTS: A total of 3135 patients with PHPT were included (596 [19.0%] surgical and 2539 [81.0%] nonsurgical). The mean (SD) age was 67.5 (14.2) years, and 2211 (70.5%) individuals were female. A total of 518 patients in the nonsurgical group developed incident diabetes during a median (IQR) follow-up of 2.2 (0.9-4.3) years, compared to 156 patients in the surgical group during a median (IQR) follow-up of 5.5 (3.3-8.0) years. Parathyroidectomy was associated with lower risk of incident diabetes (hazard ratio [HR], 0.68 [95% CI, 0.65-0.71]; P < .001). Results were consistent across multiple sensitivity analyses. Subgroup analyses revealed more prominent protective associations among younger patients (age </=65 years vs >65 years: HR, 0.64 [95% CI, 0.60-0.68] vs HR, 0.68 [95% CI, 0.63-0.72]; interaction P < .001) and those with more severe PHPT (parathyroid hormone [PTH] > twice the upper limit of normal vs PTH </= twice the upper limit of normal: HR, 0.58 [95% CI, 0.53-0.63] vs HR, 0.73 [95% CI, 0.69-0.77]; calcium > 2.8 vs calcium </= 2.8 mmol/L : HR, 0.58 [95%CI, 0.54-0.63] vs HR, 0.69 [95%CI, 0.66-0.73]; interaction P < .001). CONCLUSIONS AND RELEVANCE: In this cohort of patients with PHPT, parathyroidectomy was associated with a lower risk of incident diabetes. The association was more prominent in younger patients and those with more severe PHPT. These results may suggest potential additional metabolic benefits of parathyroidectomy in PHPT.
PubMed-ID: 40864441
DOI: 10.1001/jamasurg.2025.3081
PMCID: PMC12392148

Utility of 4-dimensional computed tomography in predicting single-gland parathyroid disease-Can we abandon intraoperative parathyroid monitoring?
Surgery, 182:109327.
M. S. Lui, J. C. Fisher, N. Berger, A. J. Gordon, K. Wright, V. Nguyen, M. J. Persky, B. Givi, C. D. Seib, J. D. Allendorf, J. D. Prescott, K. N. Patel and I. Suh. 2025.
BACKGROUND: Four-dimensional computed tomography is routinely used to localize parathyroid disease, with consistently excellent parathyroid gland localization rates reported. This study evaluated whether pairing 4-dimensional computed tomography results with preoperative clinical variables can accurately predict single-gland disease in primary hyperparathyroidism. METHODS: Patients with primary hyperparathyroidism who underwent both 4-dimensional computed tomography imaging and parathyroidectomy between January 2019 and September 2021 at a large academic health system were included. Patient demographics, preoperative characteristics, and peri- and postoperative data were collected. The accuracy of 4-dimensional computed tomography in correctly identifying patients with single-gland disease with and without preoperative calcium and parathyroid hormone levels was calculated. Single-gland disease was defined by intraoperative parathyroid hormone decrease >50% and a hypercellular gland on pathology. RESULTS: One hundred

seventy-five patients had 4-dimensional computed tomography results suggestive of single gland disease. One hundred fifty-two patients (87%) were predicted correctly to have single-gland disease. The predictive accuracy increased when stratifying by preoperative calcium (>/=10.5 mg/dL, >/=11 mg/dL, and >/=12 mg/dL) and parathyroid hormone levels (>/=65 pg/mL, >/=100 pg/mL, and >/=200 pg/dL). The accuracy further increased when stratifying by age (</=50 years). Accuracy for single gland disease was 100% when combined with any of the following: (1) calcium >/=12 mg/dL, (2) parathyroid hormone >/=200 pg/dL, or (3) calcium >/=11 mg/dL in patients </=50 years. CONCLUSION: Four-dimensional computed tomography alone accurately predicted single gland disease in 87% of patients with primary hyperparathyroidism. When combined with preoperative calcium, parathyroid hormone and age thresholds, predictive accuracy for single-gland disease approached 100%. Given the high likelihood of single-gland disease in these scenarios, clinicians may consider offering focused unilateral parathyroidectomy without intraoperative parathyroid hormone monitoring in selected patients.
PubMed-ID: 40138877
DOI: 10.1016/j.surg.2025.109327

Cardiovascular Morbidity in Patients Undergoing Successful Surgery for Primary Hyperparathyroidism.
Clin Endocrinol (Oxf), 103(5):669-81.
M. Nilsson, J. G. Smith, M. Thier, E. Nordenstrom, A. Bergenfelz and M. Almquist. 2025.
OBJECTIVE: Although previous studies have shown reduced cardiovascular events following parathyroidectomy (PTX), it is unclear whether this extends to contemporary patients diagnosed and treated with milder disease than previously. The aim of this nation-wide study was to determine the effect on cardiovascular events after PTX, and to comprehensively evaluate cardiovascular disease manifestations in patients with primary hyperparathyroidism, (pHPT). DESIGN: The cohort consisted of 5009 patients who underwent PTX and were identified from the Scandinavian Quality Register for Thyroid, Parathyroid and Adrenal Surgery. Patients were matched with 14,983 population controls. METHODS: Data was linked with the National Patient and Death Registries. Incidence rate ratios (IRRs) were estimated before and after PTX for recurrent events of acute myocardial infarction, stroke, transient ischemic attack (TIA), and first-onset diagnoses of coronary artery disease, heart failure, aortic and mitral valve stenosis, carotid artery stenosis, peripheral artery disease, and aortic aneurysm (AA). Serum calcium and gland weight were analysed as predictors. RESULTS: TIA was increased in patients pre-and postoperatively with a peak 1-4 years before PTX (IRR: 2.06, CI 95%: 1.31-3.25). The incidence rates for acute myocardial infarction and stroke were not increased pre- and postoperatively. Mitral valve stenosis (IRR: 3.22, 1.51-6.85), and heart failure (IRR: 1.37, 1.11-1.67) were increased preoperatively, but not postoperatively. AA was increased pre- and postoperatively. CONCLUSIONS: The incidence rates for mitral valve stenosis and heart failure were increased preoperatively in patients with pHPT, normalizing after surgery. In contrast, the incidence of TIA and AA remained elevated postoperatively.
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DOI: 10.1111/cen.70015
PMCID: PMC12492784

Permanent hypoparathyroidism following total thyroidectomy - Incidence and preventative strategies without imaging adjuncts.
Am J Surg, 243:116196.
A. Niu, L. Zhou, A. Papachristos, H. Serrao-Brown, A. Aniss, M. Sywak and S. Sidhu. 2025.
INTRODUCTION: Permanent hypoparathyroidism (pHypoPT) is the most common permanent complication of total thyroidectomy. We aim to describe the incidence and predictors of hypoparathyroidism in a consecutive series of patients treated in a high-volume centre and define strategies to reduce the risk of pHypoPT. METHODS: 1182 patients who underwent total thyroidectomy between April 2018 and June 2022 were analyzed. Temporary hypoparathyroidism (tHypoPT) was defined as PTH <0.4 pmol/L (<4 pg/mL) at day one post-operatively, or clinical or biochemical evidence of hypocalcemia. pHypoPT was defined as an ongoing need for calcitriol supplementation to maintain normocalcemia at 12 months. Symptomatic tHypoPT (OR 43.97, p < 0.001) and number of parathyroid glands in the operative specimen (OR 2.31, p = 0.022) were also significantly associated with pHypoPT. RESULTS: Biochemical tHypoPT occurred in 205 (17.4 %) patients whilst pHypoPT occurred in 6 (0.5 %) patients. On multivariate analysis, parathyroid auto-transplantation (PA) independently reduced the risk of pHypoPT (OR 0.04, p = 0.004). CONCLUSIONS: The risk of pHypoPT after total thyroidectomy is 0.5 % when performed by high-volume surgeons. PA represents an important technique that reduces the risk of pHypoPT.
PubMed-ID: 39824725
DOI: 10.1016/j.amjsurg.2025.116196

Is the (18)F-choline PET-CT more cost-effective than standard protocol for locating a parathyroid adenoma?
Langenbecks Arch Surg, 410(1):235.
J. Ortega-Serrano, S. Serrano-Lopez, R. Alfonso-Ballester, R. Marti-Fernandez, M. Lapena-Rodriguez, R. D. Exposito and N. Cassinello-Fernandez. 2025.
PURPOSE: The most common cause (> 80% of cases) of primary hyperparathyroidism (PHPT) is parathyroid adenoma. Its diagnosis is conventionally made by cervical ultrasound and (99m)Tc-MIBI scintigraphy. However [(18)F-Choline PET-CT ([(18)F-FCh PET-CT) offers greater sensitivity and specificity, although at a high cost, which prevents it from being a first-line diagnostic method. METHODS: Observational retrospective cohort study of 100 consecutive patients operated on for PHPT by parathyroidectomy in a tertiary hospital. Patients were divided into two groups: Group 1, patients with successful diagnosis using conventional tests (42 patients) and Group 2, patients with an initial failed diagnosis who required (18)F-FCh PET-CT (52 patients). A group with an ideal diagnostic strategy using only (18)F-FCh PET-CT was simulated and the costs were compared with the groups in the sample. RESULTS: The sample finally analyzed 94 patients, 78.7% female, mean age 61.73 years. 55,3 % of the patients required a (18)F-FCh PET-CT for the location diagnosis. The group 2 required more consultations, more complementary tests and a longer interval between the first consultation and the intervention. The ideal diagnostic strategy (euro1,399.77/patient) represents a lower cost than the other strategy (euro1,730.61/patient). CONCLUSION: The diagnosis of location of a parathyroid adenoma with (18)F-FCh PET-CT required fewer complementary tests and consultations, reducing the interval until surgical intervention, with no difference in surgical results. The costs if (18)F-Ch PET-CT is performed as the only location diagnostic test are lower when a group of patients is studied, so its use is recommended as a first line diagnostic tool. CLINICAL TRIAL NUMBER: Not applicable.
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PMCID: PMC12313737

Transcriptome sequencing reveals distinct atypical parathyroid tumor subtypes.
Endocr Relat Cancer, 32(6)
H. S. Park, M. Kim, S. Y. Jo, G. J. Kim, J. J. Jeong, N. Hong, S. Kim and Y. Rhee. 2025.
Atypical parathyroid tumors (APTs) are a rare subtype of parathyroid neoplasms characterized by diagnostic challenges and an uncertain prognosis. This study aimed to validate the subtypes of APTs using transcriptome sequencing. We applied a clustering model developed for our previous study in which we had successfully distinguished parathyroid cancer from adenomas using gene expression patterns. Sixteen patients with APT who had undergone parathyroidectomy were enrolled, and we analyzed their baseline data, pathologic reports and follow-up records and performed transcriptome sequencing of their APT samples. We then used our clustering model to classify tumors as either cancer- or adenoma-type APTs and compared these results with clinical findings. The median age of patients was 48.9 years, with median calcium and parathyroid hormone (PTH) levels of 11.4 mg/dL and 420.0 pg/mL, respectively. Pathologic and immunohistochemical results did not reveal any remarkable differences between adenoma-type and cancer-type APTs. However, clustering analysis classified four of the 16 APTs as being cancer-type and 12 as being adenoma-type tumors. Cancer-type patients had a median age of 30.0 years, with median calcium and PTH levels of 12.6 mg/dL and 800.8 pg/mL, respectively, clinically resembling parathyroid cancer. One patient exhibited a somatic CDC73 two-hit mutation and positive WT1 staining, suggesting a high malignant potential. Clustering analysis through transcriptome sequencing shows promise for risk stratification of patients with APTs. For those classified as having cancer-type tumors, close monitoring and long-term follow-up may be warranted.
PubMed-ID: 40434298
DOI: 10.1530/ERC-25-0057
PMCID: PMC12170948

Giant Parathyroid Adenomas: A 28-Year Experience at a Tertiary Super-Specialty Hospital.
World J Surg, 49(7):1811-9.
G. Puri, P. Ranjan, B. K. Singh, R. Khadgawat, N. Damle, P. Priyadarshini, S. Agarwal, C. J. Das, K. Sharma, A. Singh and S. Chumber. 2025.
BACKGROUND: Giant parathyroid adenomas represent a distinct clinical entity forming a subset under primary hyperparathyroidism (PHPT). They comprise lesions weighing more than 3.5 g. Our study aims to determine the clinical presentation, biochemical profile, outcomes, and pathological characterization of patients with giant parathyroid adenoma. MATERIALS AND METHODS: Retrospective review of data of patients who underwent parathyroid surgery between January 1995 and December 2022 by a single surgeon. A total of 561 patients were identified, and out of these,

78 had glands measuring more than 3.5 g. RESULTS: The mean age was 42 years, and 51 (65%) were females. The most common complaint was bone pain (46%), followed by renal calculi (38%), with 15 (19%) patients presenting with hypercalcemic crisis. Median calcium value was 12.3 mg/dL, with median PTH, vitamin D, and ALP of 1025 pg/mL, 23 ng/mL, and 664 U/L, respectively. Fifty-three (68%) patients underwent focused parathyroidectomy, and 22 (28%) underwent neck exploration, with median postoperative calcium and PTH being 8.35 mg/dL and 37.8 pg/mL, respectively. The median weight was 7 g with a range from 3.58 g to a whopping 31 g. Symptomatic postoperative hypocalcemia was seen in 54 (69%), with 28 (36%) requiring intravenous calcium supplementation, and this was positively correlated with the preoperative ALP and PTH values. CONCLUSION: Giant parathyroid adenomas present with florid symptoms with hypercalcemia and often hypercalcemic crisis. The biochemical workup, localization, and surgical management are similar to any other case of PHPT. Postoperatively these patients are prone to hypocalcemia, and the intravenous requirement of calcium can be predicted by preoperative ALP levels.
PubMed-ID: 40468583
DOI: 10.1002/wjs.12627

Parathyroid autotransplantation: Nonsense or nuance?
Am J Surg, 243:116279.
N. Swaminathan and C. C. Frye. 2025.
PubMed-ID: 40050188
DOI: 10.1016/j.amjsurg.2025.116279

The relationship between postoperative parathormone suppression and surgical cure in primary hyperparathyroidism.
Front Endocrinol (Lausanne), 16:1629719.
M. T. Unlu, N. Aygun, M. Kostek, O. Caliskan and M. Uludag. 2025.
INTRODUCTION: In primary hyperparathyroidism(pHPT), suppression in other glands due to autonomy of pathological gland is frequently observed. In this retrospective study, we aimed to evaluate contribution of suppression of remaining parathyroid glands in pHPT in predicting surgical cure. METHODS: We retrospectively analyzed data from patients diagnosed with pHPT and operated at our institution between 2014 and 2022. Patients who demonstrated either a decrease of more than 50% in intraoperative parathormone levels or a normal parathormone (PTH) level at the 6th postoperative hour were included. Patients were categorized into two groups based on their PTH levels at the 6th postoperative hour: those with PTH suppression (PTH < 15 ng/L) and those without (PTH > 15 ng/L). We analyzed the outcomes in terms of persistent disease and biochemical markers. RESULTS: Among 196 patients who met the inclusion criteria, 124 exhibited PTH suppression while 72 did not. Persistent disease was significantly more common in the non-suppressed group (19.4% vs. 5.65%, p<0.001). Furthermore, postoperative PTH suppression strongly correlated with surgical cure, indicated by a significant difference in the rate of normocalcemia after 6 months. Excised parathyroid tissue volumes were determined significantly lower in group 1 compared to group (0.85 +/- 0.88cm3vs2.04 +/- 3.79cm3,p=0.035, respectively).There was no significant difference between two groups in terms of gender, preoperative Ca, magnesium, vitamin D and postoperative Ca levels. CONCLUSION: Early postoperative PTH suppression is highly associated with surgical cure. The rate of pPHPT is significantly higher in non-suppressed patients. Therefore, in follow-up strategies of postoperative patients, the possibility of a remnant pathological gland should be considered especially in those without early PTH suppression.
PubMed-ID: 40810066
DOI: 10.3389/fendo.2025.1629719
PMCID: PMC12344557

Postsurgical Hypoparathyroidism: Standardization of definition and terminology is needed.
Am J Surg:116489.
S. M. Wiseman and S. Kruijff. 2025.
PubMed-ID: 40571464
DOI: 10.1016/j.amjsurg.2025.116489

Do stricter criteria for intraoperative parathyroid hormone monitoring reduce the risk of persistence or reoperation in primary hyperparathyroidism? A receiver operating characteristic analysis.
Langenbecks Arch Surg, 410(1):220.
H. W. Wolf, S. Canovi and C. A. Nebiker. 2025.
PURPOSE: Intraoperative parathyroid hormone (PTH) measurement is a beneficial tool in the surgical management of

primary hyperparathyroidism. The expected degree of intraoperative PTH reduction, which guides surgical decision-making, determines the sensitivity and specificity of this test. While stricter criteria may enhance diagnostic accuracy, an optimal threshold has not been conclusively established. The aim of this study was to identify the PTH reduction threshold that provides the highest sensitivity and specificity for achieving biochemical cure. PATIENTS AND METHODS: A retrospective analysis was conducted on 141 patients who underwent parathyroidectomy for primary hyperparathyroidism, focusing on the intraoperative drop in PTH and surgical success. A receiver operating characteristic analysis was performed to identify the optimal threshold that balances sensitivity and specificity in predicting biochemical cure. RESULTS: The mean percentage reduction at the end of surgery was 73.93% (SD +/- 16.54%) with an overall cure rate of 94%. The area under the curve was 0.73 for a 50% PTH reduction, 0.77 for a 60% reduction, and 0.68 for a 70% reduction. CONCLUSION: The optimal balance between sensitivity and specificity was achieved with a 60% intraoperative PTH reduction. Stricter criteria increase sensitivity but may also raise the risk of surgical overtreatment.
PubMed-ID: 40637883
DOI: 10.1007/s00423-025-03796-4
PMCID: PMC12245973

Plasma metabolomics for the preoperative diagnosis of parathyroid carcinoma.
Endocr Relat Cancer, 32(7)
J. Xiao, M. Cui, Q. Zheng, S. Yang, T. Chen and Y. Hu. 2025.
Parathyroid carcinoma (PC) is a rare endocrine malignancy with a poor prognosis. Preoperative diagnosis remains a major challenge in clinical practice because of limited diagnostic methods and non-specific clinical features. This study aimed to describe the distinct plasma metabolic profiles of PC and parathyroid adenoma (PA) patients and identify promising biomarkers for the preoperative differential diagnosis of PC. A total of 115 patients were enrolled in this retrospective study, including 70 patients (24 PC and 46 PA) in the discovery cohort and 45 patients (15 PC and 30 PA) in the validation cohort. Plasma samples were collected before operation. LC-MS/MS analysis was utilised on the discovery cohort to explore the metabolic profile and find out differentially abundant metabolites. Subsequently, potential diagnostic biomarkers were verified in an external validation cohort to find out novel biomarkers for the differential diagnosis of PC before surgery. Compared with the plasma samples of PA patients, a total of three upregulated and 42 downregulated metabolites were identified by MS/MS in the plasma samples of PC patients. The differentially abundant metabolites were significantly enriched in the arachidonic acid, tryptophan, and hormone metabolism pathways. Notably, 7-ketodeoxycholic acid ($P = 0.002$, AUC = 0.804) and tryptophan ($P < 0.001$, AUC = 0.838) were confirmed to show high accuracy in differential diagnosis in the validation cohort. Therefore, metabolomics analysis of parathyroid neoplasms revealed significant differences in metabolic profiles between PAs and PCs. The plasma levels of 7-ketodeoxycholic acid and tryptophan could serve as potential diagnostic biomarkers for PC.
PubMed-ID: 40525887
DOI: 10.1530/ERC-24-0192
PMCID: PMC12231172

Adrenals

Meta-Analyses

Tools to Predict Unilateral Primary Aldosteronism and Optimise Patient Selection for Adrenal Vein Sampling: A Systematic Review.
Clin Endocrinol (Oxf), 103(1):3-12.
E. Ng, S. M. Gwini, W. Zheng, P. J. Fuller and J. Yang. 2025.
OBJECTIVE: Primary aldosteronism (PA), the most common endocrine cause of hypertension, is evaluated using adrenal vein sampling (AVS), to determine if aldosterone excess is bilateral or unilateral. AVS is invasive and technically challenging; it would ideally be used only in those with unilateral PA who are candidates for surgical cure. Those with bilateral PA would benefit from a direct path to medical management before AVS. Strategic patient selection for AVS would enable judicious and cost-efficient use of this procedure. This review evaluates the diagnostic accuracy of published algorithms that aim to predict unilateral PA and therefore facilitate informed selection for AVS. DESIGN: This systematic review was performed by searching Medline and EMBASE databases to identify published models that sought to subtype PA (PROSPERO registration CRD42021277841). Algorithms reported to predict unilateral PA and therefore select patients for AVS, using AVS and/or surgical outcomes as the gold standard, were systematically evaluated. RESULTS: There were 28 studies evaluating 63 unique predictive algorithms, of which 14 were tested in multiple cohorts. These were grouped into 5 categories; those combining biochemical, radiological and demographic characteristics, those involving confirmatory testing those using biochemical results only, those involving dynamic testing, and anatomical imaging. The algorithm with the highest sensitivity for unilateral PA which has been validated in at least two cohorts, involved serum potassium, CT imaging, PAC, ARR and female sex (sensitivity 78-96%). In a hypothetical scenario of 1000 people with PA where 30% have unilateral PA, this top performing algorithm would appropriately select 234-289 people for AVS and allow 143-324 to correctly bypass AVS. CONCLUSIONS: Accurate algorithms to inform selection for AVS will ensure that AVS is only performed in patients with a high probability of unilateral PA without clear evidence of the side of lateralisation. This will lower the demand for this invasive procedure, avoid unnecessary procedural complications, and reduce associated health care costs. Further validation of the top-performing algorithms in larger and diverse cohorts will support their use in routine practice.
PubMed-ID: 40099563
DOI: 10.1111/cen.15225
PMCID: PMC12134443

The role of adrenal-sparing surgery in the management of aldosterone-producing adenoma: a systematic review and meta-analysis.
Eur J Endocrinol, 193(3):S36-S52.
A. Artiles Medina, V. Gomez Dos Santos, C. Minguez Ojeda, A. Sanjuanbenito, J. Gomez-Ramirez, E. Mercader, F. A. Hanzu, L. Zarain, O. Vidal, A. Muriel and M. Araujo-Castro. 2025.
OBJECTIVE: The indication for laparoscopic partial adrenalectomy (LPA) in patients with primary aldosteronism due to aldosterone-producing adenoma (APA) remains controversial. This study aimed to determine the functional and surgical outcomes of LPA in this context. METHODS: This is a systematic review and meta-analysis. MEDLINE and Embase were searched until May 2024. Biochemical and clinical outcomes were defined according to the PASO criteria. RESULTS: A total of 3515 articles were initially identified, and eventually 20 studies (8 comparative and 12 single-arm) were included. The pooled biochemical success and clinical response rates (hypertension improvement) were estimated to be 100% (95% CI 99-100) and 91% (95% CI 48-99), respectively. The postoperative complication risk was very low (1%, 95% CI 0-4). The pooled recurrence risk was 0% (95% CI 0-1) over a mean follow-up of 25.9 months (range: 12-39 months). Eight comparative studies were combined in quantitative analyses. The biochemical success (OR 0.80, 95% CI 0.38-1.72), clinical cure (OR 1.07, 95% CI 0.77-1.50), recurrence (OR 1.57, 95% CI 0.25-9.77), and need for steroid supplementation (odds ratio [OR] 0.96, 95% CI 0.27-3.44) rates were similar between LPA and total adrenalectomy groups. Notwithstanding, LPA had a lower postoperative complication risk than total adrenalectomy (OR 0.51, 95% CI 0.31-0.82). CONCLUSIONS: Our systematic review underscores that LPA for treating APA has similar functional outcomes in terms of biochemical success and clinical response compared with total adrenalectomy, with fewer complications. However, given the observational nature of the currently available studies and the heterogeneity among them in the study population and surgical outcomes definitions, a clinical trial should be conducted to confirm these results.

PubMed-ID: 40919663
DOI: 10.1093/ejendo/lvaf180

Randomized controlled trials

- None -

Consensus Statements/Guidelines

Spanish consensus on the diagnosis and management of adrenocortical carcinoma.
Endocr Relat Cancer, 32(5)
M. Araujo-Castro, C. Alvarez-Escola, A. Casteras, A. Carmona-Bayonas, M. D. Chiara, F. A. Hanzu, J. Hernando, J. L. Vercher-Conejero, M. Rodriguez-Fraile, V. Gomez Dos Santos, P. Jimenez-Fonseca, A. Giraldo, N. Valdes, O. Vidal, M. Del Olmo-Garcia and J. Capdevila. 2025.
Adrenocortical carcinoma (ACC) is a rare endocrine malignancy with an estimated incidence of 0.7-2 cases per million/year. The rarity of this disease, coupled with limited preclinical models and clinical trials, has hindered progress, resulting in poor outcomes, with a 5-year survival rate of approximately 35%. Currently, the only available curative treatment is complete surgical resection of the adrenal tumor. For unresectable or metastatic ACC, the current standard therapeutic modalities are mitotane, chemotherapy, radiotherapy and locoregional treatments; however, these are noncurative. Mitotane has an adrenolytic and anti-steroidogenic effect, and it is used in the adjuvant setting for high-risk patients, as systemic therapy for metastatic disease, and/or to control hormonal secretion. While key pathways in ACC pathogenesis have been identified as potential therapeutic targets, results with targeted therapies remain modest, showing that there is a clinical unmet need for novel treatments or new combinations of exiting drugs. Effective management requires a multidisciplinary team of experts to optimize outcomes for patients. This article presents a multidisciplinary consensus on the diagnosis, management, prognosis and follow-up of patients with ACC, and the approach to two special contexts, ACC in pregnant women and hormone-producing ACC. The consensus was coordinated by the Spanish Society of Endocrinology and Nutrition (SEEN) and the Spanish Group of Neuroendocrine and Endocrine Tumors (GETNE), with contribution from experts from related societies including the Spanish Association of Surgeons (AEC), Spanish Society of Urology (AEU), Anatomic-Pathology (SEAP), Nuclear Medicine (SEMNIM), Medical Oncology (SEOM) and Radiotherapeutic Oncology (SEOR).
PubMed-ID: 40215284
DOI: 10.1530/ERC-25-0034
PMCID: PMC12053981

Society for Endocrinology Clinical Practice Guideline for the Evaluation of Androgen Excess in Women.
Clin Endocrinol (Oxf), 103(4):540-66.
Y. S. Elhassan, J. M. Hawley, L. Cussen, A. Abbara, S. A. Clarke, P. Kempegowda, R. K. Dhillon-Smith, P. Thadani, M. Busby, L. Owusu-Darkwah, R. Marrington, W. C. Duncan, R. K. Semple, R. Quinton and M. W. O'Reilly. 2025.
CONTEXT: Androgen excess is common in women and refers to clinical or biochemical evidence of elevated androgenic steroids such as testosterone. It is associated with underlying polycystic ovary syndrome in the majority of cases. However severe androgen excess is less common and may indicate the presence of underlying adrenal or ovarian neoplasms, genetic disorders or severe insulin resistance syndromes. Currently there are few consensus guidelines to assist clinicians with a standardised management approach to the patient with severe androgen excess. DESIGN: Clinical practice guideline. METHODS: This guideline has been developed with expertise from colleagues in endocrinology, gynaecology, clinical biochemistry and nursing, and furthermore provides a unique patient perspective to guide clinicians. RESULTS: The Society for Endocrinology commissioned this new guideline to collate multi-disciplinary guidance for clinical practitioners in the investigation of severe androgen excess. Recommendations have been made in the areas of clinical assessment, biochemical work up, dynamic testing and imaging, informed where possible by the best available evidence. CONCLUSION: This guideline will provide guidance for clinicians in their approach to patients with severe androgen excess.
PubMed-ID: 40364581
DOI: 10.1111/cen.15265
PMCID: PMC12413683

Expert Consensus on the Primary Aldosteronism Severity Classification and its strategic application in indicating adrenal venous sampling.
Eur J Endocrinol, 193(1):85-96.
M. Murakami, M. Naruse, H. Kobayashi, M. Parasiliti-Caprino, F. Bioletto, D. Brudgam, I. Stufchen, M. Reincke, M. St-Jean, I. Kraljevic, D. Kastelan, P. I. Nevalainen, M. Araujo-Castro, N. Sukor, M. F. Nijhoff, J. Matrozova, O. Ragnarsson, Z. Shafigullina, N. Matikainen, A. Markou, G. Piaditis, S. Izawa, T. Katabami, T. Ichijo, A. Tanabe, M. Tsuiki, M. Kakutani, N. Wada, S. Masuda, A. V. Bacca, F. Beuschlein, G. Maiolino, H. Falhammar, M. A. Grytaas, K. Lovas, M. Q. Almeida, R. M. Furnica, T. Puar, P. Kmiec, S. Masi, I. Bourdeau, L. Amar, M. C. Dennedy, F. Fallo, J. Deinum, S. O'Toole, T. Yamada, M. Quinkler, A. Lacroix and T. Kocjan. 2025.
OBJECTIVE: Severity classifications are essential for many diseases to prioritize patient management tasks such as diagnosis, treatment, and follow-up. Primary aldosteronism (PA), a common cause of secondary hypertension, lacks a standardized severity scale despite generally requiring invasive diagnostics like adrenal venous sampling (AVS). This study aimed to develop a global expert consensus-based classification for PA severity to improve clinical decision-making. METHODS: A panel of 45 international experts from 40 centers across four continents used the Delphi method to create a consensus severity classification for PA. This classification was then applied retrospectively to 2593 PA patients from 26 centers to assess its association with the disease subtype. RESULTS: After four rounds, the Primary Aldosteronism Severity Classification (PASC), which integrates biochemical and clinical parameters including serum potassium, blood pressure, and basal plasma aldosterone concentration, was established. Primary Aldosteronism Severity Classification classifies PA into mild (3 and 4 points), moderate (5-7 points), and severe (8 and 9 points). Among the cohort from 26 centers, 13.9%, 63.0%, and 23.1% were classified as mild, moderate, and severe, respectively, aligning with lateralized subtype prevalence rates of 14.7%, 44.6%, and 72.6%. CONCLUSION: Primary Aldosteronism Severity Classification is a newly developed simplified, semi-quantitative classification of PA severity. The correlation between PASC and lateralized PA subtype supports its potential to provide graded recommendations of AVS prior to surgical indication in each patient.
PubMed-ID: 40485198
DOI: 10.1093/ejendo/lvaf117

Other Articles

Predicting treatment outcome in congenital adrenal hyperplasia using urine steroidomics and machine learning.
Eur J Endocrinol, 193(1):10-20.
O. Abawi, G. Sommer, M. Grossl, U. Halbsguth, T. du Toit, S. E. Hannema, C. de Bruin, E. Charmandari, E. L. T. van den Akker, A. B. Leichtle and C. E. Fluck. 2025.
OBJECTIVE: Treatment monitoring of individuals with congenital adrenal hyperplasia (CAH) remains unsatisfactory. Comprehensive 24 h urine steroid profiling provides detailed insight into adrenal steroid pathways. We investigated whether 24 h urine steroid profiling can predict treatment control in children and adolescents with CAH using machine learning (ML). DESIGN: Prospective observational cohort study. METHODS: This study included children with 21-hydroxylase deficiency. On 24 h urines of 2 consecutive visits 40 steroids were measured by gas chromatography-mass spectrometry. Treatment outcome was clinically classified as undertreated, optimally treated or overtreated. We used sparse partial least squares discriminant analysis (sPLS-DA) to investigate prediction of treatment outcome. We computed area under the ROC-curve (AUC) of 2 sPLS-DA models: (1) using only 24 h urine metabolites and (2) adding clinical variables. RESULTS: We included 112 visits (68 optimal, 44 undertreatment) from 59 patients: 27 (46%) girls, 46 (78%) classic CAH, and 19 (32%) prepubertal. Mean age at first visit was 11.9 +/- 4.0 years and mean BMI SDS 0.6 +/- 1.1. SPLS-DA using 24 h urine metabolites showed clear clustering of optimally treated patients on 2 components, while undertreated patients were more heterogeneous (AUC 0.88). The model selected pregnanetriol and 17alpha-hydroxypregnanolone contributing to excluding optimal treatment and 5 metabolites contributing to excluding undertreatment: 17beta-estradiol, cortisone, tetrahydroaldosterone, androstenetriol, and etiocholanolone. Addition of clinical variables marginally improved classification (AUC 0.90). CONCLUSIONS: Using ML on 24 h urine steroid profiling predicted treatment outcome in children with CAH, even in the absence of clinical data, suggesting that routine comprehensive 24 h urine steroid profiling could improve treatment monitoring in CAH.
PubMed-ID: 40515610
DOI: 10.1093/ejendo/lvaf121

Long-term outcomes in patients with congenital adrenal hyperplasia treated with hydrocortisone modified-release hard capsules.
Eur J Endocrinol, 193(1):76-84.
W. Arlt, A. Brac de la Perriere, A. L. Hirschberg, D. P. Merke, J. D. C. Newell-Price, A. Prete, D. A. Rees, N. Reisch, P. A. Touraine, H. Bendfeldt, J. Porter, H. Coope and R. J. M. Ross. 2025.
BACKGROUND: Hydrocortisone modified-release hard capsules (MRHC, development name Chronocort) replace the physiological overnight cortisol rise and improve the biochemical control of congenital adrenal hyperplasia (CAH). AIM: This study aims to evaluate long-term safety, tolerability, and efficacy of MRHC. METHODS: This is an open-label follow-on study. RESULTS: Ninety-one patients with classic CAH, mean age 37 years, 68% female, 32% male, entered the study and 22 discontinued. Median treatment duration was 4 years (range 0.2-5.8). Median hydrocortisone dose at study entry was 30 mg/day and reduced to 20 mg/day after 24 weeks and stayed stable thereafter until 48 months ($P < .0001$). Disease control improved on MRHC for the steroid disease markers serum 17-hydroxyprogesterone (17OHP) ($P < .03$) and androstenedione (A4) ($P < .002$). After 4 years, the majority of patients had a 17OHP < 4-fold upper limit of normal (ULN) (71%) and an A4 <ULN (90%). Measurement of 17OHP and A4 at 09:00 h and 13:00 h gave similar results. Of the 37 women < 50 years of age who were not on contraceptives over the whole study period, 5 became pregnant (13.5%). Of the men, 13.8% (4/29) had a partner pregnancy. Seven patients had an adrenal crisis with 1 patient reporting 8 of these giving an incidence of 3.9 crises per 100 patient years. CONCLUSIONS: Modified-release hard capsule treatment resulted in hydrocortisone dose reduction followed by a stable dose with improved biochemical control associated with fertility. Biochemical control could be reliably monitored by a single blood sample taken between 09:00 and 13:00 h. The incidence of adrenal crises was below that reported previously in patients with CAH.
PubMed-ID: 40576296
DOI: 10.1093/ejendo/lvaf130

Unexpected discrepancies between steroid intra-tissular content in adrenal tumors and clinical diagnosis of steroid excess.
Eur J Endocrinol, 193(1):106-16.
F. Bonnet-Serrano, L. Thomeret, N. Benanteur, P. Vaduva, F. Violon, L. Bouys, B. Ragazzon, A. Berthon, K. Perlemoine, H. Wilmot-Roussel, C. Zientek, S. Nakib, M. Gaillard, M. Sibony, C. Laguillier-Morizot, M. C. Menet, L. Guignat, R. Libe, L. Groussin, J. Guibourdenche, A. Jouinot, G. Assie and J. Bertherat. 2025.
OBJECTIVE: Adrenocortical tumor (ACT) morbidity is associated with steroid secretion, depending on tumor type. Indeed, adrenal steroidogenesis is a finely regulated process, altered in ACT. These alterations are usually characterized by blood steroid assays, also depending on steroid gonadal production and metabolism. Our aim was to determine steroid content directly in ACT tissues and to compare it with clinical diagnosis of steroid excess. METHODS: A profile of 13 steroids was analyzed in ultra-high-performance liquid chromatography coupled to tandem mass spectrometry (Thermo Fisher Scientific(R)) in frozen tissue samples from 75 ACT, 7 Cushing's disease, and 9 normal adrenals. RESULTS: Steroid levels were 10-1000 times higher in tissue from normal adrenal than normal concentrations expected in blood. Concentration ratios between tissue from normal adrenal and blood reference values were lower for distal products than for steroid precursors. In adrenocortical cancers, intra-tissular steroid content was lower than in unilateral benign tumors despite clear clinical steroid excess. Unexpectedly, in overt-Cushing adenomas, intra-tissular cortisol levels were not higher and androstenedione levels were not lower than in non-functioning adenomas. Adrenal differentiation score based on transcriptome was well correlated with intra-tissular cortisol levels. CONCLUSION: Discrepancies observed between steroid levels measured in ACT tissue and clinical diagnosis of steroid excess suggest a dysregulation of steroid export depending on tumor type, opening new perspectives for diagnosis and treatment of steroid excess.
PubMed-ID: 40515607
DOI: 10.1093/ejendo/lvaf129

Cytological Assessment of Adrenal Tumours: Insights From 22-Years Single Centre Experience.
Clin Endocrinol (Oxf), 103(2):157-66.
A. Carasel, J. Calissendorff, C. C. Juhlin and H. Falhammar. 2025.
OBJECTIVE: The incidence of adrenal tumours has increased in the last decades, mainly due to increased use of imaging. The diagnostic evaluation of adrenal masses can be complex and, in some cases, necessitates cytological evaluation. However, concerns remain regarding the potential complications associated with adrenal gland biopsy. DESIGN: We conducted a retrospective cohort study to evaluate the safety and diagnostic effectiveness of cytology in patients who

underwent fine-needle aspiration (FNA) of adrenal glands at Karolinska University Hospital in Stockholm, Sweden, between 2000 and 2022. The aim was to evaluate the accuracy of the sample and the complication rate. PATIENTS AND MEASUREMENTS: A total of 241 patients and 251 FNAs were included, with 10 patients undergoing two FNAs each. Data on clinical, radiological and laboratory presentation was collected and corelated with cytological findings and outcomes. RESULTS: Diagnostic FNA was obtained in 90% of patients (n = 217) with endoscopic ultrasound technique being most successful (95.8%), followed by CT (88.7%) and transabdominal ultrasound technique (86.7%). The sensitivity and the specificity were 93.8% respectively 96.7%. More than half of the FNA samples (52.7%) indicated a diagnosis consistent with metastases to the adrenal gland. The complication rate was 7.9% (n = 20). Based on the FNA results, adrenalectomy was performed on 13.6%, while 52.8% of the patients with benign findings were managed conservatively. Chemotherapy was started for 78.7% of patients with malignant findings. CONCLUSION: FNA of the adrenal glands is a safe, minimally invasive diagnostic procedure that can be useful in the assessment of adrenal lesions.
PubMed-ID: 40269585
DOI: 10.1111/cen.15254
PMCID: PMC12223696

Improved and individualized approach to adrenal surgery.
Endocr Relat Cancer, 32(7)
T. Carling and M. LaRue. 2025.
Adrenal surgery has undergone significant advancements, driven by technological innovations, enhanced surgical techniques, and a deeper understanding of adrenal gland pathophysiology. This review highlights the transition toward modern, individualized adrenal surgery, emphasizing minimally invasive techniques, precision medicine, and the development of specialized centers performing more than 500 adrenalectomies a year. Minimally invasive adrenalectomy, specifically the mini back scope adrenalectomy (MBSA, also known as posterior retroperitoneoscopic adrenalectomy), has become the standard of care for most adrenal pathologies, enabling precise function-preserving (partial) adrenalectomy, and offering reduced morbidity, shorter hospital stays, and faster recovery compared to open and transabdominal surgery, whether robotic or laparoscopic. Molecular pathology and enhanced imaging modalities have improved preoperative planning and intraoperative decision-making, allowing for precise tumor localization and preservation of adrenal function. Molecular profiling of adrenal tumors has provided insights into tumor behavior, enabling tailored surgical approaches. In addition, multidisciplinary collaboration has been crucial in developing comprehensive treatment strategies, particularly for complex cases such as familial pheochromocytomas, equivocal unilateral and bilateral primary hyperaldosteronism, and ACTH-independent adrenal hypercortisolism due to bilateral adrenal lesions, adrenocortical carcinoma, and metastatic adrenal disease. Patient-specific factors, including genetic predispositions and comorbidities, are increasingly considered to optimize surgical outcomes and personalize postoperative care. As we enter this improved and individualized era of adrenal surgery, ongoing research and technological advancements are expected to continue to enhance patient outcomes and expand the indications for adrenal surgery.
PubMed-ID: 40549414
DOI: 10.1530/ERC-24-0296

Impact of surgical technique on hemodynamic instability in patients with pheochromocytoma: a single-centre retrospective cohort study.
Surg Endosc, 39(7):4166-76.
A. H. Chaman Baz, J. van de Wal, S. A. A. Willems, F. d'Ancona, X. Zhu, H. Timmers and J. F. Langenhuijsen. 2025.
BACKGROUND: Endoscopic adrenalectomy by either transperitoneal laparoscopic (TLA) or posterior retroperitoneoscopic approach (PRA) is the preferred treatment for pheochromocytoma (PCC). PRA shows advantages in patient outcome, but blood pressure fluctuations may occur due to limited working space and increased CO(2)-pressure. We investigated the impact of surgical technique on intraoperative hemodynamic instability in patients with PCC. METHODS: Patients who had endoscopic adrenalectomy for PCC consecutively from 2007 to 2022 were included in this retrospective cohort study. The primary outcome was hemodynamic instability (HI-score) and secondary outcomes were hemodynamic parameters and drug administration. RESULTS: Overall, 101 patients met the inclusion criteria, 57 had TLA and 44 PRA. The two groups were similar in baseline characteristics. The HI-score was higher in PRA than in TLA (97 vs 46, $p < 0.001$) due to more frequent (IQR: 2-5 vs IQR: 1-3, $p = 0.025$) and longer episodes of hypotension (5.6% vs 7.1%, $p = 0.013$), and longer episodes of bradycardia (9.9% vs 16.9%, $p = 0.038$). On the contrary, TLA patients had higher maximum systolic blood pressure (169 mmHg vs 157 mmHg, $p = 0.046$), more frequent episodes of tachycardia (31.6% vs 6.8%, $p = 0.002$) and higher maximum heart rate (90 bpm vs 80 bpm, $p = 0.024$). PRA patients needed more vasoconstrictive drugs (97.7% vs 78.9%, $p = 0.017$) and fluid infusion (1111 ml/h vs 798 ml/h, $p = 0.004$), whereas TLA patients received more vasodilating

drugs (64.9% vs 38.6%, p = 0.009). CONCLUSIONS: PRA was associated with higher hemodynamic instability than TLA reflected by hypotension, need for vasoconstrictive drugs and fluid infusion in a selected cohort of patients with pheochromocytoma.
PubMed-ID: 40374952
DOI: 10.1007/s00464-025-11794-2
PMCID: PMC12222387

Sex differences in management and outcomes in pheochromocytomas and paragangliomas.
Front Endocrinol (Lausanne), 16:1597908.
M. A. J. Dahl, J. Calissendorff and H. Falhammar. 2025.
PURPOSE: The aim of this study was to investigate sex differences in the management and outcomes of patients with pheochromocytomas and paragangliomas (PPGLs). METHODS: This is a retrospective cohort study including all patients diagnosed with PPGLs attending the Department of Endocrinology at Karolinska University Hospital between June 2005 and August 2024. The collected data included patient characteristics, biochemical, genetical, pharmacological and vital parameters noted during initial PPGL presentation and during follow-up, including survival. RESULTS: In total, 196 patients diagnosed with PPGLs (108 females and 88 males) were included. Paragangliomas were more prevalent in females than in males (23.1% vs 11.4%, P=0.04). Females required a lower final dose of preoperative phenoxybenzamine (50.8 +/- 19.8 vs 87.5 +/- 75.7 mg, P=0.04), while the final dose of preoperative doxazosin was non-significant lower (22.3 +/- 13.6 vs 26.0 +/- 13.9 mg, P=0.07). Moreover, females were less likely having laparoscopic surgery than males (55.2% vs 71.1%, P=0.03). After surgery, more females achieved remission from their type 2 diabetes compared to males (23.4% vs 11.8%, P=0.04). Despite similar age at diagnosis and similar follow-up time, no sex differences were identified in metastasis risk, blood pressure outcomes after surgery, or survival. CONCLUSION: Females presented more often with paragangliomas which may explain why they were less likely to have laparoscopic surgery. Remission of type 2 diabetes occurred more commonly in females after surgery. Most other outcomes were similar between sexes. More research is needed to explore differences in outcomes between sexes in PPGLs.
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DOI: 10.3389/fendo.2025.1597908
PMCID: PMC12206822

Adrenal Vein Sampling in Primary Aldosteronism-Is The Gold Standard Losing Its Luster?
J Clin Endocrinol Metab, 110(8):e2800-e3.
J. Deinum and A. F. Turcu. 2025.
The first primary aldosteronism (PA) case, documented in 1954, was attributed to a sizable aldosterone-producing adenoma, which was palpable during exploratory surgery. By the 1960s, expected aldosterone-producing adenomas in several other, equally severe PA cases escaped localization with ether radiographic modalities available at the time (aortography and retroperitoneal pneumography) or during intraoperative exploration. Adrenal vein sampling (AVS) was, hence, introduced in an effort to accurately guide adrenalectomy. Computed tomography eventually became available in the 1970s, albeit with limited initial performance. Over the following decades, cross-sectional imaging underwent major advancements in spatial resolution, scanning time, and manufacturing capacity, broadening its use at a global scale. Nevertheless, AVS has remained the most trusted modality for identifying PA cases that could benefit from surgery. This clinical practice standard has been anchored in 2 major arguments: (1) a rising detection of nonfunctional incidentalomas and (2) histological documentation of millimetric sources of clinically overt PA. Numerous limitations of AVS (an invasive, costly, and technically challenging procedure, with scarce availability) have driven efforts to develop alternative modalities to localize PA sources. In addition, growing understanding of PA pathophysiology has challenged the gold-standard status of AVS for PA subtyping. This perspective discusses the evolving role of AVS in contemporary PA management.
PubMed-ID: 40171612
DOI: 10.1210/clinem/dgaf204
PMCID: PMC12261075

From hyperplasia to carcinoma: a molecular driven adrenal disease.
Eur J Endocrinol, 192(6):K55-K9.
E. Dybal, M. Decaussin-Petrucci, F. Descotes, G. Raverot, J. C. Lifante, C. Sajous, J. Lopez and H. Lasolle. 2025.
Bilateral Macronodular Adrenocortical Disease (BMAD) is characterized by bilateral benign macronodules and, frequently, autonomous cortisol secretion. Germline molecular alterations of tumor suppressor genes are identified in around 30% of cases, the most frequent being ARMC5. Even if adrenocortical nodular disease often occurs with tumor suppressor gene

pathogenic variant, the association with adrenal cortical carcinoma (ACC) is rare and no functional studies have proven a link between these two diseases. We reported the case of a woman with an adrenal Cushing's syndrome developed on BMAD. Over 20 years later, ACC was diagnosed, developed inside a benign nodule of macronodular adrenal gland. Germline genotyping showed no alteration in CDKN1B, KDM1A, PRKACA, PRKAR1A, MEN1, APC, ARMC5, or TP53 genes. Next-generation sequencing has been performed in the ACC and the adjacent macronodular tissue, showing a progressive accumulation of somatic protumoral molecular alterations between the benign nodular part of the adrenal gland and the ACC. Therefore, we hypothesize that BMAD could be an early event of ACC development and may beneficiated from more systematic radiological monitoring.
PubMed-ID: 40448333
DOI: 10.1093/ejendo/lvaf105

Adrenocortical carcinoma: a practical guide for clinicians.
Lancet Diabetes Endocrinol, 13(5):438-52.
M. Fassnacht, S. Puglisi, O. Kimpel and M. Terzolo. 2025.
Adrenocortical carcinoma is a rare endocrine malignancy. The management of patients with adrenocortical carcinoma is challenging for several reasons, including its heterogeneous but frequently aggressive biological behaviour; tumour-related hormonal excess (eg, Cushing's syndrome or virilisation); the overall paucity of evidence regarding diagnostic investigation and treatment; the approval of only one drug (mitotane); and the scarcity of centres with sufficient experience. In this Review, we present 25 questions on the most important aspects of the clinical management of adult patients with adrenocortical carcinoma that we have frequently asked ourselves over the past 25 years. We offer our personal answers and perspectives, drawing upon published evidence as well as more than 60 years of collective clinical experience and insights from our management of more than 1700 patients across two centres in Germany and Italy.
PubMed-ID: 40086465
DOI: 10.1016/S2213-8587(24)00378-4

Does size still matter? - Feasibility of posterior retroperitoneoscopic adrenalectomy for tumors >6cm.
Langenbecks Arch Surg, 410(1):189.
J. Feka, B. Soliman, M. Arikan, M. Sacher, T. Binter, L. Hargitai, C. Scheuba and P. Riss. 2025.
PURPOSE: Retroperitoneoscopic adrenalectomy (RPA) has proven to be safe and feasible with favorable postoperative courses. The role of RPA for tumor sizes larger than 6 cm is still controversial. The aim of the study was to evaluate the postoperative outcome for removal of larger adrenal tumors via the retroperitoneoscopic route. METHODS: In this retrospective study, from 105 conducted RPA procedures, thirteen patients with adrenal tumor sizes larger than 6 cm received RPA in our hospital between January 2017 and December 2020. Clinicopathological factors, length of hospital stay, operative time and postoperative outcomes were included in this analysis. RESULTS: From this patient cohort, six (46.15%) were female and seven (53.85%) were male with a mean age of 53.85 +/- 7.89 years and a mean BMI of 28.64 +/- 3.61 kg/m2, Cushing's syndrome being the most common diagnosis (53.85%). Mean lesion size was 73.31 +/- 10.39 mm, tumor size varied from 60 mm up to 92 mm. Two patients (15.38%) required conversion to open laparotomy due to uncontrollable bleeding or an unclear view on the basis of adhesions. Postoperative complications were noted for one patient (7.69%), who suffered from a small superficial wound infection. Neither capsule ruptures nor mortality were documented. The median hospital stay was 3 days. CONCLUSION: A re-evaluation of the arbitrarily placed cut-off should be discussed, since even with a slightly higher but nevertheless acceptable risk of conversion rate, RPA offers many advantages.
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DOI: 10.1007/s00423-025-03769-7
PMCID: PMC12166009

Genotype-specific neoplastic risk profiles in patients with VHL disease.
Endocr Relat Cancer, 32(5)
A. Ganner, A. M. Ferrara, P. Sekula, F. Schiavi, J. H. Joo, G. Sanso, M. Q. Almeida, A. L. Knoblauch, C. J. Gizaw, K. Krzystolik, S. C. Astheimer, M. I. Achatz, A. Vieites, D. Donegan, T. Hundsberger, J. Lubinski, I. Yildirim Simsir, T. Bandgar, K. Hasse-Lazar, A. Pawlaczek, W. Zandee, K. Yu, C. E. Kater, L. Rostomyan, X. P. Qi, T. Deutschbein, H. Remde, T. N. Dallagnol, M. Yukina, R. Baudrand, C. E. Andreescu, T. Kunavisarut, N. D. Ishak, X. Le Guillou Horn, G. Shutler, M. Jovanovic, M. Peczkowska, J. Calissendorff, F. Circosta, M. J. Bugalho, E. P. M. Corssmit, O. Gimm, M. Quinkler, A. Goldmann, S. Watutantrige Fernando, S. Zovato, L. S. Santana, F. Freitas-Castro, C. Rothermundt, J. Zimmermann, A. Durmaz, A. Aykut, L. Vroonen, T. Krauss, C. Taschner, J. Ruf, J. H. Klingler, S. Glasker, S. Lang, F. Bucher, H. Agostini, C. Jilg, W. Schultze-

Seemann, B. Bausch, A. Bergfeld, K. Rhein, T. Uslar, A. Concistre, C. C. Juhlin, J. C. Casali-da-Rocha, L. Petramala, U. Tsoy, E. Grineva, X. D. Fang, F. Kotsis, T. Schaefer, T. P. Links, O. Makay, G. F. C. Fagundes, J. Ngeow, N. Shah, G. Opocher, M. Barontini, C. Larsson, A. Januszewicz, J. Viana Lima, N. Wohllk, C. Letizia, G. Donatini, E. R. Maher, D. Beltsevich, I. Bancos, C. Cybulski, M. K. Walz, A. Kottgen, C. Eng, H. P. H. Neumann and E. Neumann-Haefelin. 2025.
Hereditary tumor predisposition syndromes pose a challenge for early detection and timely treatment of tumors. In von Hippel-Lindau disease, desirable personalized surveillance programs are lacking due to insufficient data on genotype-specific risk profiles of individual mutations. To describe neoplastic risk profiles for carriers of pathogenic and likely pathogenic VHL germline mutations, our observational study recruited 1,350 participants from 40 centers worldwide. 432 different VHL germline mutations were observed, with p.Asn78Ser, p.Arg161Ter, p.Arg161Gln, p.Arg167Gln, p.Arg167Trp and p.Tyr98His being the six most frequent, occurring in a total of 493 carriers (36.5%) and in >/=30 patients each. Age-related penetrance risks for retinal hemangioblastoma, central nervous system hemangioblastoma, renal cell carcinoma, pancreatic neuroendocrine tumors and pheochromocytoma/paraganglioma in carriers of the most frequent VHL mutations were assessed. In addition, the number of organs affected, the frequency of surgery and the outcome are reported. Pairwise comparisons of the age-dependent tumor penetrance of these six mutations showed that 47 out of 90 pairs were significantly different. The most significant associations were found in p.Tyr98His (n = 19), followed by p.Arg161Ter (n = 10). All pairwise comparisons of mutations affecting different codons showed at least one significant ($P < 0.05$) difference, except for p.Asn78Ser vs p.Arg161Ter. Thus, tumor risk varied by VHL mutation type and location, but did not differ between the truncating mutation p.Arg161Ter and the missense mutation p.Asn78Ser. Our study demonstrates the importance of mutation-specific phenotype prediction. With appropriate validation, the data have important implications for risk assessment and decision making in tumor prevention for carriers of the respective VHL mutations.
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DOI: 10.1530/ERC-24-0260
PMCID: PMC12060576

Histopathological evaluation based on CYP11B2 staining predicts outcomes in unilateral primary aldosteronism.
Eur J Endocrinol, 192(6):763-75.
T. S. Goldbaum, F. L. Ledesma, A. G. Guimaraes, J. Okubo, E. Z. Kawahara, V. F. Calsavara, L. A. Bortolotto, J. L. Chambo, M. Fragoso, M. A. A. Pereira, A. Pio-Abreu, G. V. Silva, J. V. Silveira, F. M. Consolim-Colombo, L. F. Drager, W. C. Nahas, A. C. Latronico, B. B. Mendonca, M. Q. Almeida and M. C. N. Zerbini. 2025.
BACKGROUND: The utility of histopathological classification based on aldosterone synthase (CYP11B2) immunostaining in unilateral primary aldosteronism (PA) for predicting clinical and biochemical outcomes after adrenalectomy remains controversial. METHODS: We conducted a cohort study involving 131 consecutive patients with unilateral PA who underwent unilateral adrenalectomy. Aldosterone-producing adrenal lesions were classified according to the HISTALDO criteria. Biochemical and clinical outcomes were assessed using the PASO criteria. RESULTS: Among the 131 adrenal lesions, classical and non-classical histology were identified in 101 (77.09%) and 30 (22.91%) cases, respectively. In the classical group, 89 cases were classified as aldosterone-producing adenoma (APA), and 12 as aldosterone-producing nodule (APN). Within the non-classical group, 27 cases (90%) had multiple aldosterone-producing micronodules, and 3 cases (30%) had multiple APNs. Patients with classical histology were younger ($P = .028$) and predominantly female ($P = .028$) compared to those with non-classical histology. Classical histology was associated with higher rates of complete biochemical success (97.03% vs 68.97%, $P < .001$) and complete hypertension remission (34.34% vs 10.71%, $P < .001$) compared to non-classical histology. Although clinical and biochemical outcomes were similar between APA and APN, their immunohistological characteristics differed (fewer clear cells and stronger CYP11B2 staining in APN). In multivariable analysis, classical histology remained independently associated with complete biochemical ($P < .001$) and clinical ($P = .037$) success. CONCLUSION: Classical histology was an independent variable associated with more severe PA, complete biochemical and hypertension remission in surgically treated patients with unilateral PA. Moreover, the distinction between APA and APN did not differentiate outcome.
PubMed-ID: 40539251
DOI: 10.1093/ejendo/lvaf118

Adrenalectomy for mild autonomous cortisol secretion?
Lancet Diabetes Endocrinol, 13(7):539-41.
A. V. Haas, N. D. L. Fisher and G. K. Adler. 2025.
PubMed-ID: 40373787
DOI: 10.1016/S2213-8587(25)00117-2

Diagnostic strategies for central adrenal insufficiency in clinical practice: authors' response.
Eur J Endocrinol, 193(1):L3-L4.
L. Haberbosch, C. J. Strasburger, L. Maurer and K. Mai. 2025.
PubMed-ID: 40515606
DOI: 10.1093/ejendo/lvaf126

Identifying factors associated with subsequent diagnosis of adrenal adenoma: a population-based historical case-control study.
Eur J Endocrinol, 193(3):383-90.
A. J. Han, S. J. Achenbach, E. J. Atkinson and I. Bancos. 2025.
OBJECTIVE: The objective of this study is to identify social/metabolic risk factors associated with subsequent diagnosis of adrenal adenoma. DESIGN: The design is a population-based historical case-control study. METHODS: Cases were adult patients diagnosed with an adrenal adenoma between 2005 and 2017 with no overt hormone excess. Controls were age- and sex-matched individuals with (1) no diagnosis of adrenal adenoma and (2) no diagnosis of adrenal adenoma with cross-sectional imaging of the chest/abdomen performed within 5 years prior to index date. The frequency of various social/metabolic risk factors present 5-10 years prior to index date and odds ratios (ORs) for adrenal adenoma diagnosis were reported. RESULTS: Six hundred seventy cases identified (median age 63 years old, 56% women). During the 5-10 years prior to index date, patients with adrenal adenomas had higher prevalence of obesity (56.7% vs 49.3%, P = .007), low socioeconomic status (36.7% vs 31.1%, P = .039), tobacco use (70.2% vs 61.4%, P = .001), and diabetes (17.5% vs 11.7%, P = .003) compared to controls with prior imaging. No difference in prevalence of hypertension, substance use, chronic kidney disease, or combined cardiovascular events was observed. Based on a multivariable analysis, increased body mass index (BMI) and tobacco use were associated with increased odds of adrenal adenoma diagnosis with ORs 1.18 (95% confidence interval [CI] 1.07-1.32) and 1.41 (95% CI 1.06-1.87), respectively. CONCLUSIONS: Compared to controls with prior imaging, patients with adrenal adenoma had higher prevalence of obesity, low socioeconomic status, tobacco use, and diabetes 5-10 years prior to index date. In particular, increased BMI and tobacco use were independent risk factors associated with increased odds of adrenal adenoma diagnosis.
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DOI: 10.1093/ejendo/lvaf184
PMCID: PMC12455730

Clinical Significance of Skeletal Fat-to-Muscle Ratio in Idiopathic Hyperaldosteronism.
Clin Endocrinol (Oxf), 103(4):429-35.
Y. Jiang, D. Li, C. C. Cao, W. Feng, R. Liu, Y. Xu and C. Cao. 2025.
OBJECTIVE: The objective of this study is to evaluate the correlation between the fat-to-muscle ratio (FMR) and insulin resistance (IR) with aldosterone production among patients with idiopathic hyperaldosteronism (IHA). METHODS: Patients with primary aldosteronism were screened from those with secondary hypertension and then subtyped via adrenal venous sampling. A total of 199 patients with IHA and 186 with essential hypertension (EH) (controls) were studied. Baseline clinical characteristics, including data on diabetes and IHA, were collected. The FMR was evaluated based on the distribution of adipose tissue and muscle, measured by a body composition analyzer. RESULTS: The prevalence of diabetes and prediabetes was significantly higher in patients with IHA compared to those with essential hypertension. IHA patients also had significantly higher hemoglobin A1c(HbA1c) levels, homeostatic model assessment of insulin resistance (HOMA-IR), and much lower quantitative insulin sensitivity check index scores than the EH group. FMR was positively associated with fasting insulin, HOMA-IR, aldosterone-to-renin ratio (ARR), and age. A higher FMR was linked to the prevalence of IHA, with a stepwise increase in risk observed from the lowest to the highest quartiles of FMR. Logistic regression analysis showed that both HOMA-IR and body mass index contributed to the elevated FMR. IHA may result from a substantial loss of muscle mass accompanied by fat accumulation. DISCUSSION: In this retrospective study, our findings suggest that FMR could serve as a valuable metric for early intervention and comanagement strategies in patients at risk of sarcopenic obesity. This approach could help block the progression from aldosterone-producing cell clusters to IHA, potentially inhibiting aldosterone overproduction in such patients.
PubMed-ID: 40391493
DOI: 10.1111/cen.15274
PMCID: PMC12413673

External validation of the S-GRAS score for predicting recurrence in patients with adrenocortical carcinoma: implications for adjuvant mitotane therapy.
Eur J Endocrinol, 193(2):320-8.
P. Jimenez-Fonseca, C. Alvarez-Escola, I. Ballester Navarro, J. Hernando Cubero, L. Gonzalez Fernandez, M. A. Mangas Cruz, C. Iglesias, J. Garcia-Donas, M. J. Picon, M. Paja, L. Gonzalez Batanero, L. Garcia, J. Molina, R. Jimeno Mate, J. Aller, M. Romero, J. Cardenas Salas, G. Gutierrez-Buey, N. Egana Zunzunegui, M. Navarro, M. J. Lecumberri, N. Valdes and A. Carmona-Bayonas. 2025.
BACKGROUND: Adrenocortical carcinoma (ACC) is a rare, aggressive malignancy with variable outcomes post-adrenalectomy. The S-GRAS score integrates 5 clinical and pathological factors to predict prognosis but requires external validation in diverse settings. METHODS: We validated the S-GRAS score in 138 ACC patients from the Spanish ICARO-GETTHI/SEEN registry (1998-2023). Model performance was assessed using discrimination, calibration, and accuracy. Exploratory refinements included non-linear modeling of age and Ki-67% and an expanded model incorporating venous invasion and tumor size. Cox models examined the interaction between S-GRAS and adjuvant mitotane. RESULTS: A total of 76 recurrence events were recorded. The S-GRAS score demonstrated good discrimination for overall survival (C-index 0.706, 95% CI, 0.628-0.785) and recurrence-free survival (C-index 0.673, 95% CI, 0.601-0.745) with well-calibrated predictions. Five-year survival rates differed significantly across score groups: 100% for scores 0-1, 81.6% for 2-3, 55% for 4-5, and 33.8% for 6-7. Non-linear modeling of Ki-67% improved performance (C-index 0.738 for RFS, 0.761 for OS), but adding clinical variables offered minimal benefit, leaving 75% of recurrence variability unexplained. Higher S-GRAS scores correlated with increased mitotane benefit (HR 0.57, 95% CI, 0.34-0.97 for score 4; HR 0.46, 95% CI, 0.23-0.94 for score 5), indicating a potential incremental benefit pattern. CONCLUSIONS: Our findings validate the S-GRAS score in a multicenter cohort and support its use in identifying candidates for adjuvant mitotane. Non-linear modeling of Ki-67% enhances predictive precision without increasing complexity, but the performance plateau of clinical variables suggests that integrating molecular biomarkers may be necessary to improve prognostic accuracy.
PubMed-ID: 40810251
DOI: 10.1093/ejendo/lvaf171

Diagnostic strategies for central adrenal insufficiency in clinical practice.
Eur J Endocrinol, 193(1):L1-L2.
I. Kraljevic, M. Solak, A. Balasko, T. Skoric Polovina and D. Kastelan. 2025.
PubMed-ID: 40515611
DOI: 10.1093/ejendo/lvaf125

MEN2: surgical precision in the era of precision medicine.
Endocr Relat Cancer, 32(6)
T. R. Kurzawinski, C. R. Butler and T. A. Aziz. 2025.
ABSTRACT: Medullary thyroid cancer, phaeochromocytoma and primary hyperparathyroidism in patients with multiple endocrine neoplasia type 2 can all be cured by surgery on the condition that they are detected early before locoregional or distant spread of malignant disease occurs and long term metabolic and structural damage to cardiovascular, renal and skeletal systems takes place. Recent scientific discoveries and technological advances made surgical decision process more precise and facilitated personalised treatments. RET analysis enables us to see this syndrome not as a monolith but as a cluster of different phenotypic presentations, each sending patient on an individual journey, which can be anticipated but not determined. Biochemical monitoring provides regular updates on transformation of endocrine cells in target endocrine organs and together with imaging helps to decide on time and extent of surgery. Advances in surgical technology allow for safer and less invasive interventions resulting in fewer complications, less trauma and better functional outcomes. Calibrating magnitude of surgery able to cure but do minimal harm, timing and performing it well is the art of the surgical precision in MEN2 patients. Surgical outcomes have improved in the last 30 years and we need to continue on this road. Precision in surgery aiming at near perfect surgical performance is achievable and this review looks at surgical decision making process through the prism of genetics and biochemical testing combined with imaging, former setting a trajectory for the disease progression with a fair degree of probability and latter assessing functional and structural changes over time.
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DOI: 10.1530/ERC-24-0251
PMCID: PMC12147403

Evaluating the value of chemokine receptor type 4-targeted PET imaging in diagnosing primary aldosteronism lateralization: A comparison with adrenal venous sampling.
Surgery, 181:109156.
N. Lu, L. Chen, F. Yu, Z. Xiao, D. Xing, J. Zhong, D. Zeng, Y. Wang, S. Tang, Y. He and M. Zhe. 2025.
BACKGROUND: Primary aldosteronism lateralization is critical for the treatment option. This study evaluated the preoperative localization diagnostic efficiency of (68)Ga-pentixafor positron emission tomography/computed tomography imaging, targeting C-X-C chemokine receptor type 4 in patients with primary aldosteronism and comparing with adrenal venous sampling, the current gold standard for primary aldosteronism lateralization. METHODS: Fifty patients with primary aldosteronism underwent adrenal venous sampling and (68)Ga-pentixafor positron emission tomography/computed tomography imaging of the adrenal region separately. Patients with lateralization determined by adrenal venous sampling or positron emission tomography/computed tomography underwent adrenalectomy, followed by pathologic diagnoses and immunohistochemical staining for aldosterone synthase (CYP11B2) and C-X-C chemokine receptor type 4, and follow up 12 months after surgery. Correlations among positron emission tomography/computed tomography and adrenal venous sampling, pathologic results, and clinical outcomes were analyzed. The positron emission tomography/computed tomography threshold for primary aldosteronism lateralization was determined using receiver operating characteristic curve analysis. RESULTS: The maximum standard uptake value, with a cutoff value of 11.95, achieved a sensitivity of 74.1% and a specificity of 100.0% for primary aldosteronism lateralization in patients with aldosterone-producing adenoma. A cutoff value of 5.85 for the maximum standard uptake value reached a sensitivity of 81.6% and a specificity of 73.1% in all patients with primary aldosteronism. The concordance rate between (68)Ga-pentixafor positron emission tomography/computed tomography and adrenal venous sampling for primary aldosteronism lateralization was 96.2% in patients with aldosterone-producing adenoma and 75.7% in all patients. Patients with positron emission tomography/computed tomography lateralization benefited from adrenalectomy, and primary aldosteronism lateralization based on positron emission tomography/computed tomography strongly correlated with pathologic classifications, CYP11B2 and C-X-C chemokine receptor type 4 expression levels, and clinical outcomes during follow-up. CONCLUSION: (68)Ga-pentixafor positron emission tomography imaging, as a noninvasive method, performed excellently in detecting aldosterone-producing adenoma and could act as an effective supplement to adrenal venous sampling in primary aldosteronism lateralization.
PubMed-ID: 39919695
DOI: 10.1016/j.surg.2025.109156

Approach to the Management of Gastrointestinal Manifestations in Patients With Phaeochromocytoma and Paraganglioma.
Clin Endocrinol (Oxf), 103(1):21-35.
M. Majumder, C. Chiang, G. Kong, M. Michael, N. Sachithanandan and E. Boehm. 2025.
OBJECTIVE: Managing gastrointestinal symptoms in patients with phaeochromocytoma and paraganglioma (PPGL) is challenging due to the risk of catecholaminergic crisis with many commonly prescribed medications, especially in functional tumours. We reviewed gastrointestinal symptom management and outcomes in PPGL patients at our centre and developed recommendations based on a literature review and our experience. DESIGN, PATIENTS, MEASUREMENT: A single-centre retrospective analysis of the management of gastrointestinal symptoms in patients with PPGL between 2019 and 2024 was completed. A literature review of gastrointestinal manifestations in PPGL was undertaken. RESULTS: Twenty-four individuals with PPGL admitted for radionuclide therapy, chemotherapy, surgery or other medical illness were included. Eighteen (75%) had metastatic disease. Fifty administration events of antiemetics for nausea or vomiting occurred. Two patients had acute colonic pseudo-obstruction. Dopamine antagonists (metoclopramide) and corticosteroids (dexamethasone) were administered to 10 and 9 patients, respectively, the majority of whom were alpha-blocked (n = 7) or had a dopaminergic/biochemically silent phenotype (n = 10). A patient with noradrenergic PPGL experienced a hypertensive episode following high-dose dexamethasone. No patients with biochemically negative/dopaminergic phenotypes or on alpha blockade experienced an antiemetic-related adverse event. Published evidence of dopamine antagonists and corticosteroids precipitating catecholaminergic crisis was mostly limited to case reports. While low-risk antiemetics (serotonin, histamine or neurokinin antagonists) are preferable, we found higher-risk antiemetics (dexamethasone and metoclopramide) can be cautiously administered in patients with a biochemically negative/dopaminergic phenotype or in those on adequate alpha blockade. Limited case reports demonstrated anti-cholinergic agents were beneficial for the management of acute colonic pseudo-obstruction. CONCLUSIONS: Optimal management of gastrointestinal symptoms in PPGL should consider disease characteristics such as primary location, secretory profile, alpha blockade and medication profile.

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DOI: 10.1111/cen.15235
PMCID: PMC12134423

Rethinking dexamethasone suppression test thresholds in the era of precision steroid profiling.
Eur J Endocrinol, 193(3):C7-C8.
Q. Meng, Y. Qin and C. Jin. 2025.
This commentary critically appraises a recent study by Rotolo et al. that highlights diagnostic discrepancies between immunoassays and LC-MS/MS in the 1 mg overnight dexamethasone suppression test (DST). While the study provides compelling evidence for method-specific thresholds, we identify key limitations: the lack of an independent gold standard, incomplete steroid profiling, absence of dexamethasone quantification, and retrospective design. We propose integrating latent-class models, expanded steroid panels, and pharmacokinetic data to refine DST accuracy. Prospective, multicentre harmonization efforts are essential to validate adjusted cut-offs and ensure diagnostic precision across platforms and patient populations.
PubMed-ID: 40845182
DOI: 10.1093/ejendo/lvaf178

Steroidogenic factor-1 regulates a core set of target genes to promote malignancy in adrenocortical carcinoma.
Eur J Endocrinol, 193(1):135-45.
J. C. D. Muzzi, C. Ruggiero, M. Doghman-Bouguerra, M. E. Colodel, J. M. Magno, J. S. S. Resende, N. Durand, J. F. de Moura, L. M. Alvarenga, L. R. Cavalli, B. C. Figueiredo, E. Lalli and M. A. A. Castro. 2025.
OBJECTIVE: Gene dosage is at the core of the biological activity of the steroidogenic factor-1 (SF-1/NR5A1) transcription factor. Its overexpression in adrenocortical carcinoma (ACC) is associated with enhanced proliferation and invasive capacities, steroid modulation, immune suppression, and poor prognosis. Surprisingly, 3 independent studies showed less than 10% agreement in identifying SF-1-regulated genes in the same ACC cell line, raising concerns about technical reproducibility and methodological consistency. This study aimed to reconcile discrepancies in SF-1-regulated gene identification across independent studies using a systematic approach. DESIGN AND METHODS: We reanalysed datasets from those studies using an in silico SF-1 regulon obtained from ACC TCGA data as an external reference to evaluate transcriptional patterns. Additionally, we assessed how threshold selection impacts the overlap between experiments and optimized this process. Furthermore, we performed functional experiments to evaluate how variations in SF-1 dosage impact target gene expression. RESULTS: Our analysis revealed comparable transcriptional patterns across all studies, reconciling transcriptional signatures and phenotypes. Threshold optimization identified consensus sets of genes responsive to SF-1 perturbations. Functional experiments confirmed that variations in SF-1 dosage significantly impact gene expression, explaining discrepancies in previous studies, and evidenced negative autoregulation of the SF-1 transcript by its encoded protein both in ACC cells and in a mouse model of Sf-1 overexpression in the adrenal cortex. CONCLUSIONS: Our findings deepen our understanding of SF-1 regulatory activity in ACC and demonstrate that dosage is critical for observed gene expression patterns. Our integrative approach improves reproducibility and biological interpretation, offering a framework to reconcile cross-study findings.
PubMed-ID: 40600578
DOI: 10.1093/ejendo/lvaf138

Prospective study of metyrapone in endogenous Cushing's syndrome (PROMPT).
Eur J Endocrinol, 193(3):391-402.
L. K. Nieman, M. Boscaro, C. Scaroni, T. Deutschbein, E. Mezosi, N. Driessens, C. E. Georgescu, M. Motyka, A. Hubalewska-Dydejczyk, B. Jarzab, D. Maiter, M. Reincke, P. Loli, B. Zampetti, A. Atmaca, C. Badiu, A. Beckers, M. Bolanowski, F. Cavagnini, N. Unger, R. Giordano, F. A. Hanzu, M. Terzolo, M. B. Nader, N. Sinaii, J. Toke and M. Toth. 2025.
OBJECTIVE: We evaluated the safety and efficacy of metyrapone treatment for Cushing's syndrome (CS). DESIGN: International, prospective, single-arm, open-label study. METHODS: Fifty adults with endogenous CS (either unsuitable for or uncontrolled after surgery) and 3 urinary free cortisol (UFC) concentrations each >/=1.5-fold the upper limit of normal (ULN) were enrolled. After 12 weeks of metyrapone titration, participants with mean 24 h UFC (mUFC) </= 2-fold ULN could enter a 24-week extension phase. Safety was assessed, and doses adjusted at weeks 1-5, 8, 12, and 24. Pre-defined endpoints included normalization of mUFC at weeks 12 (primary), 24, and 36, and proportion of "responders" (normalization or >/=50% decrease of baseline mUFC), time to eucortisolemia, salivary cortisol day-curve, and quality of life (QoL). RESULTS: Of the 49 evaluable participants, 47 completed the 12-week visit; 40 were evaluated at week 24 and 35 at week 36. The primary endpoint was met in 46.9% of participants (95% CI 32.5%-61.7%), with efficacy maintained at

week 24 (52.5%; 95% CI 37.5%-67.1%) and week 36 (48.6%; 95% CI 33.0%-64.4%). The responder rates were 80.9%, 77.5%, and 71.4% at weeks 12, 24, and 36, respectively. Forty-seven participants (94%) developed mild-to-moderate adverse events (AEs), mostly during the first 12 weeks and most commonly nausea (38%), fatigue (26%), and headache (22%); 8 experienced severe AEs. Six participants developed reversible adrenal insufficiency during titration. Clinical features and QoL improved. CONCLUSION: Metyrapone is a safe and effective treatment for endogenous CS.
PubMed-ID: 40966724
DOI: 10.1093/ejendo/lvaf181

Disrupted ACTH and cortisol response to osmotic and non-osmotic stress in patients with arginine vasopressin deficiency.
Eur J Endocrinol, 193(1):1-9.
A. Nikaj, C. Atila, I. Chifu, E. Ferrante, Z. Erlic, J. B. Drummond, R. Indirli, R. Drexhage, A. S. Powlson, M. Gurnell, B. S. Soares, J. Hofland, F. Beuschlein, M. Fassnacht, B. Winzeler, J. Refardt and M. Christ-Crain. 2025.
OBJECTIVE: Arginine vasopressin (AVP), synthesized in the hypothalamus and stored in the posterior pituitary, regulates osmotic balance and stress responses. During stress, AVP enhances corticotropin-releasing hormone-stimulated adrenocorticotropic hormone (ACTH) secretion, with cortisol and AVP providing negative feedback regulation. Disruption in AVP production might impair this feedback, leading to sustained cortisol elevations. The current analysis aims to investigate the effect of hypertonic saline (osmotic stress) and arginine infusion (non-osmotic stress) on the hypothalamic-pituitary-adrenal (HPA) axis response between patients with AVP-Deficiency and primary polydipsia (PP). DESIGN: Secondary sub-analysis of a prospective diagnostic study conducted at seven tertiary centers that utilized hypertonic saline and arginine infusion for diagnostic evaluation of patients with hypotonic polyuria-polydipsia syndrome. METHODS: ACTH and cortisol levels were measured at baseline and the expected peak for both stimulation tests and groups. A pooled linear mixed-effects model (without stimulation type as a variable) was used to compare hormone responses between groups, followed by stimulation test-specific linear regression models to assess differences between both tests. RESULTS: Twenty patients with AVP-Deficiency and 10 patients with PP were included. In the pooled analysis, patients with AVP-Deficiency showed a significantly greater increase in plasma ACTH [7.0 ng/L (95% CI, 0.8-13.3), P = .04] and plasma cortisol [106 nmol/L (95% CI, 24-188), P = .02] compared to patients with PP. Upon hypertonic saline, the changes in plasma ACTH [0.3 ng/L (95% CI, -10.0 to 11.0)] and plasma cortisol [78 nmol/L (95% CI, -32 to 188)] were similar. However, upon arginine infusion, plasma ACTH [9.2 ng/L (95% CI, 1.8-17)] and plasma cortisol [141 nmol/L (95% CI, 40-242)] increases were significantly greater in patients with AVP-Deficiency. CONCLUSION: An altered ACTH and cortisol response pattern to stress in patients with AVP-Deficiency was observed, indicating impaired regulation of the HPA axis. This alteration was primarily driven by differences observed for non-osmotic stress.
PubMed-ID: 40498919
DOI: 10.1093/ejendo/lvaf119

Psychotropic drug use in patients with autoimmune Addison's disease: a Swedish population-based cohort study.
Eur J Endocrinol, 193(2):262-9.
S. Oster, T. Spelman, S. Bensing and J. Skov. 2025.
OBJECTIVE: The effect of autoimmune Addison's disease (AAD) on mental health is not well known. The aim of this study was to examine the use of psychotropic drugs around diagnosis and after long-term follow-up in Swedish individuals with AAD. DESIGN AND METHODS: In this population-based cohort study, national health and population registers and the Swedish Addison Registry were used to identify individuals diagnosed with AAD between July 2006 and December 2019 and matched population controls. The Swedish Prescribed Drug Register was used to retrieve information on annual dispensations (yes/no) of anti-psychotics [Anatomical Therapeutic Chemical (ATC) N05A], anxiolytics (ATC N05B), hypnotics/sedatives (ATC N05C), and anti-depressants (ATC N06A), from 3 years before to 3 years after diagnosis. A cross-sectional analysis of the year 2019 was also performed. RESULTS: A total of 963 persons with AAD and 9366 matched controls were identified. Use of hypnotics/sedatives, anxiolytics, and anti-depressants was significantly higher in patients with AAD the year preceding diagnosis [ORs 1.72 (1.40-2.11), 1.38 (1.07-1.78), and 1.29 (1.05-1.59), respectively]. After diagnosis, use of hypnotics/sedatives remained significantly higher [ORs 1.42 (1.13-1.78) to 1.78 (1.45-2.19)]. We found no difference in dispensation of other psychotropic drugs after diagnosis. In the cross-sectional analysis of 2019, the increased dispensation of hypnotics/sedatives remained elevated [odds ratio (OR) 1.31 (1.01-1.70)]. CONCLUSIONS: Prescription patterns suggest that early symptoms of AAD are associated with or mistaken for mental health disorders. Furthermore, insomnia is common in patients with AAD.
PubMed-ID: 40751493
DOI: 10.1093/ejendo/lvaf155

The Landmark Series: Evaluation and Management of Adrenal Incidentalomas.
Ann Surg Oncol, 32(7):4712-9.
L. Owei and H. Wachtel. 2025.
Adrenal incidentalomas are adrenal masses >/= 1 cm discovered on imaging studies for unrelated clinical conditions. The prevalence of adrenal incidentalomas has increased as a byproduct of the widespread use of cross-sectional imaging, particularly in older adults. The clinical significance of adrenal incidentalomas varies based on tumor size, hormonal activity, and imaging characteristics. While most adrenal incidentalomas are benign and asymptomatic, a significant minority are hormonally active or malignant, necessitating careful evaluation and management. Adrenal hormone secretion can have significant clinical implications. Biochemical testing is crucial to assess for hormone excess, including steroid hormones (mineralocorticoids, glucocorticoids, and androgens), which are made in the adrenal cortex, as well as catecholamines, which are made in the adrenal medulla. Non-contrast computed tomography (CT) is the preferred modality for evaluating adrenal nodules as it allows for assessment of tissue density in Hounsfield units (HU). Benign lesions typically have an homogeneous appearance with HU </= 10. Contrast-enhanced CT with delayed washout can help differentiate benign tumors from malignant tumors. Tumors >/= 4 cm, or those with indeterminate features may require further imaging, such as magnetic resonance imaging (MRI) or positron emission tomography (PET)/CT. The management of adrenal incidentalomas is determined by hormonal secretion and imaging characteristics. Surgical resection is recommended for functional tumors and those that are suspicious for malignancy, including tumors >/= 4 cm in size and those with rapid growth. Non-functional tumors < 4 cm may undergo imaging surveillance. The goal of this review is to summarize the contemporary literature and guidelines on adrenal incidentalomas, and to describe the key principles regarding evaluation and management.
PubMed-ID: 40304946
DOI: 10.1245/s10434-025-17296-8
PMCID: PMC12130141

Phenotype of pheochromocytoma and paraganglioma by germline mutation: a Korean multicenter study.
Endocr Relat Cancer, 32(5)
M. J. Park, S. S. Park, B. H. Lee, J. S. Jang, W. W. Kim, S. J. Kim, Y. M. Lee, K. E. Lee, T. Y. Sung, M. W. Seong, W. Lee, J. M. Koh, J. H. Kim and S. H. Lee. 2025.
Recent advances in genetic testing have challenged the traditional genotype-phenotype correlation in pheochromocytomas and paragangliomas (PPGL). We aimed to characterize the genotype-phenotype correlations in PPGL in a large Korean cohort and compare our findings with those from other countries. We retrospectively analyzed 627 patients with PPGL from two centers who underwent genetic testing for germline pathogenic variants (PVs) from 2000 to 2023 to examine the prevalence of clusters and their correlation with specific phenotypes. Moreover, we systematically reviewed 44 studies that investigated the frequency of germline PVs based on geographical differences. Germline PVs were identified in 29.7% of patients (n = 186). The prevalence of cluster 1A, 1B and 2 PVs was 10.6% (n = 67), 8.0% (n = 50) and 11.1% (n = 69), respectively. Cluster 1 patients were presented with more aggressive features, including younger age at diagnosis (39 years), higher rates of extra-adrenal (44.4%), and metastatic (27.8%) tumors, than did the wild-type and cluster 2 groups (P < 0.001). Cluster 1A patients had significantly higher metastasis rates than cluster 1B patients (38.8 vs 12.5%; P < 0.001). The cluster 2 group showed a high recurrence risk but rarely developed metastases. The cluster 1-to-cluster 2 ratio among Koreans (1.7) was lower than that among Europeans (2.9) and North Americans (3.3). This study underscores the genetic and clinical heterogeneity of PPGL among Korean patients based on genetic clusters and highlights geographic variations in PVs. These findings have significant implications for risk stratification, surveillance and management strategies for patients with PPGL.
PubMed-ID: 40063012
DOI: 10.1530/ERC-24-0269

Machine learning-based classification of adrenal tumors using clinical, hormonal, and body composition data.
Eur J Endocrinol, 193(2):204-15.
S. S. Park, J. Noh, J. Kim, T. Kim, H. J. Seo, C. H. Ahn, J. Choo, M. H. Choi and J. H. Kim. 2025.
OBJECTIVE: Accurate diagnosis of adrenal tumors, including mild autonomous cortisol secretion (MACS), adrenal Cushing's syndrome (ACS), primary aldosteronism (PA), pheochromocytoma (PCC), and nonfunctioning adrenal adenomas (NFAs), is crucial but challenging. We aimed to develop a machine learning (ML)-based single-step diagnostic method for differentiating adrenal tumors by integrating clinical data, serum adrenal hormone profiles (SAPs), and body composition data. METHODS: A total of 641 patients with adrenal tumors (MACS = 141, ACS = 64, PA = 265, PCC = 78, and NFA = 93),

excluding adrenal metastases and adrenocortical carcinoma, were enrolled from Seoul National University Hospital. Patients were randomly divided into training and test cohorts at a 4:1 ratio. The ML models were developed to differentiate adrenal tumors using 32 clinical data points, 49 SAP markers, and 15 body composition data points. RESULTS: The best-performing ML model for differentiating all 5 adrenal tumors achieved a balanced accuracy of 0.78, sensitivity of 0.77, specificity of 0.93, and area under the curve (AUC) of 0.89. To distinguish MACS, ACS, PA, and PCC from NFA, the accuracies were 0.85, 0.94, 0.78, and 0.86, with AUCs of 0.96, 0.99, 0.90, and 0.94, respectively. The ML model differentiating between NFA and the other functioning adrenal tumors exhibited an accuracy of 0.75 and an AUC of 0.79. The SAP features were identified as the most critical for differentiation, whereas body composition data contributed only minimally. CONCLUSIONS: The ML model demonstrates high diagnostic accuracy in differentiating adrenal tumor subtypes by integrating clinical data, body composition, and SAP, potentially reducing the need for invasive procedures and aiding clinical decision-making.
PubMed-ID: 40729515
DOI: 10.1093/ejendo/lvaf145

Locally advanced pheochromocytoma/paraganglioma exhibit high metastatic recurrence and disease specific mortality rates: long-term follow-up of 283 patients.
Eur J Endocrinol, 192(6):705-16.
W. Raber, A. Scheuba, R. Marculescu, H. Esterbauer and J. Rohrbeck. 2025.
IMPORTANCE: Data on locally advanced (LAP) pheochromocytoma/paraganglioma (PPGL), based on capsular, vascular or periadrenal fat invasion, tumor emboli and extra-adrenal extension, are scarce. OBJECTIVE: To compare outcomes of patients with LAP and without (nLAP). DESIGN: Retrospective cohort study, 1981-2024, prospectively supplemented 2020-2024. SETTING: Referral center. OUTCOMES: Overall, metastatic and nonmetastatic recurrence, overall (OAS) and disease-specific survival (DSS). RESULTS: Of 283 patients followed for 11.3 +/- 8.8 (mean +/- SD) years, 79 (27.9%) had LAP. Compared to patients with nLAP (n = 204), patients with LAP had more overall (n = 17 vs. 31, hazard ratio 2.4, 95% CI 1.4-5.0) and metastatic (11 vs. 9, HR 6.8, 2.2-20.6) and similar (6 vs. 22, HR 1.2, 0.5-3.0) nonmetastatic recurrences. OAS was comparable (12 vs. 42 nonsurvivors, HR 1.2, 0.6-2.3), but mortality from metastatic disease was higher with LAP (2 vs. 4 deaths, HR 12.2, 1.8-82.8). Extra-adrenal tumor location was predictive of metastatic and nonmetastatic recurrence but not of OAS or DSS, tumor size of metastatic recurrence and of DSS, cluster 1 and 2 pathogenic variants of overall and nonmetastatic recurrence but not of OAS or DSS. LAP with tumor emboli and extra-adrenal extension predicted overall (HR 4.5, 1.3-14.2 and 5.0, 1.4-13.7) and metastatic recurrence (HR 24.6, 6.4-91.8 and 6.5, 1.6-23.4), OAS (HR 21.2, 2.8-108, tumor emboli only) and DSS (HR 22.6, 3.5-183 and 13.1, 1.7-120), LAP with vessel invasion nonmetastatic recurrence (HR 3.6, 1.2-10.0). CONCLUSION: Patients with LAP vs. nLAP have higher metastatic recurrences and worse DSS. Tumor emboli and extra-adrenal extension indicated lower DSS, warranting a close follow-up.
PubMed-ID: 40393073
DOI: 10.1093/ejendo/lvaf104

Evaluation of prognostic factors in advanced pediatric ACC.
Endocr Relat Cancer, 32(5)
M. Riedmeier, S. Agarwal, S. R. R. Antonini, S. Ekinci, M. Fassnacht, B. C. Figueiredo, C. Hartel, J. P. Meena, S. D. Marks, J. Munarin, S. Puglisi, G. Tuli, B. Yalcin, P. G. Schlegel, A. Wiegering and V. Wiegering. 2025.
Therapeutic options of advanced pediatric adrenocortical carcinoma (pACC) are limited, and achieving valuable risk stratification remains challenging. We refined the value of prognostic factors with an emphasis on resection status. Retrospective international data from 106 patients with advanced pACC from various collaborating centers of the international pACC working groups ENSAT-PACT, IC-PACT and/or from individual international collaboration diagnosed were collected. One hundred six patients aged 0.1-18.1 (median 7.6) years were diagnosed with pACC, with 42 tumor stage III and 64 stage IV, respectively. Eighty percent (85/106) of the tumors were hormone-producing, with a mean Ki67 index for both stage groups of 29%. Patient survival was 45% (48/106) with a mean follow-up of 17.7 months. Higher age, tumor stage IV and increased Ki67 index worsened the prognosis on overall survival. Resection status had an essential impact on survival, as the patients with R0 resection (n = 32) had a better overall survival (71% for stage III patients; 80% for stage IV patients) than patients with R1 (n = 24) (45% for stage III; 69% for stage IV), R2 (n = 33) (17% for stage III; 15% for stage IV) and Rx (n = 7) (0% for stage III; 17% for stage IV). Of the ten patients with tumor spillage, only a few (57% of stage III; 0% of stage IV patients) survived. The resection status has a significant impact on overall survival in pACC. Therefore, tumor surgery should only be undertaken by experienced surgeons proficient in adrenalectomy and oncology, ideally within specialized pediatric oncological centers with a multidisciplinary team setting.

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DOI: 10.1530/ERC-24-0135

Inflammation-based score in pediatric adrenocortical carcinoma.
Endocr Relat Cancer, 32(5)
M. Riedmeier, J. Idkowiak, H. Frey, S. R. R. Antonini, G. F. L. Canali, C. F. Classen, N. Dominguez-Pinilla, M. Fassnacht, S. Fuchs, C. Hartel, D. Janus, R. de Krijger, T. Kutluk, N. L. Bui, J. P. Meena, M. Mezoued, J. Munarin, M. M. van Noesel, N. O. Kose, S. H. Pearce, T. Perwein, S. Puglisi, J. Del Rivero, P. G. Schlegel, I. Schmid, G. Tuli, J. Walenciak, B. Yalcin and V. Wiegering. 2025.
Inflammation-based scores have been demonstrated to be independent prognostic factors in predicting outcomes in adult adrenocortical carcinoma (ACC). We aimed to investigate the prognostic role of these scores in pediatric adrenocortical carcinoma (pACC) patients. An international multicenter analysis was conducted on a pediatric cohort from 21 ACC centers. Pretreatment inflammation-based scoring parameters, including neutrophil-to-lymphocyte ratio (NLR), derived neutrophil-to-lymphocyte ratio (dNLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR) and serum albumin, as well as clinical parameters, were analyzed. The primary endpoint was 10-year overall survival (OS). One hundred twenty-nine pediatric patients (50.4% females, mean age 87 months) across all tumor stages with a median follow-up of 36 months were included. 107/108 patients underwent primary surgery, and 62/106 received systemic treatment at the time of diagnosis. Of 102 patients, 27 died from disease. In the univariable analysis, NLR >/=5 (HR 8.0, 95% CI 3.4-19.1), MLR >/=0.28 (HR 4.2, 95% CI 1.7-10.4), PLR >/=190 (HR 4.5, 95% CI 2.0-10.4) and dNLR >/=1.44 (HR 5.9, 95% CI 2.3-15.5), as well as clinical parameters age >/=4 years (HR 5.5, 95% CI 1.9-15.8), tumor stage IV (HR 5.7, 95% CI 2.7-11.9) and incomplete resection status (HR 8.0, 95% CI 3.6-17.7) were significantly associated with reduced 10-year OS. After multivariable adjustment, only tumor stage IV (HR 336.7, 95% CI 5.8-19,518.1) and MLR >/=0.28 (HR 247.1, 95% CI = 3.1-19,907.5) were significantly associated with an unfavorable outcome. Inflammation-based scores tend to have prognostic value in pACC and could serve as prognostic tools after further validation in future studies with sufficient case numbers.
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DOI: 10.1530/ERC-24-0244
PMCID: PMC12002726

Genetic Testing Referral Rates for Pheochromocytoma and Paraganglioma in an Academic Tertiary Centre.
Clin Endocrinol (Oxf), 103(2):147-56.
B. Ruhle, N. E. Kim, S. Ngo, E. G. Hughes, D. P. Sajed, R. Yu, J. X. Wu, M. W. Yeh and M. J. Livhits. 2025.
BACKGROUND: Clinical guidelines recommend genetic counselling for all patients with pheochromocytoma or paraganglioma (PPGL). Barriers to accessing genetics evaluation are incompletely understood. The objective of this study was to identify individual- and provider-level barriers to genetic testing. METHODS: Retrospective study of patients with PPGL who underwent resection at a tertiary academic centre. Study outcomes included referral rates for genetic counselling and completion of germline testing. RESULTS: Of 224 patients who underwent resection of PPGL, 75% were referred for genetic counselling, and 49% completed testing. Genetic testing was highest after 2019. More individuals 50 years or younger underwent testing compared to over 50 (65% vs. 37%, $p < 0.001$). Medicare insurance was associated with lower rates of testing compared to commercial insurances (32% vs. 64%, $p = 0.006$). Controlling for individual and temporal factors, head and neck paragangliomas were least likely to undergo genetic testing (OR 0.13, 95% CI: 0.05-0.31). Reasons for not undergoing testing included insurance denial, time constraints, and patient uncertainty. Twenty-two percent (14/68) of patients with pheochromocytoma had a positive finding (FH, MSH3, MUTYH, NF1, RET, SDHD and VHL), while 46% (19/41) of patients with paraganglioma had a positive finding (MSH6, SDHA, SDHB, SDHD, TMEM127 and VHL). CONCLUSION: Germline testing was performed in less than half of patients with PPGL, and 30% who underwent tested carried a pathogenic mutation, reinforcing the importance of genetics evaluation. Older age, Medicare coverage, and head and neck paragangliomas were associated with lower rates of genetic testing, presenting opportunities to improve education and equity in the management of patients with PPGL.
PubMed-ID: 40235160
DOI: 10.1111/cen.15248
PMCID: PMC12223699

A Novel Natural Language Processing Model for Triaging Head and Neck Patient Appointments.
Otolaryngol Head Neck Surg, 173(1):126-33.
S. Seo, A. S. Ding, S. A. Ahmad, K. Z. Xin, M. L. Jiam, V. Xin, L. J. Mady, C. G. Gourin, W. K. Mydlarz, N. R. London, Jr., W.

Koch, C. Fakhry and N. T. Jiam. 2025.
OBJECTIVE: Inaccurate patient triage contributes to suboptimal clinical capacity management and delays in patient care, which in cancer patients may significantly increase morbidity and mortality. We developed a natural language processing (NLP) model as an adjunctive tool for head and neck (H&N) patient triage workflows. This study assesses the model's ability to categorize and triage patient appointments based on available documentation. STUDY DESIGN: A retrospective cohort study. SETTING: An academic institution. METHODS: A total of 83 new patients seeing an H&N surgeon from January to April 2024 with at least 1 referral record (clinic note, imaging, or pathology report) available were included in this study. Referral clinic, imaging, and pathology reports were entered into the NLP model to predict pathology type (non-endocrine H&N neoplasm, thyroid, parathyroid, and benign lesions), malignancy risk, and appointment urgency. The gold standard was the final diagnosis from pathology reports or surgeons' clinic notes. RESULTS: The NLP model achieved an accuracy of 81.9% for pathology type and 86.8% for urgency level. Sensitivity was high for non-endocrine H&N neoplasms (88.9%), thyroid pathology (88.9%), and parathyroid pathology (100%), although lower for benign lesions (67.9%). Specificity was 86.8% for non-endocrine H&N neoplasms, 91.9% for thyroid pathology, 97.6% for parathyroid pathology, and 96.4% for benign lesions. Prediction of appointment urgency achieved a Matthews correlation coefficient of 0.698, reflecting strong predictive performance. CONCLUSION: This novel NLP model demonstrated robust performance characteristics for predicting H&N diagnoses based on referring documents and excelled at identifying patients requiring urgent care based on malignancy risk. This tool may help H&N practice coordinators screen referrals, potentially optimizing patient care.
PubMed-ID: 40277144
DOI: 10.1002/ohn.1244

Improving diagnosis in primary aldosteronism using HISTALDO and nodule size metrics.
Eur J Endocrinol, 193(2):278-88.
K. Solhuslokk Hose, A. Stenman, H. Falhammar, C. Volpe, C. Larsson, J. Zedenius and C. C. Juhlin. 2025.
BACKGROUND: Primary aldosteronism (PA) is the leading cause of secondary hypertension. The 2022 WHO classification introduced the HISTALDO system, separating solitary aldosterone-producing adenomas/nodules (APA/APN; classical histology) from multiple nodules/micronodules (MAPN/MAPM; non-classical histology). Surgery often cures classical cases, while non-classical cases frequently recur. HISTALDO uses CYP11B2 immunohistochemistry, but interpretation is challenged by background nodules. A "B2 ratio" (size ratio of the largest to second-largest CYP11B2-positive nodule) has been proposed to aid diagnosis. OBJECTIVE: To assess whether standardized tissue sampling and the B2 ratio improve PA diagnosis and correlate with outcomes. METHODS: A prospective study of 75 unilateral PA patients undergoing adrenalectomy (2017-2022) at Karolinska University Hospital. CYP11B2 immunohistochemistry was performed using a standardized protocol, and the B2 ratio was calculated in cases with multiple CYP11B2-positive nodules (HISTALDO B2R). Outcomes were assessed using Primary Aldosteronism Surgical Outcome criteria. RESULTS: HISTALDO classified 20 cases as classical and 55 as non-classical (median B2 ratio 9). Using a B2 ratio cut-off >/=8.1, 29/55 non-classical cases were reclassified, yielding 49 classical and 26 non-classical cases under HISTALDO B2R. Higher B2 ratios correlated with complete clinical response (P = .0038) and fewer antihypertensive medications postoperatively (R = -0.4, P = .0022). A trend for B2 ratio as an independent predictor of complete response was observed (OR = 1.07, P = .058). CONCLUSIONS: HISTALDO may over-report non-classical histology. Adding the B2 ratio improves diagnostic accuracy, distinguishing APA with background zona glomerulosa activity from true multinodular disease, facilitating patient management and follow-up.
PubMed-ID: 40729417
DOI: 10.1093/ejendo/lvaf157

A global real-world study assessing total time to adrenalectomy in primary aldosteronism.
Eur J Endocrinol, 193(1):65-75.
C. Ter, X. H. Koh, H. Tran, I. Bancos, M. Bassiony, M. Araujo-Castro, M. Paja, M. Gonzalez Boillos, E. Gkaniatsa, M. Reincke, C. Adolf, T. V. Tran, M. Stowasser, D. Nayak, M. A. Grytaas, A. F. Turcu, J. Matrozova, N. Sukor, F. Ismail, T. Kocjan, M. Parasiliti-Caprino, R. Baudrand, T. Uslar, M. Tsuiki, M. Murakami, J. Yang, C. Ng, T. Katabami, M. Naruse, M. St-Jean, F. Ceccato, S. E. Saffari, A. E. D. Teo and T. H. Puar. 2025.
BACKGROUND: Primary aldosteronism (PA) is a common treatable cause of hypertension. When caused by unilateral adrenal disease, it is potentially curable by adrenalectomy. However, specialized tests and other factors may delay definitive treatment. We assessed the time to adrenalectomy (TTA) for patients worldwide. METHODS: We conducted an international, multicentre retrospective study involving 39 centres from 15 countries to determine the total time taken from the first presentation to adrenalectomy and the intervals between each stage (screening, confirmatory, subtyping,

and adrenalectomy). We included patients with PA who underwent adrenalectomy from January 1, 2018, to October 30, 2022. Post-adrenalectomy outcomes were evaluated using the Primary Aldosteronism Surgery Outcome criteria. We performed multivariable quantile and linear regression to identify characteristics associated with longer TTA. RESULTS: We included 861 patients, mean age 49.3 +/- 11.1 years, and 44.5% were women. Overall median TTA was 13.5 months, IQR: 6.6-24.5. Median intervals were 0.1 months (screening), 1.0 months (confirmatory), 4.1 months (subtyping), and 4.3 months (adrenalectomy). On multivariable analysis, median TTA was increased by 5.4 months for each additional adrenal vein sampling (AVS) procedure. Other factors associated with longer TTA included adrenalectomy post-COVID-19, younger age, and additional screening tests. Compared with countries with routine AVS, those without AVS had a shorter TTA (6.1 vs 15.1 months, P < .001), but greater likelihood of absent/partial biochemical success post-adrenalectomy (27.4% vs 12.4%, P < .001). CONCLUSION: Primary aldosteronism management is time-consuming worldwide, especially for subtyping tests and adrenalectomy. While omitting AVS reduces overall time, patients are less likely to achieve biochemical cure post-adrenalectomy.
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DOI: 10.1093/ejendo/lvaf124
PMCID: PMC12224190

Discordance and shortcomings of aldosterone suppression tests in primary aldosteronism.
Eur J Endocrinol, 193(3):348-58.
C. H. Tsai, S. Parisien-La Salle, J. M. Brown, A. Newman, C. C. Chang, V. C. Wu, Y. H. Lin and A. Vaidya. 2025.
BACKGROUND: The saline suppression test (SST) and the captopril challenge test (CCT) have traditionally been used to confirm or exclude primary aldosteronism (PA). New guidelines recommend using these tests to predict the likelihood of unilateral PA. This study evaluated the diagnostic accuracy, consistency, and clinical implications of these tests. METHODS: We conducted a retrospective study of 531 patients with high-probability features of PA who underwent both SST and CCT to evaluate their accuracy and ability to predict unilateral PA. Adrenal lateralization and surgical treatment decisions were guided by individualized clinical judgment rather than strictly relying on SST/CCT results. RESULTS: The rate of PA diagnosis ranged from 47.8% to 97.2% based on SST and CCT criteria. Discordance rates between SST and CCT ranged from 10.9% to 51.6%. In analyses restricted to only patients with clinically overt PA, where suppression testing is not considered necessary, the positivity rates of the SST and CCT were still suboptimal and test discordance persisted. Among patients with lateralizing PA, 6.6% to 27.9% had either a negative SST or CCT interpretation, and among those who achieved Primary Aldosteronism Surgical Outcome-defined biochemical cure after unilateral adrenalectomy, 4.1% to 39.8% had either a negative SST or CCT, and up to 5.1% had false-negative results on both tests. CONCLUSIONS: Well-established aldosterone suppression tests for PA demonstrated substantial inconsistency, false-negative interpretations, and the inability to reliably predict lateralization outcomes in PA. Aldosterone suppression testing, using SST and CCT, lack accuracy for the diagnosis and subtyping of PA in high-risk patients.
PubMed-ID: 40796325
DOI: 10.1093/ejendo/lvaf170
PMCID: PMC12405916

Challenges in circulating miRNA analysis in adrenocortical tumors.
Endocr Relat Cancer, 32(6)
B. Vekony, G. Nyiro, H. Butz, B. K. Szeredas, V. Toth, P. Ferdinandy, A. Patocs and P. Igaz. 2025.
The differentiation of benign and malignant adrenocortical tumors is of major clinical relevance. Circulating microRNAs (miRNAs) hold promise as blood-borne biomarkers of adrenocortical cancer (ACC). There are, however, many difficulties with their use, including technical and biological standardization challenges. Our aim was to evaluate the interchangeability of quantitative polymerase chain reaction (qPCR) and digital PCR (dPCR) for measuring circulating miRNAs and to investigate whether K2- and K3-EDTA as anticoagulants influence the measurements. Blood samples were drawn simultaneously from 20 participants into K2- and K3-EDTA tubes. Three miRNAs shown to be associated with ACC (miR-483-5p, miR-210-3p, miR-21-5p), together with two controls (miR-16-5p, cel-miR-39-3p), were analyzed using RT-qPCR and dPCR. qPCR and dPCR results showed different correlations in K2- and K3-EDTA samples, with K2 performing better regarding DeltaCt values. Moreover, proportional biases related to low or high miRNA expressions between the two methods were observed. In qPCR measurements, K3-EDTA samples showed larger standard deviations, particularly for cel-miR-39. While raw Ct values differed between K2- and K3-EDTA only for miR-483-5p, DeltaCt values showed statistically significant differences across all miRNAs except for miR-483-5p. dPCR results were not affected by the choice of anticoagulant. In conclusion, this is the first study demonstrating that dPCR and qPCR results are not easily interchangeable for circulating miRNA, particularly for abundant or rare miRNAs, making cross-validation studies

challenging. K2- and K3-EDTA could potentially influence qPCR outcomes, underscoring the need for standardized protocols. A consensus-based methodology could improve reproducibility, enhancing miRNA-based biomarker utility in adrenocortical tumor diagnostics.
PubMed-ID: 40472370
DOI: 10.1530/ERC-25-0045

Pituitary tumor-transforming gene 1 and endocrine cancers: an up-to-date review through history, current insights and future perspectives.
Endocr Relat Cancer, 32(6)
E. Vergani, E. Teveroni, F. Mancini, F. Di Nicuolo, S. Raia, S. Chiloiro, F. Pierconti, A. Bianchi, A. M. Isidori, A. Pontecorvi and D. Milardi. 2025.
Pituitary tumor-transforming gene 1 (PTTG1), discovered in 1997 by Pei and Melmed, takes part in cellular replication, cell cycle control, DNA repair mechanisms, organogenesis, metabolism regulation, cellular transformation, and senescence. Its biological actions include protein-protein interactions, modulation of gene transcription, and other than intracellular and autocrine mechanisms, even paracrine activities. For the reasons mentioned above, PTTG1 stands out as a multifaceted regulator of cancer biology; it is involved in genomic and chromosomal instability, local invasiveness, neo-lymphangiogenesis, and metastatic spreading. In solid neoplasms, endocrine neoplasms, although deemed rare, have experienced a significant increase in diagnostic incidence in recent years. Endocrine cancers are still a major challenge in healthcare and research since several questions remain unanswered, even though researchers have made considerable efforts to uncover their causes. Twenty-seven years have passed since PTTG1's discovery, and several works have been published. However, only the tip of the iceberg has been unveiled. Herein, we review current knowledge of PTTG1's action in endocrine cancers, such as pituitary, thyroid, testicular, adrenal, pancreatic, and ovarian.
PubMed-ID: 40472369
DOI: 10.1530/ERC-24-0163

A predictive nomogram for incomplete clinical success after unilateral adrenalectomy in patients with primary aldosteronism.
Front Endocrinol (Lausanne), 16:1628564.
P. Wang, L. Liu, S. Lu, X. Zhu, R. Zhu, Y. Yang, G. Zhou and X. Cao. 2025.
INTRODUCTION: Incomplete clinical success after unilateral adrenalectomy for primary aldosteronism (PA) remains a significant challenge, often characterized by persistent hypertension despite biochemical remission. OBJECTIVE: This study aimed to develop and validate a preoperative predictive nomogram to estimate the probability of incomplete clinical success in PA patients undergoing unilateral adrenalectomy. MATERIALS AND METHODS: A retrospective analysis was conducted on 58 PA patients who underwent adrenalectomy. Independent predictors of non-complete clinical success were identified using multivariate logistic regression. A nomogram was developed based on age, highest systolic blood pressure (SBP), and lateralization index (LI). Model performance was evaluated through the concordance index (C-index), calibration plots, and decision curve analysis, with internal validation performed via bootstrapping (1,000 resamples). RESULTS: Age (OR 1.117), highest SBP (OR 1.241), and LI (OR 1.044) were independently associated with incomplete clinical success. The nomogram showed strong discriminative ability (C-index: 0.829) and good calibration. Internal validation confirmed its reliability (AUC: 0.844, sensitivity 84.2%, specificity 75.0%). CONCLUSION: This nomogram offers a reliable, easy-to-use tool for preoperative risk stratification of PA patients, facilitating personalized postoperative management. External validation in multicenter cohorts is warranted.
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DOI: 10.3389/fendo.2025.1628564
PMCID: PMC12328156

Mitotane treatment of adrenocortical carcinoma induces tumoural secretion of GDF-15: impact on poor prognosis and impaired responsiveness to immunotherapy.
Eur J Endocrinol, 193(1):146-55.
I. Weigand, A. S. Triebig, T. Maier, T. Anderlik, H. Remde, L. S. Landwehr, O. Kimpel, M. Reuter, J. Schreiner, F. Wedekink, O. Scherf-Clavel, E. Hoster, K. C. Wollert, I. Budde, B. Altieri, P. Schwarzlmueller, M. Reincke, J. Wischhusen, M. Fassnacht and M. Kroiss. 2025.
PURPOSE: Treatment options for adrenocortical carcinoma (ACC), where mitotane remains a mainstay of therapy, are unsatisfactory. Response rates of ACC to immune checkpoint inhibition (ICI) are disappointing, and immune cells are scarce in ACC. Growth/differentiation factor 15 (GDF-15) is a cytokine impairing tumoural immune infiltration. We here

aimed to assess the value of serum GDF-15 for the prognosis of ACC and as a predictor of response to ICI. METHODS: GDF-15 was measured in serum samples of 151 patients and correlated with clinical data. Serum GDF-15 was analysed in a second cohort of 46 ACC patients who received ICI, including 14 responders. mRNA expression of GDF15 and genes related to immune response was quantified in 58 ACC tumour samples. RESULTS: We found GDF-15 induction in ACC cells and patients upon mitotane treatment. In ACC patients, serum GDF-15 concentration below the median was associated with significantly longer patient survival. GDF-15 levels in responders to ICI were significantly lower than in non-responders (P = .0379), and patients with low GDF-15 levels had a significant longer progression-free survival than patients with higher GDF-15 serum levels (P = .036). Expression of pro-inflammatory immune-related genes was lower in ACC tissue with GDF-15 expression above the median. CONCLUSIONS: Mitotane increases GDF-15 levels and is associated with poor response to ICI. GDF-15 may mediate reduced infiltration with immune cells in ACC.
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DOI: 10.1093/ejendo/lvaf135

Clinical and genetic features of older patients with pheochromocytomas and paragangliomas: A multicenter retrospective study.
J Endocrinol Invest,
X. Xu, Y. Shen, J. Jiang, Y. Pang, K. Cheng, Z. Li, Y. Wang, J. Chen, A. Yu, J. Wang, M. Li, J. Zhang and L. Liu. 2025.
PURPOSE: The genetic background and catecholamine phenotype of pheochromocytomas and paragangliomas (PPGLs) influence the age at diagnosis. However, few studies have systematically investigated clinical features of older patients with PPGLs. This study was based on one of the largest PPGL cohorts in China and aimed to summarize the clinical and genetic characteristics of older PPGL patients, especially concerning intraoperative hemodynamics and genetic background. METHODS: This retrospective study involved 897 patients with abdominal PPGLs from two Chinese centers. DNA from tumor samples was sequenced using next-generation sequencing. Clinical information, intraoperative hemodynamic data, and pathogenic variants were collected and compared between younger (</= 50 years) and older (> 50 years) patients. RESULTS: Older patients had a higher rate of incidental tumors (40.5% vs. 48.2%, P = 0.022), fewer typical catecholamine-related symptoms (49.8% vs. 42.4%, P = 0.032), lower plasma normetanephrine levels (7.61 vs. 5.17, P = 0.003) and higher proportion exceeding the normal glycemic range (21.7% vs. 34.4%, P = 0.01) compared to younger patients. The proportion of older patients receiving alpha-adrenergic receptor blockers for preoperative preparation decreased to 74% compared to 82.4% in younger patients (P = 0.003). During surgery, older patients showed hemodynamic changes indicative of vascular and cardiac aging. Specifically, older patients had lower minSBP, DBP, minMAP, and heart rate, while the SBP fluctuation was higher (P = 0.008). Additionally, younger patients have significantly higher mutation rates for SDHB (5.5% vs. 1.0%, P < 0.001) and VHL (13.3% vs. 7.3%, P = 0.003). HRAS mutations are more prevalent in older patients (10.5% vs. 21.3%, P < 0.001). IDH1 mutations occurred exclusively in older patients (0.56%, 5/887). CONCLUSION: Older patients with PPGLs have unique clinical and genetic characteristics. These differences highlight the importance of personalized diagnosis and treatment for various age groups, particularly in developing preoperative preparation strategies to improve vascular and cardiac function in older patients.
PubMed-ID: 40833586
DOI: 10.1007/s40618-025-02689-z

Progress in treatment and follow-up of pheochromocytoma.
Eur J Surg Oncol, 51(8):110144.
Y. Zhou, Y. Tai and J. Shang. 2025.
Pheochromocytoma (PHEO) is an uncommon neuroendocrine tumor originating from the chromaffin cells of the adrenal medulla. These tumors are capable of producing and releasing substantial amounts of catecholamine (CA) hormones. Individuals with PHEO often experience transient blood pressure fluctuations, headaches, and palpitations, among other symptoms. In extreme cases, they may develop severe complications, including cardiovascular and cerebrovascular incidents, myocardial disorders, and gastrointestinal issues. At the advanced stage, PHEO can affect multiple organs, potentially leading to pheochromocytoma crisis. However, the clinical manifestations of pheochromocytoma may be diverse. Some patients have no typical triad of headache, palpitations, and sweating, and are not accompanied by obvious clinical symptoms or signs. There are only abnormalities in imaging and biochemical indicators, which will pose a challenge for early diagnosis. The primary treatment options for PHEO encompass surgical and non-surgical approaches. In contrast to many other adrenal pathologies, there is currently no consensus on the optimal surgical versus non-surgical management of PHEO. Laparoscopic surgery, as opposed to traditional open surgery, offers numerous benefits. However, whether retroperitoneal or transperitoneal laparoscopic adrenalectomy remains controversial. Da Vinci robot-assisted adrenalectomy has the advantages of highly precise operation and excellent hemostasis capabilities. The day surgery

management model for adrenalectomy procedures has proven to be both safe and feasible. However, current research on its long - term effectiveness and wide - scale application still has limitations. Additionally, the application of the Senhance robot in urology, particularly in adrenalectomy, has seen relatively little investigation thus far. In terms of non-surgical treatment for pheochromocytoma, chemotherapy, radionuclide therapy, targeted therapy and immunotherapy, as well as radiofrequency ablation and microwave ablation chemotherapy have all advanced significantly. This article aims to review the latest advancements in the treatment of pheochromocytoma.
PubMed-ID: 40373734
DOI: 10.1016/j.ejso.2025.110144

Clinical Utility of Dual-Time (68)Ga-Pentixafor PET/CT in Diagnosing and Subtyping Primary Aldosteronism.
Clin Endocrinol (Oxf), 102(5):499-509.
R. Zuo, S. Liu, X. Ren, W. Li, Z. Xia, L. Xu and H. Pang. 2025.
OBJECTIVES: This study aimed to compare the clinical efficacy of dual-time (68)Ga-pentixafor PET/CT with adrenal vein sampling (AVS) in PA lateralization. METHODS AND METHODS: We retrospectively analysed 161 patients with PA. We assessed the diagnostic performance of dual-time (68)Ga-pentixafor PET/CT in diagnosing unilateral primary aldosteronism (UPA) and aldosterone-producing adenoma (APA). We also explored the relationship between (68)Ga-pentixafor PET/CT findings, postoperative outcomes, and the presence of the KCNJ5 gene mutation. RESULTS: The diagnostic accuracy of (68)Ga-pentixafor PET at 10 and 40 min for UPA (75.2% and 76.4%, respectively) surpassed that of CT (55.3%, $p < 0.01$). The optimal cutoff for diagnosing APA was 10 min lesion-to-normal adrenal ratio = 1.95, yielding an AUC of 91.9%, with sensitivity, specificity, and accuracy of 76.0%, 91.3%, and 83.3%, respectively. This high diagnostic efficacy extended to subgroups with nodules >/= 1 or < 1 cm, and the largest AUC of (68)Ga-pentixafor PET/CT for diagnosis APA with lesions >/= 1 and < 1 cm is 88.2% and 97.0%, respectively. The lateralization results provided by (68)Ga-pentixafor PET/CT corroborated the surgical treatment decision in 92.0% of PA patients, and more than 95% achieved clinical and/or biochemical cure or improvement. The PET positive rate of KCNJ5 mutation was higher than that of KCNJ5 wild-type, with optimal diagnostic efficacy at 40 min lesion-to-liver ratio = 4.79 (AUC 81.3%, sensitivity 90.0%, specificity 66.7%). CONCLUSION: Dual-time (68)Ga-pentixafor PET/CT exhibits robust diagnostic efficacy in PA lateralization. Furthermore, (68)Ga-pentixafor PET/CT holds promise as an imaging marker for predicting the presence of the KCNJ5 mutation in PA patients.
PubMed-ID: 39865783
DOI: 10.1111/cen.15204

NET

Meta-Analyses

Management of liver metastases from non-functional gastroenteropancreatic neuroendocrine tumors: a systematic review.
Front Endocrinol (Lausanne), 16:1601185.
J. S. Xue, Y. Yang, Z. Huang, H. Zhao, X. Chen and J. Q. Cai. 2025.
The liver is the most common metastatic organ of neuroendocrine tumors (NETs). NET liver metastases (NETLMs) are categorized into simple liver metastasis (type I), complex liver metastasis (type II) and diffuse liver metastasis (type III), of which diffuse liver metastasis accounts for the highest percentage, up to 60-70%. Radical resection is recommended for all patients with type I and partial type II liver metastases without extrahepatic metastases in G1 and G2 grades, with a 5-year survival rate of 65%-70%. But for patients with G3 or type III liver metastases, treatment is controversial. Ablation and TAE/TACE are commonly used localized treatments. Somatostatin analogue (octreotide and lanreotide) are efficacious in the treatment of better-differentiated NETs and can prolong the progression-free survival (PFS) of patients. Targeted drugs such as sunitinib, everolimus, sofantinib and cabozantinib are used to control tumor growth and improve symptoms. In addition, peptide receptor radionuclide therapy (PRRT), has been approved by the FDA for the treatment of progressive somatostatin receptor-positive gastroenteropancreatic NETs and has shown potential for prolonging PFS and improving survival. Multidisciplinary treatment is crucial for patients with NETLMs with high tumor load, and neoadjuvant therapy combined with surgery may lead to a better prognosis. However, the choice of treatment, indications for combination therapy, and disease prognosis still require further research and exploration. This review summarizes and evaluates the current treatment strategies and development trend of NETLM treatment through a literature review and provides new ideas as well as insights.
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DOI: 10.3389/fendo.2025.1601185
PMCID: PMC12328144

Randomized controlled trials

Traction-assisted endoscopic submucosal resection (TA-ESD) for rectal neuroendocrine tumors: a randomized multi-center trial.
Surg Endosc, 39(8):5430-8.
S. Wu, Y. Zhou, D. Ji, X. Cai, L. Shen, X. Yu, J. Xia, M. Zhu, X. Zhao, Y. Shi, M. Ning, X. J. Wan and Z. X. Dong. 2025.
BACKGROUND AND AIM: Endoscopic resection is the first-line choice for the treatment of rectal neuroendocrine tumors (NETs). This study aimed to compare the efficacy and safety of a modified traction-assisted endoscopic submucosal resection (TA-ESD) and traditional endoscopic submucosal resection (ESD). METHODS: In this multi-center prospective randomized controlled trial, patients with small rectal NET(< 2 cm) were 1:1 randomized into TA-ESD or traditional ESD groups. The operation time was selected as the primary endpoint, while en bloc resection rate, R0 resection rate, complications, length of hospitalization were chosen as secondary endpoints. RESULTS: A total of 44 patients (22 TA-ESD and 22 ESD patients) were enrolled in this study, of which 40 patients (19 TA-ESD and 21 ESD patients) were pathologically confirmed rectal NET patients. The median operation time was shorter in the TA-ESD group than in the ESD group (7.3 (5.4-9.6) vs. 12.2 (7.8-21.0) minutes, Difference (95% CI) -4.5 (-10.0, -1.3), P = 0.0054). Furthermore, the rates of en bloc resection and R0 resection were 22 (100%) and 22 (100%) in TA-ESD group and ESD group, respectively. Perforation occurred in one patient in the ESD group during the operation and no postoperative complication was recorded in both groups. CONCLUSION: Compared with traditional ESD, modified TA-ESD is more suitable for the treatment of small rectal NETs than traditional ESD due to its shorter operation time and improved R0 resection rate.
PubMed-ID: 40634728
DOI: 10.1007/s00464-025-11934-8
PMCID: PMC12287171

Consensus Statements/Guidelines

- None -

Other Articles

Results of Surgical Reintervention After Suboptimal Initial Resection for Locoregional Neuroendocrine Tumors of the Small Intestine.
World J Surg, 49(5):1343-50.
D. K. Bartsch, N. Krasser-Gercke, M. Jesinghaus, J. Gorlach, F. Eilsberger, A. Rinke and E. Maurer. 2025.
BACKGROUND: Complete resection is the only chance for cure in small intestine neuroendocrine neoplasms (SI-NEN). Previous ENETS guidelines proposed standards for the surgery of SI-NEN, which should be followed to provide long-term disease-free survival. AIM: To analyze the results of reintervention for locoregional SI-NEN (stages I-III) after suboptimal initial resection. METHODS: Perioperative characteristics of all patients who underwent surgical reintervention after suboptimal initial resection (SIR) of locoregional SI-NEN were retrieved from a prospective database. Patient characteristics, initial and redo procedures, imaging before reintervention, pathological results of SIR, and after reintervention, including missed primary tumors and lymph node metastases, were retrospectively analyzed. RESULTS: During a 15 years period, 21 of 93 (22%) patients had surgical reinterventions after SIR. In 20 of 21 (95%) cases, the initial resection was performed outside an ENETS center of excellence. Ten (48%) of those cases were emergency operations because of the bowel obstruction or bowel bleeding. Seven SIR (33%) cases were performed laparoscopically, and in another 5 (24%) cases, a complete endoscopic mucosa resection was performed. Imaging before reintervention visualized residual disease in 15 of 21 (71%) patients. Surgical reintervention included either lymphadenectomy alone (LAD, n = 3) or small bowel resection plus systematic LAD (n = 12) or right hemicolectomy/ileocecal resection with systematic LAD (n = 6), respectively. In 19 of 21 (90%) patients, a R0 resection could be achieved. One patient (5%) experienced postoperative clinically relevant complications. According to pathology, in 10 (48%) patients lymph node metastases, in 6 (29%) patients additional primary tumors, and in 5 (24%) patients, both lymph nodes metastases and primary tumors were left behind in the SIR. After mean follow-up of 52 months, 16 (76%) of 21 patients were free of disease, 4 (19%) patients were alive with disease, and 1 patient deceased of an unrelated cause. CONCLUSION: The proposed standards to resect locoregional SI-NEN should be followed to avoid SIR, although the prognosis after adequate surgical reintervention is good.
PubMed-ID: 40238178
DOI: 10.1002/wjs.12582
PMCID: PMC12058433

Pancreatic neuroendocrine tumors: Do we need more nuanced staging?
Am J Surg, 246:116383.
E. Chen and J. B. Rose. 2025.
PubMed-ID: 40374420
DOI: 10.1016/j.amjsurg.2025.116383

MiR-7-5p as a Diagnostic and Monitoring Biomarker for Neuroendocrine Tumors: Insights from the SKY-NET Multicenter Study.
Ann Surg,
Y. Higuchi, K. Shoda, H. Konishi, T. Nakayama, R. Shibata, R. Saito, S. Maruyama, K. Shiraishi, S. Furuya, Y. Kawaguchi, H. Amemiya, A. Shiozaki and D. Ichikawa. 2025.
OBJECTIVE: This study aimed to identify and validate miR-7-5p as a non-invasive biomarker for diagnosing and monitoring neuroendocrine tumors (NETs). SUMMARY BACKGROUND DATA: The incidence of NETs has been increasing globally in recent years, yet standardized non-invasive biomarkers for early detection and monitoring of these malignancies are lacking. Although diagnostic imaging is valuable, its resource-intensive nature limits its practicality for routine screening. Thus, reliable, non-invasive biomarkers are urgently needed. METHODS: In the multicenter SKY-NET study, we performed comprehensive genome-wide transcriptome profiling to identify candidate microRNAs (miRNAs) in the tissues of patients with NET. Promising candidates were validated in plasma samples from two independent cohorts using quantitative polymerase chain reaction. RESULTS: We identified miR-7-5p as a diagnostic candidate for NET. In the multicenter SKY-NET

study, miR-7-5p exhibited robust diagnostic performance in both tissue and plasma samples, with high sensitivity and specificity. The biomarker differentiated NET tissues from normal tissues, with an area under the receiver operating characteristic curve (AUC) of 0.97 and 0.88 for tissue and plasma samples, respectively. In an independent clinical cohort, plasma miR-7-5p maintained strong diagnostic performance (AUC=0.85). Notably, plasma miR-7-5p levels correlated with tumor dynamics, reflecting treatment response and disease recurrence. CONCLUSION: MiR-7-5p demonstrates substantial potential as a non-invasive biomarker for diagnosing and monitoring NET. Our findings support its potential as a diagnostic tool and for assessing disease progression, offering a new avenue for early detection and treatment evaluation in patients with NET.
PubMed-ID: 40657762
DOI: 10.1097/SLA.0000000000006816

Intraoperative differentiation of pancreatic neoplastic lesions using optical coherence tomography (OCT).
Langenbecks Arch Surg, 410(1):227.
M. Kist, P. Strenge, T. Keck, A. Weber, P. Bronsert, T. S. A. Abdalla, U. F. Wellner and M. Thomaschewski. 2025.
PURPOSE: The diagnostic methods for accurately differentiating the dignity of pancreatic neoplasms are limited. Worrisome features on MRI and endosonography guide the way to resection or conservative treatment with a relevant rate of failure. Intraoperative minimal invasive optical coherence tomography could be a solution for this challenge. The aim of this study is to investigate whether optical coherence tomography is suitable for differentiating of pancreatic neoplastic lesions. METHODS: In this exploratory study, four patient's specimens of pancreatic resections (white adipose tissue, intraductal papillary mucinous neoplasm (IPMN), pancreatic ductal adenocarcinoma (PDAC) based on IPMN and neuroendocrine pancreatic carcinoma) were prospectively examined ex vivo immediately after resection in the operating room using an optical coherence tomography system (Callisto 930nm, Thorlabs GmbH). In detail, the study investigated whether and in what way endocrine tumors, adenocarcinomas, premalignant and benign cysts differ morphologically in optical coherence tomography imaging compared to healthy pancreatic tissue. The final histopathological findings of the pancreatic specimens served as a reference and were correlated. RESULTS: The samples examined ranged from typical fatty tissue, intraductal papillary mucinous neoplasm (IPMN), a moderate differentiated (G2) pancreatic ductal adenocarcinoma (PDAC) based on an intraductal papillary mucinous neoplasm (IPMN) and a neuroendocrine pancreatic carcinoma. Optical coherence tomography was feasible to replicate key histological characteristics and tissue architecture in correlation to conventional Hematoxylin-eosin histology. CONCLUSION: Optical coherence tomography imaging has the potential to differentiate between benign, pre-malignant and malignant pancreatic pathologies by morphology and should be examined in larger collectives.
PubMed-ID: 40679633
DOI: 10.1007/s00423-025-03810-9
PMCID: PMC12274226

Therapy-related myeloid neoplasms in 177Lu-DOTATATE treated neuroendocrine tumor patients: how great is the risk?
Endocr Relat Cancer, 32(6)
Y. Kusne, M. M. Patnaik, T. R. Halfdanarson and M. B. Sonbol. 2025.
Peptide receptor radionuclide therapy (PRRT) with lutetium-177-Dotatate (177Lu-DOTATATE) has transformed neuroendocrine tumor (NET) treatment, improving progression-free survival, symptom control, and quality of life. However, long-term hematologic toxicities, including therapy-related myeloid neoplasms (tMN), are increasingly recognized. These rare but severe complications, such as myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML), appear multifactorial, influenced by prior cytotoxic therapies, radiation exposure, clonal hematopoiesis, and germline predispositions. This review synthesizes data on PRRT-related hematologic toxicities, including findings from pivotal studies and real-world evidence. We explore risk factors, underlying mechanisms, and the potential role of biomarkers, such as clonal hematopoiesis and germline mutations, in predicting toxicity. Emerging approaches, including alpha particle radioligand therapy and advanced dosimetry, are explored as strategies to optimize patient selection and minimize adverse outcomes. To maximize the benefits of PRRT while safeguarding patient safety, future efforts should focus on integrating predictive biomarkers, refining treatment sequencing, and developing personalized risk-stratified approaches to therapy.
PubMed-ID: 40446156
DOI: 10.1530/ERC-25-0025

Lenvatinib as salvage therapy in advanced and progressive GI-NET.
Endocr Relat Cancer, 32(8)
A. Mathew, J. Capdevila, N. Unger, W. Fendler, S. Theurer, F. Weber, D. Fuhrer and H. Lahner. 2025.
The efficacy of lenvatinib in treating gastrointestinal neuroendocrine tumors (GI-NETs) has been explored in preclinical studies and early-phase clinical trials, but real-world data remain limited. Data of sixteen patients (median age 65 years; 62.5% female) with advanced and progressive GI-NET who were treated with lenvatinib at the ENETS Center, University Hospital Essen, between July 2019 and February 2024 were analyzed. Patients received all other approved therapies and showed progression within 2 months. Salvage therapy with lenvatinib was initiated after approval from health insurance. Most NETs originated in the small intestine (94%) with a median Ki-67 index of 3.5%. Before lenvatinib, patients received a median of four lines of treatment (range 3-7), including somatostatin analogs (100%), everolimus (100%), chemotherapy (25%) and PRRT (88%). Surgery of the primary and/or metastatic lesions was performed in 81% and ablative therapies in 38%. The median time between NET diagnosis and the initiation of lenvatinib was 100 months. The overall response rate on salvage therapy was 29% and the clinical benefit rate was 100%. The median progression-free survival (PFS) on lenvatinib was 10 months and the median overall survival (OS) after the initiation of lenvatinib reached 113 months. Hypertension was associated with significantly longer PFS (24.5 months, P = 0.007), whereas weight loss correlated with shorter PFS (4 months, P = 0.0032). In this retrospective single-center case analysis, lenvatinib demonstrated promising results in heavily pre-treated and rapidly progressing GI-NET. With an OS of 9.4 years after start of salvage therapy, these results highlight the value of lenvatinib as a therapeutic option for advanced GI-NET patients with otherwise limited treatment alternatives.
PubMed-ID: 40748172
DOI: 10.1530/ERC-25-0165

Impact of treatment on quality of life in neuroendocrine neoplasm survivors.
Endocr Relat Cancer, 32(8)
R. Modica, E. Benevento, A. La Salvia, R. Mazzilli, C. Pandozzi, G. Pecora, L. Barrea, A. Colao, A. Faggiano and N. Group. 2025.
Neuroendocrine neoplasms (NENs) are a heterogeneous group of tumors, ranging from well-differentiated, slow-growing neuroendocrine tumor (NET) with long-term survival, to aggressive high-grade neuroendocrine carcinoma (NEC). Advances in treatment and earlier diagnosis have led to improved survival outcomes; however, data regarding patients' quality of life (QoL) during therapy and in the post-treatment phase remain limited. This narrative review aims to analyze available data on QoL in NEN patients undergoing medical therapies, including nutritional considerations, to improve and personalize therapeutic strategies. A literature search was performed using online databases, including MEDLINE (via PubMed) and Scopus, employing multiple keyword combinations up to October 2024. Somatostatin analogs (SSAs) and radioligand therapy (RLT) have demonstrated good tolerability profiles and efficacy on QoL, especially in patients with carcinoid syndrome, impacting on both physical and emotional domains. In contrast, multikinase inhibitors have been associated with declines in general health status, and sexual and physical function. Data on chemotherapy are conflicting, with some evidence suggesting a favorable QoL profile due to tumor control. Interestingly, approximately 30% of NEN survivors report persistence of symptoms related to depression. Both treatment-related side effects and disease-related symptoms may impact QoL, affecting nutritional status, which should be carefully considered. Despite standardized QoL, assessments are lacking in nutritional studies, and adherence to a Mediterranean diet seems to positively influence symptom burden in NEN patients. In conclusion, evidence supports that SSA and RLT contribute to improved QoL, likely due to symptom control. Further research is needed to better characterize the QoL impact of other therapies using standardized assessment tools, in order to optimize therapeutic management.
PubMed-ID: 40663359
DOI: 10.1530/ERC-24-0303

Defining Biological Borderline Resectable Non-functioning Pancreatic Neuroendocrine Tumors (NF-PanNETs): A Predictive Model for Preoperative Assessment of Early Recurrence Risk.
Ann Surg, 282(5):734-41.
S. Partelli, G. Guarneri, P. M. V. Rancoita, I. De Martino, L. Provinciali, L. De Mestier, S. Dokmak, J. Hallet, A. Sauvanet and M. Falconi. 2025.
OBJECTIVE: This study aimed to develop and validate a preoperative predictive model to identify patients at high risk of early recurrence (ER), with a view to establish a framework for biological borderline resectability of non-functioning pancreatic neuroendocrine tumors (NF-PanNETs). BACKGROUND: Radical surgery is curative for most localized NF-PanNETs, but a subset of patients experiences ER. No standardized criteria define preoperative high-risk disease.

METHODS: A retrospective multicentric study was conducted at 3 tertiary centers. Patients undergoing curative resection for localized NF-PanNETs were included, and preoperative clinicopathologic and imaging variables were analyzed. ER was defined as a recurrence within 24 months. A classification tree model was developed, and performance was assessed using the area under the curve (AUC) of the receiver operating characteristic curve. RESULTS: A total of 496 patients were analyzed, with 290 in the derivation cohort and 206 in the validation cohort. ER occurred in 55 patients (11%), including 26 (9%) in the derivation and 29 (14%) in the validation cohort. The median disease-free survival for ER patients was 16 months (interquartile range: 10-20 months). Neoplastic venous thrombosis was the strongest predictor of ER, with an ER probability of 71%. Among patients without venous thrombosis, those with a Ki-67 index >/=5% and tumor size >/=3 cm had an ER probability of 41% in case of adenopathy and 19% otherwise. The model achieved an AUC of 0.91 in the derivation cohort and 0.84 in the validation cohort. CONCLUSIONS: This externally validated model provides a reliable preoperative tool to identify NF-PanNETs at high risk of ER and introduces the concept of biological borderline resectable NF-PanNETs.
PubMed-ID: 40747911
DOI: 10.1097/SLA.0000000000006867

Peptide receptor radionuclide therapy in malignant insulinoma.
Endocr Relat Cancer, 32(6)
D. A. Pattison, G. Kong, T. Akhurst, M. Burge, C. Chiang, M. S. Hofman, T. J. Hung, A. Love, M. Michael, S. Okano, A. S. Ravi Kumar, N. Sachithanandan, D. Wyld and R. J. Hicks. 2025.
The management of malignant insulinoma (MI) presents dual management challenges of hypoglycaemia and tumour control. This study aims to analyse long-term outcomes of PRRT for the treatment of MI. We retrospectively reviewed consecutive patients with MI treated with [177Lu]Lu-DOTATATE (LuTATE) at two Australian NET centres between 2004 and 2022. Follow-up for hypoglycaemia, molecular imaging, radiologic and biochemical responses, treatment-related side-effects, progression-free and overall survival were assessed. Of 15 patients (seven female; median age 60, range 26-82) treated for intractable hypoglycaemia, WHO grade (G) was known in 12 patients (three G1, six G2 and three G3). PRRT was administered in a median of seven cycles (range 1-15), with a median cumulative activity of 42 GBq (range 4-117 GBq) and radiosensitizing chemotherapy in 9/15 (60%) patients. Resolution of hypoglycaemia was observed in 14/15 (93%) patients after a median of 2.5 months (range 0.2-23.5), but recurred in 7/14 cases after a median of 17.7 months (range 7.6-48.3). Patients with recurrent hypoglycaemia had a longer time to hypoglycaemia resolution (median 3.0 vs 0.5 months), were more likely G3 (57 vs 0%) and experienced higher mortality (86 vs 29%). In all seven cases, PRRT re-treatment was successful. The mean duration of hypoglycaemia remission was 23.8 months (range 9.2-101). The median progression-free and overall survival was 17.9 months (95% CI, 8.5-43.2) and 50.1 months (95% CI, 23.0-ND), respectively. Side-effects included G3/4 myelosuppression in 4/15 patients and hypoglycaemia flare (hospitalisation >48 h) in 7/15 patients. PRRT provides durable hypoglycaemic and oncologic disease control of MI with manageable toxicity including hypoglycaemia flare requiring multidisciplinary care.
PubMed-ID: 40424062
DOI: 10.1530/ERC-25-0018

A Reassessment of the Clinical Utility of (68)Ga-DOTATATE PET/CT in Patients With Gastroenteropancreatic Neuroendocrine Tumors.
J Surg Oncol, 131(7):1336-42.
O. Prela, B. Caveney, M. Strawderman, D. Linehan, E. Galka, L. Schoeniger, A. Hezel, N. Badri and D. R. Carpizo. 2025.
BACKGROUND: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are a rare and biologically diverse group of tumors that are challenging to image. (68)Ga-DOTATATE PET/CT is the most sensitive imaging tool for these tumors, and while its use has increased over time, its clinical impact remains unclear, particularly for clinical scenarios involving surveillance after treatment. We sought to reassess its clinical utility across all stages. METHODS: Retrospective study of pathologically confirmed GEP-NET patients between 1/1/2020 and 9/1/2022 at a tertiary care center. Demographic, clinical, and radiographic data were analyzed. The primary objective was to determine if PET/CT use was associated with a change in clinical management. The secondary objective was to determine if PET/CT was superior in identifying primary or metastatic lesions compared to traditional imaging. RESULTS: One hundred twenty-four patients with GEP-NETs underwent 207 PET/CT scans. The majority of scans were obtained for disease surveillance (70.2%) or staging (37.9%), and the remaining (3.2%) were used to aid in diagnosis or before PRRT initiation (3.2%). Following PET/CT scan, 51 patients (41.1%) had a change in clinical management, with change being higher among those with metastatic disease (44.9% vs. 14.5%). Of the 124, 72 patients had traditional imaging available for comparison. In this subgroup, 34 patients (47.2%) had new lesions identified on PET/CT that were not identified using traditional imaging resulting in a change in management in

79.4% favoring patients with M1 versus M0 disease (26.9% M0 vs. 58.7% M1, p = 0.010). CONCLUSION: (68)Ga-DOTATATE PET/CT imaging is clinically most useful for initial staging and in surveillance and monitoring response to therapy in the metastatic setting. It is least useful for surveillance in the early-stage setting and does not support its use following curative intent surgery. It remains superior to unlabeled imaging in sensitivity and the additional disease burden detected is highly likely to change management.
PubMed-ID: 39757730
DOI: 10.1002/jso.28061
PMCID: PMC12186107

Clinical, genetic, radiological characteristics and management of mediastinal paragangliomas: a literature review and case series.
Endocr Relat Cancer, 32(5)
M. Quinn, Y. Kemkem, G. White, P. Touska, D. Christodoulou, A. Jacques, L. Breen, B. McGowan, M. Joshi, F. Ul Hassan, K. Harrison-Phipps, J. G. Hubbard, R. Obholzer, L. Izatt, P. Carroll and A. Velusamy. 2025.
Paragangliomas (PGLs) are neuroendocrine tumours (NETs) that arise from neural crest-derived cells. Up to 40% of cases occur due to the presence of a pathogenic germline variant (PGV) in a known gene. Mediastinal PGLs are rare but are being diagnosed with increasing frequency. Treatment generally involves surgery but is complicated in mediastinal PGLs due to their anatomy. Here, we will perform a literature review and discuss our experience with 18 such cases. Cases were identified via the Guy's and St Thomas' NHS Foundation Trust NET multidisciplinary team database. Tumours ranged in size from 0.6 x 0.6 to 6.8 x 4.9 cm. 72.2% were associated with a PGV of SDHB or SDHD. 22.2% developed metastatic disease, but it was only possible to attribute 50% of these to a mediastinal primary. 68Ga-DOTATATE PET CT demonstrated 100% sensitivity. The literature review identified 233 cases. A PGV was reported in 81% of cases, with metastatic disease in approximately 39.2%. It was not possible to confirm that all cases of metastatic disease were secondary to a mediastinal primary. Our experience confirms the high rate of mediastinal PGLs arising in the presence of a PGV. The lower rate of metastatic disease in our cohort (11.1%) likely represents earlier diagnosis thanks to the application of screening protocols and the increased sensitivity of 68Ga-DOTATATE PET CT. With this increased sensitivity, we have diagnosed small mediastinal PGLs that were not evident on alternative imaging modalities. In the absence of growth or catecholamine secretion, the need to intervene on these is unclear.
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PMCID: PMC11964478

Predictors Based on the Radiologic Characteristics for Aggressiveness of Small (< 20 mm) Nonfunctioning Pancreatic Neuroendocrine Tumors.
J Surg Oncol, 131(6):1142-8.
S. J. Ren, F. Yang, Q. Q. Tan, C. Liu, X. B. Liu, C. L. Tan and X. Wang. 2025.
BACKGROUND AND OBJECTIVES: To find the association between preoperative computed tomography (CT) features combined with tumor marker and known high-risk factors of small nonfunctioning pancreatic neuroendocrine tumors (NF-PNETS), thereby selecting appropriate treatment strategy for these patients. METHOD: One hundred fourteen patients with NF-PNETs< 20 mm who underwent surgical operation were retrospectively analyzed from 2009 to 2023. Univariate and multivariable logistic regression analyses were performed to find the relationship between preoperative clinical psychological and CT features and high-risk factors. The overall survival (OS) rates with and without high-risk factors were compared. RESULTS: Of 114 patients, 29(25%) had at least one of these high-risk factors. Main pancreatic duct dilation (OR, 3.315; 95% CI, 1.079-10.184; p = 0.036), irregular tumor margin (OR, 2.955; 95% CI, 1.021-8.551; p = 0.046), positive tumor marker (OR, 6.047; 95% CI, 1.408-25.963; p = 0.015) were associated with increased odds of having any of these high-risk factors. The time to death differed significantly between patients with and without high-risk factors. Patients combining with high-risk factors were associated with lower 3- and 5-year OS (100% vs. 81.8%, 93.1% vs. 81.8%, respectively; p = 0.035 for both). CONCLUSION: Main pancreatic duct dilation, irregular tumor margin and positive tumor marker could screen a subset of patients recommended for surgery.
PubMed-ID: 39699960
DOI: 10.1002/jso.28049

World first hybrid neuroendocrine cell line sharing properties of NET G3 and dedifferentiated NEC.
Eur J Endocrinol, 193(3):359-73.
D. Rogoll, L. S. Landwehr, J. Schreiner, P. Hartrampf, L. Frey, E. Hartmann, A. Meining, S. Gulden, H. Schnaidt, S. Y. Chan, S. Jittavisutthikul, C. Wen-Hui, C. Stigloher, R. A. Werner, M. Scheurlen, T. Bumm and A. Weich. 2025.
BACKGROUND: Current therapies for neuroendocrine neoplasms (NENs) are limited, especially for fast-growing dedifferentiated NECs, which exhibit low somatostatin receptor (SSTR) expression and poor prognosis. Well-differentiated neuroendocrine tumors (NETs), on the other hand, retain SSTR expression, making them amenable to receptor-targeted therapies. In dedifferentiated NEC, C-X-C motif chemokine receptor 4 (CXCR4) has been shown to be abundantly expressed, making it a potential target for alternative treatment and diagnostic strategies. A major challenge in developing targeted therapies is the lack of primary patient-derived cell lines that maintain receptor profiles suitable for preclinical evaluation of established or innovative receptor-targeted approaches. METHODS: We established the MS-18 cell line from a metastatic rectal NEC. Neuroendocrine differentiation markers, SSTRs1-5, CXCR4, epithelial and mesenchymal markers, drug transporters (ABCB1, ABCG2), and Ki-67 were analyzed using qPCR and immunoblotting. Somatostatin receptor and CXCR4 function was evaluated by radiouptake assays. Electron microscopy, karyotyping, and CGH were performed, and the cell's in vivo engraftment rate was evaluated in a mouse NSG model. Viability studies on conventional therapeutic agents were performed. Extended molecular profiling of the primary tumor, liver metastasis, and MS-18 cell line was conducted. RESULTS: MS-18 cells showed strong expression of neuroendocrine markers (synaptophysin, neuron-specific enolase) and preserved epithelial differentiation (high E-cadherin, absence of mesenchymal markers). SSTR1, SSTR2, and SSTR5 were highly expressed, while SSTR3 and SSTR4 were absent. Uniquely, MS-18 cells exhibited strong CXCR4 expression. The proliferation index (Ki-67: 90%) matched that of the primary tumor. Elevated ABCG2 expression contributed to resistance to etoposide. Molecular profiling revealed no pathogenic mutations in key genes commonly altered in NENs, including MEN1, DAXX, ATRX, mTOR, PTEN, TP53, and RB1. The successful in vivo engraftment rate was high (4/5). CONCLUSION: The MS-18 cell line is the first patient-derived cell line with a transitional phenotype between differentiated NET and dedifferentiated NEC, showing strong expression of SSTR2 and CXCR4 and absence of driver mutations in key NET-/NEC-associated genes. It offers a unique platform for preclinical evaluation of targeted therapies.
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DOI: 10.1093/ejendo/lvaf159

Impact of multikinase inhibitors in reshaping the treatment of advanced gastroenteropancreatic neuroendocrine tumors.
Endocr Relat Cancer, 32(6)
A. R. Siebenhuner, J. Refardt, G. P. Nicolas, R. Kaderli, M. A. Walter, A. Perren and E. Christ. 2025.
Neuroendocrine tumors (NETs) pose a considerable challenge due to their increasing incidence and frequently late-stage diagnosis. The arrival of multikinase inhibitors (MKIs) into clinical practice has brought notable progress in the management of advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs). This review aims at exploring the impact of MKIs in reshaping the treatment landscape for advanced GEP-NETs. Current approaches in managing advanced GEP-NETs are discussed, including somatostatin analogs, surgery, peptide receptor radionuclide therapy, and approved systemic treatments such as everolimus or sunitinib. The limitations and challenges faced in treating these tumors remain significant. Here, we review the clinical evidence supporting the use of everolimus as a targeted therapy, which has demonstrated improved progression-free survival (PFS), and the need for alternative therapies. Discussions focus on the clinical effectiveness and the emerging role of both established and novel MKIs in the treatment of GEP-NETs, including recent evidence from the CABINET trial and other emerging agents such as surufatinib, axitinib, pazopanib, and lenvatinib. We explore the clinical evidence that showcases sunitinib's and other MKIs' effectiveness in prolonging PFS compared to placebo in advanced GEP-NETs. Recently, MKIs have shown to have a significant impact for the treatment of advanced GEP-NETs. There remain several unmet needs that must be addressed, particularly regarding optimal treatment sequencing and the development of predictive biomarkers. Ongoing research and the use of current and emerging MKIs hold great potential to advance the treatment landscape for advanced GEP-NETs significantly.
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DOI: 10.1530/ERC-25-0052
PMCID: PMC12177888

Targeting anti-apoptosis as a therapeutic strategy in neuroendocrine neoplasms.
Endocr Relat Cancer, 32(7)
V. Sukrithan, U. Ahmed, H. Krause, N. Gandhi, A. Elliott, A. Hinton, P. Walker, A. Vanderwalde, Y. Zhou, D. C. Patel, E. Lou, H. P. Soares, K. A. Rogers and B. Konda. 2025.
BCL-2 is an anti-apoptotic protein expressed by aggressive neuroendocrine neoplasms (NENs). We report a case of a patient with a pancreatic neuroendocrine tumor (pNET) who received venetoclax, a BCL-2-targeting drug for the treatment of chronic lymphocytic leukemia. We further characterized BCL2 expression in NENs from a large multi-institutional patient cohort. Clinical data were abstracted from the records of a patient with a pNET. Next-generation sequencing of DNA (592-gene panel or whole exome) and RNA (whole transcriptome) was performed on 636 NENs of pancreatic (P-NENs), small bowel (SB-NENs), colorectal (CR-NENs), and lung (L-NENs) origin by Caris Life Sciences. Comparisons were performed against site-matched non-NEN cancers. BCL2- or MKI67- high and low cohorts were defined based on the top and bottom quartiles of gene expression. The patient with a pNET who received venetoclax had a partial response in the primary tumor that lasted 30 months. CR-, L-, and P-NENs had significantly higher expression of BCL2 compared to non-NEN counterparts. BCL2 expression was significantly higher in MKI67-high tumors among all NEN subtypes. In P-NENs, there was a higher prevalence of RB1 mutations in BCL2-high vs BCL2-low (40 vs 4.9%, $P < 0.005$). Patients with BCL2-high P-NENs had significantly decreased overall survival (HR 1.94, 95% CI 1.0-3.76, $P = 0.047$). Immune checkpoint gene expression and T cells were enriched in BCL2-high tumors across all subtypes. In summary, we report the first known case of a pancreatic NET with response to venetoclax. BCL2 expression correlated with high MKI67 expression, worse survival, and a highly immune-enriched microenvironment.
PubMed-ID: 40512124
DOI: 10.1530/ERC-24-0341

Prognosis of small pancreatic neuroendocrine neoplasms: Functionality matters.
Am J Surg, 246:116302.
Q. Tan, L. Liu, X. Liu, C. Tan and X. Wang. 2025.
BACKGROUND: This study aimed to evaluate potential difference in clinicopathological characteristics, prognosis as well as the genetic bases between insulinomas and non-functional pancreatic neuroendocrine neoplasms (NF-PNENs). METHOD: We analyzed data from 241 patients who underwent resection for PNENs measuring 1-2 cm at West China Hospital between 2002 and 2020. RESULTS: NF-PNENs were more likely to show lymph node involvement ($P < 0.001$), perineural invasion ($P = 0.025$), and a more advanced tumor grade ($P < 0.001$). In multivariate analysis, NF-PNENs, when combined with lymph node metastasis and WHO G2/G3 grading, independently decreased recurrence-free survival [hazard ratio (HR), 4.72; $P = 0.014$]. Whole exome sequencing revealed that most of the top 20 somatic mutated genes (90 %, 36/40) between insulinomas and NF-PNENs are different. Besides, all copy number variant (CNV) patterns were present in NF-PNENs, whereas insulinomas were more likely to exhibit CNV amplification. CONCLUSION: Insulinomas and small NF-PNENs exhibit distinct tumor biology, prognosis, and genetic backgrounds, which may inform changes in surgical management and postoperative follow-up strategies for these patients.
PubMed-ID: 40140248
DOI: 10.1016/j.amjsurg.2025.116302

The Landmark Series: Surgical Management of Functioning and Non-Functioning Pancreatic Neuroendocrine Tumors.
Ann Surg Oncol, 32(7):4720-8.
J. Tobias, C. N. Clarke, A. Gangi and X. M. Keutgen. 2025.
Pancreatic neuroendocrine tumors (PNETs) are comparatively rare pancreatic malignancies that exhibit diverse biologic behavior, ranging from indolent tumors to widely metastatic cancers, with up to 15 % secreting hormones that cause symptoms. As a consequence, the management of PNETs is highly individualized and can include active surveillance of small (1-2 cm) and very small (< 1 cm) nonfunctioning tumors without worrisome features, parenchymal-sparing resection of appropriately located tumors, anatomic pancreatectomy and, in select cases, debulking of metastatic disease, particularly in the liver. This review synthesizes society recommendations and contemporary evidence guiding the surgical management of PNETs. Innovations in molecular profiling and systemic therapies hold promise to refine surgical algorithms for this heterogeneous tumor.
PubMed-ID: 40319207
DOI: 10.1245/s10434-025-17390-x
PMCID: PMC12130066

Cabozantinib in Advanced Neuroendocrine Tumors.
N Engl J Med, 392(18):1869.
D. I. Tsilimigras. 2025.
PubMed-ID: 40334169
DOI: 10.1056/NEJMc2503524

Charting the Course: Insights into Neuroendocrine Tumor Dynamics in the United States.
Ann Surg, 281(6):968-75.
C. Wu, Z. Song, S. Balachandra, S. Dream, H. Chen, J. B. Rose, S. Bhatia and A. Gillis. 2025.
OBJECTIVE: To explore changing trends and characteristics in neuroendocrine tumors (NETs) epidemiology, focusing on demographics, clinical aspects, and survival, including the impact of social determinants of health (SDOH) on outcomes. BACKGROUND: The escalating incidence and prevalence of NETs underscore the pressing need for updated epidemiologic data to reveal the evolving landscape of this condition. Access to current information is imperative for informing clinical strategies and public health initiatives targeting NETs. METHODS: A retrospective, population-based study analyzed NET patient data from 1975 to 2020, using the Surveillance, Epidemiology, and End Results (SEER 8, 12, 18) program. We calculated annual age-adjusted incidence, prevalence, and 5-year overall survival (OS) rates. Survival trends from 2000 to 2019 were examined, employing the Fine-Gray model to evaluate cancer-specific mortality. RESULTS: NETs' age-adjusted incidence rate quadrupled from 1.5 per 100,000 in 1975 to 6.0 per 100,000 in 2020. A decline in incidence occurred from 6.8 per 100,000 in 2019 to 6.0 per 100,000 in 2020. All-cause survival multivariable analysis demonstrated high grade (HR: 2.95, 95% CI: 2.63-3.09, P <0.001), single patients (HR: 1.49, 95% CI: 1.45-1.54, P <0.001), and Black patients (HR: 1.17, 95% CI:1.13-1.22, P <0.001) all had worse survival than their controls. CONCLUSIONS: Our study shows a steady increase in NETs incidence until 2019, with a decline in 2020. Understanding the reasons behind this trend is vital for improved management and public health planning. Further research should focus on the factors driving these changes to enhance our understanding of NET epidemiology.
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DOI: 10.1097/SLA.0000000000006331
PMCID: PMC11538379

General

Meta-Analyses

Survival probabilities in patients with ectopic Cushing's syndrome-a systematic review and a single-arm meta-analysis.
Eur J Endocrinol, 192(6):S53-S65.
M. Piasecka, E. Papakokkinou, A. Piasecki, H. Falhammar and O. Ragnarsson. 2025.
OBJECTIVE: We aimed to estimate 1- and 5-year survival probabilities in patients with different forms of ectopic Cushing's syndrome (ECS) and identify factors influencing survival. METHODS: In this systematic review and meta-analysis, we searched the online databases PubMed, Scopus, and Web of Science up to October 18, 2023, for studies reporting survival in patients with ECS. Data extraction and risk of bias assessment were performed by 3 independent investigators. Primary outcome was survival in patients with ECS and secondary outcome was factors influencing survival. RESULTS: We included 40 studies with a total of 1148 patients. The pooled mean 1-year survival probability for ECS of mixed etiologies was 78% while the mean pooled 5-year survival probability was 47%. The 5-year survival probabilities for patients with pulmonary neuroendocrine neoplasm (NEN) was 81%, occult ECS 66%, thymic NEN 50%, and pancreatic NEN 40%. Only 8 studies reported factors influencing survival, where total resection of the primary tumor was associated with better overall survival, and unresectable tumors, metastatic disease at diagnosis, severe hypercortisolism, hypokalemia, and new-onset diabetes mellitus were associated with worse prognosis. CONCLUSION: Survival in ECS varies considerably, mainly due to the underlying origin of the tumor, tumor stage, and severity of the hypercortisolism. Further studies analyzing the importance of factors affecting survival are needed.
PubMed-ID: 40455890
DOI: 10.1093/ejendo/lvaf114

Treatments for MEN1-associated endocrine tumours: three systematic reviews and a meta-analysis.
Lancet Diabetes Endocrinol, 13(8):685-98.
K. A. English, C. R. C. Pieterman, F. Marini, K. E. Lines, T. Cuny, R. Saulle, O. A. Shariq, Z. Mitrova, F. Castinetti, S. G. Waguespack, M. L. Brandi, R. V. Thakker, G. D. Valk and S. Minozzi. 2025.
BACKGROUND: Multiple endocrine neoplasia type 1 (MEN1) is a rare hereditary disorder characterised by the combined occurrence of parathyroid, pancreatic, and pituitary tumours. Current treatments are based on very low-quality evidence. Our aims were to determine treatment outcomes in patients with MEN1 for: subtotal parathyroidectomy versus less than subtotal parathyroidectomy for primary hyperparathyroidism (Q1); surgery versus active surveillance for non-functioning pancreatic neuroendocrine tumours sized 2 cm or less (Q2); and dopamine agonist responses of prolactinomas in patients with MEN1 versus patients without MEN1 (Q3). METHODS: We conducted three systematic reviews and one meta-analysis. Four electronic databases (MEDLINE Ovid, Embase Ovid, The Cochrane Library, and Web of Science) were searched from Dec 1, 2001, to Feb 13, 2023, with no language restrictions. Study designs included randomised controlled trials, prospective and retrospective cohort studies, and case-controlled and case series. Adults and children with MEN1-associated tumours were included in all three systematic reviews. For each clinical question, three pairs of authors independently screened abstracts and assessed the full text for final inclusion, discordant views were resolved by senior authors. Dichotomous outcomes were calculated using risk ratios or hazard ratios for time-to-event analyses, with 95% CIs. Continuous outcomes were ascertained using mean difference with 95% CIs. Where feasible, outcomes from individual studies were analysed through meta-analysis, using a random-effects model. The systematic reviews were prospectively registered (PROSPERO reference numbers CRD42023409912, CRD42023409936, and CRD42023409949). FINDINGS: For primary hyperparathyroidism (Q1), 990 non-duplicate records were screened for title and abstract, of which 23 studies with 1073 patients were eligible for meta-analysis. These studies showed that subtotal parathyroidectomy had a significantly lower risk of persistent primary hyperparathyroidism (RR 0.32, 95% CI 0.20-0.52; I(2)=0%) and recurrent primary hyperparathyroidism (RR 0.78, 0.62-0.97; I(2)=27%), when compared with less than subtotal parathyroidectomy, although the risk of post-operative hypoparathyroidism was higher (RR 2.64, 1.63-4.29; I(2)=0%). For non-functioning pancreatic neuroendocrine tumours sized 2 cm and less (Q2), 1583 non-duplicate records were screened for title and abstract, of which three cohort studies were eligible for analysis. These studies showed that combined metastatic disease and mortality rates were comparable between patients in the surgery group (two [7%] of 27 to three [20%] of 15) and patients in the active surveillance group (one [3%] of 33 to four [8%] of 50]). For prolactinomas (Q3), 475 non-duplicate records were screened for title and abstract, of which ten studies with 505 patients were eligible for analysis. These studies showed that dopamine agonist treatment failure rates to normalise serum prolactin were

similar between patients with MEN1 (zero of one to one [33%] of three) and patients without MEN1 (four [6%] of 68 to nine (82%) of 11), n=23 studies). GRADE certainty scores for all were low or very low. INTERPRETATION: In patients with MEN1, subtotal parathyroidectomy achieved greater reductions in persistence and recurrence of primary hyperparathyroidism than less than subtotal parathyroidectomy; for non-functioning pancreatic neuroendocrine tumours sized 2 cm or less, the few available studies suggest that active surveillance might be comparable to surgical resection; and for prolactinomas, dopamine agonist therapy appears to have comparable efficacy as in patients without MEN1. FUNDING: None.
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DOI: 10.1016/S2213-8587(25)00118-4

Randomized controlled trials

- None -

Consensus Statements/Guidelines

Multiple endocrine neoplasia type 1 (MEN1): recommendations and guidelines for best practice.
Lancet Diabetes Endocrinol, 13(8):699-721.
M. L. Brandi, C. R. C. Pieterman, K. A. English, K. E. Lines, O. A. Shariq, F. Marini, T. Cuny, M. A. Lewis, C. A. Stratakis, N. D. Perrier, S. G. Waguespack, F. Castinetti, G. D. Valk, R. V. Thakker and P. Delphi Expert. 2025.
Multiple endocrine neoplasia type 1 (MEN1) is characterised by combined occurrence of parathyroid tumours, duodenopancreatic neuroendocrine tumours, and anterior pituitary adenomas. Some patients might also develop thymic and bronchopulmonary neuroendocrine tumours, and adrenal tumours. MEN1 is an autosomal dominant disorder caused by mutations in the tumour-suppressor gene MEN1, which encodes a scaffold protein, menin. Without treatment, patients with MEN1 have high morbidity and premature mortality, which can be mitigated by early tumour detection and intervention. Identification of individuals at high risk for MEN1 can be facilitated by genetic testing of patients and their first-degree relatives, and undertaking periodic clinical, biochemical, and radiological screening in patients and MEN1 mutation carriers. However, no consensus exists regarding the optimal assessment and management of MEN1. To provide such recommendations, a multidisciplinary group was convened to undertake systematic reviews and a meta-analysis of the literature, and to use a Delphi approach for the development of consensus statements. 55 clinical recommendations were developed to guide clinicians, patients, and stakeholders about approaches for MEN1 in adults and children.
PubMed-ID: 40523372
DOI: 10.1016/S2213-8587(25)00119-6

Other Articles

Experience evolves into evidence in the new MEN1 guidelines.
Lancet Diabetes Endocrinol, 13(8):640-2.
A. F. Daly. 2025.
PubMed-ID: 40523373
DOI: 10.1016/S2213-8587(25)00160-3

Genomic testing for RET in the clinic: UK and global perspective.
Endocr Relat Cancer, 32(5)
L. Izatt. 2025.
ABSTRACT: RET is a key oncogene in neuroendocrine cancer. Pathogenic germline variants lead to multiple different phenotypes, including multiple endocrine neoplasia type 2, medullary thyroid cancer (MTC), Hirschsprung disease and kidney malformations. Pathogenic somatic variants are also associated with MTC, and RET rearrangements are observed in

papillary thyroid cancer, non-small cell lung cancer and pan-cancer syndromes. Testing for both germline and somatic variants is now feasible in everyday clinical practice, and their identification has important clinical consequences, both for affected individuals and their families. This mini-review will discuss current germline and somatic testing strategies in the UK and worldwide, as well as reporting and test outcomes (including variants of uncertain significance or incidental findings). It will explore actions following identification of a pathogenic germline variant, including predictive, reproductive and childhood testing, and somatic testing of RET variants in solid tumours informing personalised cancer treatment. Finally, it will discuss the challenge of delivering rapid and equitable access to genomic testing to ensure that all individuals can benefit promptly and appropriately to improve clinical outcomes.
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DOI: 10.1530/ERC-24-0230
PMCID: PMC12020483

Practice Readiness of Chief Residents in a National Sample During the First Year of EPA Assessments.
Ann Surg, 282(4):601-7.
B. Lindeman, C. Scott-Smith, A. Jones, G. A. Sarosi, Jr., R. M. Minter, S. Jung, J. Jesneck, R. Thanawala, J. D. Mellinger, J. Buyske and K. J. Brasel. 2025.
OBJECTIVES: Identify the prevalence of practice-ready formative entrustable professional activity (EPA) assessments obtained by residents in their final year of general surgery training. BACKGROUND: EPA microassessments will be required for admissibility to American Board of Surgery general surgery certification beginning in 2028. EPA implementation began in July 2023 as the initial step in complying with these requirements. METHODS: EPA microassessments using the ABS entrustment scale (1=limited participation, 2=direct supervision, 3=indirect supervision, 4=practice ready) were completed in real time through a secure application. Deidentified data were downloaded at year end for programs, faculty assessors, and individual residents. Assessments of PGY5 residents by faculty were included. Descriptive statistics were utilized to summarize entrustment ratings and compared across the academic year (July 1, 2023-May 31, 2024) with chi 2 tests. RESULTS: A majority of PGY5 residents (n=1032, 67%) were assessed with 12,611 microassessments (mean 12.2/resident). All EPAs were assessed, with the most in gallbladder disease (n=2950). Median entrustment was practice-ready for all EPAs except renal replacement therapy and thyroid/parathyroid disease (median rating indirect supervision for both). Overall, 63% of microassessments (n=7946) during the chief year were practice-ready, with 59% (5571/9460) intraoperatively and 75% nonoperatively (2375/3151). In July 2023, 56% of PGY5 microassessments were rated indirect supervision or lower compared with 26% in May 2024. CONCLUSIONS: The majority of formative microassessments of PGY5 residents in general surgery training programs demonstrate practice readiness for 16 of 18 EPAs. Competence of chief residents grows from the beginning to the end of the PGY5 year for core general surgery activities.
PubMed-ID: 40662595
DOI: 10.1097/SLA.0000000000006839

A Dwindling Matter: An Analysis of Medicare Reimbursement for Endocrine Surgery Procedures From 2000 to 2023.
Ann Surg, 281(6):891-900.
A. T. Saxton, A. J. Monreal, M. T. Stang, H. S. Kazaure and R. P. Scheri. 2025.
OBJECTIVE: To evaluate Medicare reimbursement trends for endocrine surgeries from 2000 to 2023. BACKGROUND: As the population ages, demand for endocrine surgeries is expected to increase. Understanding reimbursement trends is essential to ensure the financial sustainability of endocrine surgery. METHODS: Data were extracted from Medicare Inpatient and Outpatient Hospital data sets, National Summary, and Physician Fee Look-up Files for nine common thyroid, parathyroid, and adrenal surgeries. Data were adjusted for inflation. Descriptive statistics, compound annual growth rate (CAGR), and linear regression models were built to evaluate practice and reimbursement trends. RESULTS: From 2000 to 2023, there was a 63.8% increase in endocrine surgery volume. However, inflation-adjusted average procedure reimbursements decreased by 43.2% from $1709 to $972 (CAGR-2.4%), which is the largest decrease for any surgical subspecialty reported in the published literature. At the current CAGR, the average estimated reimbursement is projected to decrease to $868 by 2030 (P <0.001). Average facility reimbursements for inpatient and outpatient hospitalizations increased. However, substantial practice pattern shifts in the study period led to decreased overall facility reimbursements, with a $17.9 million decrease in total inpatient reimbursements between 2016 and 2021 that was only partially offset by a $3.2 million increase in outpatient hospital reimbursements. CONCLUSION: Medicare procedure reimbursements for endocrine surgeries have been outpaced by inflation, with large decreases since 2000. Concurrent changes in practice patterns have also resulted in markedly fewer inpatient stays, leading to lower total facility reimbursements. Our data raise concern over the financial sustainability of the endocrine surgery field as the demand for endocrine surgery procedures increases.

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DOI: 10.1097/SLA.0000000000006423