*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)

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## Preliminary

Dear Members,

Finally, the first ESES collection of 2024 is complete, sorry for being late, this is my first review, even if still done with Ulrich's help. I ask you to be patient cause I'm still learning how to master reviews and this takes time. I hope to become as efficient as Ulrich has been in all these years.

Please let me have your feedback about my job so I can improve.

Sincerely yours

Paola Sartori

## Journals covered

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|---|---|---|---|
| Acta Cytol | 1.8 | J Bone Miner Res | 6.2 |
| Am J Kidney Dis | 13.2 | J Clin Endocrinol Metab | 5.8 |
| Am J Nephrol | 4.2 | J Clin Oncol | 45.3 |
| Am J Surg | 3.0 | J Endocrinol | 4.0 |
| Am Surgeon | 1.0 | J Endocrinol Invest | 5.4 |
| Ann Surg | 9.0 | J Nephrol | 3.4 |
| Ann Surg Oncol | 3.7 | J Nucl Med | 9.3 |
| ANZ J Surg | 1.7 | J Surg Oncol | 2.5 |
| Br J Surg | 9.6 | Lancet | 168.9 |
| Cancer | 6.2 | Langenbecks Arch Surg | 2.3 |
| Chirurgie (formerly: Chirurg) | 0.9 | Laryngoscope | 2.6 |
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Journal names are links to the journal's homepage!, IF2022: Impact factor

# Thyroid

## Meta-Analyses

**Impact of radioiodine therapy on recurrence and survival outcomes in intermediate-risk papillary thyroid carcinoma -A systematic review and meta-analysis**.
*Clin Endocrinol (Oxf)*, 100(2):181-91.
K. R. Chandekar, S. Satapathy and C. Bal. 2024.
OBJECTIVE: The utility of radioiodine (RAI) therapy in intermediate-risk papillary thyroid carcinoma (PTC) remains a topic of ongoing discussion. This systematic review and meta-analysis aimed to consolidate existing evidence on the impact of postoperative RAI therapy on recurrence and survival outcomes in intermediate-risk PTC. METHODS: A literature search was performed using relevant keywords in PubMed, Scopus, and EMBASE. Articles from January 2008 to March 2023 were included. Odds ratios (ORs) and hazard ratios (HRs) were extracted from the individual articles, and pooled estimates were generated using meta-analysis. RESULTS: Eleven articles comprising 56,266 intermediate-risk PTC patients were included. 41,530 (73.8%) patients underwent postoperative RAI therapy, while 14,736 (26.2%) patients were kept on no-RAI (NOI) follow-up. No significant reduction in rates of structural disease recurrence was noted with RAI therapy in comparison to NOI follow-up (pooled univariate OR, 0.73, 95% confidence interval [CI], 0.29-1.87, I(2) = 75%). RAI therapy was not a significant predictor of better recurrence-free survival (pooled multivariate HR, 0.21; 95% CI, 0.01-3.74, I(2) = 94%). Interestingly, RAI therapy was associated with an overall survival benefit compared to NOI follow-up (pooled multivariate HR, 0.63; 95% CI, 0.48-0.82, I(2) = 79%). CONCLUSIONS: This meta-analysis did not establish a conclusive benefit of RAI therapy in preventing structural disease recurrence or improving recurrence-free survival in intermediate-risk PTC. However, these results need to be interpreted with caution owing to significant heterogeneity in the existing literature. A prospective, randomised clinical trial is the need of the hour to better understand the effect of RAI therapy on long-term outcomes.
PubMed-ID: 38050454
DOI: 10.1111/cen.15001

**Total thyroidectomy versus unilateral lobectomy for unilateral multifocal papillary thyroid carcinoma: systematic review and meta-analysis**.
*Updates Surg*, 76(1):33-41.
H. Chen, Y. Liu, D. Huang, X. Zhang and L. She. 2024.
The optimal surgical procedure(s) for unilateral multifocal papillary thyroid carcinomas is currently controversial. As such, the present study aimed to compare the efficacies of total thyroidectomy and lobectomy in patients with unilateral multifocal papillary thyroid carcinoma. A literature search of the PubMed/Medline, Embase, Web of Science, Cochrane Library, Wan Fang, and Zhi Wang databases for relevant studies, published from inception to October 31, 2022, was performed. Two researchers independently extracted data from the included studies. Lymph node metastasis, vocal fold paralysis, parathyroid injury, postoperative recurrence, and disease-free survival were evaluated. The meta-analysis included 7 studies comprising 1540 patients, of whom 496 and 1044 underwent lobectomy and total thyroidectomy, respectively. Compared with lobectomy, total thyroidectomy resulted in more vocal cord paralysis (odds ratio [OR] 0.35 [95% confidence interval (CI) 0.13 to 0.96]; P = 0.04) and parathyroid injury (OR 0.11 [95% CI 0.03-0.39]; P = 0.001) but with better disease-free survival (OR 0.21 [95% CI 0.09-0.49]; P = 0.000), although vocal cord paralysis and parathyroid injury, in large part, resolved within 1 year after surgery. In addition, there was no difference in postoperative lymph nodes metastasis (OR 0.74 [95% CI 0.13-4.21]; P = 0.737) and postoperative recurrence (OR 2.37 [95% CI 0.42-13.38]; P = 0.33). Excluding studies that deviated from the general trend, total thyroidectomy was beneficial in reducing recurrence. Compared with lobectomy, total thyroidectomy was beneficial in reducing recurrence and disease-free survival and may be considered a more optimal approach for unilateral multifocal papillary thyroid carcinoma.
PubMed-ID: 38127193
DOI: 10.1007/s13304-023-01726-x

**Oncologic outcomes and surgical completeness of remote-access thyroidectomy: a systematic review and network meta-analysis**.
*Langenbecks Arch Surg*, 409(1):117.
V. C. Nguyen, D. W. Lee, C. M. Song, Y. B. Ji, J. S. Park and K. Tae. 2024.
BACKGROUND: The oncologic safety and surgical completeness of remote-access thyroidectomies are not yet clearly established. This study evaluates the oncologic outcomes and surgical completeness of three prevalent remote-access thyroidectomies: the gasless transaxillary approach (GTAA), bilateral axillo-breast approach (BABA), and transoral approach (TOA), in comparison with conventional transcervical thyroidectomy (CTT). METHODS: Literature searches were conducted in PubMed, EMBASE, and the Cochrane Library databases, covering the period from 2000 to 2023. Network meta-analyses were performed on selected studies, focusing on recurrence and surgical completeness. Surgical completeness was assessed using stimulated serum thyroglobulin levels and the count of retrieved lymph nodes. RESULTS: The review included 48 studies, encompassing a total of 16,356 patients. The number of retrieved lymph nodes was comparable among BABA, TOA, and CTT, while GTAA might be less effective. Stimulated serum thyroglobulin levels showed no significant differences across the four groups. However, the proportion of patients with stimulated thyroglobulin levels below 1.0 ng/mL was significantly lower in GTAA compared to the other groups. The overall recurrence rates were 1.31% for CTT, 0.89% for GTAA, 0.62% for BABA, and 0% for TOA, with no significant differences in recurrence rates when adjusted for follow-up duration. CONCLUSIONS: This study demonstrated that the oncologic outcomes of GTAA, BABA, and TOA are comparable to those of CTT, based on recurrence rates. In terms of surgical completeness, BABA and TOA showed equivalence to CTT, whereas GTAA might be inferior to the other techniques.
PubMed-ID: 38598044
DOI: 10.1007/s00423-024-03316-w

**Comparison of surgical outcomes of transoral robotic and endoscopic thyroidectomy: A systematic review and network meta-analysis**.
*Head Neck*, 46(3):688-701.
V. C. Nguyen, C. M. Song, Y. B. Ji, S. Oh, J. H. Jeong and K. Tae. 2024.
This study aimed to compare surgical outcomes of transoral robotic thyroidectomy (TORT) and transoral endoscopic thyroidectomy vestibular approach (TOETVA), concurrently compared with conventional transcervical thyroidectomy (CTT). A network meta-analysis, comprising 23 studies, was performed in this study. The operative time of the CTT group was significantly shorter than that of the TOETVA and TORT groups. The hospital stay of the TOETVA group was significantly longer than that of the CTT group. Rates of transient recurrent laryngeal nerve palsy and total complications were higher in association with TOETVA than with TORT. No significant differences were found between the three groups in intraoperative blood loss, retrieved lymph nodes, postoperative pain, and other complications. Cosmetic satisfaction was significantly superior with TORT and TOETVA than with CTT. Compared with CTT, TOETVA and TORT showed superior cosmesis but no significant difference in surgical outcomes except for operative time and hospital stay.
PubMed-ID: 38229250
DOI: 10.1002/hed.27644

**Tyrosine kinase inhibitors for radioiodine refractory differentiated thyroid cancer: A systematic review and meta-analysis**.
*Clin Endocrinol (Oxf)*, 100(4):379-88.
J. Yu, Z. Liu, Y. Su, X. Peng and Y. Xie. 2024.
BACKGROUND: The poor overall prognosis of radioiodine refractory thyroid cancer is an inevitable challenge in managing this disease. A series of trials have demonstrated the antitumor activity of tyrosine kinase inhibitors (TKIs) in radioiodine refractory differentiated thyroid cancer (RAIR-DTC). However, the available evidence cannot determine the optimal choice of TKI in RAIR-DTC. METHODS: This study searched PubMed, EMBASE, Cochrane databases, and the ClinicalTrials website. The Cochrane bias risk tool was used to assess the risk of bias, and to evaluate randomized clinical trials (RCT) of RAIR-DTC patients treated with the TKI system. Outcomes, including progression-free survival (PFS), overall survival (OS), and adverse events (AEs) were reported. RESULTS: Seven studies involving 1310 patients with RAIR-DTC was conducted to compare the PFS and OS of various TKI monotherapies with placebo. The results showed that all TKI monotherapies had a statistically significant benefit in terms of PFS compared with placebo, with lenvatinib demonstrating the greatest benefit (hazard ratio [HR] 0.19, 95% credible interval [CrI] 0.14-0.25). In terms of OS, only apatinib (HR 0.42, 95% CrI 0.18-0.97) and anlotinib (HR 0.36, 95% CrI 0.18-0.73) showed statistically significant benefits compared with placebo. TKIs also had a higher incidence of AEs of grade 3 or higher compared with placebo. The findings suggest that lenvatinib may be the preferred TKI for the treatment of RAIR-DTC, although its high incidence of AEs should be considered. The results also

indicate that TKI treatment may be similarly effective in RAIR-DTC patients with BRAF or RAS mutations and in those with papillary or follicular subtypes of the disease, regardless of prior TKI treatment. CONCLUSIONS: The results of this meta-analysis suggest that targeted therapy with TKIs may be beneficial for patients with radioiodine-refractory advanced or metastatic differentiated thyroid cancer. Among the TKIs analyzed, lenvatinib appeared to be the most effective at improving PFS, although it also had the highest incidence of AEs. Further research through direct randomized controlled trials is needed to determine the optimal choice of TKI for treating patients with RAIR-DTC. This study is beneficial for formulating patients' treatment plans and guides clinicians' decision-making.
PubMed-ID: 38351437
DOI: 10.1111/cen.15027

## Randomized controlled trials

**Autofluorescence-guided hemithyroidectomy in a low-volume thyroid institution with no experience in parathyroid surgery: randomized clinical trial**.
*Br J Surg*, 111(4):undefined-undefined.
A. Abood, L. Rolighed, T. Ovesen, S. H. Madsen, P. Vestergaard and F. Triponez. 2024.
BACKGROUND: Recent studies suggest that low-volume surgeons with no experience in parathyroid surgery are at increased risk of causing parathyroid gland damage during thyroid surgery. The aim of this RCT was to evaluate the impact of using autofluorescence in hemithyroidectomy on parathyroid gland identification and preservation in a low-volume institution with no experience in parathyroid surgery. METHODS: Patients referred for hemithyroidectomy were randomized 1 : 1 to either autofluorescence-guided hemithyroidectomy (the near-infrared autofluorescence group) or conventional hemithyroidectomy (the control group). The primary outcome was parathyroid gland identification rate. Secondary outcomes were the rate of parathyroid gland autotransplantation and the rate of inadvertent parathyroid gland excision. RESULTS: A total of 170 patients were randomized to either autofluorescence-guided hemithyroidectomy (84 patients) or conventional hemithyroidectomy (86 patients). In the near-infrared autofluorescence group, 81.0% of parathyroid glands were identified, compared with 57.0% in the control group (P < 0.001). Autofluorescence enabled parathyroid gland visualization before the naked eye in 46.3% of cases. Surgeons had lower confidence in the parathyroid gland identification process in the control group than in the near-infrared autofluorescence group (59.1% versus 87.5% respectively; P < 0.001). In the near-infrared autofluorescence group, the parathyroid gland autotransplantation rate was initially high, but declined over time. There was no difference in the rate of inadvertent parathyroid gland excision. CONCLUSION: Autofluorescence guidance significantly improved the parathyroid gland identification rate in hemithyroidectomy in a low-volume institution with no experience in parathyroid surgery and provided an increase in surgical confidence. The pattern of parathyroid gland autotransplantation in autofluorescence-guided surgery indicates the presence of a learning curve. REGISTRATION NUMBER: NCT05044351 (http://www.clinicaltrials.gov).
Damage to the parathyroid glands is common during thyroid surgery. The main reason for that is that they can be difficult to see during surgery. The aim of this study was to see if the use of a new near-infrared camera during thyroid surgery could make it easier to see the parathyroid glands. Patients, where removal of part of their thyroid gland was planned, were randomly assigned to one of two groups. In the first group, the near-infrared camera was used, whereas it was not used in the other group. When the near-infrared camera was used, more parathyroid glands were found and the surgeons felt more secure in their handling of parathyroid glands.
eng.
PubMed-ID: 38573333
DOI: 10.1093/bjs/znae075

**Randomized double-blind placebo-controlled trial on levothyroxine and liothyronine combination therapy in totally thyroidectomized subjects: the LEVOLIO study**.
*Eur J Endocrinol*, 190(1):12-22.
G. Brigante, D. Santi, G. Boselli, G. Margiotta, R. Corleto, M. L. Monzani, A. Craparo, M. Locaso, S. Sperduti, N. Roy, L. Casarini, T. Trenti, S. Tagliavini, M. C. De Santis, L. Roli, V. Rochira and M. Simoni. 2024.
OBJECTIVE: Despite having normal thyroid-stimulating hormone levels, many hypothyroid patients are dissatisfied with the treatment. The primary aim of this study was to evaluate the effect of twice-daily, combination therapy with levothyroxine (LT4) and liothyronine (LT3), at doses adapted according to TSH-level, on peripheral tissues as reflected by sex hormone binding globulin (SHBG) levels in totally thyroidectomized patients. Changes in other tissue markers and

quality of life considering DIO2-rs225014 and MCT10-rs17606253 genetic variants were also assessed. DESIGN: Double-blind, randomized, placebo-controlled. METHODS: One hundred and forty-one subjects were randomized to LT4 + LT3 group (LT4 + LT3 in the morning and LT3 in the evening; n = 70) or placebo group (LT4 in the morning and placebo in the evening; n = 71). Pituitary-thyroid axis compensation was assessed after 6, 12, and 24 weeks. Clinical parameters, quality of life, and tissue markers (sex hormone binding globulin, serum lipids, bone markers) were evaluated at 12 and 24 weeks. DIO2 and MCT10 single nucleotide polymorphisms were genotyped. RESULTS: The LT4 + LT3 group was treated with mean daily LT3 doses of 5.00 microg, with a mean daily LT4 reduction of 15 microg. After 6 months of treatment, neither SHBG and other tissue markers nor quality of life differed significantly between groups. Combination treatment required greater dose adjustments than placebo (25% vs 54%, P < .001), due to thyroid-stimulating hormone reduction, without hyperthyroidism signs or symptoms. At the end of treatment, the LT4 + placebo group had significantly lower fT3/fT4 compared to the LT4 + LT3 group (0.26 +/- 0.05 vs 0.32 +/- 0.08, P < .001). No preference for combination therapy was found. Genetic variants did not influence any outcomes. CONCLUSIONS: Six months of combination therapy with twice-daily LT3 dose adapted according to TSH-level do not significantly change peripheral tissue response or quality of life, despite an increase in the fT3/fT4 ratio.
PubMed-ID: 38124252
DOI: 10.1093/ejendo/lvad172

**Effect of chewing gum of different weights before surgery on sore throat after total thyroidectomy: A randomized controlled trial**.
*World J Surg*, 48(1):130-7.
S. Zou, L. Guo, C. Xu, T. Liu, L. Li, S. Pan and D. Qi. 2024.
BACKGROUND: Postoperative sore throat (POST) is a common postoperative complication. COMPLICATION: Chewing gum can inhibit the growth of oral bacteria, cleanse, and lubricate the oral cavity, which can help reduce postoperative sore throat. We hypothesize that chewing gum before surgery could relieve POST. METHODS: Patients planned to undergo total thyroidectomy under general anesthesia with tracheal intubation were randomized to swallow saliva twice or chew 1.4 g/2.8 g of gum for 2 minutes before surgery. A standard anesthesia protocol was performed. The numerical rating scale scores of POST at 1, 24, and 48 h after surgery were collected. The primary outcome was the incidence of moderate/severe POST (numerical rating scale score >3) within 48 h. RESULTS: Data from 148 patients (control group, n = 50; 1.4 g group, n = 48; and 2.8 g group, n = 50) were included in the analysis. Within 48 h, there was a significant difference among the three groups in the incidence of moderate/severe POST (control group: 74% vs. 1.4 g group: 65% vs. 2.8 g group: 50%. P = 0.04). The 2.8 g group had less incidence of moderate/severe POST than the control group (Odds Ratio = 0.351 95% Confidence Interval: (0.152 and 0.814) P = 0.02). CONCLUSION: Chewing 2.8 g gum before total thyroidectomy can reduce the incidence of moderate/severe POST within 48 h after surgery.
PubMed-ID: 38284756
DOI: 10.1002/wjs.12025

## Consensus Statements/Guidelines

*- None -*

## Other Articles

**Validating the risk of hypoparathyroidism after total thyroidectomy in a population-based cohort: plea for improved follow-up**.
*Br J Surg*, 111(1):undefined-undefined.
M. Anneback, C. Osterman, J. Arlebrink, S. Mellerstedt, N. Papathanasakis, G. Wallin, O. Hessman, M. Annerbo and O. Norlen. 2024.
BACKGROUND: A previous nationwide study from Sweden showed that the rate of permanent hypoparathyroidism is high and under-rated in the Swedish Quality Register. This retrospective population-based study aimed to validate the rate and diagnosis of permanent hypoparathyroidism found in the previous study. A secondary aim was to assess the relationship between the rate of low parathyroid hormone (PTH) levels within 24 h after surgery and the rate of permanent hypoparathyroidism. METHODS: All patients who underwent total thyroidectomy from 2005 to 2015 in a region of Sweden

were included. Data were retrieved from local health records, the National Patient Registry, the Swedish Prescribed Drug Registry, and the Swedish Quality Register. A strict definition of permanent hypoparathyroidism was used, including biochemical data and attempts to stop the treatment. RESULTS: A total of 1636 patients were included. Altogether, 143 patients (8.7 per cent) developed permanent hypoparathyroidism. Of these, 102 (6.2 per cent) had definitive permanent hypoparathyroidism, whereas 41 (2.5 per cent) had possible permanent hypoparathyroidism, because attempts to stop the treatment were lacking (28) or patients were lost to follow-up (13). The agreement between the Swedish Quality Register and the chart review was 29.3 per cent. A proportion of 23.2 per cent with a PTH level below the reference value corresponded to a 6.7 per cent rate of permanent hypoparathyroidism. CONCLUSION: The risk of permanent hypoparathyroidism after total thyroidectomy is high. Some patients are overtreated because attempts to stop the treatment are lacking. Quality registers might underestimate the risk of permanent hypoparathyroidism. Approximately one-quarter of all patients with low PTH levels immediately after surgery developed permanent hypoparathyroidism.
The parathyroid glands control calcium levels in the blood. If they do not make enough hormone, calcium levels are low. Parathyroid dysfunction can happen after thyroid surgery, if the glands are hurt or removed by mistake. This is a problem because people with this condition may have symptoms and need ongoing treatment with vitamin D and calcium. They might also face other health issues and need regular visits to their doctor. Finding out how often long-term parathyroid dysfunction happens can be tricky because it requires a full year of follow-up and attempts to stop the treatment. This information is often missing from many studies and registers. Some recent studies have shown that this condition is more common than previously thought. It would be helpful to have a quick way to know how common long-term parathyroid gland dysfunction will be within a unit or hospital, without having to wait for the follow-up. This would help doctors to assess how good they are at taking care of patients. It would also support research on new methods to avoid parathyroid dysfunction. The goal of the study was to see how often long-term parathyroid dysfunction occurs after thyroid surgery, using a strict definition and complete long-term follow-up. Another aim was to assess the link between low parathyroid hormone levels right after surgery and the rate of long-term parathyroid dysfunction. All individuals who had the entire thyroid gland removed for benign disease between 2005 and 2015 in a region of Sweden were included. Data were collected from local health records at six hospitals. Patient information, surgical details, blood tests, and treatment details were gathered from the medical charts. Data were also collected from the national quality register. A high rate of long-term parathyroid dysfunction was seen in this large study of 1636 patients, Some patients may have been overtreated, because no attempts had been made to stop the treatment. The rate of long-term parathyroid dysfunction in patients with a normal early parathyroid hormone level was very low. About 23 per cent of all patients had a low early parathyroid hormone level, which corresponded to a 6.7 per cent rate of long-term parathyroid dysfunction. The authors believe that parathyroid hormone measurement could help predict the rate of permanent hypoparathyroidism, but more studies are needed to be sure.
eng.
PubMed-ID: 37995259
DOI: 10.1093/bjs/znad366
PMCID: PMC10776524

**Feasibility of Autofluorescence Using Overlay Imaging for the Detection of Parathyroid Glands: Defining Standards**.
*Ann Surg Oncol*, 31(2):1116-24.
M. Arikan, J. Hegazy, S. Mertlitsch, T. Binter, L. Hargitai, C. Scheuba and P. Riss. 2024.
BACKGROUND: The aim of this study is to define standards for the use of near-infrared autofluorescence (NIRAF)-based overlay imaging via EleVision IR (Medtronic, Dublin, Ireland) and to evaluate its clinical applicability. PATIENTS AND METHODS: This prospective study included 189 patients who had undergone open thyroid and/or parathyroid surgery and in whom EleVision IR was applied to visualize at least one parathyroid gland (PG) between January 2021 and May 2022 in a tertiary referral care center. Whether the PGs were first localized by the surgeon or by overlay imaging was noted. Handling of the device, application time and duration, distance, infrared intensity (IR%), and the angle of each measurement were analyzed. In thyroidectomies, the specimens were subsequently scanned for further PGs. NIRAF patterns and intensities were described. RESULTS: Overall, 543 PGs were analyzed in 158 (83.6%) surgeries of thyroid glands (TGs) and in 49 (25.9%) surgeries for hyperparathyroidism. In 111 (58.7%) patients, identical numbers of PGs were detected by the surgeon and by overlay imaging. While a larger number of PGs was identified by the surgeon in 48 (25.4%) patients, overlay imaging served to detect more PGs in 30 (15.9%) cases. In four (2.1%) patients, PGs were visualized post-thyroidectomy due to their autofluorescence on the specimen. NIRAF-based overlay imaging was applied to depict the PGs early on after exposure by the surgeon. The ideal distance for the measurement ranged between 8 and 12 cm with an angle of 90 degrees and a mean IR% of 34.5% (+/- 17.6). CONCLUSIONS: Considering the standard operating procedures, NIRAF-based overlay imaging can be used as an adjunct tool for intraoperative localization.

PubMed-ID: 37957502
DOI: 10.1245/s10434-023-14552-7
PMCID: PMC10761391

**Correlation of TIRADS scoring in thyroid nodules with preoperative fine needle aspiration biopsy and postoperative specimen pathology**.
*Head Neck*, 46(4):849-56.
C. Atar, K. Dalci, Y. Aktar, N. Totik, U. Topal, I. C. Eray, A. T. Akcam and G. Sakman. 2024.
INTRODUCTION: The aim of our study is to determine the value of Thyroid Imaging Reporting and Data Systems (TIRADS) scoring in predicting malignancy in thyroid nodules by examining its relationship with fine needle aspiration biopsy and postoperative histopathological results. MATERIALS AND METHODS: In this study, patients who underwent surgery after ultrasonographic examination and fine needle aspiration biopsy for thyroid nodules at the General Surgery Clinic of Cukurova University Faculty of Medicine between January 2014 and November 2021 were retrospectively analyzed. The thyroid ultrasonography and fine needle aspiration biopsy of the included patients were performed by a clinician with 15 years of experience. The ultrasonographic features of the nodules were re-evaluated by the same clinician, and the American College of Radiology (ACR) TIRADS score was determined. Fine needle aspiration biopsy results were grouped according to Bethesda criteria. Postoperative histopathological examination results were divided into two groups: benign and malignant. The ACR TIRADS score was compared with fine needle aspiration biopsy and histopathological results. The performance of the ACR TIRADS score in predicting malignancy was determined. RESULTS: 79.8% of the 397 patients were female, and the mean age was 50.9 +/- 12.8 years. The mean diameter of the nodules was 27.4 +/- 15.8 mm. There was a significant, positive, but weak correlation between ACR TIRADS and Bethesda ($p < 0.001$) ($r = 0.33$). When the ACR TIRADS score was compared with histopathological results, it was found that the rate of malignancy increased as the TIRADS score increased ($p < 0.001$). The rates of malignancy diagnosis were 0% for TR1, 13.2% for TR2, 21.7% for TR3, 50.3% for TR4, and 72.4% for TR5. The area under the receiver operating characteristic curve for TIRADS in predicting malignancy was 0.747 (95% CI: 0.699-0.796, $p < 0.001$). TIRADS can distinguish malignancy with 75% accuracy. The optimal cutoff point was determined as TR4 with 80.3% sensitivity and 60.8% specificity. CONCLUSION: The ACR TIRADS scoring system is an effective risk classification system for thyroid nodules, providing 75% accuracy in predicting malignancy, with 80.3% sensitivity and 60.8% specificity values.
PubMed-ID: 38197158
DOI: 10.1002/hed.27622

**Hemithyroidectomy, does the indication influence the outcome?**
*Langenbecks Arch Surg*, 409(1):1.
E. Beka, H. Hanna, P. Olofsson and O. Gimm. 2023.
PURPOSE: Hemithyroidectomies are mainly performed for two indications, either therapeutically to relieve compression symptoms or diagnostically for suspicious nodule(s). In case of the latter, one could consider the approach to be rather extensive since the majority of patients have no symptoms and will have benign disease. The aim of this study is to investigate the complication rates of diagnostic hemithyroidectomy and to compare it with the complication rates of compressive symptoms hemithyroidectomy. METHODS: Data from patients who had undergone hemithyroidectomy either for compression symptoms or for excluding malignancy were extracted from a well-established Scandinavian quality register (SQRTPA). The following complications were analyzed: bleedings, wound infections, and paresis of the recurrent laryngeal nerve (RLN). Risk factors for these complications were examined by univariable and multivariable logistic regression. RESULTS: A total of 9677 patients were included, 3871 (40%) underwent surgery to exclude malignancy and 5806 (60%) due to compression symptoms. In the multivariable analysis, the totally excised thyroid weight was an independent risk factor for bleeding. Permanent (6-12 months after the operation) RLN paresis were less common in the excluding malignancy group ($p = 0.03$). CONCLUSION: A range of factors interfere and contribute to bleeding, wound infections, and RLN paresis after hemithyroidectomy. In this observational study based on a Scandinavian quality register, the indication "excluding malignancy" for hemithyroidectomy is associated with less permanent RLN paresis than the indication "compression symptoms." Thus, patients undergoing diagnostic hemithyroidectomy can be reassured that this procedure is a safe surgical procedure and does not entail an unjustified risk.
PubMed-ID: 38062331
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PMCID: PMC10703970

**Patient-reported oral function and psychological well-being outcomes of papillary thyroid cancer patients (PTC) after surgery: a cross-sectional study**.
*Surg Endosc*, 38(2):813-20.
J. Chen, J. Fang, J. Liu, T. Lu, X. Zheng and S. Wang. 2024.
BACKGROUND: This study was performed to evaluate the differences in oral function and psychological well-being between patients with PTC after the gasless transoral endoscopic thyroidectomy vestibular approach (gasless-TOETVA) and patients with PTC after open surgery. METHODS: PTC patients who underwent radical surgery from May 2021 to August 2022 were included in this study. Postoperative data on oral function and psychological well-being, including the Oral Health Impact profile-14 (OHIP-14) and State-Trait Anxiety Inventory Form Y, were collected and analyzed. RESULTS: 212 patients were included in the analysis. Among them, 102 patients who received gasless-TOETVA were assigned to the gasless-TOETVA group, while the remaining 110 patients who underwent open surgery were categorized as the open group. Although the OHIP-14 score in the gasless-TOETVA group was higher than that of the open group from 6 months to 1 year after surgery ($p = 0.012$), the difference in OHIP-14 scores between the two groups disappeared 1 year after surgery ($p = 0.155$). There were no differences between the gasless-TOETVA group and the open group in state-anxiety scores. However, the gasless-TOETVA group had significantly lower trait-anxiety scores than the open group at all follow-up time periods. Furthermore, within the gasless-TOETVA group, patients who were more than 1 year post-surgery showed significantly increased trait-anxiety scores compared to those of patients who were less than 1 year post-surgery (Delta = 3.4; $p = 0.032$). In contrast, the open group showed a decreasing trend in trait-anxiety scores, but there was no statistically significant difference between patients who had surgery less than 1 year ago and those who had surgery more than 1 year ago (Delta = - 2.2; $p = 0.094$). CONCLUSION: Gasless TOETVA had a temporary impact on oral function, but it did not alleviate the state of anxiety. Furthermore, we observed a significant increase in trait-anxiety scores among PTC patients who underwent gasless-TOETVA after 1 year.
PubMed-ID: 38062180
DOI: 10.1007/s00464-023-10603-y

**Neurophysiology of the Superior Laryngeal Nerve in an In Vivo Rat Model**.
*Laryngoscope*, 134(4):1778-84.
D. J. Cvancara, J. A. de Leon, H. C. Baertsch, Z. Jaleel, G. Kinney, V. Martinez and N. K. Bhatt. 2024.
OBJECTIVE: The superior laryngeal nerve (SLN) is fundamental in laryngeal sensation, cough reflex, and pitch control. SLN injury has substantial consequences including altered sensation, aspiration, and dysphonia. To date, in vivo measurement of the SLN remains elusive. The purpose of this study was to assess the feasibility of recording motor and sensory evoked potentials in a rat SLN model. METHODS: Twenty-two rat hemi-laryngeal preparations (n = 11) were obtained from 4-month-old Sprague-Dawley rats and included in this study. Compound motor action potentials (CMAPs) and motor unit number estimation (MUNE) were calculated by stimulating the SLN at the point of medial extension near the carotid artery and by placing a recording electrode on the cricothyroid muscle. Sensory response was determined through stimulation of the SLN and laryngoscopic visualization of a laryngeal adductor reflex (LAR). SLN and cricothyroid muscle cross-sections were stained and histologic morphometrics were quantified. RESULTS: Laryngeal evoked potentials were successfully obtained in all trials. Mean CMAP latency and negative durations were 0.99 +/- 0.57 ms and 1.49 +/- 0.57 ms, respectively. The median MUNE was 2.06 (IQR 1.88, 3.51). LAR was induced with a mean intensity of 0.69 +/- 0.20 mV. Mean axon count, myelin thickness, and g-ratio were 681 +/- 192.2, 1.72 +/- 0.26, and 0.45 +/- 0.04, respectively. CONCLUSIONS: This study demonstrates the feasibility of recording evoked response potentials following SLN stimulation. We hypothesize that this work will provide a tractable animal model to study changes in laryngeal sensation and cricothyroid motor function with aging, neurodegenerative disease, aspiration, or nerve injury. LEVEL OF EVIDENCE: NA Laryngoscope, 134:1778-1784, 2024.
PubMed-ID: 37787452
DOI: 10.1002/lary.31087

**Effect of Radioactive Iodine Therapy on Cancer-Specific Survival of Papillary Thyroid Cancer Tall Cell Variant**.
*J Clin Endocrinol Metab*, 109(3):e1260-e6.
P. Dai, W. Zhao, X. Zheng, H. Luo and X. Wang. 2024.
CONTEXT: Radioactive iodine (RAI) therapy is often used as an adjuvant treatment to reduce the risk of recurrence in patients with papillary thyroid cancer (PTC). However, the effect of RAI therapy on cancer-specific survival (CSS) in patients with tall cell variant (TCV) remains controversial. OBJECTIVE: This study aimed to investigate the impact of RAI therapy on CSS in patients with TCV-PTC by analyzing data from the Surveillance, Epidemiology, and End Results database. METHODS: We identified 1281 patients with TCV-PTC in the SEER database who underwent total thyroidectomy between 2004 and

2019. Of these, 866 (67.6%) patients received RAI therapy and 415 (32.4%) did not. Propensity score matching was conducted to balance the baseline characteristics between the 2 groups. Cox proportional hazards regression models were used to estimate the hazard ratio (HR) and 95% CI for the effect of RAI therapy on CSS. RESULTS: After propensity score matching, 373 pairs of patients were included in the analysis. The results showed no significant difference in CSS between the RAI therapy group and the non-RAI therapy group (HR 0.54, 95% CI 0.25-1.17, P = .120). Subgroup analyses indicated similar results. CONCLUSION: RAI therapy may not improve CSS in patients with TCV-PTC after total thyroidectomy. Future studies with larger sample sizes, longer follow-up periods, and better study designs are needed to confirm or refine our research findings.
PubMed-ID: 37804527
DOI: 10.1210/clinem/dgad580

**A comparison of swallowing related quality of life in patients undergoing transoral endoscopic versus open thyroid surgery**.
*World J Surg*, 48(2):379-85.
P. Deshmukh, B. Shiva, S. K. Yadav, P. Agarwal, D. Sharma and G. Johri. 2024.
INTRODUCTION: It is important for the endoscopic thyroid surgeon to understand the pros and cons of trans-oral endoscopic thyroidectomy-vestibular approach (TOETVA) vis-a-vis, open conventional thyroidectomy (OTx) so he/she can help patients in making informed choices regarding the type of procedure to opt for. Swallowing related quality of life (SWAL-QoL) has not been compared between the two approaches. Using a rigorous qualitative methodology and validated reliable tool, this study set out to compare the swallowing related quality of life in patients undergoing TOETVA versus OTx. METHODS: Prospective study at 3 time points in patients planned for hemithyroidectomy (Preoperative, 1 week and 12 weeks). Data were collected on patients at a tertiary teaching institute in India. Participants ranged from age 18-60 years with a diagnosis of benign euthyroid nodule undergoing hemithyroidectomy. Exclusion criteria were-(1) pre-existing vocal cord abnormalities, (2) undergoing surgery for recurrent nodules, and (3) any neuro-muscular disease affecting swallowing ability. Main outcome measure was comparison of swallowing related quality of life domain scores between patients undergoing hemithyroidectomy via either endoscopic trans-oral or open approach. RESULTS: Of the 82 included patients, 40 underwent TOETVA and 42 OTx. Both the groups were comparable in terms of demographic and clinicopathological profile. The mean preoperative SWAL-QOL scores were comparable in all domains. Mean SWAL-QoL scores for all domains on postoperative day 7 were significantly better in TOETVA group with domains burden, eating desire, mental health and communication having medium effect sizes. Physical symptom domain was better in the OTx group but had a small effect size. The difference in SWAL-QoL domains between the two groups persisted for 3 months also. CONCLUSION: Swallowing related quality of life after trans-oral endoscopic thyroidectomy compared to conventional open surgery has not been reported in the literature. Our findings suggest that trans-oral endoscopic thyroidectomy results in significant superior swallowing related quality of life in the majority of domains.
PubMed-ID: 38686757
DOI: 10.1002/wjs.12012

**Impact of near-infrared fluorescence imaging plus indocyanine green fluorescence on postoperative hypoparathyroidism rates after total thyroidectomy and central neck lymph node dissection**.
*Br J Surg*, 111(2):undefined-undefined.
S. Di Lorenzo, J. L. Carrillo Lizarazo, G. Dionigi, J. L. Kraimps and G. Donatini. 2024.
BACKGROUND: Patients with thyroid carcinoma often undergo cervical lymph node dissection, which is associated with high rates of both transient and permanent postoperative hypoparathyroidism. The impact of near-infrared fluorescence imaging + indocyanine green (ICG) fluorescence on postoperative hypoparathyroidism rates after total thyroidectomy and central neck lymph node dissection was evaluated. METHODS: All patients undergoing surgery between January 2019 and March 2023 were included and divided into three groups: a control group (parathyroid glands identified visually), a near-infrared fluorescence imaging alone group, and a near-infrared fluorescence imaging + ICG fluorescence group. The primary outcome was the transient and permanent postoperative hypoparathyroidism rates. Secondary outcomes were: length of surgery and number of parathyroid glands identified, inadvertently resected, and autotransplanted. RESULTS: A total of 131 patients were included in the study (47 in the control group, 45 in the near-infrared fluorescence imaging alone group, and 39 in the near-infrared fluorescence imaging + ICG fluorescence group). The transient hypoparathyroidism rate was 48.9% in the control group, 37.8% in the near-infrared fluorescence imaging alone, and 5.1% in the near-infrared fluorescence imaging + ICG fluorescence group (P < 0.0001), while the permanent hypoparathyroidism rate was 8.5% in the control group, 2.2% in the near-infrared fluorescence imaging alone group, and 0% in the near-infrared fluorescence imaging + ICG fluorescence group (P = 0.096). The number of parathyroid glands identified was 159

of 188 in the control group, 165 of 180 in the near-infrared fluorescence imaging alone group, and 149 of 156 in the near-infrared fluorescence imaging + ICG fluorescence group (P = 0.002). Inadvertent resection of parathyroid glands occurred for 29 of 188 in the control group, 15 of 180 in the near-infrared fluorescence imaging alone group, and 7 of 156 in the near-infrared fluorescence imaging + ICG fluorescence group (P = 0.002), with subsequent parathyroid gland autotransplantation for 2 of 29 in the control group, 2 of 15 in the near-infrared fluorescence imaging alone group, and 3 of 7 in the near-infrared fluorescence imaging + ICG fluorescence group (P = 0.040). There was no difference in the median operating time between groups. CONCLUSION: The use of near-infrared fluorescence imaging + ICG fluorescence decreased both transient and permanent hypoparathyroidism rates in patients undergoing total thyroidectomy and central neck lymph node dissection.
PubMed-ID: 38381933
DOI: 10.1093/bjs/znae022

**Fluorescence imaging to visualize the recurrent laryngeal nerve during thyroidectomy procedures: analysis of 65 cases and 81 nerves**.
*Surg Endosc*, 38(3):1406-13.
F. Dip, J. Falco, K. White and R. Rosenthal. 2024.
BACKGROUND: Recurrent laryngeal nerve (RLN) injury after thyroidectomy is relatively common. Locating the RLN prior to thyroid dissection is paramount to avoid injury. We developed a fluorescence imaging system that permits nerve autofluorescence. We aimed to determine the sensitivity and specificity of fluorescence imaging at detecting the RLN relative to thyroid and other background tissue and compared it to white light. METHODS: In this prospective study, 65 patients underwent thyroidectomy from January to April 2022 (16 bilateral thyroid resections) using white and fluorescent light. Fluorescence intensity [relative fluorescence units (RFU)] was recorded for RLN, thyroid, and background. RFU mean, minimum, and maximum values were calculated using Image J software. Thirty randomly selected pairs of white and fluorescent light images were independently reviewed by two examiners to compare RLN detection rate, number of branches, and length and minimum width of nerves visualized. Parametric and nonparametric statistical analysis was performed. RESULTS: All 81 RNLs observed were visualized more clearly under fluorescence (mean intensity, micro = 134.3 RFU) than either thyroid (micro = 33.7, $p < 0.001$) or background (micro = 14.4, $p < 0.001$). Forest plots revealed no overlap between RLN intensity and that of either other tissue. Sensitivity and specificity for RLN were 100%. All 30 RLNs and all 45 nerve branches were clearly visualized under fluorescence, versus 17 and 22, respectively, with white light (both $p < 0.001$). Visible nerve length was 2.5 x as great with fluorescence as with white light (micro = 1.90 vs. 0.76 cm, $p < 0.001$). CONCLUSIONS: In 65 patients and 81 nerves, RLN detection was markedly and consistently enhanced with autofluorescence neuro-imaging during thyroidectomy, with 100% sensitivity and specificity.
PubMed-ID: 38168731
DOI: 10.1007/s00464-023-10627-4

**History of Bariatric Surgery Before Thyroid Surgery: Recommendations for Prevention and Management of Postoperative Hypocalcemia**.
*Otolaryngol Head Neck Surg*, 170(3):989-91.
H. W. Eberly, B. Y. Sciscent, F. Jeffrey Lorenz, N. Goyal and D. Goldenberg. 2024.
Hypocalcemia following thyroidectomy is a common and potentially life-threatening complication. It is caused by intraoperative injury to the parathyroid glands or their blood supply. Although several studies have shown that patients with a prior history of bariatric surgery may be at an increased risk for hypocalcemia after thyroidectomy, no clear recommendations exist for preventing and managing this condition in this population. This paper highlights the significance of understanding this risk and of obtaining a history of prior bariatric surgery before thyroidectomy. We propose concise recommendations for preventing and managing hypocalcemia following thyroidectomy in patients with a history of bariatric surgery.
PubMed-ID: 38044480
DOI: 10.1002/ohn.604

**Artificial Intelligence Model Assisting Thyroid Nodule Diagnosis and Management: A Multicenter Diagnostic Study**.
*J Clin Endocrinol Metab*, 109(2):527-35.
E. J. Ha, J. H. Lee, D. H. Lee, J. Moon, H. Lee, Y. N. Kim, M. Kim, D. G. Na and J. H. Kim. 2024.
CONTEXT: It is not clear how to integrate artificial intelligence (AI)-based models into diagnostic workflows. OBJECTIVE: To develop and validate a deep-learning-based AI model (AI-Thyroid) for thyroid cancer diagnosis, and to explore how this improves diagnostic performance. METHODS: The system was trained using 19 711 images of 6163 patients in a tertiary

hospital (Ajou University Medical Center; AUMC). It was validated using 11 185 images of 4820 patients in 24 hospitals (test set 1) and 4490 images of 2367 patients in AUMC (test set 2). The clinical implications were determined by comparing the findings of six physicians with different levels of experience (group 1: 4 trainees, and group 2: 2 faculty radiologists) before and after AI-Thyroid assistance. RESULTS: The area under the receiver operating characteristic (AUROC) curve of AI-Thyroid was 0.939. The AUROC, sensitivity, and specificity were 0.922, 87.0%, and 81.5% for test set 1 and 0.938, 89.9%, and 81.6% for test set 2. The AUROCs of AI-Thyroid did not differ significantly according to the prevalence of malignancies (>15.0% vs </=15.0%, P = .226). In the simulated scenario, AI-Thyroid assistance changed the AUROC, sensitivity, and specificity from 0.854 to 0.945, from 84.2% to 92.7%, and from 72.9% to 86.6% (all P < .001) in group 1, and from 0.914 to 0.939 (P = .022), from 78.6% to 85.5% (P = .053) and from 91.9% to 92.5% (P = .683) in group 2. The interobserver agreement improved from moderate to substantial in both groups. CONCLUSION: AI-Thyroid can improve diagnostic performance and interobserver agreement in thyroid cancer diagnosis, especially in less-experienced physicians.
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DOI: 10.1210/clinem/dgad503

**Lymph node imaging for thyroid cancer**.
*Clin Endocrinol (Oxf)*, 100(1):96-101.
S. A. Holoubek and R. S. Sippel. 2024.
Cervical lymph nodes (LNs) in the central (level VI) and lateral (levels II-V) compartments of the neck are the most common sites of locoregional metastases associated with thyroid cancer. Prophylactic nodal dissections are uncommon in modern thyroid surgery and are not routinely performed due to concern for increased morbidity and do not offer improved survival. Therefore, a selective approach for LN dissections is increasingly important. Preoperatively, this is most frequently assessed with cervical ultrasound (US). Contrast-enhanced computed tomography (CT) of the neck can also be used for preoperative assessment. Both US and CT imaging can be used to characterise LNs in levels II-VI and their risk of malignancy based on size, morphology, and growth. US-guided fine-needle aspiration of equivocal LN with thyroglobulin (Tg) washout can also determine if a LN harbours malignancy. For postoperative surveillance after total thyroidectomy, both US and CT continue to play an important role at 6-12 months intervals. These patients may also benefit from additional biochemical data such as Tg levels in addition to LN and thyroid bed imaging. Thyroid uptake scans may also play a role in LN surveillance postoperatively for well-differentiated thyroid carcinoma in certain clinical contexts. Less commonly, positron emitted tomography may play a role, but is typically reserved for patients with aggressive or radioactive iodine refractory disease.
PubMed-ID: 38009335
DOI: 10.1111/cen.14993

**A national study of postoperative thyroid hormone supplementation rates after thyroid lobectomy**.
*Surgery*, 175(4):1029-33.
Q. L. Hu, L. Chen, E. J. Kuo, J. A. Lee, J. H. Kuo, J. D. Wright and C. M. McManus. 2024.
BACKGROUND: The American Thyroid Association updated guidelines in 2015 to allow lobectomy for low-risk thyroid cancers. The objectives of this study were (1) to determine thyroid hormone supplementation rates after lobectomy and (2) to evaluate the effect of the American Thyroid Association guideline change on lobectomy and hormone supplementation rates among thyroid cancer patients. METHODS: The Merative MarketScan Databases was used to identify adult (>/=age 18) patients who underwent thyroidectomy for benign nodules or thyroid cancer. The association between indication for surgery and postoperative thyroid hormone supplementation was examined using chi(2) analyses and multivariable logistic regression models. Among patients with thyroid cancer, lobectomy and hormone supplementation rates were compared in the periods before (2008-2015) and after the guideline change (2016-2019). RESULTS: Of the 81,926 patients identified, 33,756 (41.2%) underwent thyroid lobectomy, 45,104 (55.1%) underwent total thyroidectomy, and 3,066 (3.7%) underwent completion thyroidectomy. Patients who underwent lobectomy for malignancy were significantly more likely to require hormone supplementation (59.3% vs 39.4% [P < .001], adjusted odds ratio 2.34 [95% confidence interval 2.20-2.48]) compared to those with benign disease. Compared to the 2008 to 2015 period, the proportion of patients who underwent lobectomy for thyroid cancer was higher in the 2016 to 2019 period (34.3% vs 30.3%, P < .001), with fewer patients requiring completion thyroidectomy (25.6% vs 29.8%, P < .001) and thyroid hormone supplementation (56.9% vs 60.1%, P = .04). CONCLUSION: The postoperative thyroid hormone supplementation rate was significantly higher in patients who had thyroid cancers compared to benign diseases. After the American Thyroid Association guidelines changed, lobectomy rates increased significantly without a concomitant increase in the completion of thyroidectomy.

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DOI: 10.1016/j.surg.2023.11.016

**Noise level and surgeon stress during thyroidectomy in an endocrine surgery operating room**.
*Head Neck*, 46(1):37-45.
S. Idrees, M. Sabaretnam, G. Chand, A. Mishra, A. Rastogi and G. Agarwal. 2024.
INTRODUCTION: Noise in the operating room is an ongoing problem that impacts the outcome of any surgery. Noise as a stressor can produce a startling reaction and activate the fight or flight response of the autonomic and endocrine systems. The psychobiology of stress as assessed by salivary cortisol level is a sensitive measure of allostatic load. This study aims to correlate, both subjectively and objectively, the salivary cortisol levels of the surgeon with noise level measurement in an endocrine surgery operating room (OR). MATERIALS AND METHODS: A prospective observational study was conducted in the Endocrine surgery OR of a tertiary care center. We recorded the noise from the shifting in of patients in the OR to shifting out using a digital sound level meter. The operating surgeon (S) provided two salivary cortisol samples (normal salivary cortisol <5 nmol/L), one baseline and another after the procedure. The questionnaire for the assessment of distraction during thyroidectomy was filled in by the S at the end of the procedure. Salivary cortisol levels were analyzed using SLV-4635 (formerly SLV-2930) DRG Instruments GmbH German using the ELISA technique. Statistical analysis was performed using SPSS 22.0. RESULTS: A total of 37 procedures with 74 salivary cortisol samples and 259 questionnaire responses from S were analyzed. All patients with only benign FNAC were operated upon (64.9% colloid). Mean TSH levels were 3.5 +/- 6.7 mIU/L. The majority had a solitary thyroid nodule (STN) (25/37, 67.6%). Nineteen patients (51.3%) underwent open hemithyroidectomy, 10 patients total thyroidectomy, and eight patients endoscopic hemithyroidectomy. The mean noise level in the OR was 70 db. The maximum and minimum noise level in the OR was 90.06 and 51.81 dB, respectively. A total of 74 salivary cortisol samples from the S were collected (baseline and post-noise exposure) and mean cortisol levels were recorded. The surgeon was more significantly affected by surrounding noise, especially during critical phases 3 of surgery, mainly, RLN dissection and parathyroid dissection as recorded by their responses in the questionnaire ($p = 0.003$). The maximum value of post-operative salivary cortisol of surgeon was recorded as 23. 48 ng/mL and the minimum value recorded was 0.49 ng/mL. The difference in baseline cortisol and post-noise exposure cortisol levels of surgeon was found to be significant ($p < 0.001$). Maximum and mean noise levels were significantly associated with post-noise exposure salivary cortisol elevation in the surgeon ($p = 0.032$ and 0.014, respectively). The noise levels during RLN dissection were borderline significant with the post-noise exposure salivary cortisol of the surgeon ($p = 0.055$). CONCLUSION: Our research is the first such study which has been done to assess noise levels and their effect on thyroidectomy using objective salivary cortisol measurement. It challenges the misconstrued notion that visceral surgeries requiring lesser instruments are not associated with noise-related stress. Noise is a major distraction and the effect of long-term effect on the entire surgical team needs to be studied.
PubMed-ID: 37860889
DOI: 10.1002/hed.27552

**Completion thyroidectomy: A safe option for high-volume surgeons**.
*Head Neck*, 46(1):57-63.
P. P. Issa, E. Hossam, J. H. Cheng, B. M. Magazine, M. Hussein, X. Luo, A. Abdelhady, J. Staav, A. LaForteza, A. L. Albuck, M. Shama, E. Toraih and E. Kandil. 2024.
BACKGROUND: The risk of complication in patients undergoing completion thyroidectomy (cT) is mixed. Several studies report increased risk in comparison to total thyroidectomy (TT) and still others reporting a comparatively decreased risk. We compared the rates of complication in patients at our institution undergoing thyroid lobectomy (TL), (TT), and cT by a single high-volume surgeon. METHODS: We performed a single-institution retrospective cohort study. Patients undergoing TL, TT, or cT by a high-volume surgeon were included. Rates of complication were collected and compared between the three cohorts. RESULTS: A total of 310 patients were included. The overall rate of complication was 4.2%. The complication rates in the TL, TT, and cT cohorts were 1%, 7.1%, and 4.5%, respectively ($p = 0.10$). Transient hypocalcemia was slightly more common in the TT cohort (6.1%) as opposed to the TL (0%) or cT (0.9%) cohort ($p = 0.01$). The cohorts also had similar rates of recurrent laryngeal nerve signal loss leading to transient dysphonia (TL: 0% vs. TT: 1% vs. cT: 3.6%, $p = 0.10$). CONCLUSIONS: While rates of complication tended to predictably decrease as approaches became less extensive, there were no significant differences in complication rates among the three surgical approaches when performed by a high-volume surgeon. Considering the low rates of complication overall, patient counseling and preference should be emphasized to provide appropriate and tailored treatment plans.
PubMed-ID: 37872858
DOI: 10.1002/hed.27551

**Fusion Oncogenes in Patients With Locally Advanced or Distant Metastatic Differentiated Thyroid Cancer**.
*J Clin Endocrinol Metab*, 109(2):505-15.
G. Ju, Y. Sun, H. Wang, X. Zhang, Z. Mu, D. Sun, L. Huang, R. Lin, T. Xing, W. Cheng, J. Liang and Y. S. Lin. 2024.
CONTEXT: Fusion oncogenes are involved in the underlying pathology of advanced differentiated thyroid cancer (DTC), and even the cause of radioactive iodine (RAI)-refractoriness. OBJECTIVE: We aimed to investigation between fusion oncogenes and clinicopathological characteristics involving a large-scale cohort of patients with advanced DTC. METHODS: We collected 278 tumor samples from patients with locally advanced (N1b or T4) or distant metastatic DTC. Targeted next-generation sequencing with a 26-gene ThyroLead panel was performed on these samples. RESULTS: Fusion oncogenes accounted for 29.86% of the samples (72 rearrangement during transfection (RET) fusions, 7 neurotrophic tropomyosin receptor kinase (NTRK) fusions, 4 anaplastic lymphoma kinase (ALK) fusions) and occurred more frequently in pediatric patients than in their adult counterparts (P = .003, OR 2.411, 95% CI 1.329-4.311) in our cohort. DTCs with fusion oncogenes appeared to have a more advanced American Joint Committee on Cancer (AJCC)_N and AJCC_M stage (P = .0002, OR 15.47, 95% CI 2.54-160.9, and P = .016, OR 2.35, 95% CI 1.18-4.81) than those without. DTCs with fusion oncogenes were associated with pediatric radioactive iodine (RAI) refractoriness compared with those without fusion oncogenes (P = .017, OR 4.85, 95% CI 1.29-15.19). However, in adult DTCs, those with fusion oncogenes were less likely to be associated with RAI refractoriness than those without (P = .029, OR 0.50, 95% CI 0.27-0.95), owing to a high occurrence of the TERT mutation, which was the most prominent genetic risk factor for RAI refractoriness in multivariate logistic regression analysis (P < .001, OR 7.36, 95% CI 3.14-17.27). CONCLUSION: Fusion oncogenes were more prevalent in pediatric DTCs than in their adult counterparts and were associated with pediatric RAI refractoriness, while in adult DTCs, TERT mutation was the dominant genetic contributor to RAI refractoriness rather than fusion oncogenes.
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DOI: 10.1210/clinem/dgad500
PMCID: PMC10795910

**Enabling Patient Empowerment in Treatment Decisions for Thyroid Cancer**.
*JAMA Surg*, 159(1):114.
P. Kaul and P. K. Garg. 2024.
PubMed-ID: 37672280
DOI: 10.1001/jamasurg.2023.3951

**Defining competencies in robotic thyroidectomy: development of a model assessing an expert operator's intraoperative performance skills and cognitive strategies**.
*Gland Surg*, 13(3):340-50.
H. Kim, H. W. Yu, J. H. Ahn, T. S. Lee and K. E. Lee. 2024.
BACKGROUND: The changing medical education environment emphasizes the need for time efficiency, increasing the demand for competency-based medical education to improve trainees' learning strategies. This study was performed to determine the competencies required for successful performance of robotic thyroidectomy (RT) and to determine the consensus of experts for performance of RT. METHODS: Data were collected through 12 semi-structured interviews with RT experts and 11 field observations. Cognitive task analysis was performed to determine the competencies required for experts to perform RT. A modified Delphi methodology was used to determine how 20 experts rated the importance of each item of RT performance on a Likert 7-point scale. The criteria for the Delphi consensus were set at a Cronbach's alpha>/=0.80 with two survey rounds. RESULTS: After 11 field observations and 12 semi-structured interviews, 89 items were identified within six modules. These items were grouped into sub-modules according to their theme. The modified Delphi survey, involving 21 experts, reached the consensus standard during the second round (Cronbach's alpha=0.954), enabling the identification of the 64 most important items within six modules related to RT performance: midline incision to isthmectomy (MID module; n=8), lateral dissection (LAT module; n=7), preservation of inferior parathyroid glands (INF module; n=16), preservation of recurrent laryngeal nerve and dissection of the ligament of Berry (BER module; n=21), dissection of the thyroid upper pole (SUP module; n=10), and specimen removal and closure (END module; n=2). CONCLUSIONS: This mixed-method study combining qualitative and quantitative methodology identified modules of core competencies required to perform RT. These modules can be used as a standard and objective guide to train surgeons to perform RT and evaluate outcomes.
PubMed-ID: 38601290
DOI: 10.21037/gs-23-467
PMCID: PMC11002486

**Accuracy and diagnostic performance of the Bethesda system for reporting thyroid cytopathology in a tertiary endocrine surgical referral center in Belgium**.
*World J Surg*, 48(2):386-92.
S. Kinet, H. Cornette, K. Van Den Heede, N. Brusselaers and S. Van Slycke. 2024.
BACKGROUND: The Bethesda System for Reporting Thyroid Cytopathology is a commonly used classification for fine needle aspiration (FNA) cytology of suspicious thyroid nodules. The risk of malignancy (ROM) for each category has recently been analyzed in three international databases. This paper compares the diagnostic performance of the Bethesda classification in a high-volume referral center in Belgium. METHODS: All consecutive thyroid procedures were registered in a prospective database from January 2010 till August 2022. Patient and surgical characteristics, preoperative Bethesda categories, and postoperative pathology results were analyzed. RESULTS: Out of 2219 consecutive thyroid procedures, 1226 patients underwent preoperative FNA. Papillary thyroid cancer was the most prevalent malignancy (N = 119, 70.4%), followed by follicular (N = 17, 10.1%) and medullary thyroid cancer (N = 15, 8.9%). Micropapillary thyroid cancer was incidentally found in 46 (3.8%) patients. Bethesda categories I, II, III, IV, V, and VI, respectively, represented 250 (20.4%; ROM 4.4%), 546 (44.5%; ROM 3.8%), 96 (7.8%; ROM 20.8%), 231 (18.8%; ROM 15.2%), 62 (5.1%; ROM 72.6%), and 41 (3.3%; ROM 90.2%) patients. Overall ROM was 13.8%. An negative predictive value (NPV) of 96.2% was found. Overall specificity was 64.2% with a positive predictive value (PPV) of 31.9%. Diagnostic accuracy was 67.8%. Compared to international databases (CESQIP, EUROCRINE, and UKRETS), ROM in this study appeared lower for Bethesda category IV (15.2 vs. 26.7% and p = 0.612). CONCLUSION: Despite being validated in numerous studies, ROM based on preoperative FNA cytology classified according to the Bethesda classification may vary among surgical centers and countries as this study reveals a higher NPV and lower PPV.
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DOI: 10.1002/wjs.12052

**Patient-reported swallowing outcomes after transoral robotic thyroidectomy: Comparison with conventional transcervical thyroidectomy**.
*Head Neck*, 46(1):64-73.
S. Y. Lee, S. R. Ryu, B. R. Yun, Y. B. Ji, C. M. Song and K. Tae. 2024.
BACKGROUND: This study aimed to evaluate the swallowing outcomes after transoral robotic thyroidectomy (TORT) and compare them with those of conventional transcervical thyroidectomy. METHOD: We enrolled 146 patients who underwent thyroidectomy (73 TORT; 73 conventional approach). We prospectively analyzed swallowing outcomes using the Swallowing Impairment Index-6 (SIS-6) questionnaire, a patient-reported measure, before and 1, 3, and 6 days; 1, 3, and 6 months; and 1 year after surgery. Propensity score-matched analysis was performed using three covariates: age, sex, and extent of thyroidectomy. RESULTS: SIS-6 scores worsened significantly immediately after surgery and progressively recovered 1 year postoperatively in both groups. Propensity score matching generated two matched groups of 22 patients each. In the propensity score-matched samples, the SIS-6 scores did not differ between the TORT and conventional groups, except at 1 day postoperatively. CONCLUSION: Patient-reported swallowing outcomes of TORT were comparable to those of the conventional transcervical procedure.
PubMed-ID: 37877746
DOI: 10.1002/hed.27557

**Radioactive iodine administration is not associated with improved disease-specific survival in classic papillary thyroid carcinoma greater than 4 cm confined to the thyroid**.
*Surgery*, 175(1):215-20.
Y. J. Lee-Saxton, F. Palacardo, J. A. Greenberg, C. E. Egan, T. E. Marshall, A. Tumati, T. Beninato, R. Zarnegar, T. J. Fahey, 3rd and B. M. Finnerty. 2024.
BACKGROUND: We aimed to evaluate the impact of radioactive iodine on disease-specific survival in intrathyroidal (N0M0) papillary thyroid carcinoma >4 cm, given conflicting data in the American Thyroid Association guidelines regarding their management. METHODS: The Surveillance, Epidemiology, and End Results database was queried for N0M0 classic papillary thyroid carcinoma >4 cm. Kaplan-Meier estimates were performed to compare disease-specific survival between radioactive iodine-treated and untreated groups. A multivariable Cox regression was performed to identify predictors of disease-specific survival. RESULTS: There were more patients aged >/=55 (41.7% vs 32.3%, P = .001) and fewer multifocal tumors (25.3% vs 30.6%, P = .006) in the no radioactive iodine group. Ten-year disease-specific survival was similar between the radioactive iodine treated and untreated groups (97.2% vs 95.6%, P = .34). Radioactive iodine was not associated with a significant disease-specific survival benefit (adjusted hazard ratio = 0.78, confidence interval [0.39-1.58],

P = .49). Age >/=55 (adjusted hazard ratio = 3.50, confidence interval [1.69-7.26], P = .001) and larger tumor size (adjusted hazard ratio = 1.04, confidence interval [1.02-1.06], P < .001) were associated with an increased risk of disease-specific death. Subgroup analyses did not demonstrate improved disease-specific survival with radioactive iodine in patients >/=55 and in tumors >5 cm. CONCLUSION: Adjuvant radioactive iodine administration in classic papillary thyroid carcinoma >4 cm confined to the thyroid did not significantly impact disease-specific survival. Thus, these patients may not require routine treatment with adjuvant radioactive iodine.
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DOI: 10.1016/j.surg.2023.04.065

**Long-Term Outcomes and Risk Factors of Radiofrequency Ablation for T1N0M0 Papillary Thyroid Carcinoma**.
*JAMA Surg*, 159(1):51-8.
X. Li, L. Yan, J. Xiao, Y. Li, Z. Yang, M. Zhang and Y. Luo. 2024.
IMPORTANCE: Radiofrequency ablation (RFA) has gained increasing interest as a minimally invasive procedure to treat low-risk papillary thyroid carcinoma (PTC). Considering the indolent nature of this disease, studies in large populations with long follow-up would be invaluable to further substantiate the effectiveness of RFA. OBJECTIVE: To evaluate the long-term (58.5 months) outcomes of patients with T1N0M0 PTC who underwent RFA and investigate risk factors for local tumor progression (LTP). DESIGN, SETTING, AND PARTICIPANTS: This cohort study included 1613 patients aged 18 years or older with T1N0M0 PTC who underwent ultrasonography-guided RFA between January 2014 and December 2020 at the Chinese People's Liberation Army General Hospital in Beijing, China. Included in the analysis were patients with PTC (confirmed by biopsy) with a maximum diameter of 20 mm or less; no evidence of extrathyroidal extension (capsular disruption or involvement of perithyroidal tissue), lymph node metastasis, or distant metastasis on ultrasonography or computed tomography; and no evidence of an aggressive subtype of PTC on biopsy. Patients with PTC larger than 2 cm, less than 12 months of follow-up, or inadequate follow-up information were excluded. Data were analyzed in April 2023. MAIN OUTCOMES AND MEASURES: Long-term progression rate, disease-free survival, and complete tumor disappearance and their associations with patient and tumor characteristics. Disease-free survival was calculated using Kaplan-Meier analysis. Cox proportional hazards regression analyses were performed to assess risk factors for LTP and complete tumor disappearance. RESULTS: The study comprised 1613 patients (mean [SD] age, 43.3 [10.2] years; 1256 women [77.9%]) with 1834 T1N0M0 PTC tumors. During a mean follow-up of 58.5 months (range, 27 to 111 months), LTP was observed in 69 patients (4.3%), including 42 (2.6%) with tumor recurrence and 27 (1.7%) with tumor persistence. Cumulative disease-free survival rates at 1, 3, 5, and 8 years were 98.0%, 96.7%, 96.0%, and 95.7%, respectively. The overall complication rate was 2.0% (32 patients), with 6 (0.4%) major complications. Independent risk factors for LTP included subcapsular tumor location 2 mm or less from the capsule or trachea (hazard ratio [HR], 3.36; 95% CI, 2.02-5.59; P < .001) and multifocal tumors (HR, 2.27; 95% CI, 1.30-3.96; P = .004). Furthermore, 1376 patients (85.3%) showed complete tumor disappearance at follow-up ultrasonographic examination. Factors associated with complete tumor disappearance included age 40 years or less (HR, 0.78; 95% CI, 0.70-0.87; P < .001), stage T1a tumors (HR, 0.37; 95% CI, 0.31-0.45; P < .001), and unifocal tumors (HR, 0.50; 95% CI, 0.42-0.60; P < .001). CONCLUSIONS AND RELEVANCE: In this cohort study, ultrasonography-guided RFA for T1N0M0 PTC had excellent long-term outcomes. Patients with unifocal T1N0M0 PTC and subcapsular tumor location more than 2 mm from the capsule or trachea may be the best candidates for RFA.
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PMCID: PMC10600723

**Quality of life and decision regret in patients with late-hypothyroidism after radioiodine treatment for Graves' disease**.
*Clin Endocrinol (Oxf)*, 100(1):87-95.
Y. Li, T. Yang, L. Ju, Y. Feng, Z. Chen, X. Xiang, T. Zhu, H. Pang and Z. Wang. 2024.
OBJECTIVE: Patients with Graves' disease often engage in shared decision-making to select an individualised treatment regimen from multiple options. Radioactive iodine (RAI) is one of the treatment choices for their condition, aims to improve quality of life and well-being. Likewise, dissatisfaction with treatment outcomes can result in decision regret. We employed validated questionnaires to assess the prospective quality of life, decision regret and relative factors involved in decision-making of patients with late hypothyroidism after RAI therapy. METHODS: A questionnaire survey was conducted among patients in hypothyroidism status for more than 1 year after RAI therapy. Disease-specific and generic QoL were assessed using the short form of thyroid-related patient-reported outcome (ThyPRO-39) questionnaire. Patient satisfaction regarding their decision to undergo RAI was assessed using the Decision Regret Scale (DRS) and patients were asked about the importance of relative factors in decision-making. RESULTS: Of 254 patients who responded to the survey, the mean age of patients was 45.3 years (range: 18-78 years) and the median time from RAI therapy to survey was 4 years

(range: 1-30 years). Patients' median and mean DRS score were 34.4 and 38.8 (range: 0-100), respectively. A total of 100 (39.4%) patients express absent-to-mild regret (score: 0-25), 154 (60.6%) patients express moderate-to-severe regret (score: >25). The mean score of the absent-to-mild regret group were significantly higher than those of the moderate-to-severe regret group on most ThyPRO-39 scales. A statistically significant positive correlation was observed between DRS score and most ThyPRO-39 scale score. There was a significant positive association between higher DRS score and longer time intervals after RAI treatment, a brief duration of hyperthyroidism, and the significance of long-time outpatient follow-up. More decision regret was negatively associated Iodine-free diet, ineffectiveness of ATD, fear of surgery. CONCLUSION: Impairment of quality of life was positively correlated with decision regret in patients with late-hypothyroidism after radioiodine therapy. Patients with insufficient information support before decision-making are more likely to have higher decision regret after treatment. Our findings suggest that health providers should fully communicate with patients and provide information support in multiple dimensions during the shared-decision-making process.
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DOI: 10.1111/cen.14986

**Impact of fine-needle aspiration cytology in thyroidectomy extent and associated surgical morbidity in thyroid cancer**.
*Langenbecks Arch Surg*, 409(1):68.
P. Lind, E. Nordenstrom, L. Johansson, G. Wallin and K. Daskalakis. 2024.
PURPOSE: To assess the impact of fine-needle aspiration cytology (FNAC) in the extent of surgery in patients with thyroid cancer (TC) and the associated surgical morbidity in primary and completion setting. METHODS: A Swedish nationwide cohort of patients having surgery for TC (n = 2519) from the Scandinavian Quality Register for Thyroid, Parathyroid and Adrenal surgery between 2004 and 2013 was obtained. Data was validated through scrutinizing FNAC and histology reports. RESULTS: Among the 2519 cases operated for TC, the diagnosis was substantiated and validated through the histology report in 2332 cases (92.6%). Among these, 1679 patients (72%) were female, and the median age at TC diagnosis was 52.3 years (range 18-94.6). Less than total thyroidectomy (LTT) was undertaken in 944 whereas total thyroidectomy (TT) in 1388 cases. The intermediate FNAC categories of atypia of undetermined significance/follicular lesion of undetermined significance (AUS/ FLUS), as well as suspicion for follicular neoplasm (SFN) lesions were more often encountered in LTT (n = 314, 33.3%) than TT (n = 63, 4.6%), whereas FNACs suspicion for malignancy and/or malignancy were overrepresented in TT (n = 963, 69.4%). Completion thyroidectomies were undertaken in 553 patients out of 944 that initially had LTT. In 201 cases with cancer lesions > 1 cm, other than FTC (Follicular TC)/ HTC (Hurthle cell TC) subjected to primary LTT, inadequate procedures were undertaken in 81 due to absent, Bethesda I or II FNAC categories, preoperatively. Complications at completion of surgery in this particular setting were 0.5% for RLN palsy (n = 1) and 1% (n = 2) for hypoparathyroidism 6 months postoperatively. The overall postoperative complication rate was higher in primary TT vs. LTT for RLN palsy (4.8% [n = 67] vs. 2.4% [n = 23]; p = 0.003) and permanent hypoparathyroidism (6.8% [n = 95] vs. 0.8% [n = 8]; p < 0.0001). CONCLUSIONS: FNAC results appear to affect surgical planning in TC as intermediate FNAC categories lead more often to LTT. Overall, inadequate procedures necessitating completion surgery are encountered in up to 15% of TC patients subjected to LTT due to absent, inconclusive, or misleading FNAC, preoperatively. However, completion of thyroidectomy in this setting did not yield significant surgical morbidity. Primary LTT is a safer primary approach compared to TT in respect of RLN palsy and permanent hypoparathyroidism complication rates; therefore, primary TT should probably be reserved for lesions > 1 cm or even larger with suspicion for malignancy or malignant FNAC.
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DOI: 10.1007/s00423-024-03258-3
PMCID: PMC10876808

**The causal relationship between autoimmune thyroid disorders and telomere length: A Mendelian randomization and colocalization study**.
*Clin Endocrinol (Oxf)*, 100(3):294-303.
X. Liu, J. Yuan, S. Liu, X. Wang, M. Tang, X. Meng, Y. Li, Y. Chai, Y. Wang, G. Tian, X. Liu, H. Zhou, C. Kou, L. Zhang, Z. Yuan and H. Zhang. 2024.
This study aimed to evaluate whether there is a causal relationship between autoimmune thyroid disorders (AITDs) and telomere length (TL) in the European population and whether there is reverse causality. In this study, Mendelian randomization (MR) and colocalization analysis were conducted to assess the potential causal relationship between AITDs and TL using summary statistics from large-scale genome-wide association studies, followed by analysis of the relationship between TL and thyroid stimulating hormone and free thyroxine (FT4) to help interpret the findings. The inverse variance weighted (IVW) method was used to estimate the causal estimates. The weighted median, MR-Egger and leave-one-out methods were used as sensitivity analyses. The IVW method results showed a significant causal relationship between

autoimmune hyperthyroidism and TL (beta = -1.93 x 10(-2) ; p = 4.54 x 10(-5) ). There was no causal relationship between autoimmune hypothyroidism and TL (beta = -3.99 x 10(-3) ; p = 0.324). The results of the reverse MR analysis showed that genetically TL had a significant causal relationship on autoimmune hyperthyroidism (IVW: odds ratio (OR) = 0.49; p = 2.83 x 10(-4) ) and autoimmune hypothyroidism (IVW: OR = 0.86; p = 7.46 x 10(-3) ). Both horizontal pleiotropy and heterogeneity tests indicated the validity of our bidirectional MR study. Finally, colocalization analysis suggested that there were shared causal variants between autoimmune hyperthyroidism and TL, further highlighting the robustness of the results. In conclusion, autoimmune hyperthyroidism may accelerate telomere attrition, and telomere attrition is a causal factor for AITDs.
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DOI: 10.1111/cen.15004

**Current guidelines for the application of radiofrequency ablation for thyroid nodules: a narrative review**.
*Gland Surg*, 13(1):59-69.
M. S. Lui and K. N. Patel. 2024.
BACKGROUND AND OBJECTIVE: Thyroid nodules are frequently incidentally found on physical exam or imaging for an unrelated work-up. Although surgery remains the gold standard for treating symptomatic benign and/or malignant thyroid nodules, radiofrequency ablation (RFA) has emerged as a minimally invasive treatment option for high risk patients and those who decline surgery. The novel application of RFA to treat thyroid disease was originally described for symptomatic, benign thyroid nodules. Since then, several studies have tried to expand its indication to treat primary and recurrent well-differentiated thyroid cancer. The high success rates and the low complication profile, has allowed for quick adoption of RFA as a treatment option for well-selected patients with benign thyroid nodules and locoregional recurrent thyroid malignancy. As such, multidisciplinary guidelines and consensus statements were developed to standardize indications, techniques, outcome measures, and follow-up to ensure the best patient care. This article summarizes the current indications and recommendations to help guide clinicians on how best to effectively and safely utilize RFA to treat thyroid disease. METHODS: A PubMed/MEDLINE search between 2000-2022 using a combination of "radiofrequency ablation", "RFA", "thyroid nodule", and "guidelines" was conducted. The inclusion criteria were articles published in English which offered recommendations on RFA use for thyroid nodules. KEY CONTENT AND FINDINGS: For symptomatic, benign thyroid nodules, RFA is effective at significantly reducing nodule volume. For large nodules, multiple RFA sessions may be needed to achieve clinically significant volume reduction. Patients undergoing RFA for autonomously functioning thyroid nodules may see symptomatic relief but success rates are variable. RFA may serve a curative or palliative role in recurrent well-differentiated thyroid cancers. There is little data describing the use of RFA for primary well-differentiated thyroid cancer >1 cm and the role of RFA for thyroid microcarcinomas remains controversial. CONCLUSIONS: RFA is a safe minimally invasive technique and may be considered, in appropriate circumstances, a first-line treatment option for benign thyroid nodules. Practices adopting RFA will likely increase as more clinicians become familiar with this technique, highlighting the importance of developing standardized guidelines.
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DOI: 10.21037/gs-23-18
PMCID: PMC10839702

**Sexual dimorphism in medullary thyroid cancer aggressiveness**.
*Endocr Relat Cancer*, 31(3)
A. Machens, K. Lorenz, F. Weber and H. Dralle. 2024.
Thyroid cancer is the only nonreproductive cancer with striking female predominance, although men with thyroid cancer develop more aggressive disease. This study aimed to quantify sex-specific differences in medullary thyroid cancer (MTC) spread after controlling for primary thyroid tumor size. Included in this retrospective analysis were all patients with unilateral solitary MTC who underwent initial neck surgery at a tertiary referral center. A total of 565 patients, 255 men and 310 women, were identified, of whom 467 had sporadic and 98 hereditary MTC. When stratified by sex, and after correction for multiple testing, men had higher preoperative basal calcitonin levels (medians of 655 vs 181 pg/mL; P < 0.001), more frequent extrathyroid extension (25 vs 9%; P < 0.001) and node metastasis (53 vs 27%; P < 0.001) with more involved nodes (medians of 2 vs 0 nodes; P < 0.001) than women but achieved less often biochemical cure (53 vs 74%; P < 0.001). Although absent in patients with very small (</=5 mm) thyroid tumors, sex disparities were immediately apparent in patients with 5.1-40 mm (node metastasis and biochemical cure) and 10.1-40 mm (extrathyroid extension) large thyroid tumors but were lost in patients with thyroid tumors >40 mm as women caught up. Sex disparities were strongest for node metastasis with a 27-41% (overall 24.0%) point difference, followed by biochemical cure with a -15-35% (overall -20.3%) point difference and extrathyroid extension with a 17-24% (14.2% overall) point difference. These findings indicate

that the male predominance in MTC aggressiveness is largely biologically driven, warranting further research.
PubMed-ID: 38174975
DOI: 10.1530/ERC-23-0301

**Decreasing utilization for postoperative radiation therapy in locoregionally advanced medullary thyroid cancer**.
*Head Neck*, 46(2):328-35.
A. Maniakas, A. Sullivan, M. I. Hu, N. L. Busaidy, M. E. Cabanillas, R. Dadu, S. G. Waguespack, S. B. Fisher, P. H. Graham, N. D. Gross, E. G. Grubbs, N. D. Perrier, J. R. Wang, B. Gunn, A. S. Garden, R. Megahed, S. Navuluri, X. Li, M. D. Williams and M. Zafereo. 2024.
BACKGROUND: Use of postoperative radiation therapy (PORT) in locoregionally advanced medullary thyroid cancer (MTC) remains controversial. The objective was to evaluate the effect of PORT on locoregional control (LRC) and overall survival (OS). METHODS: Retrospective cohort study of 346 MTC patients separated into PORT and no-PORT cohorts. Relative indications for PORT, as well as changes in patterns of treatment, were recorded. RESULTS: 49/346 (14%) received PORT. PORT was associated with worse OS; adjusted HR = 2.0 (95%CI 1.3-3.3). PORT was not associated with improved LRC, even when adjusting for advanced stage (Stage III p = 0.892; Stage IV p = 0.101). PORT and targeted therapy were not associated with improved OS compared to targeted therapy alone; adjusted HR = 1.2 (95%CI 0.3-4.1). CONCLUSIONS: Use of PORT in MTC has decreased and its indications have become more selective, coinciding with the advent of effective targeted therapies. Overall, PORT was not associated with improved LRC or OS.
PubMed-ID: 38009416
DOI: 10.1002/hed.27584

**Thyrotoxicosis, not hyperthyroidism, is a frequent sequelae of parathyroidectomy**.
*Am J Surg*, 230:7-8.
C. R. McHenry. 2024.
PubMed-ID: 38087726
DOI: 10.1016/j.amjsurg.2023.11.023

**Outcomes of Patients With Graves Disease 25 Years After Initiating Antithyroid Drug Therapy**.
*J Clin Endocrinol Metab*, 109(3):827-36.
A. E. Meling Stokland, M. Austdal, B. G. Nedrebo, S. Carlsen, H. B. Hetland, L. Breivik, H. O. Ueland, T. Watt, P. K. Cramon, K. Lovas, E. S. Husebye and G. A. Ueland. 2024.
CONTEXT: Graves disease (GD) is a leading cause of hyperthyroidism. Detailed investigations and predictors of long-term outcomes are missing. OBJECTIVE: This work aimed to investigate the outcomes in GD 25 years after initiating antithyroid drug treatment, including disease course, clinical and biochemical predictors of relapse, and quality of life. METHODS: A retrospective follow-up was conducted of GD patients that participated in a randomized trial from 1997 to 2001. Demographic and clinical data were obtained from medical records and questionnaires. Biobank samples were analyzed for inflammatory biomarkers and compared with age- and sex-matched healthy individuals. RESULTS: We included 83% (182/218) of the patients from the original study. At the end of follow-up, normal thyroid function was achieved in 34%. The remaining had either active disease (1%), spontaneous hypothyroidism (13%), or had undergone ablative treatment with radioiodine (40%) or thyroidectomy (13%). Age younger than or equal to 40 years, thyroid eye disease (TED), smoking, and elevated levels of interleukin 6 and tumor necrosis factor receptor superfamily member 9 (TNFRS9) increased the risk of relapsing disease (odds ratio 3.22; 2.26; 2.21; 1.99; 2.36). At the end of treatment, CD40 was lower in patients who maintained normal thyroid function (P = .04). At the end of follow-up, 47% had one or more autoimmune diseases, including vitamin B12 deficiency (26%) and rheumatoid arthritis (5%). GD patients who developed hypothyroidism had reduced quality of life. CONCLUSION: Careful lifelong monitoring is indicated to detect recurrence, hypothyroidism, and other autoimmune diseases. Long-term ATD treatment emerges as a beneficial first-line treatment option, especially in patients with young age at onset or presence of TED.
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DOI: 10.1210/clinem/dgad538
PMCID: PMC10876387

**Contemporary trends in extent of surgery for differentiated thyroid cancer with extrathyroidal extension**.
*Am J Surg*, 228:173-9.
K. B. Montgomery, J. M. Fazendin, H. Chen and K. K. Broman. 2024.
OBJECTIVE: Although lobectomy is acceptable for patients with small, low-risk differentiated thyroid cancer (DTC), gross

extrathyroidal extension (ETE) remains an indication for total thyroidectomy (TT). Here we investigate evolving trends in extent of surgery for + ETE DTC. METHODS: Patients with +ETE DTC who underwent resection from 2010 to 2020 were identified using the National Cancer Database. The primary outcome was performance of TT versus lobectomy. RESULTS: Among 5851 patients, most were female (79.7%), white (80.0%), and had minimal ETE (91.8%). Ninety-two percent of patients received TT. Year of treatment was influential ($p < 0.001$), with increasing lobectomy rates in later years. On multivariable analyses, a decreased likelihood of TT was seen in years 2015 through 2020. CONCLUSIONS: Most patients with +ETE DTC underwent guideline-concordant TT, but lobectomy rates doubled over the study period. These findings may reflect increased preference for lobectomy in low-risk DTC, but could undertreat patients with high-risk features.
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DOI: 10.1016/j.amjsurg.2023.09.021
PMCID: PMC10922190

**The weepy cry - short neural signal bursts in intraoperative neuromonitoring**.
*Langenbecks Arch Surg*, 409(1):102.
P. C. B. Munk, M. E. Merkelbach and W. Lamade. 2024.
PURPOSE: This study aimed to establish an in-vitro alternative to existing in-vivo systems to analyze nerve dysfunction using continuous neuromonitoring (C-IONM). METHODS: Three hundred sixty-three recurrent laryngeal nerves (RLN) (N((pigs)) = 304, N((cattle)) = 59) from food industry cadavers were exposed by microsurgical dissection following euthanasia. After rinsing with Ringer's lactate, they were tempered at 22 degrees C. Signal evaluation using C-IONM was performed for 10 min at 2 min intervals, and traction forces of up to 2N were applied for a median time of 60 s. Based on their post-traumatic electrophysiological response, RLNs were classified into four groups: Group A: Amplitude >/= 100%, Group B: loss of function (LOS) 0-25%, Group C: >/= 25-50%, and Group D: > 50%. RESULTS: A viable in-vitro neuromonitoring system was established. The median post-traumatic amplitudes were 112%, 88%, 59%, and 9% in groups A, B, C, and D, respectively. A time-dependent further dynamic LOS was observed during the 10 min after cessation of strain. Surprisingly, following initial post-traumatic hyperconductivity, complete LOS occurred in up to 20% of the nerves in group A. The critical threshold for triggering LOS was 2N in all four groups, resulting in immediate paralysis of up to 51.4% of the nerves studied. CONCLUSION: Consistent with in-vivo studies, RLN exhibit significant intrinsic electrophysiological variability in response to tensile forces. Moreover, nerve damage progresses even after the complete cessation of strain. Up to 20% of nerves with transiently increased post-traumatic amplitudes above 100% developed complete LOS, which we termed the "weepy cry." This time-delayed response must be considered during the interpretation of C-IONM signals.
PubMed-ID: 38514480
DOI: 10.1007/s00423-024-03240-z
PMCID: PMC10957688

**Modified Radical Neck Dissection for Papillary Thyroid Carcinoma via a Combined Endoscopy Approach: The Transoral Approach and the Chest Approach**.
*Ann Surg Oncol*, 31(4):2357-8.
D. Q. Ngo, D. T. Le, Q. X. Ngo and Q. Van Le. 2024.
BACKGROUND: Recently, modified radical neck dissection (MRND) for papillary thyroid carcinoma (PTC) has been performed by the transoral endoscopic approach.(1) However, dissection of level II lymph nodes using only the transoral approach is highly difficult because of the inadequate axis of surgical view. Hence, we decided to combine the transoral and chest approaches to perform MRND. To the best of our knowledge, this is the first video case of MRND using the combined approach. PATIENT AND METHODS: A 35-year-old woman was diagnosed with cT1aN1bM0 right PTC (metastatic to right level III lymph nodes). The patient underwent total thyroidectomy, bilateral central neck dissection (CND), and right MRND via a combined endoscopic approach: the transoral and chest approaches. Total thyroidectomy and bilateral central neck dissection were performed via the transoral approach, similar to prior studies.(2-6) The chest approach can help the surgeon to perform level II and the transoral approach was used to dissect the lymph node of levels III and IV. RESULTS: The total time for total thyroidectomy, bilateral CND, and right MRND was 190 min. The time for MRND was 90 min. The number of harvested lymph nodes were 14 in the right lateral compartments, and the number of metastatic lymph nodes were 2 in the lateral compartments. There were no major postoperative complications. The patient was completely satisfied with the cosmetic result. CONCLUSIONS: The combined approach of the transoral and chest approaches was sufficient to perform total thyroidectomy and MRND for levels II, III, and IV.
PubMed-ID: 38198005
DOI: 10.1245/s10434-024-14899-5

**The Frequency of Differentiated Thyroid Cancer Recurrence in 2302 Patients With Excellent Response to Primary Therapy**.
*J Clin Endocrinol Metab*, 109(2):e569-e78.
I. Palyga, M. Rumian, A. Kosel, M. Albrzykowski, P. Krawczyk, A. Kalwat, D. Gasior-Perczak, A. Walczyk, A. Kuchareczko, J. Kopczynski, M. Chrapek, S. Gozdz and A. Kowalska. 2024.
CONTEXT: Discrepant data on the recurrence rate of differentiated thyroid cancer (DTC) are reported. OBJECTIVE: To evaluate the frequency and risk factors of true recurrence in DTC patients with excellent responses (ExR) to initial therapy. METHODS: A retrospective analysis of the 2302 consecutive DTC patients with ExR to primary therapy, treated during 24 years at single center. The percentage of recurrence and cumulative recurrence rate (CRR) were analyzed. Risk factors for recurrence for patients with papillary thyroid cancer (PTC) were investigated and methods for establishing a diagnosis of recurrence were evaluated. RESULTS: Of DTC patients, 32 (1.4%) experienced recurrence. PTC patients with recurrence were more likely to have younger age (P = .0182), larger tumor size (P = .0013), lymph node metastases (P = .0013), incomplete resection (P = .0446), higher ATA risk (P = .0002), and had more frequently been treated with 131I (P = .0203). CRRs at 5, 10, 15, 20, and 24 years after surgery were 1.2%, 1.9%, 2.5%, 2.9%, and 2.9%, respectively. The CRRs according to histological type were highest for poorly differentiated thyroid cancer (PDTC), lower for oncocytic (OTC) and follicular thyroid cancer (FTC), and lowest for PTC. Most recurrences occurred within the first 5 years of observation. The most effective method for detecting local recurrence was ultrasonography with fine needle aspiration cytology, and for distant metastases, 18F-FDG PET. CONCLUSION: True recurrence is rare in DTC patients. PTC patients with ExR to primary therapy and N0/Nx can be dismissed from oncological follow-up. Despite ExR to primary therapy, DTC patients with N1, and PDTC, OTC, FTC should remain under oncological follow-up.
PubMed-ID: 37768152
DOI: 10.1210/clinem/dgad571

**Comparison of postoperative pain between transoral and conventional thyroidectomy: a propensity score-matched analysis**.
*Surg Endosc*, 38(3):1512-22.
M. K. Park, V. C. Nguyen, E. Kim, C. M. Song, Y. B. Ji, J. H. Jeong and K. Tae. 2024.
BACKGROUND: The extent of postoperative pain following transoral thyroidectomy is not well-understood and remains a subject of debate. This study aims to analyze and compare postoperative pain levels between patients undergoing transoral and conventional transcervical thyroidectomy. METHODS: A prospective evaluation on postoperative pain was conducted in 310 patients undergoing conventional thyroidectomy and 194 undergoing transoral thyroidectomy. Pain levels were evaluated using the numerical rating scale (NRS, ranging from 0 to 10) through preoperative and postoperative questionnaires at specified time points: 1, 3, and 6 days, and 1 and 3 months following surgery. Propensity score-matched analysis was carried out based on six covariates: sex, age, body mass index, extent of thyroidectomy, tumor size, and central neck dissection. RESULTS: After propensity score matching based on the six covariates, 121 patient pairs were identified from each group. Within this matched cohort, postoperative pain scores significantly worsened 1 day after surgery but showed progressive recovery up to 3 months post-surgery in both groups. The transoral group exhibited higher postoperative pain scores than the conventional group from day 1 (4.43 +/- 2.6 vs. 3.11 +/- 2.5, $p < 0.001$) to day 6 (1.76 +/- 1.9 vs. 1.13 +/- 1.6, $p = 0.016$) post-surgery, with no significant difference noted at 1 month. Among transoral procedures, pain scores were significantly higher for the endoscopic approach compared to the robotic approach on days 1 (5.52 +/- 2.3 vs. 4.29 +/- 2.3, $p = 0.028$) and 3 (3.52 +/- 2.5 vs. 2.64 +/- 2.0, $p = 0.047$) post-surgery. CONCLUSIONS: Postoperative pain was significantly higher in transoral thyroidectomy compared to conventional thyroidectomy up to 6 days post-surgery. Within the transoral group, the robotic procedure resulted in lower pain levels than the endoscopic approach during the early postoperative period.
PubMed-ID: 38253696
DOI: 10.1007/s00464-023-10656-z

**Thyroid Cancer Polygenic Risk Score Improves Classification of Thyroid Nodules as Benign or Malignant**.
*J Clin Endocrinol Metab*, 109(2):402-12.
N. Pozdeyev, M. Dighe, M. Barrio, C. Raeburn, H. Smith, M. Fisher, S. Chavan, N. Rafaels, J. A. Shortt, M. Lin, M. G. Leu, T. Clark, C. Marshall, B. R. Haugen, D. Subramanian, K. Crooks, C. Gignoux and T. Cohen. 2024.
CONTEXT: Thyroid nodule ultrasound-based risk stratification schemas rely on the presence of high-risk sonographic features. However, some malignant thyroid nodules have benign appearance on thyroid ultrasound. New methods for thyroid nodule risk assessment are needed. OBJECTIVE: We investigated polygenic risk score (PRS) accounting for inherited thyroid cancer risk combined with ultrasound-based analysis for improved thyroid nodule risk assessment.

METHODS: The convolutional neural network classifier was trained on thyroid ultrasound still images and cine clips from 621 thyroid nodules. Phenome-wide association study (PheWAS) and PRS PheWAS were used to optimize PRS for distinguishing benign and malignant nodules. PRS was evaluated in 73 346 participants in the Colorado Center for Personalized Medicine Biobank. RESULTS: When the deep learning model output was combined with thyroid cancer PRS and genetic ancestry estimates, the area under the receiver operating characteristic curve (AUROC) of the benign vs malignant thyroid nodule classifier increased from 0.83 to 0.89 (DeLong, P value = .007). The combined deep learning and genetic classifier achieved a clinically relevant sensitivity of 0.95, 95% CI [0.88-0.99], specificity of 0.63 [0.55-0.70], and positive and negative predictive values of 0.47 [0.41-0.58] and 0.97 [0.92-0.99], respectively. AUROC improvement was consistent in European ancestry-stratified analysis (0.83 and 0.87 for deep learning and deep learning combined with PRS classifiers, respectively). Elevated PRS was associated with a greater risk of thyroid cancer structural disease recurrence (ordinal logistic regression, P value = .002). CONCLUSION: Augmenting ultrasound-based risk assessment with PRS improves diagnostic accuracy.
PubMed-ID: 37683082
DOI: 10.1210/clinem/dgad530

**Diagnostic performance of molecular testing in indeterminate (Bethesda III and IV) thyroid nodules with Hurthle cell cytology**.
*Surgery*, 175(1):221-7.
R. Raghunathan, X. R. Longstaff, E. G. Hughes, S. J. Li, V. R. Sant, C. H. Tseng, J. Rao, J. X. Wu, M. W. Yeh and M. J. Livhits. 2024.
BACKGROUND: Indeterminate thyroid nodules with Hurthle cell cytology remain a diagnostic challenge. The low benign call rate and positive predictive value of first-generation molecular tests precluded their use to rule out malignancy. We examined the diagnostic performance of current tests. METHOD: This subset analysis of our prospective randomized trial compared the benign call rate and positive predictive value of Afirma Gene Sequencing Classifier and Thyroseq v3 in Bethesda III and IV nodules with Hurthle cell cytology. Molecular test samples were obtained at initial fine-needle aspiration (8/2017-7/2022) and reflexively sent for processing. RESULTS: Molecular testing was performed on 140 Hurthle cell nodules. Of 79 nodules tested with the Afirma Gene Sequencing Classifier, the benign call rate was 84% (66/79). Nine of 66 nodules with benign results were resected, with no malignancies. Twelve of 13 nodules with suspicious results were resected, revealing 3 malignancies-2 papillary thyroid carcinomas and one Hurthle cell carcinoma (positive predictive value 25%). Of 61 nodules tested with Thyroseq v3, the benign call rate was 56% (34/61; (P < .01 versus Afirma Gene Sequencing Classifier). Five of 34 nodules with negative results were resected, with no malignancies. Nineteen of 27 nodules with positive results were resected, revealing 3 malignancies-2 papillary thyroid carcinomas and 1 Hurthle cell carcinoma (positive predictive value 16%). CONCLUSION: The high benign call rate of current molecular tests in Hurthle cell nodules strengthens their value in enabling patients to avoid surgery.
PubMed-ID: 37926582
DOI: 10.1016/j.surg.2023.05.046

**Hypoparathyroidism and mortality after total thyroidectomy: A nationwide matched cohort study**.
*Clin Endocrinol (Oxf)*, 100(4):408-15.
R. Reinke, S. Udholm, C. F. Christiansen, M. Almquist, S. Londero, L. Rejnmark, T. B. Rasmussen and L. Rolighed. 2024.
OBJECTIVE: Total thyroidectomy (TT) carries a risk of hypoparathyroidism (hypoPT). Recently, hypoPT has been associated with higher overall mortality rates. We aimed to evaluate the frequency of hypoPT and mortality in patients undergoing TT in Denmark covering 20 years. DESIGN: Retrospective Cohort study. PATIENTS AND MEASUREMENTS: Using population-based registries, we identified all Danish individuals who had undergone TT between January 1998 and December 2017. We included a comparison cohort by randomly selecting 10 citizens for each patient, matched on sex and birth year. HypoPT was defined as treatment with active vitamin D after 12 months postoperatively. We used cumulative incidence to calculate risks and Cox regression to compare the rate of mortality between patients and the comparison cohort. We evaluated patients in different comorbidity groups using the Charlson Comorbidity Index and by different indications for surgery. RESULTS: 7912 patients underwent TT in the period. The prevalence of hypoPT in the study period was 16.6%, 12 months postoperatively. After adjusting for potential confounders the risk of death due to any causes (hazard ratio; 95% confidence intervals) following TT was significantly increased (1.34; 1.15-1.56) for patients who developed hypoPT. However, subgroup analysis revealed mortality was only increased in malignancy cases (2.48; 1.99-3.10) whereas mortality was not increased when surgery was due to benign indications such as goitre (0.88; 0.68-1.15) or thyrotoxicosis (0.86; 0.57-1.28). CONCLUSIONS: The use of active vitamin D for hypoPT was prevalent one year after TT. Patients with hypoPT did not have an increased risk of mortality following TT unless the indication was due to malignancy.

PubMed-ID: 38375986
DOI: 10.1111/cen.15037

**Radiofrequency ablation of benign thyroid nodules: A prospective, multi-institutional North American experience**.
*Surgery*, 175(1):139-45.
J. O. Russell, D. D. Desai, J. E. Noel, M. Hussein, E. Toraih, S. Seo, S. Wolfe, M. Omar, P. Issa, L. A. Orloff, R. P. Tufano and E. Kandil. 2024.
BACKGROUND: Radiofrequency ablation for benign thyroid nodules aims to achieve a volume reduction rate of >/=50%. However, factors that predict treatment success have not been defined in a large-scale study. METHODS: A prospective cohort study of biopsy-proven benign thyroid nodules treated with radiofrequency ablation at 3 institutions was performed. Patient demographics, nodule sonographic features, procedural data, and nodule volume reduction were evaluated. Binary logistic regression analysis was performed to identify features associated with treatment response. RESULTS: A total of 620 nodules were analyzed. The pooled median volume reduction rate at 12 months was 70.9% (interquartile range 52.9-86.6). At 1 year follow-up, 78.4% of nodules reached treatment success with a volume reduction rate >/=50%. The overall complication rate was 3.2% and included temporary voice changes (n = 14), vasovagal episodes (n = 5), nodule rupture (n = 3), and lightheadedness (n = 2). No permanent voice changes occurred. Four patients developed postprocedural hypothyroidism. Large baseline nodule volume (>20 mL) was associated with a lower rate of successful volume reduction (odds ratio 0.60 [0.37-0.976]). Large nodules achieved treatment success by 12-month follow-up at a rate of 64.5%, compared with 81.4% for small nodules and 87.2% for medium nodules. CONCLUSION: To our knowledge, this is the largest North American cohort of patients with benign thyroid nodules treated with radiofrequency ablation. Overall, radiofrequency ablation was an effective treatment option with a low risk of procedural complications. Large volume nodules (>20 mL) may be associated with a lower rate of successful reduction with radiofrequency ablation treatment.
PubMed-ID: 37953141
DOI: 10.1016/j.surg.2023.07.046

**Selpercatinib Before Surgery for the Treatment of RET-Altered Thyroid Cancers**.
*Ann Surg Oncol*, 31(4):2202-3.
A. L. Sarvestani, J. Lambdin, M. Hu, M. Cabanillas, S. G. Waguespack, J. M. Hernandez and M. E. Zafereo. 2024.
PubMed-ID: 38245643
DOI: 10.1245/s10434-023-14854-w

**Development of a tool to calculate the probability of hypocalcemia after total thyroidectomy: a prospective study**.
*Langenbecks Arch Surg*, 409(1):33.
C. S. P. Soares, K. H. Koga, S. M. Moriguchi, S. A. Terra, J. V. Tagliarini, P. H. D. de Vasconcelos Affonso, M. da Silva Pechutti and G. M. F. da Silva Mazeto. 2024.
PURPOSE: This study aimed to evaluate the ability of the percentage of decrease in serum PTH level in the first 8 h after total thyroidectomy (TT) to predict hypocalcemia requiring Ca supplementation and develop a tool to predict it. METHODS: 97 patients who underwent TT with measurement of preoperative parathyroid hormone (PTH) levels were prospectively evaluated 1 and 8 h after TT; postoperative magnesium (Mg2PO) and phosphorus levels were evaluated on the 2nd day after surgery. The percentage of decrease in PTH level 1 h (%dPTH1h) and 8 h (%dPTH8h) postoperatively and predictors of hypocalcemia requiring Ca supplementation were evaluated and an equation was developed to predict this outcome. RESULTS: %dPTH1h ($p = 0.002$), %dPTH8h ($p = 0.001$) and (Mg2PO) ($p < 0.01$) were isolated predictors of postoperative hypocalcemia requiring Ca supplementation. The data obtained led to the development of two tools to predict this complication. CONCLUSIONS: The percentage of decrease in PTH level 1 h and 8 h postoperatively and the magnesium level on the 2nd day after surgery were predictors of more severe hypocalcemia, and an auxiliary tool for predicting this complication was developed.
PubMed-ID: 38195723
DOI: 10.1007/s00423-024-03229-8

**Medullary Thyroid Carcinoma: Why are One in Four Patients Treated Out of Concordance from the ATA Guidelines?**
*Ann Surg Oncol*, 31(2):709-10.
T. Szabo Yamashita and E. G. Grubbs. 2024.
PubMed-ID: 38032463
DOI: 10.1245/s10434-023-13249-1

**ASO Author Reflections: The Role of Surgery in the Precise Treatment of Primary Thyroid Lymphoma**.
*Ann Surg Oncol*, 31(3):1522.
Y. Tang, T. Yan and Z. Yang. 2024.
PubMed-ID: 38071717
DOI: 10.1245/s10434-023-14644-4

**Subgroup analysis of steadily increased trends in medullary thyroid carcinoma incidence and mortality in the USA, 2000-2020: a population-based retrospective cohort study**.
*Endocr Relat Cancer*, 31(5)
Z. Tao, X. Deng, B. Guo, Z. Ding and Y. Fan. 2024.
The incidence rate of medullary thyroid carcinoma (MTC) continues to grow, along with its mortality rate in the USA. However, the subgroup trends in MTC have not yet been established. This population-based retrospective cohort study was based on the Surveillance, Epidemiology, and End Results (SEER) 17/12 registry database. Subgroup analysis was performed through clinicopathological and treatment-related characteristics. Annual average percentage change (AAPC) was calculated using joinpoint regression analysis. A total of 3833 MTC patients and 536 death cases were diagnosed in the SEER database. Between 2000 and 2019, the incidence (AAPC = 1.64) and mortality (AAPC = 3.46) rates of MTC continued to rise. Subgroup analysis showed the proportion of elderly patients (65-84 years) gradually increased in incidence between 2000 and 2020. Patients with early-stage tumors, such as tumors </=20 mm, showed the same trends. Aspects of treatment, the implementation rate of total thyroidectomy (AAPC = 0.38) and lymph node dissection (AAPC = 1.06) also increased persistently in almost all of the age subgroups. The incidence and mortality of MTC consistently increased from 2000 to 2019. Subgroup analysis indicated a significant increase in elderly patients and early-stage patients, and more attention should be paid to the management of these increased subgroups.
PubMed-ID: 38376827
DOI: 10.1530/ERC-23-0319
PMCID: PMC11046345

**ATA risk stratification in papillary thyroid microcarcinoma has low positive predictive value when identifying recurrence**.
*Am J Surg*, 229:106-10.
A. Tran, R. J. Weigel and A. C. Beck. 2024.
BACKGROUND: Rising incidence of papillary thyroid microcarcinomas (PTMC) has raised concerns for overdiagnosis. Utility of the American Thyroid Association Risk Stratification System (ATA-RSS) 2015 in predicting risk of disease recurrence in patients with PTMC was assessed. METHODS: Electronic health records of patients who underwent total thyroidectomy were queried. ATA-RSS 2015 risk stratification was performed on those with PTMC, and validity for predicting disease recurrence was calculated. RESULTS: With 10-year median follow up, recurrence was higher in PTMC patients with high/intermediate vs low ATA risk (33 % vs 4 %, p = 0.002). Sensitivity of ATA-RSS for detecting recurrence was 60 %, specificity 90 %, PPV 33.3 %, NPV 96.6 %, and accuracy 88 %. When microscopic extrathyroidal extension (ETE) was excluded as an intermediate risk criterion, PPV improved to 50 % and accuracy improved to 92.5 % CONCLUSIONS: ATA-RSS 2015 predicts recurrence in PTMC with high NPV but low PPV. Exclusion of microscopic ETE improved PPV, which may help prevent overtreatment.
PubMed-ID: 37968147
DOI: 10.1016/j.amjsurg.2023.11.003

**Regional Collaboration and Trends in Clinical Management of Thyroid Cancer**.
*Otolaryngol Head Neck Surg*, 170(1):159-68.
S. P. J. van Dijk, H. I. Coerts, I. Loncar, C. M. J. van Kinschot, E. M. von Meyenfeldt, W. Edward Visser, C. van Noord, H. F. Zengerink, M. R. J. Ten Broek, C. Verhoef, R. P. Peeters and T. M. van Ginhoven. 2024.
OBJECTIVE: This study examines the trends in the management of thyroid cancer and clinical outcomes in the Southwestern region of The Netherlands from 2010 to 2021, where a regional collaborative network has been implemented in January 2016. STUDY DESIGN: Retrospective cohort study. SETTING: This study encompasses all patients diagnosed with thyroid cancer of any subtype between January 2010 and June 2021 in 10 collaborating hospitals in the Southwestern region of The Netherlands. METHODS: The primary outcome of this study was the occurrence of postoperative complications. Secondary outcomes were trends in surgical management, centralization, and waiting times of patients with thyroid cancer. RESULTS: This study included 1186 patients with thyroid cancer. Median follow-up was 58

[interquartile range: 24-95] months. Surgery was performed in 1027 (86.6%) patients. No differences in postoperative complications, such as long-term hypoparathyroidism, permanent recurrent nerve paresis, or reoperation due to bleeding were seen over time. The percentage of patients with low-risk papillary thyroid carcinoma referred to the academic hospital decreased from 85% (n = 120/142) in 2010 to 2013 to 70% (n = 120/171) in 2014 to 2017 and 62% (n = 100/162) in 2018 to 2021 (P < .01). The percentage of patients undergoing a hemithyroidectomy alone was 9% (n = 28/323) in 2010 to 2013 and increased to 20% (n = 63/317; P < .01) in 2018 to 2021. CONCLUSION: The establishment of a regional oncological network coincided with a de-escalation of thyroid cancer treatment and centralization of complex patients and interventions. However, no differences in postoperative complications over time were observed. Determining the impact of regional oncological networks on quality of care is challenging in the absence of uniform quality indicators.
PubMed-ID: 37595096
DOI: 10.1002/ohn.481

**Retracting the thyroid matters: Who develops asymptomatic transient thyrotoxicosis after parathyroidectomy**.
*Am J Surg*, 230:9-13.
R. Wang, G. Stidham, K. Lovell, J. L. McMullin, A. Gillis, J. Fazendin, B. Lindeman and H. Chen. 2024.
BACKGROUND: Hyperthyroidism after parathyroidectomy is not a well-understood complication. We sought to determine the incidence and risk factors of hyperthyroidism after parathyroidectomy. MATERIALS AND METHODS: This is a prospective study of 91 patients undergoing parathyroidectomy. Pre- and post-operative thyroid-stimulating hormone(TSH) and free thyroxine(T4) levels at two-week follow-ups were collected. Bivariate analyses were conducted to compare demographics, laboratory results, and intraoperative findings between patients with normal and suppressed post-parathyroidectomy TSH. RESULTS: Twenty-two(24.2 %) patients had suppressed TSH after parathyroidectomy and 2(2.2 %) reported symptoms of hyperthyroidism. All hyperthyroidism resolved within 6 weeks. No patients required medical treatment. Compared to the normal TSH group, the suppressed TSH group had significantly more bilateral explorations(91.0 % vs. 58.0 %, p = 0.006), and superior parathyroid resections(95.5 % vs. 65.2 %, p = 0.006). CONCLUSION: Transient hyperthyroidism is common following parathyroidectomy, which is likely associated with intraoperative thyroid manipulation. Gentle retraction of thyroid glands in parathyroidectomy is warranted, especially during superior parathyroid gland resection.
PubMed-ID: 38296712
DOI: 10.1016/j.amjsurg.2024.01.014

**Graves' disease: Unveiling a novel etiology of secondary hyperparathyroidism**.
*Am J Surg*, 229:182-3.
C. Wu, P. Zmijewski, R. Akhund, Z. Song, A. Allahwasaya, M. A. Murcy, J. Fazendin, B. Lindeman, A. Gillis and H. Chen. 2024.
PubMed-ID: 37957045
DOI: 10.1016/j.amjsurg.2023.10.041

**Pregnancy and Progression of Differentiated Thyroid Cancer: A Propensity Score-Matched Retrospective Cohort Study**.
*J Clin Endocrinol Metab*, 109(3):837-43.
W. C. Xiao, X. Li, R. Shan, F. Mei, S. B. Song, J. Chen, B. K. Sun, C. H. Yuan and Z. Liu. 2024.
CONTEXT AND OBJECTIVE: Differentiated thyroid cancer (DTC) is very common in women of reproductive age. However, it remains unclear whether pregnancy is associated with DTC progression before surgical treatment. METHODS: This retrospective cohort study, conducted at the Peking University Third Hospital in Beijing, China between January 2012 and December 2022, included 311 eligible women aged 20 to 45 years. To control for potential confounders, we first used propensity score matching (PSM) to match the pregnant group (n = 48) with the nonpregnant group (n = 154) on age, tumor size, tumor type, and Hashimoto's thyroiditis status at baseline, and then used Cox proportional risk models stratified by the matched pairs to estimate the association of pregnancy with DTC progression. RESULTS: After PSM, the pregnant and nonpregnant groups were well comparable at baseline (standardized difference < 10% and P > .05). Over an average observation period of 2.5 years, we observed no difference between the pregnant group and the matched nonpregnant group in DTC progression-free survival (hazard ratio [HR] = 0.96; 95% CI, 0.56 to 1.65; P = .895), tumor enlargement-free survival (HR = 0.99; 95% CI, 0.56 to 1.76; P = .969) or lymph node metastasis-free survival (LNM) (HR = 0.67; 95% CI, 0.21 to 2.13; P = .498). The postoperative pathological characteristics also showed no significant difference between the pregnant and nonpregnant groups (P > .05). CONCLUSION: Pregnancy seemed to be irrelevant to DTC progression-free survival before surgical treatment. Further prospective cohort studies are needed to translate this finding into clinical practice.

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DOI: 10.1210/clinem/dgad557

**Long-term impact of prophylactic central neck dissection in non-invasive classic papillary thyroid carcinoma**.
*Eur J Surg Oncol*, 50(1):107305.
Z. Xu, Z. Mao, S. Chen, Z. Mo, J. Zhou, Z. Chen, R. Zarnegar, T. J. Fahey Iii, W. Wang and L. Teng. 2024.
BACKGROUND: The utilization of prophylactic central neck dissection (pCND) in cases of non-invasive clinical node-negative (cN0) papillary thyroid carcinoma (PTC) remains a topic of debate, with a dearth of long-term evidence. MATERIALS AND METHODS: We retrospectively reviewed 1181 cN0 PTC patients from 1997 to 2011. Of these, 641 underwent pCND (pCND + group) and 540 did not (pCND-group). Propensity score matching (PSM) was used to identify similar patients. Event-free survival and long-term complications including permanent hyperparathyroidism and permanent recurrent laryngeal nerve (RLN) paralysis were analyzed after PSM. RESULTS: The pCND + group had more aggressive characteristics. In the matched cohort after PSM, the 5-year, 10-year, and 15-year EFS rates were 98.9 %, 98.2 %, and 97.1 % for the pCND + group, and 97.7 %, 97.1 %, and 97.1 % for the pCND-group, respectively. There was no statistically significant difference in EFS rates between the two groups (Log Rank P = 0.38). There was no statistically significant difference in the incidence of permanent hyperparathyroidism (3.3 % vs. 1.5 %, P = 0.08) and permanent RLN paralysis (1.7 % vs. 0.9 %, P = 0.13) between the pCND+ and pCND- groups. CONCLUSION: Our study, with a median follow-up duration of 107 months, indicates that pCND does not lead to a significant reduction in nodal recurrence among non-invasive cN0 PTC patients.
PubMed-ID: 38070466
DOI: 10.1016/j.ejso.2023.107305

**IRS1 promotes thyroid cancer metastasis through EMT and PI3K/AKT pathways**.
*Clin Endocrinol (Oxf)*, 100(3):284-93.
F. Yu, D. Huang, Y. Kuang, J. Dong, Q. Han, J. Zhou and X. Teng. 2024.
OBJECTIVE: Insulin receptor substract 1 (IRS1) protein is an important signal transduction adapter for extracellular signal transduction from insulin-like growth factor-1 receptor and its family members to IRS1 downstream proteins. IRS1 has been reported to be involved in tumourigenesis and metastasis in some of solid tumors. Investigating the role of IRS1 in thyroid cancer can help to screen high risk patients at the initial diagnosis. DESIGN, PATIENTS AND MEASUREMENTS: Immunohistochemical assay was used to detect the expression levels of IRS1 in 131 metastatic thyroid cancer tissues. Wound healing, cell invasion and colony formation assays were used to study the functions of IRS1 in vitro. RNA sequencing (RNA-seq) and Western blot analysis analyses were performed to examine the underlying regulation mechanisms of IRS1 in thyroid cancer cells. RESULTS: IRS1 was highly expressed in thyroid cancers and its expression was positively associated with distant metastasis and advanced clinical stages. In vitro studies demonstrated that IRS1 is an important mediator of migration, invasion and colony formation of thyroid cancer cells. RNA-seq showed that IRS1 promoted the metastasis of thyroid cancer by regulating epithelial-mesenchymal transition and phosphoinositide 3-kinase (PI3K)/AKT pathway. CONCLUSIONS: IRS1 overexpression contributes to the aggressiveness of thyroid cancer and is expected to be a stratified marker and a potential therapeutic target for thyroid cancer.
PubMed-ID: 38172081
DOI: 10.1111/cen.15005

**Gasless Single-Incision Endoscopic Surgery via Subclavicular Approach for Lateral Neck Dissection in Patients with Papillary Thyroid Cancer**.
*Ann Surg Oncol*, 31(3):1498-508.
G. Zheng, W. Ding, X. Liu, Y. Liu, H. Sun, X. Song and H. Zheng. 2024.
BACKGROUND: The technical difficulties and trauma of remote access methods in endoscopic surgery (ES) for lateral neck dissection (LND) can be daunting for most patients with papillary thyroid cancer (PTC) and surgeons. The purpose of study was to introduce gasless single-incision ES via a subclavicular approach (ESSA) and to explore its safety and efficacy for LND. METHODS: Between January 2022 and February 2023, we retrospectively reviewed 17 patients with PTC who underwent ESSA for LND. In addition, 22 patients who received video-assisted ES (VAES) and 48 patients who underwent open surgery (OP) for LND during the same period were included. Clinicopathological characteristics, complications, and efficacy of the lymph node yield (LNY) were compared between the ESSA and the other two groups (VAES and OP). RESULTS: The LNY from central and lateral neck dissection by ESSA was comparable to that by VAES (9.2 +/- 8.1 vs. 9.5 +/- 4.2, P = 0.986, and 33.5 +/- 11.6 vs. 30.6 +/- 9.2, P = 0.382, respectively) and OP (9.2 +/- 8.1 vs. 11.0 +/- 5.4, P = 0.420, and 33.5 +/- 11.6 vs. 31.5 +/- 7.9, P = 0.383, respectively). Swallowing impairment scores at 1 and 3 months were significantly

lower after ESSA than those after VAES (1.8 +/- 1.0 vs. 3.0 +/- 1.2, P = 0.003, and 0.9 +/- 0.8 vs. 1.7 +/- 0.8, P = 0.006, respectively). The cosmetic satisfaction rate 1 month after surgery was significantly higher in the ESSA group than that in the VAES group (100 vs. 31.8%, P < 0.001). CONCLUSIONS: ESSA is a safe and minimally invasive procedure that provides a scarless cervical appearance and has good efficacy for LND. Therefore, ESSA may be a feasible choice for selected patients with N1b PTC with cervical cosmetic needs.
PubMed-ID: 38099992
DOI: 10.1245/s10434-023-14639-1

**ASO Author Reflections: A Promising Approach of Endoscopic Surgery for Lateral Neck Dissection in Patients with N1b Papillary Thyroid Cancer**.
*Ann Surg Oncol*, 31(3):1521.
G. Zheng, H. Zheng and X. Song. 2024.
PubMed-ID: 38105380
DOI: 10.1245/s10434-023-14725-4

# Parathyroids

## Meta-Analyses

**Management of Postthyroidectomy Hypoparathyroidism and Its Effect on Hypocalcemia-Related Complications: A Meta-Analysis**.
*Otolaryngol Head Neck Surg*, 170(2):359-72.
S. P. J. van Dijk, M. H. E. van Driel, C. M. J. van Kinschot, M. F. M. Engel, G. J. H. Franssen, C. van Noord, W. E. Visser, C. Verhoef, R. P. Peeters and T. M. van Ginhoven. 2024.
OBJECTIVE: The aim of this Meta-analysis is to evaluate the impact of different treatment strategies for early postoperative hypoparathyroidism on hypocalcemia-related complications and long-term hypoparathyroidism. DATA SOURCES: Embase.com, MEDLINE, Web of Science Core Collection, Cochrane Central Register of Controlled Trials, and the top 100 references of Google Scholar were searched to September 20, 2022. REVIEW METHODS: Articles reporting on adult patients who underwent total thyroidectomy which specified a treatment strategy for postthyroidectomy hypoparathyroidism were included. Random effect models were applied to obtain pooled proportions and 95% confidence intervals. Primary outcome was the occurrence of major hypocalcemia-related complications. Secondary outcome was long-term hypoparathyroidism. RESULTS: Sixty-six studies comprising 67 treatment protocols and 51,096 patients were included in this Meta-analysis. In 8 protocols (3806 patients), routine calcium and/or active vitamin D medication was given to all patients directly after thyroidectomy. In 49 protocols (44,012 patients), calcium and/or active vitamin D medication was only given to patients with biochemically proven postthyroidectomy hypoparathyroidism. In 10 protocols (3278 patients), calcium and/or active vitamin D supplementation was only initiated in case of clinical symptoms of hypocalcemia. No patient had a major complication due to postoperative hypocalcemia. The pooled proportion of long-term hypoparathyroidism was 2.4% (95% confidence interval, 1.9-3.0). There was no significant difference in the incidence of long-term hypoparathyroidism between the 3 supplementation groups. CONCLUSIONS: All treatment strategies for postoperative hypocalcemia prevent major complications of hypocalcemia. The early postoperative treatment protocol for postthyroidectomy hypoparathyroidism does not seem to influence recovery of parathyroid function in the long term.
PubMed-ID: 38013484
DOI: 10.1002/ohn.594

## Randomized controlled trials

*- None -*

## Consensus Statements/Guidelines

**Primary hyperparathyroidism in adults-(Part I) assessment and medical management: Position statement of the endocrine society of Australia, the Australian & New Zealand endocrine surgeons, and the Australian & New Zealand bone and mineral society**.
*Clin Endocrinol (Oxf)*, 100(1):3-18.
F. Milat, S. K. Ramchand, M. Herath, J. Gundara, S. Harper, S. Farrell, C. M. Girgis, R. Clifton-Bligh, H. G. Schneider, S. M. C. De Sousa, A. J. Gill, J. Serpell, K. Taubman, J. Christie, R. W. Carroll, J. A. Miller and M. Grossmann. 2024.
OBJECTIVE: To formulate clinical consensus recommendations on the presentation, assessment, and management of primary hyperparathyroidism (PHPT) in adults. METHODS: Representatives from relevant Australian and New Zealand Societies used a systematic approach for adaptation of guidelines (ADAPTE) to derive an evidence-informed position statement addressing nine key questions. RESULTS: PHPT is a biochemical diagnosis. Serum calcium should be measured in patients with suggestive symptoms, reduced bone mineral density or minimal trauma fractures, and in those with renal stones. Other indications are detailed in the manuscript. In patients with hypercalcaemia, intact parathyroid hormone, 25-hydroxy vitamin D, phosphate, and renal function should be measured. In established PHPT, assessment of bone mineral density, vertebral fractures, urinary tract calculi/nephrocalcinosis and quantification of urinary calcium excretion is warranted. Parathyroidectomy is the only definitive treatment and is warranted for all symptomatic patients and should

be considered for asymptomatic patients without contraindications to surgery and with >10 years life expectancy. In patients who do not undergo surgery, we recommend annual evaluation for disease progression. Where the diagnosis is not clear or the risk-benefit ratio is not obvious, multidisciplinary discussion and formulation of a consensus management plan is appropriate. Genetic testing for familial hyperparathyroidism is recommended in selected patients. CONCLUSIONS: These clinical consensus recommendations were developed to provide clinicians with contemporary guidance on the assessment and management of PHPT in adults. It is anticipated that improved health outcomes for individuals and the population will be achieved at a decreased cost to the community.
PubMed-ID: 34931708
DOI: 10.1111/cen.14659

## Other Articles

**Near-Infrared Autofluorescence Identification of Ectopic Parathyroid Lesions**.
*Laryngoscope*, 134(1):496-500.
K. Abe, T. Takahashi, Y. Yokoyama, R. Shodo, Y. Ueki, K. Yamazaki and A. Horii. 2024.
Ectopic parathyroid lesions can be difficult to detect. In the present study, we used near-infrared autofluorescence imaging (NIFI) in three cases of ectopic parathyroid lesions. Our results suggest that NIFI may be a confirmation tool for parathyroid pathology and an intraoperative navigation tool in vivo and ex vivo. Laryngoscope, 134:496-500, 2024.
PubMed-ID: 37140028
DOI: 10.1002/lary.30728

**Predictive Risk Score for Postparathyroidectomy Hungry Bone Syndrome in Patients With Secondary Hyperparathyroidism**.
*J Clin Endocrinol Metab*, 109(3):603-10.
W. Amjad, S. P. Ginzberg, J. E. Passman, J. Heintz, R. R. Kelz and H. Wachtel. 2024.
PURPOSE: Secondary hyperparathyroidism (SHPT) frequently affects patients with end-stage renal disease. Hungry bone syndrome (HBS) is a common complication among patients who undergo parathyroidectomy for SHPT and may cause prolonged hospitalization or require intensive care. The objective of this study is to develop a scoring system to stratify patients according to their risk of developing HBS. METHODS: A retrospective cohort study was performed using the US Renal Data System (2010-2021). Univariable and multivariable logistic regression models were developed and weighted beta-coefficients from the multivariable model were used to construct a risk score for the development of HBS. Positive and negative predictive values were assessed. RESULTS: Of 17 074 patients who underwent parathyroidectomy for SHPT, 19.4% developed HBS. Intensive care unit admission was more common in patients who developed HBS (33.5% vs 24.6%, $P < .001$). On multivariable logistic regression analysis, younger age, renal osteodystrophy, longer duration of dialysis, longer duration of kidney transplant, and higher Elixhauser score were significantly associated with HBS. A risk score based on these clinical factors was developed, with a total of 6 possible points. Rates of HBS ranged from 8% in patients with 0 points to 44% in patients with 6 points. The risk score had a poor positive predictive value (20.3%) but excellent negative predictive value (89.3%) for HBS. CONCLUSION: We developed a weighted risk score that effectively stratifies patients by risk for developing HBS after parathyroidectomy. This tool can be used to counsel patients and to identify patients who may not require postoperative hospitalization.
PubMed-ID: 37897423
DOI: 10.1210/clinem/dgad636

**Outcomes of subtotal parathyroidectomy for renal hyperparathyroidism**.
*Surgery*, 175(3):788-93.
K. A. Baugh, L. Yip, K. M. Ramonell, S. E. Carty and K. L. McCoy. 2024.
BACKGROUND: Renal hyperparathyroidism due to end-stage kidney disease is associated with considerable morbidity, and when refractory is treated with parathyroidectomy. Recurrent renal hyperparathyroidism is a major surgical complication, yet initial target parathyroid remnant size and outcomes, including rates of recurrence are not well elucidated. METHODS: This is a single-institution retrospective cohort study of patients who underwent initial subtotal parathyroidectomy for renal hyperparathyroidism on dialysis, from 1990-2022. The subtotal parathyroidectomy was defined as resection of 3 parathyroid glands +/- partial resection of the fourth gland leaving a remnant of approximately 75-100 mg, and postresection intraoperative parathyroid hormone goal was 150-250 pg/mL. Clinical data were examined for outcomes.

RESULTS: Among 204 patients who met inclusion criteria, 139 (68%) had follow-up data; 58% (80/139) were women and median age was 45 years. Surgical complications included 2 hematomas (1.4%), 1 recurrent laryngeal nerve injury (<1%), and no patient required readmission for intravenous calcium. Using a target remnant size of 75-100 mg, recurrent renal hyperparathyroidism was uncommon (14/139, 10%) and arose at a median interval of 58.6 months (range, 8-180). In cases of recurrence, the postresection intraoperative parathyroid hormone level was less likely to drop <250 pg/mL (40%, 4/10 vs nonrecurrence 65%, 80/123; P = .11) with a slightly lower median decrease (70% vs 81% in nonrecurrence, P = .8); however, neither were significant. Recurrence did not occur in the 19 patients who later received kidney transplantation (P = .2). CONCLUSION: In subtotal parathyroidectomy for renal hyperparathyroidism, use of a target 75-100 mg remnant size results in low complication rates. Durable cure appears to be more likely with renal transplantation.
PubMed-ID: 37945480
DOI: 10.1016/j.surg.2023.09.016

**Lithium-associated primary hyperparathyroidism:: An evaluation of screening and referral patterns in a southeastern veteran population**.
*Surgery*, 175(1):187-92.
L. E. Hendrick, A. M. Fleming, J. W. Sullivan, L. S. Usdan, R. D. Childress, H. Oktaei, S. R. Kode, P. V. Dickson and O. M. DeLozier. 2024.
BACKGROUND: Long-term lithium therapy has a well-established but under-recognized association with primary hyperparathyroidism. Rates of hypercalcemia, screening for primary hyperparathyroidism, and referral for parathyroidectomy were evaluated among United States veterans on long-term lithium therapy. METHODS: Patients undergoing chronic long-term lithium therapy (>12 months) were identified from 1999 to 2022. Demographics, long-term lithium therapy duration, post-treatment calcium, parathyroid hormone, creatinine, and vitamin D levels were abstracted. Rates of screening for hypercalcemia (calcium >/=10.2 mg/dL), primary hyperparathyroidism (parathyroid hormone >/=30 pg/mL in the setting of hypercalcemia), referral for parathyroidectomy, and outcomes were evaluated. RESULTS: A total of 1,356 patients underwent long-term lithium therapy, 514 of whom received chronic long-term lithium therapy. Baseline characteristics of patients with and without post-treatment hypercalcemia were compared. Of 148 patients with post-treatment hypercalcemia, 112 (74.7%) underwent no further evaluation for primary hyperparathyroidism, while 36 (25.3%) patients had a parathyroid hormone level recorded. Although 33 (91.7%) hypercalcemic patients screened positive for primary hyperparathyroidism, only 5 (13%) were referred for parathyroidectomy. Of the 4 patients who underwent parathyroidectomy, mean calcium was 11.2 mg/dL (range 11.1-11.4), and mean parathyroid hormone was 272 pg/mL (range 108-622). Three patients were localized on preoperative imaging, 2 of whom underwent unilateral exploration with cure, with 1 experiencing recurrence at 31 months. The remaining patient who localized preoperatively underwent bilateral exploration and had 2 ipsilateral glands resected and persistence. The patient who did not localize preoperatively underwent bilateral exploration with 3 gland resection and cure. CONCLUSIONS: Screening for primary hyperparathyroidism and referral for parathyroidectomy are underutilized in United States veterans undergoing chronic long-term lithium therapy. Institutional protocols to standardize screening, surveillance, and referrals to endocrinology/endocrine surgery could benefit this population at increased risk for primary hyperparathyroidism.
PubMed-ID: 37925259
DOI: 10.1016/j.surg.2023.04.069

**Sonographic Features of Atypical and Initially Missed Parathyroid Adenomas: Lessons Learned From a Single-Center Cohort**.
*J Clin Endocrinol Metab*, 109(2):439-48.
S. Ilgan, B. I. Aydogan, O. Emer, C. Anil, A. Gursoy, M. Cesur and B. Bilezikci. 2024.
CONTEXT: Awareness of typical and atypical ultrasonographic (US) features of parathyroid adenomas (PAs) is crucial since US is the most widely used first-line imaging modality. OBJECTIVE: The purpose of this study was to describe the atypical features of PAs on US and other possible factors leading to a false negative examination in a large single-center cohort. MATERIALS AND METHODS: The US records of 457 PAs in 445 patients with biochemically proven primary hyperparathyroidism (PHPT) were evaluated in a prospectively maintained database. Atypical size, composition, shape, echogenicity, location, and vascular pattern on US were noted. For patients who previously had at least one negative US examination in referring centers, the main possible reason was defined accordingly. RESULTS: The study group included 359 female and 86 male patients with PHPT. Typical sonographic features were observed in 231 PAs (51%), whereas 226 (49%) had at least one atypical US feature. The most common atypical features were atypical size (29%), followed by atypical echogenicity (19%), shape (8%), location (7%), and composition (7%), respectively. There were 122 initially missed PAs in all groups. The most frequent main atypical US features leading to false negative examinations were atypical size

(22.1%) and atypical location (18.8%). Inexperience was third most common reason (16.3%) for false negative US examinations. CONCLUSIONS: Almost half of PAs have at least one atypical feature on US. Awareness of the high prevalence of atypical US features could increase the accuracy of US examination and potentially decrease demand for more expensive second-line imaging modalities.
PubMed-ID: 37668359
DOI: 10.1210/clinem/dgad527

**Radiofrequency ablation as a treatment modality for primary hyperparathyroidism: a systematic literature review**.
*Gland Surg*, 13(1):87-99.
P. P. Issa, E. Kandil and G. S. Lee. 2024.
BACKGROUND: Primary hyperparathyroidism (pHPT) is an endocrine disorder typically characterized by elevated serum calcium and elevated parathyroid hormone (PTH). While parathyroidectomy is the standard treatment, non-operative intervention such as radiofrequency ablation (RFA) has been adopted as an alternative for the management of pHPT, as it has been utilized in other endocrine glands such as thyroid and adrenal. In this literature review, we aim to evaluate the current practice of RFA for pHPT. METHODS: A systematic literature search using PubMed, Web of Science, and Embase through June 2022 was conducted. Studies included in the review consisted of patient cohorts who had an unequivocal diagnosis of pHPT and underwent the treatment of pHPT with RFA. When more than one study was published from a similar cohort of patients, only the study with the most number of patients was considered. Studies included were assessed for bias using the critical appraisal instruments from the Joanna Briggs Institute (JBI) System. RESULTS: A total of 14 studies describing 167 parathyroid glands treated in 163 patients were reviewed. The overall cure rate was 91.2%, with 5 patients undergoing more than one ablation. The most common adverse effect encountered was temporary dysphonia. Incomplete ablation and missed multiglandular disease were the most common reasons for RFA treatment failure. CONCLUSIONS: RFA may be an effective and safe alternative to parathyroidectomy in select patients with a well-localized, well-located parathyroid adenoma. Additional long-term data are needed to refine its role in the pHPT treatment algorithm.
PubMed-ID: 38323227
DOI: 10.21037/gs-22-546
PMCID: PMC10839703

**Heterogeneous parathyroid near-infrared autofluorescence patterns are associated with single adenomas in primary hyperparathyroidism**.
*Head Neck*, 46(3):592-8.
S. M. Lee, P. H. Dedhia and J. E. Phay. 2024.
BACKGROUND: Primary adenoma (PA) and multi-gland hyperplasia (MGH) account for 85% and 15% of primary hyperparathyroidism (PHPT) cases, respectively. Near-infrared autofluorescence (NIRAF) enhances intraoperative parathyroid identification. We hypothesized that PA would display a more heterogeneous NIRAF pattern compared to MGH. METHODS: Patients undergoing surgery for sporadic PHPT were categorized based on the presence of PA or MGH. To quantify heterogeneity, we utilized ratios of (1) mean parathyroid gland (PG) NIRAF over background NIRAF (mean ratio), (2) minimum and (3) maximum PG NIRAF over mean PG NIRAF (minimum and maximum ratios). Additionally, a heterogeneity score was quantified using mean ratio (mean PG NIRAF over background NIRAF), and overall NIRAF (mean NIRAF of eight random 15 x 15 pixel areas). A point was assigned to ratios <0.8 or >1.2. Images were quantified by ImageJ software. Mann-Whitney test was performed for all comparisons. RESULTS: Of 78 patients, 63 had a single PA and 15 had MGH, totaling 102 PGs. There was no difference between their mean ratios. PA had a lower minimum ratio compared to that of MGH (0.86 +/- 0.01 vs. 0.93 +/- 0.01, p = 0.001) and a brighter maximum ratio (1.21 +/- 0.02 vs. 1.12 +/- 0.01, p = 0.0008). PA also scored higher on their heterogeneity scores compared to MGH (1.27 +/- 0.23 vs. 0.33 +/- 0.15, p = 0.001). CONCLUSION: Single parathyroid adenomas display a more heterogeneous autofluorescence pattern compared to that of multi-gland hyperplasia. Intraoperative characterization of PGs by real-time NIR imaging patterns may be a beneficial adjunct during parathyroid surgery.
PubMed-ID: 38133490
DOI: 10.1002/hed.27599

**Surgical strategy in lithium-associated hyperparathyroidism: A population-based study**.
*World J Surg*, 48(2):408-15.
I. L. Nilsson, D. Thorsteinsson, C. Nylen, A. Koman, F. Granath and R. Branstrom. 2024.
BACKGROUND: The extent of parathyroidectomy (PTX) recommendation in patients with lithium-associated

hyperparathyroidism (LAH) remains controversial. The primary objectives of this study were to analyze extent of surgery, complications, and long-term outcomes. METHODS: A population-based study, including all primary hyperparathyroidism (PHPT) patients who underwent PTX in Sweden between 2008 and 2017. Data on exhibited lithium prescriptions, morbidity, surgical approach, and outcomes were collected from relevant national registers and the Scandinavian Quality Register of Thyroid, Parathyroid, and Adrenal Surgery. Patients with lithium exposure before PTX were defined as having LAH. Descriptive summary statistics and regression models were used to evaluate differences in comorbidities, surgical approach, and outcomes between LAH and PHPT not exposed to lithium (non-LAH). RESULTS: Lithium exposure was significantly more common among PHPT (n = 202, 2.3%) than in controls (n = 416, 0.5%); OR 5.0 (95% CI 4.2-5.9). The risk of LAH correlated to the length of lithium exposure. In the LAH-group, the surgical procedures were more extensive and associated with a higher risk of postoperative bleeding, wound infections, persistent hypercalcemia, and hypocalcemia that remained after adjustment for the higher percentage of multiglandular disease. However, the cumulative risk of re-admission for PHPT was similar the first years after PTX and primarily elevated for patients with >5 years duration of lithium exposure prior to surgery. CONCLUSIONS: The findings support the perception of LAH as a complex entity. We recommend a functionally oriented approach, aimed to obtain and maintain normocalcemia for as long as possible, minimizing the risk of permanent hypoparathyroidism, and accepting some risk of recurrence.
PubMed-ID: 38686807
DOI: 10.1002/wjs.12071

**Recurrence After Surgery for Primary Hyperparathyroidism in 517 Patients With Multiple Endocrine Neoplasia Type 1: An Association Francophone de Chirurgie Endocrinienne and Groupe d'etude des Tumeurs Endocrines study**.
*Ann Surg*, 279(2):340-5.
N. Santucci, E. Ksiazek, F. Pattou, G. Baud, E. Mirallie, S. Frey, C. Tresallet, F. Sebag, C. Guerin, M. Mathonnet, N. Christou, G. Donatini, L. Brunaud, S. Gaujoux, F. Menegaux, H. Najah, C. Binquet, P. Goudet and J. C. Lifante. 2024.
OBJECTIVE: To assess recurrence according to the type of surgery for primary hyperparathyroidism (pHPT) in multiple endocrine neoplasia type 1 ( MEN1 ) patients and to identify the risk factors for recurrence after the initial surgery. BACKGROUND: In MEN1 patients, pHPT is multiglandular, and the optimal extent of initial parathyroid resection influences the risk of recurrence. METHODS: MEN1 patients who underwent initial surgery for pHPT between 1990 and 2019 were included. Persistence and recurrence rates after less than subtotal parathyroidectomy (LTSP) and subtotal parathyroidectomy (STP) were analyzed. Patients with total parathyroidectomy with reimplantation were excluded. RESULTS: Five hundred seventeen patients underwent their first surgery for pHPT: 178 had LTSP (34.4%) and 339 STP (65.6%). The recurrence rate was significantly higher after LTSP (68.5%) than STP (45%) ( $P < 0.001$). The median time to recurrence after pHPT surgery was significantly shorter after LTSP than after STP: 4.25 (1.2-7.1) versus 7.2 (3.9-10.1) years ( $P < 0.001$). A mutation in exon 10 was an independent risk factor of recurrence after STP (odds ratio = 2.19; 95% CI: 1.31; 3.69; $P = 0.003$). The 5 and 10-year recurrent pHPT probabilities were significantly higher in patients after LTSP with a mutation in exon 10 (37% and 79% vs 30% and 61%; $P = 0.016$). CONCLUSIONS: Persistence, recurrence of pHPT, and reoperation rate are significantly lower after STP than LTSP in MEN1 patients. Genotype seems to be associated with the recurrence of pHPT. A mutation in exon 10 is an independent risk factor for recurrence after STP, and LTSP may not be recommended when exon 10 is mutated.
PubMed-ID: 37389888
DOI: 10.1097/SLA.0000000000005980

**Primary Hyperparathyroidism and the PAS Score**.
*Am J Surg*, 229:196-7.
T. S. Wang. 2024.
PubMed-ID: 37977977
DOI: 10.1016/j.amjsurg.2023.11.006

# Adrenals

## Meta-Analyses

**Predicting Bilateral Subtypes of Primary Aldosteronism Without Adrenal Vein Sampling: A Systematic Review and Meta-analysis**.
*J Clin Endocrinol Metab*, 109(2):e837-e55.
E. Ng, S. M. Gwini, W. Zheng, P. J. Fuller and J. Yang. 2024.
CONTEXT: Primary aldosteronism (PA) is the most common endocrine cause of hypertension. The final diagnostic step involves subtyping, using adrenal vein sampling (AVS), to determine if PA is unilateral or bilateral. The complete PA diagnostic process is time and resource intensive, which can impact rates of diagnosis and treatment. Previous studies have developed tools to predict bilateral PA before AVS. OBJECTIVE: Evaluate the sensitivity and specificity of published tools that aim to identify bilateral subtypes of PA. METHODS: Medline and Embase databases were searched to identify published models that sought to subtype PA, and algorithms to predict bilateral PA are reported. Meta-analysis and meta-regression were then performed. RESULTS: There were 35 studies included, evaluating 55 unique algorithms to predict bilateral PA. The algorithms were grouped into 6 categories: those combining biochemical, radiological, and demographic characteristics (A); confirmatory testing alone or combined with biochemical, radiological, and demographic characteristics (B); biochemistry results alone (C); adrenocorticotropic hormone stimulation testing (D); anatomical imaging (E); and functional imaging (F). Across the identified algorithms, sensitivity and specificity ranged from 5% to 100% and 36% to 100%, respectively. Meta-analysis of 30 unique predictive tools from 32 studies showed that the group A algorithms had the highest specificity for predicting bilateral PA, while group F had the highest sensitivity. CONCLUSIONS: Despite the variability in published predictive algorithms, they are likely important for decision-making regarding the value of AVS. Prospective validation may enable medical treatment upfront for people with a high likelihood of bilateral PA without the need for an invasive and resource-intensive test.
PubMed-ID: 37531636
DOI: 10.1210/clinem/dgad451

**Time to Benefit of Surgery vs Targeted Medical Therapy for Patients With Primary Aldosteronism: A Meta-analysis**.
*J Clin Endocrinol Metab*, 109(3):e1280-e9.
S. Samnani, I. Cenzer, G. A. Kline, S. J. Lee, G. L. Hundemer, C. McClurg, J. L. Pasieka, W. J. Boscardin, P. E. Ronksley and A. A. Leung. 2024.
CONTEXT: Primary aldosteronism (PA) is one of the most common causes of secondary hypertension, but the comparative outcomes of targeted treatment remain unclear. OBJECTIVE: To compare the clinical outcomes in patients treated for primary aldosteronism over time. METHODS: Medline and EMBASE were searched. Original studies reporting the incidence of mortality, major adverse cardiovascular outcomes (MACE), progression to chronic kidney disease, or diabetes following adrenalectomy vs medical therapy were selected. Two reviewers independently abstracted data and assessed study quality. Standard meta-analyses were conducted using random-effects models to estimate relative differences. Time to benefit meta-analyses were conducted by fitting Weibull survival curves to estimate absolute risk differences and pooled using random-effects models. RESULTS: 15 541 patients (16 studies) with PA were included. Surgery was consistently associated with an overall lower risk of death (hazard ratio [HR] 0.34, 95% CI 0.22-0.54) and MACE (HR 0.55, 95% CI 0.36-0.84) compared with medical therapy. Surgery was associated with a significantly lower risk of hospitalization for heart failure (HR 0.48 95% CI 0.34-0.70) and progression to chronic kidney disease (HR 0.62 95% CI 0.39-0.98), and nonsignificant reductions in myocardial infarction and stroke. In absolute terms, 200 patients would need to be treated with surgery instead of medical therapy to prevent 1 death after 12.3 (95% CI 3.1-48.7) months. CONCLUSION: Surgery is associated with lower all-cause mortality and MACE than medical therapy for PA. For most patients, the long-term surgical benefits outweigh the short-term perioperative risks.
PubMed-ID: 37946600
DOI: 10.1210/clinem/dgad654
PMCID: PMC10876395

## Randomized controlled trials

**Sunitinib for metastatic progressive phaeochromocytomas and paragangliomas: results from FIRSTMAPPP, an academic, multicentre, international, randomised, placebo-controlled, double-blind, phase 2 trial**.
*Lancet*, 403(10431):1061-70.
E. Baudin, B. Goichot, A. Berruti, J. Hadoux, S. Moalla, S. Laboureau, S. Nolting, C. de la Fouchardiere, T. Kienitz, T. Deutschbein, S. Zovato, L. Amar, M. Haissaguerre, H. Timmers, P. Niccoli, A. Faggiano, M. Angokai, L. Lamartina, F. Luca, D. Cosentini, S. Hahner, F. Beuschlein, M. Attard, M. Texier, M. Fassnacht, C. Endocan and E. Networks. 2024.
BACKGROUND: No randomised controlled trial has ever been done in patients with metastatic phaeochromocytomas and paragangliomas. Preclinical and first clinical evidence suggested beneficial effects of sunitinib. We aimed to evaluate the safety and efficacy of sunitinib in patients with metastatic phaeochromocytomas and paragangliomas. METHODS: FIRSTMAPPP is a multicentre, international, randomised, placebo-controlled, double-blind, phase 2 trial done at 14 academic centres across four European countries. Eligible participants were adults (aged >/=18 years) with sporadic or inherited progressive metastatic phaeochromocytomas and paragangliomas. Patients were randomly assigned (1:1) to receive either oral sunitinib (37.5 mg per day) or placebo. Randomisation was stratified according to SDHB status (mutation present vs wild type) and number of previous systemic therapies (0 vs >/=1). Primary endpoint was the rate of progression-free survival at 12 months according to real-time central review (Response Evaluation Criteria in Solid Tumours version 1.1). On the basis of a two-step Simon model, we aimed for the accrual of 78 patients, assuming a 20% improvement of the 12-month progression-free survival rate from 20% to 40%, to conclude that sunitinib is effective. Crossover from the placebo group was allowed. This trial is registered with ClinicalTrials.gov, number NCT01371201, and is closed for enrolment. FINDINGS: From Dec 1, 2011, to Jan 31, 2019, a total of 78 patients with progressive metastatic phaeochromocytomas and paragangliomas were enrolled (39 patients per group). 25 (32%) of 78 patients had germline SDHx variants and 54 (69%) had used previous therapies. The primary endpoint was met, with a 12-month progression-free survival in 14 of 39 patients (36% [90% CI 23-50]) in the sunitinib group. In the placebo group, the 12-month progression-free survival in seven of 39 patients was 19% (90% CI 11-31), validating the hypotheses of our study design. The most frequent grade 3 or 4 adverse events were asthenia (seven [18%] of 39 and one [3%] of 39), hypertension (five [13%] and four [10%]), and back or bone pain (one [3%] and three [8%]) in the sunitinib and placebo groups, respectively. Three deaths occurred in the sunitinib group: these deaths were due to respiratory insufficiency, amyotrophic lateral sclerosis, and rectal bleeding. Only the latter event was considered drug related. Two deaths occurred in the placebo group due to aspiration pneumonia and septic shock. INTERPRETATION: This first randomised trial supports the use of sunitinib as the medical option with the highest level of evidence for anti-tumour efficacy in progressive metastatic phaeochromocytomas and paragangliomas. FUNDING: French Ministry of Health, through the National Institute for Cancer, German Ministry of Education and Research, and the German Research Foundation within the CRC/Transregio 205/2, EU Seventh Framework Programme, and a private donator grant.
PubMed-ID: 38402886
DOI: 10.1016/S0140-6736(23)02554-0

## Consensus Statements/Guidelines

**International consensus on mitotane treatment in pediatric patients with adrenal cortical tumors: indications, therapy, and management of adverse effects**.
*Eur J Endocrinol*, 190(4):G15-G24.
M. Riedmeier, S. R. R. Antonini, S. Brandalise, T. Costa, C. M. Daiggi, B. C. de Figueiredo, R. R. de Krijger, K. E. De Sa Rodrigues, C. Deal, J. Del Rivero, G. Engstler, M. Fassnacht, G. C. Fernandes Luiz Canali, C. A. F. Molina, E. N. Gonc, M. Gultekin, H. R. Haak, T. Guran, E. J. Hendriks Allaird, J. Idkowiak, M. Kuhlen, D. Malkin, J. P. Meena, C. Pamporaki, E. Pinto, S. Puglisi, R. C. Ribeiro, L. D. R. Thompson, B. Yalcin, M. Van Noesel and V. Wiegering. 2024.
OBJECTIVE: Mitotane is an important cornerstone in the treatment of pediatric adrenal cortical tumors (pACC), but experience with the drug in the pediatric age group is still limited and current practice is not guided by robust evidence. Therefore, we have compiled international consensus statements from pACC experts on mitotane indications, therapy, and management of adverse effects. METHODS: A Delphi method with 3 rounds of questionnaires within the pACC expert consortium of the international network groups European Network for the Study of Adrenal Tumors pediatric working group (ENSAT-PACT) and International Consortium of pediatric adrenocortical tumors (ICPACT) was used to create 21 final consensus statements. RESULTS: We divided the statements into 4 groups: environment, indications, therapy, and adverse

effects. We reached a clear consensus for mitotane treatment for advanced pACC with stages III and IV and with incomplete resection/tumor spillage. For stage II patients, mitotane is not generally indicated. The timing of initiating mitotane therapy depends on the clinical condition of the patient and the setting of the planned therapy. We recommend a starting dose of 50 mg/kg/d (1500 mg/m(2)/d) which can be increased up to 4000 mg/m2/d. Blood levels should range between 14 and 20 mg/L. Duration of mitotane treatment depends on the clinical risk profile and tolerability. Mitotane treatment causes adrenal insufficiency in virtually all patients requiring glucocorticoid replacement shortly after beginning. As the spectrum of adverse effects of mitotane is wide-ranging and can be life-threatening, frequent clinical and neurological examinations (every 2-4 weeks), along with evaluation and assessment of laboratory values, are required. CONCLUSIONS: The Delphi method enabled us to propose an expert consensus statement, which may guide clinicians, further adapted by local norms and the individual patient setting. In order to generate evidence, well-constructed studies should be the focus of future efforts.
PubMed-ID: 38552173
DOI: 10.1093/ejendo/lvae038

## Other Articles

**Effect of mild cortisol cosecretion on body composition and metabolic parameters in patients with primary hyperaldosteronism**.
*Clin Endocrinol (Oxf)*, 100(3):212-20.
N. Mansour, D. Bruedgam, U. Dischinger, L. Kurzinger, C. Adolf, R. Walter, O. Ocal, V. F. Schmidt, J. Rudolph, J. Ricke, N. Reisch, M. Reincke, M. Wildgruber and D. Heinrich. 2024.
OBJECTIVE: To investigate the effects of simultaneous cortisol cosecretion (CCS) on body composition in computed tomography (CT)-imaging and metabolic parameters in patients with primary aldosteronism (PA) with the objective of facilitating early detection. DESIGN: Retrospective cohort study. PATIENTS: Forty-seven patients with PA and CCS confirmed by 1-mg dexamethasone suppression test (DST) with a cutoff of >/=1.8 microg/dL were compared with PA patients with excluded CCS (non-CCS, n = 47) matched by age and sex. METHODS: Segmentation of the fat compartments and muscle area at the third lumbar region was performed on non-contrast-enhanced CT images with dedicated segmentation software. Additionally, liver, spleen, pancreas and muscle attenuation were compared between the two groups. RESULTS: Mean cortisol after DST was 1.2 microg/dL (33.1 nmol/L) in the non-CCS group and 3.2 microg/dL (88.3 nmol/L) in the CCS group with mild autonomous cortisol excess (MACE). No difference in total, visceral and subcutaneous fat volumes was observed between the CCS and non-CCS group (p = .7, .6 and .8, respectively). However, a multivariable regression analysis revealed a significant correlation between total serum cholesterol and results of serum cortisol after 1-mg DST (p = .026). Classification of the patients based on visible lesion on CT and PA-lateralization via adrenal venous sampling also did not show any significant differences in body composition. CONCLUSION: MACE in PA patients does not translate into body composition changes on CT-imaging. Therefore, early detection of concurrent CCS in PA is currently only attainable through biochemical tests. Further investigation of the long-term clinical adverse effects of MACE in PA is necessary.
PubMed-ID: 38164017
DOI: 10.1111/cen.15013

**Treating Primary Aldosteronism-Induced Hypertension: Novel Approaches and Future Outlooks**.
*Endocr Rev*, 45(1):125-70.
N. Mullen, J. Curneen, P. T. Donlon, P. Prakash, I. Bancos, M. Gurnell and M. C. Dennedy. 2024.
Primary aldosteronism (PA) is the most common cause of secondary hypertension and is associated with increased morbidity and mortality when compared with blood pressure-matched cases of primary hypertension. Current limitations in patient care stem from delayed recognition of the condition, limited access to key diagnostic procedures, and lack of a definitive therapy option for nonsurgical candidates. However, several recent advances have the potential to address these barriers to optimal care. From a diagnostic perspective, machine-learning algorithms have shown promise in the prediction of PA subtypes, while the development of noninvasive alternatives to adrenal vein sampling (including molecular positron emission tomography imaging) has made accurate localization of functioning adrenal nodules possible. In parallel, more selective approaches to targeting the causative aldosterone-producing adrenal adenoma/nodule (APA/APN) have emerged with the advent of partial adrenalectomy or precision ablation. Additionally, the development of novel pharmacological agents may help to mitigate off-target effects of aldosterone and improve clinical efficacy and

outcomes. Here, we consider how each of these innovations might change our approach to the patient with PA, to allow more tailored investigation and treatment plans, with corresponding improvement in clinical outcomes and resource utilization, for this highly prevalent disorder.
PubMed-ID: 37556722
DOI: 10.1210/endrev/bnad026
PMCID: PMC10765166

**Surgical Management of Metastatic Adrenocortical Carcinoma**.
*World J Surg*, 48(1):110-20.
J. E. Passman, W. Amjad, S. P. Ginzberg, J. M. Soegaard Ballester, C. Finn and H. Wachtel. 2024.
INTRODUCTION: Adrenocortical carcinoma (ACC) is a notoriously aggressive cancer with a dismal prognosis, especially for patients with metastatic disease. Metastatic ACC is classically a contraindication to operative management. Here, we evaluate the impact of primary tumor resection and metastasectomy on survival in metastatic ACC. METHODS: We performed a retrospective cohort study of patients with metastatic ACC (2010-2019) utilizing the National Cancer Database. The primary outcome was overall survival (OS). Cox proportional hazards models were developed to evaluate the associations between surgical management and survival. Propensity score matching (PSM) was utilized to account for selection bias in receipt of surgery. RESULTS: Of 976 subjects with metastatic ACC, 38% underwent surgical management. Median OS across all patients was 7.6 months. On multivariable Cox proportional hazards regression, primary tumor resection alone (HR: 0.523; p<0.001) and primary resection with metastasectomy (HR: 0.372; p<0.001) were significantly associated with improved OS. Metastasectomy alone had no association with OS (HR: 0.909; p=0.740). Primary resection with metastasectomy was associated with improved OS over resection of the primary tumor alone (HR: 0.636; p=0.018). After PSM, resection of the primary tumor alone remained associated with improved OS (HR 0.593; p<0.001), and metastasectomy alone had no survival benefit (HR 0.709; p=0.196) compared with non-operative management; combined resection was associated with improved OS over primary tumor resection alone (HR 0.575, p=0.008). CONCLUSION: In metastatic ACC, patients may benefit from primary tumor resection alone or in combination with metastasectomy, however further research is required to facilitate appropriate patient selection.
PubMed-ID: 38463201
DOI: 10.1002/wjs.12014
PMCID: PMC10919939

**Defining Optimal Management of Non-metastatic Adrenocortical Carcinoma**.
*Ann Surg Oncol*, 31(2):1097-107.
J. E. Passman, W. Amjad, J. M. Soegaard Ballester, S. P. Ginzberg and H. Wachtel. 2024.
BACKGROUND: Adrenocortical carcinoma (ACC) is an aggressive, deadly malignancy. Resection remains the primary treatment; however, there is conflicting evidence regarding the optimal approach to and extent of surgery and the role of adjuvant therapy. We evaluated the impact of surgical technique and adjuvant therapies on survival in non-metastatic ACC. METHODS: We performed a retrospective cohort study of subjects who underwent surgery for non-metastatic ACC between 2010 and 2019 utilizing the National Cancer Database. The primary outcome was overall survival. Cox proportional hazards models were developed to identify associations between clinical and treatment characteristics and survival. RESULTS: Overall, 1175 subjects were included. Their mean age was 54 +/- 15 years, and 62% of patients were female. 67% of procedures were performed via the open approach, 22% involved multi-organ resection, and 26% included lymphadenectomy. Median survival was 77.1 months. Age (hazard ratio [HR] 1.019; p < 0.001), advanced stage (stage III HR 2.421; p < 0.001), laparoscopic approach (HR 1.329; p = 0.010), and positive margins (HR 1.587; p < 0.001) were negatively associated with survival, while extent of resection (HR 1.189; p = 0.140) and lymphadenectomy (HR 1.039; p = 0.759) had no association. Stratified by stage, laparoscopic resection was only associated with worse survival in stage III disease (HR 1.548; p = 0.007). Chemoradiation was only associated with improved survival in patients with positive resection margins (HR 0.475; p = 0.004). CONCLUSION: Tumor biology and surgical margins are the primary determinants of survival in non-metastatic ACC. Surgical extent and lymphadenectomy are not associated with overall survival. In advanced disease, the open approach is associated with improved survival.
PubMed-ID: 37925657
DOI: 10.1245/s10434-023-14533-w

**ASO Author Reflections: Surgical Decision-Making in Adrenocortical Carcinoma: When Less is More**.
*Ann Surg Oncol*, 31(2):1140-1.
J. E. Passman and H. Wachtel. 2024.
PubMed-ID: 37993746
DOI: 10.1245/s10434-023-14630-w

**Impact of adrenal surgeon volume on outcome: analysis of 4464 operations from the United Kingdom Registry of Endocrine and Thyroid Surgery (UKRETS)**.
*Br J Surg*, 111(2):undefined-undefined.
S. Rajan, N. Patel, M. Stechman, S. P. Balasubramanian, R. Mihai and S. Aspinall. 2024.
BACKGROUND: There is a surgeon volume-outcome effect in adrenal surgery but the threshold for high-volume surgeon remains controversial. This study aimed to determine predictors of high-risk adrenal operations and to explore whether these should be restricted to high-volume surgeons. METHODS: Patients undergoing adrenal surgery and registered in the United Kingdom Registry of Endocrine and Thyroid Surgery between 2004 and 2021 were analysed. Outcomes included postoperative complications, duration of hospital stay, and mortality. Factors included in multivariable analysis were age, sex, diagnosis, surgical approach, laterality, and surgeon volume. Patients with missing data were excluded. RESULTS: A total of 4464 of 6174 patients (72.3%) were analysed. Postoperative complications occurred in 418 patients (9.4%) and 14 (0.3%) died. Median duration of hospital stay was 3 (i.q.r. 2-5) days. Co-variables significantly associated with an increase or decrease in postoperative complications (P < 0.050) were age (OR 1.02, 95% c.i. 1.01 to 1.03), adrenal cancer (OR 1.64, 1.14 to 2.36), minimally invasive approach (OR 0.317, 0.248 to 0.405), bilateral surgery (OR 1.66, 1.03 to 2.69), and surgeon volume (OR 0.98, 0.96 to 0.99). An increase or decrease in mortality was associated with patient age (OR 1.08, 1.03 to 1.13), minimally invasive approach (OR 0.08, 0.02 to 0.27), and bilateral surgery (OR 6.93, 1.40 to 34.34). The incidence of postoperative complications was significantly lower above a threshold of 12 operations per year (P = 0.034) and 20 per year (P < 0.001), but not six per year (P = 0.540). Median duration of hospital stay was 2 days for surgeons doing over 20 operations per year, compared with 3 days for those undertaking fewer than 20, fewer than 12 or fewer than 6 operations per year. CONCLUSION: Increasing surgical volume is associated with shorter hospital stay and fewer complications. This analysis supports the case for centralization of surgery for adrenal cancer and bilateral tumours to higher-volume surgeons performing a minimum of 12 operations per year.
The adrenal glands are found in the fatty tissue at the back of the abdomen above each kidney, and produce steroid and adrenaline hormones. Surgery on tumours of the adrenal gland is uncommon compared with surgery for other tumours such as those of the breast, bowel, kidney, and lung. Research has shown that the more adrenal operations a surgeon undertakes per year, the better the overall outcomes for patients undergoing that type of surgery. In this study, the outcomes from adrenal operations recorded over 18 years in the national adrenal surgical registry by members of the British Association of Endocrine and Thyroid Surgeons were analysed. The results confirmed previous findings showing that postoperative complications and length of hospital stay were reduced for patients operated by surgeons who did more adrenal operations per year. Operations done by keyhole surgery had better outcomes. Operations done either in older patients, or for the rare adrenal cancer tumours had worse outcomes, as did operations in which both adrenal glands were removed. The authors recommended that all surgeons performing adrenal surgery should monitor the outcomes of their operations, ideally in a national registry, and discuss these with patients before surgery; and undertake a minimum of 6 adrenal operations per year, but a minimum of 12 per year if doing surgery for adrenal cancer or surgery to remove both adrenal glands.
eng.
PubMed-ID: 38306505
DOI: 10.1093/bjs/znae002

**Monitoring adrenal insufficiency through salivary steroids: a pilot study**.
*Eur J Endocrinol*, 190(4):327-37.
L. Tucci, F. Fanelli, I. Improta, V. Bissi, C. Lena, G. Galante, M. Mezzullo, M. Magagnoli, A. B. Lalumera, G. Colombin, K. Coscia, L. Rotolo, V. Vicennati, U. Pagotto and G. Di Dalmazi. 2024.
BACKGROUND: Various glucocorticoid replacement therapies (GRTs) are available for adrenal insufficiency (AI). However, their effectiveness in restoring glucocorticoid rhythm and exposure lacks adequate biochemical markers. We described the diurnal salivary cortisol (SalF) and cortisone (SalE) rhythm among different GRTs and analysed the associations between saliva-derived parameters and life quality questionnaires. METHODS: Control subjects (CSs, n = 28) and AI patients receiving hydrocortisone (HC, n = 9), cortisone acetate (CA, n = 23), and dual-release hydrocortisone once (DRHC-od, n = 10) and twice a day (DRHC-td, n = 6) collected 9 saliva samples from 07:00 to 23:00. Patients compiled Pittsburgh

Sleep Quality Index, Hospital Anxiety and Depression Scale, and Addison disease-specific quality-of-life questionnaires. SalE and SalF were measured by liquid chromatography-mass spectrometry. Exposure was monitored using SalE for HC and DRHC and SalF for CA. Area under the curve (AUC) was computed. Different GRTs were compared by Z-scores calculated from saliva-derived parameters. Questionnaire results predictors were evaluated with multiple regression analysis. RESULTS: Compared with controls, all GRTs resulted in glucocorticoid overexposure in the morning. Hydrocortisone, CA, and DRHC-td caused overexposure also in afternoon and evening. Compared with other treatments, CA determined increased Z-score-07:00 ($P < .001$), DRHC-td determined increased Z-score-AUC07:00-->14:00 ($P = .007$), and DRHC-od induced lower Z-score-AUC14:00-->23:00 ($P = .015$). Z-scores-AUC14:00-->16:00 >/= .619 best predicted questionnaire scores. CONCLUSIONS: None of the GRTs mimics normal glucocorticoid rhythmicity and exposure. SalE, SalF, and Z-score may be useful markers for monitoring and comparing different GRTs. Excess glucocorticoid in early afternoon best associated with depressive symptoms and worse life and sleep quality.
PubMed-ID: 38571387
DOI: 10.1093/ejendo/lvae037

# NET

## Meta-Analyses

*- None -*

## Randomized controlled trials

*- None -*

## Consensus Statements/Guidelines

**Surgery for advanced pancreatic neuroendocrine neoplasms: recommendations based on a consensus meeting of the European Society of Endocrine Surgeons (ESES)**.
*Br J Surg*, 111(2):undefined-undefined.
D. J. Van Beek, K. Van Den Heede, I. Borel Rinkes, O. Norlen, S. Van Slycke, P. Stalberg and E. Nordenstrom. 2024.
PubMed-ID: 38364061
DOI: 10.1093/bjs/znae017

## Other Articles

**Impact of sex on treatment decisions and outcome in patients with neuroendocrine neoplasms**.
*Endocr Relat Cancer*, 31(3)
J. Beck, A. Siebenhuner, D. Wild, E. Christ and J. Refardt. 2024.
Sex differences affect the management of several diseases in both male and female patients. However, the influence of sex on neuroendocrine neoplasms (NENs) has been scarcely investigated. Thus, this study aimed to compare tumor characteristics, treatment decisions, and overall survival in patients with NENs, stratified by sex. The retrospective analysis of the SwissNET cohort covered NENs of gastroenteropancreatic, pulmonary, or unknown origin from July 2014 to September 2022. The analysis included 1985 patients (46% female and 54% male). No significant difference in tumor grading was found between male and female patients. However, male patients presented with higher staging at time of diagnosis and with more lymph node and bone metastases. Surgery was performed more often in female compared to male patients (73.4% vs 68.7%, P = 0.023). Male patients received peptide receptor nuclide therapy (PRRT) earlier than female patients (7.8 months vs 13.1 months from time of diagnosis, P = 0.003). The median overall survival was significantly shorter for male compared to female patients (male: 18 years, female: not reached, P < 0.001, hazard ratio (HR) 1.55 (1.19-2.01), P = 0.001). Multivariable analyses revealed advanced age (HR 1.02 (1.01-1.04)), cancer of unknown origin (HR 2.01 (1.09-3.70)), higher grading (G3: HR 6.74 (4.22-10.76)), having metastases at the time of diagnosis (HR 2.11 (1.47-3.02)), and surgical treatment (HR 0.67 (0.48-0.93)) as independent predictors for overall survival. In conclusion, male sex was associated with worse outcome in NEN patients, likely due to more advanced tumor stage at the time of diagnosis. Further investigations are required to understand the underlying mechanisms of these sex differences.
PubMed-ID: 38117915
DOI: 10.1530/ERC-23-0235

**Live to fight another day: Combining parenchymal sparing resection and ablative therapy in neuroendocrine tumor liver metastases**.
*Am J Surg*, 229:15-6.
R. J. Bello and C. N. Clarke. 2024.
PubMed-ID: 37985321
DOI: 10.1016/j.amjsurg.2023.11.015

**Evolution of Surgical Management and Outcomes of Neuroendocrine Tumor Liver Metastases**.
*Ann Surg Oncol*, 31(4):2192-3.
R. J. Bello and C. N. Clarke. 2024.
PubMed-ID: 38273173
DOI: 10.1245/s10434-024-14903-y

**Diagnosis and staging of small intestinal neuroendocrine tumors with CT enterography and PET with Gallium-68: preoperative risk stratification protocol**.
*Langenbecks Arch Surg*, 409(1):63.
A. Bonomi, U. Fumagalli Romario, L. Funicelli, G. Conti, M. Realis Luc, F. Ceci, S. Pozzi, D. Radice, N. Fazio and E. Bertani. 2024.
PURPOSE: Pre-operative diagnosis and staging of small intestine neuroendocrine tumors (SI-NETs) remain sub-optimal, with open palpation during surgery still considered the gold standard. This limits a standardized implementation of minimally invasive surgery (MIS). The aim of this single-center retrospective study was to assess a tailored diagnostic work-up to identify candidates at low risk of undetected disease who may benefit from MIS. METHODS: Patients diagnosed with SI-NETs between 2013 and 2022 who underwent contrast-enhanced computed tomography enterography (CTE) and Ga68-DOTATOC-positron emission tomography-CT (68 Ga DOTATATE PET/CT) preoperatively and subsequently underwent open surgical resection were included. Imaging studies were reassessed by two radiologists. Combined use of CTE and 68 Ga DOTATATE PET/CT in determining primary lesion disease burden (number of lesions) and LN disease stage (distal and proximal relative to superior mesenteric vessels) was assessed, using surgical reports and pathology as gold standard. RESULTS: Overall, 56 patients were included. Sensitivity of CTE and 68 Ga DOTATATE PET/CT for at least one primary SI-NET was 100% and 94%, respectively. In the presence of concordance between studies, combined use of CTE and 68 Ga DOTATATE PET/CT for detection of single primary tumors improved specificity to 89% (n = 25/28) with a positive predictive value of 87.5% (n = 21/24). Distal LN disease was identified in 89.2% of cases (n = 33/37). The association of single lesion and distal LN disease was found pre-operatively in 32% of patients (n = 18). CONCLUSION: Combined use of CTE and 68 Ga DOTATATE PET/CT enables identifying low-risk surgical candidates (single SI-NET lesions with distal LN disease).
PubMed-ID: 38363374
DOI: 10.1007/s00423-024-03254-7

**The Search for a Reliable Biomarker in MEN1 Duodenopancreatic Neuroendocrine Tumors**.
*J Clin Endocrinol Metab*, 109(3):e1301-e2.
D. Bulzico. 2024.
PubMed-ID: 37646771
DOI: 10.1210/clinem/dgad521

**Risk Factor Analysis of Lymph Node Metastasis for Rectal Neuroendocrine Tumors: Who Needs a Radical Resection in Rectal Neuroendocrine Tumors Sized 1-2 cm?**
*Ann Surg Oncol*, 31(4):2414-24.
J. S. Choi, M. J. Kim, R. Shin, J. W. Park, S. C. Heo, S. Y. Jeong, K. J. Park and S. B. Ryoo. 2024.
BACKGROUND: Rectal neuroendocrine tumors (NETs) have malignant potential, and lymph node (LN) or distant metastases can occur; however, treatment of NETs 1-2 cm in size is controversial. OBJECTIVE: This study aimed to identify predictive factors for LN metastasis and prognostic factors for recurrence of rectal NETs, especially tumors 1–2 cm in size. METHODS: Between October 2004 and November 2020, 453 patients underwent endoscopic or surgical treatment for rectal NETs in Seoul National University Hospital. The data on these patients were prospectively collected in our database and reviewed retrospectively. In cases of local excision, we evaluated LN metastasis with radiologic imaging, including computed tomography or magnetic resonance imaging before treatment and during the follow-up periods. RESULTS: LN metastasis was observed in 40 patients (8.8%). A higher rate of LN metastasis was observed in larger-sized tumors, advanced T stage, lymphovascular invasion (LVI), perineural invasion (PNI), and high tumor grade. In multivariable analysis, the significant risk factors for LN metastasis were tumor size (1 </= size < 2 cm: hazard ratio [HR] 64.07; size >/=2 cm: HR 102.37, p < 0.001) and tumor grade (G2: HR 3.63, p = 0.034; G3: HR 5.09, p = 0.044). In multivariable analysis for tumors 1-2 cm in size, the risk factor for LN metastasis was tumor grade (G2: HR 6.34, p = 0.013). CONCLUSIONS: Tumor grade and size are important predictive factors for LN metastasis. In NETs 2 cm in size, tumor grade is also important for LN metastasis, and radical resection should be considered.

PubMed-ID: 38194045
DOI: 10.1245/s10434-023-14829-x

**Risk factors for positive resection margins after endoscopic resection for gastrointestinal neuroendocrine tumors**.
*Surg Endosc*, 38(4):2041-9.
L. Han, J. Li, C. Liang, Y. Chu, Y. Wang, L. Lv, D. Liu and Y. Tan. 2024.
BACKGROUND: In recent years, the incidence of gastrointestinal neuroendocrine tumors (GI-NETs) has remarkably increased due to the widespread use of screening gastrointestinal endoscopy. Currently, the most common treatments are surgery and endoscopic resection. Compared to surgery, endoscopic resection possesses a higher risk of resection margin residues for the treatment of GI-NETs. METHODS: A total of 315 patients who underwent surgery or endoscopic resection for GI-NETs were included. We analyzed their resection modality (surgery, ESD, EMR), margin status, Preoperative marking and Prognosis. RESULTS: Among 315 patients included, 175 cases underwent endoscopic resection and 140 cases underwent surgical treatment. A total of 43 (43/175, 24.57%) and 10 (10/140, 7.14%) patients exhibited positive resection margins after endoscopic resection and surgery, respectively. Multivariate regression analysis suggested that no preoperative marking and endoscopic treatment methods were risk factors for resection margin residues. Among the patients with positive margin residues after endoscopic resection, 5 patients underwent the radical surgical resection and 1 patient underwent additional ESD resection. The remaining 37 patients had no recurrence during a median follow-up of 36 months. CONCLUSIONS: Compared with surgery, endoscopic therapy has a higher margin residual rate. During endoscopic resection, preoperative marking may reduce the rate of lateral margin residues, and endoscopic submucosal dissection may be preferred than endoscopic mucosal resection. Periodical follow-up may be an alternative method for patients with positive margin residues after endoscopic resection.
PubMed-ID: 38429572
DOI: 10.1007/s00464-024-10706-0

**Relation between WHO Classification and Location- and Functionality-Based Classifications of Neuroendocrine Neoplasms of the Digestive Tract**.
*Neuroendocrinology*, 114(2):120-33.
N. C. Helderman, M. Suerink, G. Kilinc, J. G. van den Berg, M. Nielsen and M. E. T. Tesselaar. 2024.
Practice of neuroendocrine neoplasms (NENs) of the digestive tract, which comprise of a highly diverse group of tumors with a rising incidence, faces multiple biological, diagnostic, and therapeutic issues. Part of these issues is due to misuse and misinterpretation of the classification and terminology of NENs of the digestive tract, which make it increasingly challenging to evaluate and compare the literature. For instance, grade 3 neuroendocrine tumors (NETs) are frequently referred to as neuroendocrine carcinomas (NECs) and vice versa, while NECs are, by definition, high grade and therefore constitute a separate entity from NETs. Moreover, the term NET is regularly misused to describe NENs in general, and NETs are frequently referred to as benign, while they should always be considered malignancies as they do have metastatic potential. To prevent misconceptions in future NEN-related research, we reviewed the most recent terminology used to classify NENs of the digestive tract and created an overview that combines the classification of these NENs according to the World Health Organization (WHO) with location- and functionality-based classifications. This overview may help clinicians and researchers in understanding the current literature and could serve as a guide in the clinic as well as for writing future studies on NENs of the digestive tract. In this way, we aim for the universal use of terminology, thereby providing an efficient foundation for future NEN-related research.
PubMed-ID: 37690447
DOI: 10.1159/000534035
PMCID: PMC10836754

**Primary Tumor Resection and Its Implications in the Modern Treatment Era of Metastatic Small Bowel Neuroendocrine Tumors : Editorial on: "Morbidity and Outcomes of Primary Tumor Management in Patients with Widely Metastatic Well-Differentiated Small Bowel Neuroendocrine Tumors"**.
*Ann Surg Oncol*, 31(4):2187-9.
X. M. Keutgen. 2024.
PubMed-ID: 38167812
DOI: 10.1245/s10434-023-14836-y

**Single center outcomes from parenchymal-sparing resections and microwave ablations for neuroendocrine tumor liver metastases**.
*Am J Surg*, 229:17-23.
F. T. Lee, J. Williams, R. Nordgren, J. L. Schwarz, N. Setia, K. Roggin, B. Polite, G. Rangrass, C. Y. Liao, J. M. Millis and X. M. Keutgen. 2024.
BACKGROUND: Reported outcomes after surgical debulking in patients with advanced neuroendocrine tumor liver metastases (NETLM) are sparse. METHODS: NETLM patients that underwent surgical debulking from 2019 to 2021 were reviewed. Trends in perioperative liver function, complications, symptom response, and progression-free survival were examined. RESULTS: 1069 liver lesions were debulked from 53 patients using a combination of parenchymal-sparing resections (PSR) and ultrasound-guided microwave ablations (MWA). Post-operative transaminitis and thrombocytopenia were common, and severity correlated with increasing number of lesions. Laboratory markers for synthetic liver function did not differ according to the number of lesions debulked. 13% of patients sustained a Clavien-Dindo grade 3 or 4 complication which was not associated with the number of lesions targeted. All patients with preoperative symptoms had improvement after surgery. Median time to progression was 10.9 months. CONCLUSIONS: PSR with MWA for large numbers of NETLM is safe and effective for symptom control and does not affect synthetic liver function.
PubMed-ID: 37802701
DOI: 10.1016/j.amjsurg.2023.09.020

**Morbidity and Outcomes of Primary Tumor Management in Patients with Widely Metastatic Well-Differentiated Small Bowel Neuroendocrine Tumors**.
*Ann Surg Oncol*, 31(4):2337-48.
A. Nigam, J. W. Y. Li, M. Fiasconaro, S. Lin, M. Capanu, D. A. Kleiman, K. Memeh, N. Raj, D. L. Reidy-Lagunes and B. R. Untch. 2024.
BACKGROUND: The benefit of primary tumor resection in distant metastatic small bowel neuroendocrine tumors (SBNETs) is controversial, with treatment-based morbidity not well-defined. We aimed to determine the impact of primary tumor resection on development of disease-specific complications in patients with metastatic well-differentiated SBNETs. PATIENTS AND METHODS: A retrospective analysis was performed of patients diagnosed with metastatic well-differentiated jejunal/ileal SBNETs at a single tertiary care cancer center from 1980 to 2016. Outcomes were compared on the basis of treatment selected at diagnosis between patients who underwent initial medical treatment or primary tumor resection. RESULTS: Among 180 patients, 71 underwent medical management and 109 primary tumor resection. Median follow-up was 116 months. Median event-free survival did not differ between treatment approaches (log-rank $p = 0.2$). In patients medically managed first, 16/71 (23%) required surgery due to obstruction, perforation, or bleeding. These same complications led to resection at presentation in 31/109 (28%) surgically treated patients. Development of an obstruction from the primary tumor was not associated with disease progression/recurrence (HR 1.14, 95% CI 0.75-1.75) with all patients recovering postoperatively. Ongoing tumor progression requiring secondary laparotomy was associated with worse mortality (HR 7.51, 95% CI 3.3-16.9; $p < 0.001$) and occurred in 20/109 (18%) primary tumor resection and 7/16 (44%) initially medically treated patients. CONCLUSIONS: Rates of event-free survival among patients with metastatic SBNETs do not differ on the basis of primary tumor management. The development of an obstruction from the primary tumor was not associated with worse outcomes with all patients salvaged. Regardless of initial treatment selected, patients with metastatic SBNET should be closely followed for early signs of primary tumor complications.
PubMed-ID: 38036927
DOI: 10.1245/s10434-023-14637-3

**Management of Gastric Neuroendocrine Tumors: A Review**.
*Ann Surg Oncol*, 31(3):1509-18.
C. Sok, P. S. Ajay, V. Tsagkalidis, D. A. Kooby and M. M. Shah. 2024.
Gastric neuroendocrine tumors (G-NET) are rare tumors arising from enterochromaffin-like cells of the gastric mucosa. They belong to a larger group called gastroenteropancreatic neuroendocrine tumors and are classified as low, intermediate, or high-grade tumors based on their proliferative indices. They are further categorized into three subtypes based on their morphologic characteristics, pathogenesis, and behavior. Types 1 and 2 tumors are characterized by elevated serum gastrin and are usually multifocal. They typically occur in the setting of atrophic gastritis or MEN1/Zollinger Ellison syndrome, respectively. Type 2 tumors are associated with the most symptoms, such as abdominal pain and diarrhea. Type 3 tumors are associated with normal serum gastrin, are usually solitary, and occur sporadically. This type has the most aggressive phenotype and metastatic potential. Treatment and prognosis for G-NET is dependent on their type, size, and stage. Type 1 has the best prognosis, and Type 3 has the worst. This review discusses the

presentation, workup, and surgical management of these tumors.
PubMed-ID: 38062290
DOI: 10.1245/s10434-023-14712-9
PMCID: PMC10922891

**Surgery as a Principle and Technical Consideration for Primary Tumor Resection of Small Bowel Neuroendocrine Tumors**.
*Ann Surg Oncol*, 31(2):1125-37.
K. Soreide, S. Stattner and J. Hallet. 2024.
Small bowel neuroendocrine tumors (SB-NETs) are increasingly identified and have become the most frequent entity among small bowel tumors. An increasing incidence, a high prevalence, and a prolonged survival with optimal modern multidisciplinary management makes SB-NETs a unique set of tumors to consider for surgical oncologists. The major goals of surgical treatment in the setting of SB-NET include control of tumor volume, control of endocrine secretion, and prevention of locoregional complications. Key considerations include assessment of multifocality and resection of mesenteric nodal masses with the use of mesenteric-sparing approaches and acceptance of R1 margins if necessary to clear disease while avoiding short bowel syndrome. A description through eight steps for consideration is presented to allow for systematic surgical planning and execution of resection. Moreover, some controversies and evolving considerations to the surgical principles and technical procedures remain. The role of primary tumor resection in the presence of (unresectable) liver metastasis is still unclear. Reports of feasibility of minimally invasive surgery are emerging, with undetermined selection criteria for appropriateness or long-term outcomes. Resection of SB-NETs should be considered in all patients fit for surgery and should follow principles to achieve surgical oncological control that is appropriate for the stage and tumor burden, considering the age and comorbidity of the individual patient.
PubMed-ID: 38006527
DOI: 10.1245/s10434-023-14610-0
PMCID: PMC10761444

**Risk of metastasis and survival in patients undergoing different treatment strategies with T1 colonic neuroendocrine tumors**.
*J Endocrinol Invest*, 47(3):671-81.
X. Wu, C. Peng, M. Lin, Z. Li, X. Yang, J. Liu, X. Yang and X. Zuo. 2024.
PURPOSE: The efficacy and safety of local excision (LE) for small (< 1–2 cm) colonic neuroendocrine tumors (NETs) is controversial due to the higher metastasis risk when compared with rectal NETs. The study aimed to evaluate the metastasis risk of T1 colonic NETs and compare patients' long-term prognosis after LE or radical surgery (RS). METHODS: The Surveillance Epidemiology and End Results database was used to identify patients with T1 colonic NETs (2004–2015). Multivariable logistic regression was performed to assess factors associated with metastasis risk. Propensity score matching was used to balance the variables. Cancer-specific survival (CSS) and overall survival (OS) were calculated to estimate the prognosis of patients with T1N0M0 colonic NETs who underwent LE or RS. RESULTS: Of the 610 patients with colonic NETs, 46 (7.54%) had metastasis at diagnosis. Tumor size (11-20 mm) (OR = 9.51; 95% confidence interval (CI): 4.32–21.45; P < 0.001), right colon (OR = 15.79; 95% CI 7.20–38.56; P < 0.001), submucosal infiltration (OR = 2.08; 95% CI 0.84–5.57; P = 0.125) were independent risk factors associated with metastasis. Of the 515 patients with T1N0M0 colonic NETs, the overall long-term prognosis of LE was as good as that of RS groups (after matching, 5-year CSS: 97.9% vs. 94.6%, P = 0.450; 5-year OS: 92.7% vs. 85.6%, P = 0.009). CONCLUSION: Tumor size (11–20 mm) and site (right colon) are associated with metastasis in T1 colonic NETs. In the absence of metastasis, LE could be a viable option for 0–10 mm T1 colonic NETs with well/moderate differentiation in the left colon in terms of long-term survival.
PubMed-ID: 37653287
DOI: 10.1007/s40618-023-02185-2

**Low Prognostic Nutritional Index Is Common and Associated with Poor Outcomes following Curative-Intent Resection for Gastro-Entero-Pancreatic Neuroendocrine Tumors**.
*Neuroendocrinology*, 114(2):158-69.
J. X. Xiang, Y. R. Qian, J. He, A. G. Lopez-Aguiar, G. Poultsides, F. Rocha, S. Weber, R. Fields, K. Idrees, C. Cho, S. K. Maithel, Y. Lv, X. F. Zhang and T. M. Pawlik. 2024.
INTRODUCTION: To investigate the impact of prognostic nutritional index (PNI) on short- and long-term outcomes of patients who underwent curative-intent resection for gastro-entero-pancreatic neuroendocrine tumors (GEP-NETs). METHODS: Patients with GET-NETs who underwent curative-intent resection were identified from a multi-center

database. The prognostic impact of clinicopathological factors including PNI on post-operative outcomes were evaluated. A novel nomogram was developed and externally validated. RESULTS: A total of 2,099 patients with GEP-NETs were included in the training cohort; 255 patients were in the external validation cohort. Median PNI (n = 973) was 47.4 (IQR 43.1-52.4). At the time of presentation, 1,299 (61.9%) patients presented with some type of clinical symptom. Low-PNI (</=42.2) was associated with gastrointestinal symptoms, as well as nodal metastasis and distant metastasis (all p < 0.05). Patients with a low PNI had a higher incidence of severe (>/=Clavien-Dindo grade IIIa: low PNI 24.9% vs. high PNI 15.4%, p = 0.001) and multiple (>/=3 types of complications: low PNI 14.5% vs. high PNI 9.2%, p = 0.024) complications, as well as a worse overall survival (OS)(5-year OS, low PNI 73.7% vs. high PNI 88.5%, p < 0.001), and RFS (5-year RFS, low PNI 68.5% vs. high PNI 79.8%, p = 0.008) versus patients with high PNI (>42.2). A nomogram based on PNI, tumor grade and metastatic disease demonstrated excellent discrimination and calibration to predict OS in both the training (C-index 0.748) and two external validation (C-index 0.827, 0.745) cohorts. CONCLUSIONS: Low PNI was common and associated with worse short- and long-term outcomes among patients with GEP-NETs.
PubMed-ID: 37703840
DOI: 10.1159/000534075

# General

## Meta-Analyses

*- None -*

## Randomized controlled trials

*- None -*

## Consensus Statements/Guidelines

*- None -*

## Other Articles

**Janice L. Pasieka MD: A champion of endocrine surgery, adventure, and family**.
*Am J Surg*, 229:207-8.
S. E. Carty. 2024.
PubMed-ID: 38171941
DOI: 10.1016/j.amjsurg.2023.12.007

**The impact of social determinants of health on thyroid cancer mortality and time to treatment**.
*Surgery*, 175(1):57-64.
R. A. Collins, C. McManus, E. J. Kuo, R. Liou, J. A. Lee and J. H. Kuo. 2024.
BACKGROUND: Whereas racial disparities in thyroid cancer care are well established, the role of social determinants of health is less clear. We aimed to assess the individual and cumulative impact of social determinants of health on mortality and time to treatment among patients with thyroid cancer. METHODS: We collected social determinants of health data from thyroid cancer patients registered in the National Cancer Database from 2004 to 2017. We created a count variable for patients in the lowest quartile of each social determinant of health (ie, low income, low education, and no insurance). We assessed the association of social determinants of health with mortality and time to treatment and the association between cumulative social determinants of health count and time to treatment using Cox regression. RESULTS: Of the 142,024 patients we identified, patients with longer time to treatment had greater mortality compared to patients treated within 90 days (90-180 days, adjusted hazard ratio 1.21 (95% confidence interval 1.13-1.29, P < .001); >180 days, adjusted hazard ratio 1.57 (95% confidence interval 1.41-1.76, (P < .001). Compared to patients with no adverse social determinants of health, patients with 1, 2, or 3 adverse social determinants of health had a 10%, 12%, and 34%, respectively, higher likelihood of longer time to treatment (1 social determinant of health, hazard ratio 0.90, 95% confidence interval 0.89-0.92, P < .001; 2 social determinants of health, hazard ratio 0.88, 95% confidence interval 0.87-0.90, P < .001; 3 social determinants of health, hazard ratio 0.66, 95% confidence interval 0.62-0.71, P < .001 for all). On subgroup analysis by race, each adverse social determinant of health was associated with an increased likelihood of a longer time to treatment for Black and Hispanic patients (P < .05). CONCLUSION: A greater number of adverse social determinants of health leads to a higher likelihood of a longer time to treatment for patients with thyroid cancer, which, in turn, is associated with an increased risk for mortality.
PubMed-ID: 37872045
DOI: 10.1016/j.surg.2023.04.062