EUROPEAN SOCIETY OF ENDOCRINE SURGEONS

ESES Review of Recently Published Literature

Collection: T. Clerici, F. Triponez, M. Demarchi, K. Lorenz, M. Elwerr, G. Franch-Arcas & C. Martinez-Santos

Compilation and design: Paola Sartori, srtpvn@gmail.com

Affiliations see next page

Sept- Dec 2024

Data retrival from Pubmed: 9-03-25

Contents

CTRL-click on category or count number jumps to the according page

Publication count:	SR/MA	RCT	CG	Other	Page
Thyroid	5	1	1	27	4
Parathyroids	1	0	1	17	17
Adrenals	1	0	0	9	25
NET	1	0	0	7	30
General	0	0	0	2	34

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

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

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

Collectors

Thomas Clerici, MD
Department of Surgery, Cantonal Hospital St. Gallen, St. Gallen, Switzerland

Frédéric Triponez, MD
Marco Demarchi, MD
Department of Thoracic and Endocrine Surgery, University Hospitals of Geneva, Geneva, Switzerland

Kerstin Lorenz, MD
Malik Elwerr, MD
Department of General-, Visceral-, and Vascular Surgery, Martin-Luther University of Halle-Wittenberg, Germany

Guzmán Franch-Arcas, MD
Endocrine Surgery, Department of General and Digestive Tract Surgery, University Hospital Salamanca, Salamanca, Spain

Cristina Martinez-Santos, MD
Endocrine Surgery, Hospital Costa del Sol Marbella, Málaga, Spain

Compilation and Coordination

Paola Vincenza Sartori
Surgery Department, Desio Hospital, Desio, Italy
mailto:srtpvn@gmail.com

Journals covered

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

Journal names are links to the journal's homepage!, IF2022: Impact factor

Thyroid

Meta-Analyses

Risk factors for surgical site infection following thyroid surgery: a systematic review and meta-analysis.
Gland Surg, 13(11):2010-22.
X. Huang, K. Huang, Y. Zhang, L. Zhou, F. Wu, S. Qian, Y. Cai and D. Luo. 2024.
BACKGROUND: Thyroid surgery is a common surgical procedure for the treatment of thyroid diseases, such as thyroid nodules, thyroid cancer, and hyperthyroidism. Despite significant advancements in surgical techniques and perioperative care, surgical site infection (SSI) remains a frequent postoperative complication, which can lead to prolonged hospital stays, increased medical costs, and decreased quality of life for patients. Identifying risk factors for SSI is crucial for developing effective prevention strategies. This study aimed to systematically investigate and quantify the incidence and risk factors associated with SSI following thyroid surgery through a meta-analysis and systematic review. METHODS: A comprehensive search strategy was employed across major databases [PubMed, Web of Science, Embase, Cochrane Library, China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), Wanfang Data] up to June 15, 2024. Additionally, we conducted a supplementary search for relevant literature up to October 4, 2024. Studies were selected based on stringent inclusion and exclusion criteria focusing on SSI risk factors in patients undergoing thyroid surgery. The methodological quality of eligible studies was critically appraised. Statistical analyses were conducted using Stata 15.1 with meta-analytic techniques to estimate means and standard deviations, and calculating odds ratio (OR) with 95% confidence interval (CI) using appropriate effect models. Publication bias was assessed using Egger's test. RESULTS: The systematic review and subsequent meta-analysis included nine studies (eight case-control and two cohort) involving a total of 127,467 patients, with 703 cases of postoperative SSI documented. Key findings indicated that prolonged surgical duration greater than 2 hours [OR =4.50; 95% CI: (2.74, 7.37); P<0.001], presence of comorbidities [OR =1.91; 95% CI: (1.16, 3.15); P=0.01], age greater than 50 years [OR =1.81; 95% CI: (1.24, 2.64); P=0.002], incision length greater than 5 cm [OR =2.79; 95% CI: (1.92, 4.04); P<0.001], lymph node dissection [OR =1.90; 95% CI: (1.28, 2.80); P=0.001], and male [OR =1.78; 95% CI: (1.38, 2.29); P<0.001] were significant risk factors for SSI after thyroid surgery. Conversely, male gender did not present a statistically significant association with SSI risk. CONCLUSIONS: Surgical duration greater than 2 hours, presence of comorbidities, age greater than 50 years, incision length greater than 5 cm, lymph node dissection, and male emerge as critical risk factors for SSI in patients recovering from thyroid surgery. However, the small number of included articles and the lack of differentiation between OR, risk ratio (RR), and hazard ratio (HR) are limitations of this analysis.
PubMed-ID: 39678408
DOI: 10.21037/gs-24-330
PMCID: PMC11635573

Clinical outcomes of outpatient thyroidectomy: A systematic review and single-arm meta-analysis.
Am J Surg, 236:115694.
H. Nakanishi, R. Wang, S. Miangul, G. E. Kim, O. A. Segun-Omosehin, N. E. Bourdakos, C. A. Than, B. E. Johnson, H. Chen and A. Gillis. 2024.
BACKGROUND: The aim of this meta-analysis is to investigate the safety of outpatient thyroidectomy based on 24-h and same-day discharge criteria. METHODS: CENTRAL, Embase, PubMed, and Scopus were searched. A meta-analysis of selected studies was performed. The review was registered prospectively with PROSPERO (CRD42022361134). RESULTS: Thirty-one studies met the eligibility criteria, with a total of 74328 patients undergoing thyroidectomy in an outpatient setting based on 24-h discharge criteria. Overall postoperative complications after outpatient thyroidectomies were 5.7% (95%CI: 0.049-0.065; I2 = 97.3%), consisting of hematoma (0.4%; 95%CI: 0.003-0.005; I2 = 83.4%), recurrent laryngeal nerve injury (0.4%; 95%CI: 0.003-0.006; I2 = 93.5%), and hypocalcemia (1.6%; 95%CI: 0.012-0.019; I2 = 93.7%). The rate of readmission was 1.1% (95%CI: 0.007-0.015; I2 = 95.4%). Results were similar for same-day criteria. CONCLUSIONS: Our analysis demonstrated that outpatient thyroidectomy is a safe procedure in the management of thyroid disease for selected patients.
PubMed-ID: 38443270
DOI: 10.1016/j.amjsurg.2024.02.037

Feasibility of remote-access and minimally invasive video-assisted approaches in lateral neck dissection for papillary thyroid carcinoma: A systematic review and network meta-analysis.

Eur J Surg Oncol, 50(9):108469.
V. C. Nguyen, C. M. Song, Y. B. Ji, J. K. Myung, J. S. Park and K. Tae. 2024.
BACKGROUND: This study was conducted to evaluate the feasibility and surgical outcomes of minimally invasive video-assisted thyroidectomy (MIVAT) and three remote-access approaches, namely the robotic bilateral axillo-breast approach (BABA-R), endoscopic breast-chest approach (BCA-E), and robotic gasless transaxillary approach (GTAA-R) in lateral neck dissection for papillary thyroid carcinoma, compared with conventional transcervical approach (CTA). METHODS: The literature search was conducted in the PubMed, EMBASE, and Cochrane Library databases, covering the period January 2000 to February 2024. A systematic review and network meta-analysis were performed to compare surgical feasibility, safety, and oncologic outcomes between approaches. RESULTS: Fourteen articles on lateral neck dissection in patients with papillary thyroid carcinoma were included after systematic screening. The number of removed and metastatic lateral lymph nodes, the extent of lateral neck dissection, the rate of transient recurrent laryngeal nerve palsy and hypoparathyroidism, serum-stimulated thyroglobulin levels, and recurrence were not significantly different between the MIVAT and three remote-access approaches. Additionally, these were comparable to those of the CTA. However, the MIVAT and remote-access approaches took a longer operative time but provided superior cosmetic outcomes compared to the CTA. CONCLUSION: Lateral neck dissection using the MIVAT and three remote-access approaches was feasible and comparable to CTA in the number of lymph nodes removed, complications, stimulated thyroglobulin level, and recurrence. The MIVAT and remote-access approaches lasted longer but provided significantly superior cosmetic outcomes compared to the CTA.
PubMed-ID: 38865930
DOI: 10.1016/j.ejso.2024.108469

Track recurrence after remote-access thyroid surgeries: A systematic review.
World J Surg, 48(11):2697-707.
M. Y. Oh and Y. J. Chai. 2024.
BACKGROUND: Remote-access thyroidectomies have gained popularity, but track recurrence, which is the implantation of thyroid tissue or lesions along the surgical access route, has been reported in case studies. This systematic review aims to review cases of track recurrence following remote-access thyroidectomies. METHODS: A comprehensive literature search was conducted using PubMed, the Web of Science, the Cochrane Library, and Google Scholar to identify case reports on track recurrence after endoscopic or robotic thyroidectomy up to June 2024. Data included patient demographics, details of the initial surgery and diagnosis, methods and timing of recurrence detection, and management strategies. RESULTS: The search yielded 1578 articles, of which 17 case reports comprising 18 patients were included. The patients (16 females and two males) had a mean age of 34.6 +/- 14.9 years. The mean size of initial tumors was 3.9 +/- 1.2 cm, with diagnoses of eight cancers and 10 benign lesions. The initial surgeries included 12 endoscopic and six robotic procedures. Track recurrence was most often detected by palpable nodules followed by routine imaging and elevated serum Tg levels. The interval between initial surgery and recurrence ranged from 3 months to 8 years. Management varied from surgical resection and radioactive iodine therapy to close observation. There were no further recurrences in all but one case postoperatively. CONCLUSION: Track recurrence after remote-access thyroidectomy is rare but significant. Proper surgical techniques, careful handling of thyroid tissue, and rigorous postoperative monitoring are essential to minimize this risk. Awareness and prompt management of track recurrence may lead to favorable outcomes.
PubMed-ID: 39343618
DOI: 10.1002/wjs.12361

The efficacy and safety of selenium supplementation versus placebo in the treatment of Graves' orbitopathy: A systematic review and meta-analysis of randomised controlled trials.
Clin Endocrinol (Oxf), 101(6):669-81.
I. Sharabati, R. M. Qafesha, M. D. Hindawi, S. Amro and B. M. Ayesh. 2024.
BACKGROUND: Selenium is a trace element crucial for thyroid function, and has potential therapeutic benefits in Graves' orbitopathy (GO). Therefore, we aim to evaluate its efficacy and safety in GO patients to provide valuable insights into its role as a therapeutic option for this condition. DESIGN: Systematic review and meta-analysis. PATIENTS: GO Patients treated with selenium compared to placebo. MEASUREMENTS: Clinical activity score (CAS), Graves' orbitopathy quality of life (GO-QOL), eye symptoms and signs, and adverse events. RESULTS: Out of 1684 records screened, four randomised controlled trials were included. Selenium was superior at 6 months in lowering the CAS (MD = -1.27, 95% confidence interval [CI] [-1.68, -0.85], p < .0001]), improving total GO-QOL (RR = 2.54, 95% CI [1.69-3.81], p < .00001), and improving the visual and the psychological functioning scores (MD = 10.84, 95% CI [4.94-16.73], p = .003), (MD = 12.76, 95% CI [8.51-17.00], p < .00001) respectively. Similarly, it significantly improved these outcomes at 12 months. It also showed a

significant decrease in the palpebral aperture at 6 months (MD = -1.49, 95% CI [-2.90, -0.08], p = .04). However, no significant differences were observed in proptosis, soft tissue involvement, ocular motility, and adverse effects. CONCLUSIONS: Selenium is effective in reducing CAS and improving the palpebral aperture and GO-QOL in patients with GO. Additionally, it is safe and has promising therapeutic implications. However, further research is needed to validate its long-term efficacy and safety.
PubMed-ID: 39138905
DOI: 10.1111/cen.15128

Randomized controlled trials

Long-Term Outcome of Low- and High-Dose Radioiodine for Thyroid Remnant Ablation.
Clin Endocrinol (Oxf), 101(6):682-9.
S. Liu, S. Wu, C. Ma, S. Wang, S. Chen, H. Wang and F. Feng. 2024.
OBJECTIVE: We conducted a prospective randomized clinical trial to compare the efficacy of low- and high-dose radioiodine for remnant ablation in patients with low-risk differentiated thyroid cancer (DTC) in China. The first-stage results showed equivalence was observed between the two groups. Here, we report recurrence and survival at 3-5 and 6-10 years and biochemical parameters. DESIGN, PATIENTS AND METHODS: Between January 2013 and December 2014, adult patients with DTC were enroled. Patients had undergone total or near-total thyroidectomy, with or without cervical lymph node dissection, with tumour stages T1-T3 with or without lymph node metastasis, but without distant metastasis. Patients were randomly assigned to the low-dose (1850 MBq) or high-dose (3700 MBq) radioiodine group. They were then followed up for 3-5 and 6-10 years. Data on biochemical abnormalities, recurrence and survival were analysed using Kolmogorov-Smirnov and chi(2) tests. RESULTS: The data of 228 patients (mean age = 42 years; 70.6% women) were analysed, with 117 patients in the low-dose group and 111 in the high-dose group. There were no significant differences in biochemical abnormalities, recurrence, or survival rates at the 6-10-year follow-up (all p > .05). Nine patients experienced recurrence in the low-dose group (8.7%), while eight patients experienced recurrence in the high-dose group (8.2%). The survival rates were 100% and 98.2% in the low- and high-dose groups, respectively. CONCLUSIONS: The long-term effectiveness and safety of low-dose (1850 MBq) radioiodine are the same as those of high-dose (3700 MBq) radioiodine for thyroid remnant ablation in Chinese patients with low-risk DTC.
PubMed-ID: 39233456
DOI: 10.1111/cen.15134

Consensus Statements/Guidelines

Consensus statement on the management of incidentally discovered FDG avid thyroid nodules in patients being investigated for other cancers.
Clin Endocrinol (Oxf), 101(5):557-61.
J. Wadsley, S. P. Balasubramanian, G. Madani, J. Munday, T. Roques, C. W. Rowe, P. Touska and K. Boelaert. 2024.
With the widespread use of 18F-fluorodeoxyglucose positron emission tomography (FDG PET/CT) in the investigation and staging of cancers, incidental discovery of FDG-avid thyroid nodules is becoming increasingly common, with a reported incidence in the range 1%-4% of FDG PET/CT scans. The risk of malignancy in an incidentally discovered FDG avid thyroid nodule is not clear due to selection bias in reported retrospective series but is likely to be less than 15%. Even in cases where the nodule is found to be malignant, the majority will be differentiated thyroid cancers with an excellent prognosis even without treatment. If, due to index cancer diagnosis, age and co-morbidities, it is unlikely that the patient will survive 5 years, further investigation of an incidental FDG avid thyroid nodule is unlikely to be warranted. We provide a consensus statement on the circumstances in which further investigation of FDG avid thyroid nodules with ultrasound and fine needle aspiration might be appropriate.
PubMed-ID: 36878888
DOI: 10.1111/cen.14905

Other Articles

Medullary Thyroid Cancer: Single Institute Experience Over 3 Decades and Risk Factors for Recurrence.
J Clin Endocrinol Metab, 109(11):2729-34.
S. Abou Azar, J. Tobias, M. Applewhite, P. Angelos and X. M. Keutgen. 2024.
CONTEXT: Medullary thyroid cancer (MTC) has a historic recurrence rate up to 50%, and surgery remains the only cure. OBJECTIVE: This study aims to assess factors related to recurrence and metastatic spread in MTC. METHODS: Retrospective chart review was performed from 1990 to 2023 at a single specialized tertiary care referral center. Descriptive analysis and regression models were used for analysis. Sixty-eight patients with MTC, who underwent surgery, were included and the main outcome measure was recurrence. RESULTS: Mean age at diagnosis was 54.9 years (42.2-64.1), 65% (n = 44) females. Lymph node and distant metastases were found in 24% (n = 16) and 4% (n = 3), respectively. RET mutations were present in 52% (n = 35): MTC risk levels were highest 6%, high 7%, and moderate 39%. Mean tumor size was 1.9 cm (1.2-3.2) and mean preoperative calcitonin was 504.4 pg/mL (133.2-1833.8). Total thyroidectomy (TT) was performed in 10 patients, TT + central neck dissection (CND) in 28, and TT + CND + lateral neck dissection (LND) in 25. On final pathology, 40% had positive central nodes and 25% had positive lateral nodes. Recurrence was 22%, median follow-up 4.7 years (1.2-28.0). Male gender (hazard ratio [HR] 5.81, P = .021), positive lateral neck nodes (HR 8.10, P = .011), and high/highest MTC risk level RET mutations (HR 8.66, P = .004) were significantly associated with recurrence. Preoperative calcitonin >2175 pg/mL was a strong predictor for distant metastasis (area under the curve [AUC] 0.893) and a good predictor for lateral neck disease (AUC 0.706). Extent of surgery was not significantly associated with recurrence (P = .634). CONCLUSION: One of 4 patients undergoing surgery for MTC will recur. Risk factors associated with recurrence are male gender, lateral lymph node metastasis, and high/highest MTC risk level mutations, but not necessarily surgery type. Preoperative calcitonin >2175 pg/mL is suggestive of advanced disease and should prompt further evaluation.
PubMed-ID: 38651609
DOI: 10.1210/clinem/dgae279

Outcomes of Cytologically Indeterminate Thyroid Nodules Managed With Genomic Sequencing Classifier.
J Clin Endocrinol Metab, 109(12):e2231-e9.
S. Ahmadi, A. Kotwal, A. Bikas, P. Xiang, W. Goldner, A. Patel, E. G. Hughes, X. Longstaff, M. W. Yeh and M. J. Livhits. 2024.
CONTEXT: Molecular testing can refine the risk of malignancy in thyroid nodules with indeterminate cytology to decrease unnecessary diagnostic surgery. OBJECTIVE: This study was performed to evaluate the outcomes of cytologically indeterminate thyroid nodules managed with Afirma genomic sequencing classifier (GSC) testing. METHODS: Adult patients who underwent a biopsy at 3 major academic centers between July 2017 and June 2021 with Bethesda III or IV cytology were included. All patients had surgery or minimum follow-up of 1 year ultrasound surveillance. The primary outcomes were the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of GSC in Bethesda III and IV nodules. RESULTS: The median nodule size of the 834 indeterminate nodules was 2.1 cm and the median follow-up was 23 months. GSC sensitivity, specificity, PPV, and NPV across all institutions were 95%, 81%, 50%, and 99% for Bethesda III nodules and 94%, 82%, 65%, and 98% for Bethesda IV nodules, respectively. The overall false-negative rate was 2%. The NPV of GSC in thyroid nodules with oncocytic predominance was 100% in Bethesda III nodules and 98% in Bethesda IV nodules. However, the PPV of oncocytic nodules was low (17% in Bethesda III nodules and 45% in Bethesda IV nodules). Only 22% of thyroid nodules with benign GSC results grew during surveillance. CONCLUSION: GSC is a key tool for managing patients with indeterminate cytology, including the higher-risk Bethesda IV category. GSC-benign thyroid nodules can be observed similarly to thyroid nodules with benign cytology.
PubMed-ID: 38415829
DOI: 10.1210/clinem/dgae112

Paediatric thyroid disease.
Clin Endocrinol (Oxf), 101(3):223-33.
T. Cheetham and C. Wood. 2024.
The spectrum of thyroid disorders presenting to paediatricians is different to that seen by adult physicians. Referrals reflect cases detected by the neonatal screening programme for congenital hypothyroidism and many of the inherited defects of thyroid hormone generation or action will be manifest in early life. Autoimmune thyroid disease can be particularly challenging to manage in the young and the potential impact of thyroid status on neurodevelopment and schooling are key considerations throughout childhood and adolescence.
PubMed-ID: 39072866
DOI: 10.1111/cen.15110

A Small Opening in the Storm Clouds: Overview of the Registry-based Study on the Management of Thyroid Storm.
J Clin Endocrinol Metab, 109(12):e2355-e7.
L. H. Duntas and M. Zarkovic. 2024.
Because of the high mortality rate of thyroid storm (TS), effective guidance for its diagnosis and treatment is essential. The diagnostic criteria introduced by the Japanese Thyroid Association in 2012, along with the Burch-Wartofsky Point Scale, constitute valuable tools for the diagnosis of TS. In 2016, Guidelines on the management of TS were produced by the Japanese Thyroid Association and the Japanese Endocrine Society. Recently, a prospective multicenter register-based study compared the prognosis and outcome of 110 new-onset TS patients with the results of previous comparable studies and evaluated the efficacy of the Guidelines. The study revealed higher Acute Physiology and Chronic Health Evaluation II scores and significant correlations between lower body mass index, postresuscitation shock, and fever with outcomes and, overall, improved TS prognosis. Most patients in the study received methimazole and potassium iodide, the timely administration of which was linked to lower fatality rates. Adherence to treatment guidelines correlates with lower mortality rates, emphasizing the importance of experienced multidisciplinary teams in intensive care unit settings and the necessity for periodic review of the guidelines to enhance therapeutic approaches and reduce mortality.
PubMed-ID: 39119880
DOI: 10.1210/clinem/dgae543

Evaluation of Hypocalcemia Following Total Laryngectomy With and Without Thyroidectomy.
Otolaryngol Head Neck Surg, 171(3):685-92.
H. W. Eberly, B. Y. Sciscent, F. Jeffrey Lorenz, N. Truong, T. S. King, D. Goldenberg and N. Goyal. 2024.
OBJECTIVE: Hypoparathyroidism and associated hypocalcemia are well-established complications following laryngectomy. This study further characterizes the rates of hypocalcemia in patients undergoing total laryngectomy (TL) with and without thyroidectomy and hemithyroidectomy. STUDY DESIGN: Retrospective cohort study. SETTING: TriNetX. METHODS: We queried TriNetX, a deidentified patient database, to identify patients who underwent TL with and without thyroidectomy and hemithyroidectomy. Rates of hypocalcemia, low parathyroid hormone (PTH), calcium, and calcitriol supplementation were compared between groups with multivariable repeated measures logistic regression. RESULTS: We identified 870 patients in the TL without thyroidectomy cohort, 158 patients in the hemithyroidectomy cohort, and 123 in the total thyroidectomy cohort. Rates of hypocalcemia differed between patients receiving total thyroidectomy versus TL alone for 0 to 1 month (odds ratio [OR]: 2.88 [1.95-4.26]) 1 to 6 months (OR: 5.08 [2.29-11.3]), and 6 to 12 months (OR: 2.63 [1.003-6.88]) postoperatively, with adjustment for age at laryngectomy, race, ethnicity, and gender. Results were similar among those who received calcium supplementation. The rate of low PTH levels differed in these groups for 0 to 1 month (OR: 5.13 [3.10-8.51]), 1 to 6 months (OR: 3.47 [1.46-8.22]), and 6 to 12 months (OR: 3.63 [1.40-9.38]) following surgery. Rates of postoperative calcium supplementation were increased for patients receiving total thyroidectomy versus TL for 1 to 6 months (OR: 2.44 [1.62-3.68]), and 6 to 12 months following surgery (OR: 1.79 [1.18-2.72]). CONCLUSION: Patients undergoing TL with total thyroidectomy have a higher risk of postoperative hypocalcemia compared to patients receiving TL alone. Risk of parathyroid injury in these patients may warrant further emphasis on PTH measurement after surgery and a multidisciplinary approach to management.
PubMed-ID: 38738927
DOI: 10.1002/ohn.804

Indolent Behavior of Malignant Bethesda III Nodules Compared to Bethesda V/VI Nodules.
J Clin Endocrinol Metab, 109(9):2317-24.
M. Endo, J. Peng, F. A. Nabhan, P. Brock, I. Azaryan, C. Long, L. E. Ryan, M. D. Ringel and J. A. Sipos. 2024.
BACKGROUND: The Bethesda system classifies all fine-needle aspiration specimens into 1 of 6 categories. We speculated that cancers within each Bethesda category would have distinct clinical behavior. METHODS: This is a retrospective analysis of patients from a single academic medical center with a histologic diagnosis of thyroid cancer who had an initial diagnosis of Bethesda III, IV, V, or VI cytology. RESULTS: A total of 556 cases were included, with 87 cases of Bethesda III, 109 cases of IV, 120 cases of V, and 240 cases of VI. Bethesda III showed similarities with V/VI compared to IV with a predominance of papillary thyroid cancer. The interval from diagnosis to surgery was longer in Bethesda III compared to Bethesda V/VI (median 78 vs 41 days, $P < .001$) (Fig. 1). Yet, patients with Bethesda III had a higher probability of achieving remission (62% vs 46%, $P < .03$), a lower possibility of recurrence (8% vs 24%, $P < .001$), and a shorter interval to achieve remission (median 1218 vs 1682 days, $P = .02$) compared to Bethesda V/VI, which did not change after adjusting for age, sex, radioactive iodine therapy, mode of surgery, and tumor size. More than 70% of Bethesda III that later presented with recurrence had T3/T4 disease or distant metastasis. CONCLUSION: Cancers with Bethesda III cytology had a less aggressive

clinical phenotype with better prognosis compared to V/VI despite histological similarities. The time to remission was shorter in Bethesda III despite a longer interval between diagnosis and surgery. The initial cytological diagnosis may guide management.
PubMed-ID: 38415340
DOI: 10.1210/clinem/dgae108

A high Ki-67 labeling index and high thyroglobulin doubling rate are significant predictors of excision-site recurrence of papillary thyroid carcinoma following airway resection for locally curative surgery.
World J Surg, 48(10):2452-62.
Y. Ito, A. Miyauchi, M. Hirokawa, M. Kawakami, M. Kihara, N. Onoda and A. Miya. 2024.
BACKGROUND: Papillary thyroid carcinoma (PTC) occasionally invades the trachea and requires airway resection. Tracheal excision site recurrence (ESR) is a serious problem. We investigated predictors of ESR in patients with PTC who underwent airway resection for locally curative surgery. METHODS: We enrolled 149 patients with PTC who underwent airway resection (median age at the initial surgery: 67 years), including partial-thickness resection (n = 73) or full-thickness resection (n = 76), for grossly curative surgery. The median postoperative follow-up period was 93 months. RESULTS: To date, 11 patients (6.7%) underwent ESR: 6 underwent full-thickness resection and 5 underwent partial-thickness resection. The time to ESR ranged from 14 to 113 months (median: 57 months) after the initial surgery. None of the 11 ESR patients underwent adjuvant external beam radiotherapy (EBRT) and none of the 4 airway resection patients who underwent EBRT developed ESR. The 5- and 10-year ESR rates were 4.3% and 11.3%, respectively. In the multivariate analysis (forward-backward stepwise selection method), a Ki-67 labeling index (LI) >/=5% (p = 0.048) and the thyroglobulin doubling rate (Tg-DR) >0.33/year (p = 0.009) (for Tg-antibody negative cases) were independent predictors of ESR. Nine of the 11 patients underwent ESR resection and only one developed a second recurrence. CONCLUSIONS: A high Ki-67 LI was a static predictor, and high Tg-DR was a dynamic predictor, of ESR in patients with PTC following airway resection. In such patients, careful postoperative monitoring for ESR is necessary and adjuvant therapies, such as EBRT, may be considered.
PubMed-ID: 39252167
DOI: 10.1002/wjs.12325

Prognostic significance of T3b in papillary thyroid carcinoma: Appropriateness of classifying T3bN0M0 in patients aged 55 years or older into stage II.
World J Surg, 48(9):2132-41.
Y. Ito, A. Miyauchi, M. Kawakami, M. Kihara and A. Miya. 2024.
BACKGROUND: Papillary thyroid carcinoma (PTC) often extends to adjacent organs. According to the 8th Tumor-Node-Metastasis Classification, extension to the strap muscles was graded as T3b. We investigated the prognostic impact of T3b and the appropriateness of T3b in patients aged >/=55 years who were classified as stage II. METHODS: We enrolled 7811 patients with M0 PTC who underwent initial surgery at the Kuma Hospital (Kobe, Japan) between January 2007 and December 2016. Tumor extension was divided into T3b, T4a1 (extension to the tracheal adventitia, tracheal cartilage, esophageal muscle layer, recurrent laryngeal nerve, cricothyroid, and inferior constrictor muscles), and sT4a2 (extension to the subcutaneous soft tissues, tracheal mucosa, esophageal mucosa, internal jugular vein, brachiocephalic vein, larynx, pharynx, and sternocleidomastoid muscle). RESULTS: In patients >/=55 years, the local recurrence-free survival (LR-FS), distant recurrence-free survival (DR-FS), and cause-specific survival (CSS) rates of T3bN0M0 were significantly poorer than those of T1/T2N0M0 but did not significantly differ from those of T3aN0M0. The LR-FS, DR-FS, and CSS rates of T3b stage II patients did not differ from those of T4a1 stage III patients but were significantly better than those of T4a2 stage III patients. T3b was an independent predictor of local recurrence and distant recurrence but not of death due to carcinoma in the multivariate analysis. In patients aged <55 years with M0 PTC, T3b had no prognostic value in both analyses. CONCLUSIONS: T3bM0 patients are appropriate to be classified as stage II in patients >/=55 years but be kept in stage I in patients <55 years.
PubMed-ID: 39085165
DOI: 10.1002/wjs.12307

Developing a large-scale quality improvement program for thyroid cancer surgery.
World J Surg, 48(12):2925-33.
C. B. Jensen, E. M. Bacon, L. N. Krumeich, H. J. Underwood, D. T. Hughes, P. G. Gauger, R. Burney and S. C. Pitt. 2024.
BACKGROUND: Surgical quality improvement (QI) plays a critical role in optimizing patient outcomes and reducing healthcare costs. QI programs focusing specifically on thyroid cancer surgical care are lacking. This study aimed to (a) select and introduce surgical quality indicators for thyroid cancer and (b) identify areas for QI at the state-level. METHODS:

A multidisciplinary team of thyroid cancer and QI experts selected 10 thyroid cancer-specific quality indicators and assessed the quality of thyroid cancer surgical care compared to current national guidelines. Analysis of the first year (January-December 2023) of data collection was performed using descriptive statistics. RESULTS: The thyroid cancer quality indicators included preoperative cytology, postoperative pathology, staging, cancer size, margin status, extrathyroidal extension, lymph nodes, postoperative complications within 30 days, documented follow-up treatment, and documented surveillance plans. 112 surgeons performed 360 thyroidectomies for thyroid cancer at 51 hospitals. Preoperative cytology was not performed in 34.3% (n = 103) of cases with thyroid cancer on final pathology. When the extent of surgery was evaluated by papillary cancer size, 50.0% (n = 38) of patients with <1 cm cancers underwent total thyroidectomy, and 13.8% (n = 4) with >4 cm underwent thyroid lobectomy. Positive margins were found in 16.2% (n = 53). Postoperatively, 19.2% (n = 69) of patients lacked documented follow-up, and 18.6% (n = 67) lacked thyroid cancer surveillance plans. CONCLUSIONS: Establishing a dedicated QI program for thyroid cancer provides a previously unharnessed opportunity to enhance the quality of thyroid cancer surgical care. Statewide surgical quality collaboratives offer a model for establishing thyroid cancer QI initiatives across diverse healthcare settings in other states and countries.
PubMed-ID: 39404618
DOI: 10.1002/wjs.12367
PMCID: PMC11619744

Concerns Regarding Thermal Ablation for Papillary Thyroid Cancer.
JAMA Surg, 159(11):1231-2.
M. Jiang, Y. Yu and A. Yang. 2024.
This Viewpoint discusses drawbacks to thermal ablation for papillary thyroid cancer.
eng.
PubMed-ID: 39320880
DOI: 10.1001/jamasurg.2024.2744

Analysis of near-infrared autofluorescence imaging for detection of inadvertently resected parathyroid glands after endoscopic thyroidectomy.
Eur J Surg Oncol, 50(11):108648.
T. C. Kuo, K. Y. Chen, C. W. Lai, M. T. Lin, C. H. Chang and M. H. Wu. 2024.
BACKGROUND: Preserving parathyroid function during thyroidectomy is crucial, but remains challenging. Real-time near-infrared autofluorescence (NIRAF) aids surgeons in intraoperative parathyroid gland (PTG) identification. However, its role in detecting PTGs unintentionally removed during surgery is unclear. STUDY DESIGN: This prospective study included adult patients undergoing endoscopic thyroidectomy. Surgeons identified and documented PTGs visually. Excised specimens underwent visual inspection and NIRAF imaging (PDE-Neo II). All fluorescent tissues were dissected and pathologically evaluated (reference standard). One scanned image per lobe was chosen to quantify autofluorescence (AF) intensity. RESULTS: Overall, 95 patients underwent endoscopic thyroidectomies, with NIRAF imaging applied to 152 excised lobes. Of these, 19 lobes displayed a total of 23 spots with increased intensity. 175 specimens were sent for pathological evaluation, and 7 were confirmed to be parathyroid tissue. NIRAF demonstrated 100.0 % sensitivity and 90.5 % specificity for predicting parathyroid tissue, with 30.4 % positive predictive value, 100.0 % negative predictive value of and 90.9 % accuracy. Quantitatively normalized, the AF signal intensity was significantly higher in NIRAF-positive tissues than negative (4.3 vs 1.2 times, $p < 0.0001$). Additionally, the AF signal intensity in regions pathologically confirmed of parathyroid tissue was higher than non-parathyroid tissue (9.1 vs 2.1 times, $p < 0.0001$). CONCLUSION: This study suggests that NIRAF has high sensitivity and specificity for detecting inadvertently resected PTGs after endoscopic thyroidectomy, contributing to preservation efforts. However, NIRAF-positive tissues still require additional confirmation through multiple methods, emphasizing other examinations to verify that they are indeed parathyroid tissues. Further research is warranted to refine NIRAF imaging parameters.
PubMed-ID: 39243694
DOI: 10.1016/j.ejso.2024.108648

Tumor desmoplasia outperforms preoperative serum calcitonin as surgical biomarker in sporadic medullary thyroid cancer.
Head Neck, 46(11):2843-52.
A. Machens, K. Lorenz, C. Bensch, C. Wickenhauser and H. Dralle. 2024.
BACKGROUND: Conceptually, thyroid tumor desmoplasia may be better suited for excluding node metastases in sporadic MTC than preoperative serum calcitonin levels. METHODS: This analysis included 181 patients with unilateral sporadic

MTC graded on the 7-grade desmoplasia scale after thyroidectomy and neck dissection. RESULTS: When thyroid tumor desmoplasia reached 1% and >/=50%, node metastases increased from 0% to 7% (median of 0 metastases) and 83% (median of 7.5 metastases), microscopic lymphatic invasion from 0% to 3% and 35%, extrathyroid extension from 0% to 5% and 22%, and extranodal growth from 0% to 0% and 44%, whereas biochemical cure declined from 100% to 95% and 25%. Thyroid tumor diameters and basal calcitonin overlapped widely among the seven desmoplasia groups, precluding differentiation by thyroid tumor size or serum calcitonin levels. CONCLUSIONS: Thyroid tumor desmoplasia, unlike serum calcitonin levels, discriminates extremely well between node-negative and node-positive sporadic MTC, opening new avenues for precision surgery.
PubMed-ID: 38850101
DOI: 10.1002/hed.27827

Origin and impact of multifocal growth in sporadic vs. hereditary medullary thyroid cancer.
Eur J Surg Oncol, 50(11):108625.
A. Machens, K. Lorenz, F. Weber and H. Dralle. 2024.
Multifocal growth is characteristic of hereditary medullary thyroid cancer (MTC), whereas origin and impact of multifocal growth is enigmatic for sporadic MTC. To address this, 460 RET-negative patients with sporadic MTC, stratified by 1 (93.3 %), 2 (5.7 %) and 3 (1.1 %) thyroid tumor foci, were compared with 219 RET-positive patients with hereditary MTC, stratified by 1 (38.4 %), 2 (45.7 %), 3 (6.4 %), 4 (6.8 %) and >/=5 (2.7 %) thyroid tumor foci. For sporadic MTC, significant associations were identified with bilateral thyroid lobe involvement, microscopic lymphatic invasion, extrathyroid extension, node and distant metastases, number of node metastases, preoperative basal calcitonin level, and decreasing biochemical cure. For hereditary MTC, significant associations were limited to bilateral thyroid lobe involvement, largest thyroid tumor diameter, and preoperative basal calcitonin level. In sporadic MTC, multifocal growth is due to lymphatic invasion with frequent node metastases, whereas in hereditary MTC, it reflects malignant progression from C-cell hyperplasia to cancer.
PubMed-ID: 39213697
DOI: 10.1016/j.ejso.2024.108625

Preference Phenotypes in Thyroid Nodule Management: A Patient Segmentation Approach.
Otolaryngol Head Neck Surg, 171(3):678-84.
M. R. Naunheim, I. Wasserman, M. R. von Sneidern, M. N. Huston, G. W. Randolph and M. G. Shrime. 2024.
OBJECTIVE: Patient preferences regarding thyroid nodules are poorly understood. Our objective is to (1) employ a discrete choice experiment (DCE) to explore risk tradeoffs in thyroid nodule management, and (2) segment respondents into preference phenotypes. STUDY DESIGN: DCE. SETTING: Thyroid surgery clinic, online survey. METHODS: A DCE including 5 attributes (cancer risk, voice concerns, incision/scar, medication requirement, follow-up frequency) was refined with qualitative patient and physician input. A final DCE including 8 choice tasks, demographics, history, and risk tolerance was administered to participants with and without thyroid disease. Analysis was performed with multinomial logit modeling and latent class analysis (LCA) for preference phenotyping. RESULTS: A total of 1026 respondents were included; 480 had thyroid disease. Risk aversion was associated with increasing age (P < .001), female gender (P < .001), and limited education (P = .038), but not previous thyroid disease. Cancer risk most significantly impacted decision-making. Of the total possible utility change from thyroid nodule decision-making, 47.8% was attributable to variations in cancer risk; 20.0% from medication management; 14.9% from voice changes; 12.7% from incision/scar; and 4.6% from follow-up concerns. LCA demonstrated 3 classes with distinct preference phenotypes: the largest group (64.2%) made decisions primarily based on cancer risk; another group (18.2%) chose based on aversion to medication; the smallest group (17.7%) factored in medication and cancer risk evenly. CONCLUSION: Cancer risk and the need to take medication after thyroid surgery factor into patient decision-making most heavily when treating thyroid nodules. Distinct preference phenotypes were demonstrated, reinforcing the need for individual preference assessment before the treatment of thyroid disorders.
PubMed-ID: 38591729
DOI: 10.1002/ohn.776

Radiomics and deep learning for large volume lymph node metastasis in papillary thyroid carcinoma.
Gland Surg, 13(9):1639-49.
Z. Ni, T. Zhou, H. Fang, X. Lin, Z. Xing, X. Li, Y. Xie, L. Hong, S. Huang, J. Ding and H. Huang. 2024.
BACKGROUND: Thyroid cancer is prone to early lymph node metastasis (LNM), and patients with large volume LNM (LVLNM) tend to have a poorer prognosis. The aim of this study was to predict LVLNM in before surgery based on radiomics and deep learning (DL). METHODS: A multicenter retrospective study was performed, including 854 papillary

thyroid carcinoma (PTC) patients from three centers. Radiomics features were extracted. Logistic regression (LR), support vector machine (SVM), K-nearest neighbors (KNN), multi-layer perceptron (MLP), random forest (RF), ExtraTrees, extreme gradient boosting (XGBoost), and light gradient boosting machine (LightGBM) algorithms were used to construct radiomics models. AlexNet, DenseNet121, inception_v3, ResNet50, and transformer algorithms were used to construct DL models. The receiver operating characteristic (ROC) curve was employed to select the better-performing model. A combined model was then created by merging radiomics features and DL features. The least absolute shrinkage and selection operator (LASSO) method was utilized to identify metabolites and radiomics features with non-zero coefficients. The performance of the models was evaluated using area under the curve (AUC), accuracy (ACC), sensitivity (SEN), specificity (SPE), positive predictive value (PPV), negative predictive value (NPV), and F1-score. RESULTS: A total of 1,357 radiomics features were extracted. Among the radiomics models, the ExtraTrees model demonstrated the optimal diagnostic capabilities with an AUC of 0.787 [95% confidence interval (CI): 0.715-0.858], and DenseNet121 DL model demonstrated the optimal diagnostic capabilities with an AUC of 0.766 (95% CI: 0.683-0.848). Furthermore, the combined model, named the Thy-DL-Radiomics model, exhibited an AUC of 0.839 (95% CI: 0.758-0.920) in the internal validation set and 0.789 (95% CI: 0.718-0.859) in the external validation set. CONCLUSIONS: A radiomics-DL features integrated model can predict LVLNM in PTC patients and provide guidance for personalized treatment.
PubMed-ID: 39421056
DOI: 10.21037/gs-24-308
PMCID: PMC11480870

Recurrence and postoperative quality of life after surgical resection of unilateral cT1-T3N1bM0 papillary thyroid carcinoma.
Gland Surg, 13(10):1740-51.
Z. Qiu, L. Zhang, X. Guo, Z. Ding, J. Han, W. Bi, B. Sun, J. Zhang and C. Nie. 2024.
BACKGROUND: Determining the optimal extent of surgery and improving postoperative quality of life for patients with papillary thyroid cancer has been an important challenge. Here, we evaluated postoperative quality of life after cT1-T3N1bM0 papillary thyroid carcinoma (PTC) to explore the optimal scope of surgical resection. METHODS: In this study, we investigated surgical outcomes in patients diagnosed with unilateral cT1-T3N1bM0 PTC, who were treated at Harbin Medical University Cancer Hospital from January 2008 to December 2018. To achieve this, we divided the patients into two distinct groups based on the extent of surgery they received: the non-total thyroidectomy group (group A) and the total thyroidectomy group (group B). To comprehensively evaluate the patients' well-being, we assessed their psychological status, disease recurrence rate, postoperative complications, and quality of life. RESULTS: A total of 362 patients diagnosed with thyroid cancer were included in this study, with group A (n=88) and group B (n=274) classified based on the extent of surgery received. Significant differences were observed between the two groups in terms of clinical and pathological characteristics, including age (chi(2)=10.962, P=0.001), sex (chi(2)=5.906, P=0.02), multifocal (chi(2)=5.515, P=0.02), contralateral glandular nodule (chi(2)=34.616, P<0.001), clinical Tumor, Node, Metastasis (TNM) stage (chi(2)=11.340, P=0.001), and complication rate (chi(2)=4.265, P=0.04). Notably, group B exhibited higher rates of postoperative complications, including temporary recurrent laryngeal nerve injury (chi(2)=4.630, P=0.03), and temporary hypocalcemia (chi(2)=3.954, P=0.047) compared to group A. However, after adjustment for propensity score matching (PSM), the recurrence rate was independent of the surgical extent in both groups. In contrast, tumour size (>1 cm) (chi(2)=4.497, P=0.03), extrathyroidal invasion (chi(2)=5.133, P=0.02) and pathological T stage (chi(2)=7.663, P=0.02) increased the risk of recurrence. Moreover, there was no significant difference in the Hospital Anxiety and Depression Scale (HADS) scores between two groups (chi(2)=1.266, P=0.53). Nevertheless, the postoperative quality of life, as well as the incidence of hoarseness (t=11.77, P<0.001), symptoms of calcium deficiency (t=8.13, P<0.001), and willingness to reduce medication (t=3.60, P<0.001) were significantly lower in group A than in group B. CONCLUSIONS: In patients with PTC diagnosed as unilateral cT1-T3N1bM0 and a contralateral glandular nodule </=2 cm, the preservation of the contralateral gland does not appear to have a significant impact on the rate of tumour recurrence in patients with tumour size (<1 cm), no extrathyroidal invasion, and pathological T stage (< T3). Instead, preserving gland potentially improves the prognosis, quality of life, and complication rates in these patients.
PubMed-ID: 39544973
DOI: 10.21037/gs-24-178
PMCID: PMC11558296

Neoadjuvant therapy to improve resectability of advanced thyroid cancer: A real-world experience.
Head Neck, 46(10):2496-507.
M. Russell, M. L. Gild, L. J. Wirth, B. Robinson, A. S. Karcioglu, A. Iwata, T. S. Athni, A. H. Abdelhamid Ahmed and G. W. Randolph. 2024.
BACKGROUND: Experience with targeted neoadjuvant treatment for locoregionally advanced thyroid cancer is nascent. METHODS: Multicenter retrospective case series examining targeted neoadjuvant treatment for locoregionally advanced thyroid cancer. The primary outcome was change in surgical morbidity as measured by two metrics developed for use in clinical trials to characterize surgical complexity and morbidity. Secondary outcomes included percentage of patients proceeding to surgery and percentage receiving an R0/R1 resection. RESULTS: Seventeen patients with varied molecular alterations, pathologies, and treatment regimens were included. Mean surgical complexity scores decreased between time points for baseline and postneoadjuvant treatment, postneoadjuvant treatment and surgery, and between baseline and surgery. Eleven patients (64.7%) underwent surgical resection, with 10 (58.8%) receiving an R0/R1 resection. CONCLUSIONS: Neoadjuvant treatment of advanced thyroid cancer improves resectability and decreases the morbidity of required surgical procedures. However, treatment is not uniformly effective.
PubMed-ID: 38488238
DOI: 10.1002/hed.27735

ASO Author Reflections: Advanced Thyroid Cancers: Individualized Treatments in the Era of the Standard Surgical Approaches.
Ann Surg Oncol, 31(9):5539-40.
L. Sessa, C. De Crea, N. Voloudakis, F. Pennestri and M. Raffaelli. 2024.
PubMed-ID: 38767801
DOI: 10.1245/s10434-024-15462-y

Single Institution Experience in the Management of Locally Advanced (pT4) Differentiated Thyroid Carcinomas.
Ann Surg Oncol, 31(9):5515-24.
L. Sessa, C. De Crea, N. Voloudakis, F. Pennestri, L. Revelli, P. Gallucci, G. Perotti, L. Tagliaferri, E. Rossi, E. D. Rossi, A. Pontecorvi, R. Bellantone and M. Raffaelli. 2024.
BACKGROUND: Locally infiltrating (T4) differentiated thyroid carcinomas (DTC) represent a challenge. Surgical strategy and adjuvant therapy should be planned balancing morbidity and oncologic outcome. A series of patients with T4 DTC who underwent multidisciplinary evaluation and treatment is reported. The main study endpoints were the oncologic outcome, complication rates, and risk factors for tumor recurrence. PATIENTS AND METHODS: All DTC cases operated between 2009 and 2021 were reviewed and T4 DTC cases were identified. En bloc resection of inferior laryngeal nerve (ILN), tracheal, and/or internal jugular vein (IJV) was performed in cases of massive infiltration. In cases of pharyngoesophageal junction (PEJ) invasion, the shaving technique was always applied. RESULTS: Among 4775 DTC cases, 60 were T4. ILN infiltration was documented in 45 cases (en bloc resection in 9), tracheal infiltration in 14 (tracheal resection in 2), PEJ invasion in 11 (R0 resection in 7 cases and < 1 cm residual tissue in 4 cases), IJV resection in 6, and laryngeal in 2. In total, 11 postoperative ILN palsy, 23 transient hypoparathyroidisms, and 2 hematomas requiring reoperation were registered. Final histology showed 7 pN0, 22 pN1a, and 31 pN1b tumors. Aggressive variants were observed in 47 patients. All but 1 patient underwent radioiodine treatment, 12 underwent adjuvant external beam radiation therapy (EBRT), and 2 underwent chemotherapy. At a median follow-up of 58 months, no tumor-related death was registered, and seven patients required reoperation for recurrence. Tracheal invasion was the only significant factor negatively impacting recurrence ($p = 0.045$). CONCLUSIONS: A multidisciplinary approach is essential for the management of T4 DTC. Individualized and balanced surgical strategy and adjuvant treatments, in particular EBRT, ensure control of locally advanced disease with acceptable morbidity.
PubMed-ID: 38700801
DOI: 10.1245/s10434-024-15356-z
PMCID: PMC11300486

From routine to rescue: Thyroidectomy for life-threatening thyrotoxicosis.
World J Surg, 48(12):2892-8.
Z. Song, R. Akhund, C. Wu, R. Wang, B. Lindeman, J. Fazendin, A. Gillis and H. Chen. 2024.
BACKGROUND: Thyroidectomies are routinely same-day elective procedures. The aim of this study was to investigate outcomes in patients who underwent uncommon urgent thyroidectomy. METHODS: We retrospectively reviewed patients diagnosed with thyrotoxicosis at a quaternary medical center between 2011 and 2023. Included patients were admitted

nonelectively with thyroidectomies performed during same hospital stay. Patient demographics, comorbidities, hospital course, and operative outcomes were analyzed. RESULTS: Thirty patients met the inclusion criteria. The majority were female (60%) and Black (60%) with a mean age of 41 +/- 14 years. At admission, 76.6% had undetectable thyrotropin levels (<0.01 microU/mL) and 26.7% were diagnosed with thyroid storm. Common presenting comorbidities included atrial fibrillation (53.3%), heart failure (40%), and liver failure (16.7%). Graves' disease was diagnosed in 83.3% of patients, while 13.3% had amiodarone-induced thyrotoxicosis. Median hospital stay before surgery was 8 days (interquartile range: 4-16). Indications for surgery were adverse medication events (30%), inadequate therapeutic effect by medication (30%), and worsening heart failure (26.7%). Postoperatively, 6.7% required reoperation for neck hematoma, 13.3% experienced temporary hypoparathyroidism, and 6.7% had hoarseness. Following surgery, 50% of patients with atrial fibrillation experienced resolution and 50% with heart failure with reduced ejection fraction showed ultrasonic improvement. Within 30 days, 20% visited the emergency department, none due to thyroidectomy complications, and 13.3% were readmitted for comorbidities. One patient (3.3%) died from liver failure. CONCLUSIONS: Patients who require an urgent thyroidectomy often have life-threatening comorbidities particularly cardiac disease. Performing thyroidectomy in these patients can potentially create clinical homeostasis for further management of their comorbidities.
PubMed-ID: 39134403
DOI: 10.1002/wjs.12312
PMCID: PMC11620921

Trends in papillary thyroid cancer mortality in Denmark according to stage and education.
Clin Endocrinol (Oxf), 101(6):573-9.
S. M. Sorensen, C. Munk, T. Maltesen, U. Feldt-Rasmussen and S. K. Kjaer. 2024.
OBJECTIVE: Few studies exist on trends in papillary thyroid cancer (PTC) survival and mortality according to stage and level of socioeconomic status. DESIGN: Nationwide cohort study. PATIENTS AND MEASUREMENTS: Patients diagnosed with PTC during 2000-2015 in Denmark were identified from the Danish Cancer Registry and followed until the end of 2020. We evaluated 5-year all-cause mortality and relative survival according to stage and 5-year mortality rates with corresponding average annual percentage changes (AAPCs) according to stage and education. Finally, we assessed the association between several factors and mortality of PTC using Cox regression. RESULTS: For the 2006 cases of PTC diagnosed during 2000-2015, relative survival tended to increase and mortality rates tended to decrease for all stages. For localized PTC, mortality rates tended to decrease among individuals with medium education (AAPC = -7.0, 95% confidence interval [CI]: -14.7 to 1.5), but showed an increasing pattern among individuals with long education (AAPC = 19.8, 95% CI: -4.2 to 50.0). For nonlocalized PTC, mortality rates showed a decreasing tendency among individuals with medium and long education (AAPC = -5.5, 95% CI: -13.2 to 2.9, and AAPC = -10.4, 95% CI: -20.8 to 1.4, respectively). Being diagnosed with PTC in a more recent calendar period and long education were associated with a lower mortality rate in the Cox regression analysis. CONCLUSIONS: A pattern of an increasing relative survival and decreasing mortality rates of PTC across all stages was seen in Denmark during 2000-2015. The decreasing pattern in mortality rates was most evident in individuals with localized stage and medium education, and in individuals with nonlocalized stage and medium or long education.
PubMed-ID: 39113277
DOI: 10.1111/cen.15119

Calcium and vitamin D substitution for hypoparathyroidism after thyroidectomy - how is it continued after discharge from hospital?
Langenbecks Arch Surg, 409(1):373.
J. I. Staubitz-Vernazza, A. K. Lederer, N. Bouzakri, O. Lozan, F. Wild and T. J. Musholt. 2024.
PURPOSE: Postoperative hypoparathyroidism (HypoPT) is one of the most feared complications after thyroid surgery. In most cases, HypoPT is transient, requiring temporary substitution with calcium and active vitamin D. The analysis was conducted to investigate how calcium and vitamin D substitution was managed in routine postoperative clinical practice after discharge from hospital. METHODS: From March 2015 to December 2023, patients with HypoPT after thyroidectomy at the university medical center (UMC) Mainz, were included in a retrospective study. The rate of continued prescription of calcium and vitamin D by external practitioners in relation to the PTH and calcium levels at the first postoperative outpatient visit at the outpatient clinic of the UMC Mainz was analyzed and critically discussed. RESULTS: Ninety-four of 332 patients (28.3%) were continuously prescribed with calcium/vitamin D supplements: 14 had PTH deficiency and hypocalcemia and 14 had normal/elevated PTH levels with hypocalcemia, 59 had PTH values below the normal range and normo- or hypercalcemia and 7 had normal or elevated PTH levels with normocalcemia. CONCLUSIONS: There are inconsistent procedures regarding the adjustment of the calcium and vitamin D substitution by the practices providing external follow-up treatment. To avoid iatrogenic suppression of PTH levels, high calcium load and potential affection of

the kidney function, a reduction scheme should be actively recommended by thyroid surgeons.
PubMed-ID: 39636417
DOI: 10.1007/s00423-024-03556-w
PMCID: PMC11621183

Primary thyroid lymphoma: A multi-center retrospective review.
Am J Surg, 237:115927.
M. W. Su, T. N. Beck, J. Knepprath, G. Romero-Velez, K. B. Heiden and C. R. McHenry. 2024.
BACKGROUND: Primary thyroid lymphoma (PTL) is rare and diagnosis is challenging. METHODS: We conducted a multicenter retrospective study of patients with PTL from 1990 to 2023 to determine method of diagnosis, treatment, and outcomes. RESULTS: The study cohort included 31 patients with PTL; all had thyroid enlargement; 21 (68 %) had compressive symptoms, 11 (35 %) had hypothyroidism and 3 had (10 %) B symptoms. Diagnosis was established from incisional biopsy in 8 (26 %), needle biopsy in 4 (13 %), excisional lymph node biopsy in 1 (3 %), and thyroidectomy specimens in 18 (58 %). 15 (48 %) patients had Hashimoto thyroiditis. Treatment included chemotherapy in 19 (61 %); surgery alone in 7 (23 %); and radiation alone or with surgery in 5 (16 %) patients. One (3 %) patient recurred, and 4 (13 %) patients died after a median 4.2 years. CONCLUSION: Diagnosis of PTL was made in only 13 % of patients preoperatively. There may be opportunity for needle biopsy to facilitate earlier diagnosis and treatment.
PubMed-ID: 39213784
DOI: 10.1016/j.amjsurg.2024.115927

Clinically Relevant Germline Variants in Children With Nonmedullary Thyroid Cancer.
J Clin Endocrinol Metab, 109(12):e2214-e21.
K. van der Tuin, D. Ruano, J. Knijnenburg, R. B. van der Luijt, H. Morreau, T. P. Links, F. J. Hes and C. Dutch Pediatric Thyroid Cancer. 2024.
CONTEXT: The underlying genetic cause of nonmedullary thyroid cancer (NMTC) in children is often unknown, hampering both predictive testing of family members and preventive clinical management. OBJECTIVE: Our objectives were to investigated the potential heritability in the largest childhood NMTC cohort that has been genotyped to date. METHODS: Nationwide retrospective cohort study in tertiary referral centers. In total, 97 patients diagnosed with pediatric NMTC between 1970 and 2020 were included in this study. Patients underwent germline whole genome sequencing. The main outcome measures were mutation detection yield in (1) clinically relevant tumor predisposition genes and (2) genes previously associated with NMTC. RESULTS: In total, 13 of 97 patients (13%) carried a germline (likely) pathogenic variant in a well-known tumor predisposition gene: APC (n = 1), BRCA2 (n = 2), CHEK2 (n = 4), DICER1 (n = 4), HOXB13 (n = 1), and MITF (n = 1). In addition, 1 patient was diagnosed with Pendred syndrome (SLC26A4) and 9 variants of high interest were found in other NMTC candidate susceptibility genes. CONCLUSION: The reported prevalence (13%) of germline variants in well-known tumor predisposing genes and the added value of a revised personal/family history and histology led us to recommend genetic counseling for all patients with childhood NMTC. The detected tumor predisposition syndromes are associated with a risk for second cancers which necessitates additional surveillance of the index patients and presymptomatic genetic testing of at risk family members.
PubMed-ID: 38415346
DOI: 10.1210/clinem/dgae107
PMCID: PMC11570363

Tracking dynamic evolution of low- and intermediate-risk differentiated thyroid cancer: Identification of individuals at risk of recurrence.
Clin Endocrinol (Oxf), 101(3):286-94.
F. Volpi, J. Alcalde, J. Larrache, E. Alegre, A. Argueta, M. D. Lozano, C. Colombo and J. C. Galofre. 2024.
OBJECTIVE: The generally good prognosis of low- and intermediate-risk differentiated thyroid cancer (DTC) underscored the need to identify those few patients who relapse. DESIGN: Records of 299 low- or intermediate-risk DTC patients (mean follow-up 8.2 +/- 6.2 years) were retrospectively reviewed. The sample was classified following the American Thyroid Association (ATA) dynamic risk stratification (DRS) system. PATIENTS AND MEASUREMENT: After classifying patients according to DRS at the first visit following initial therapy (FU1), structural recurrence occurred in 2/181 (1.1%), 5/81 (6.2%) and 13/26 (50.0%) with excellent, indeterminate and biochemical incomplete response to treatment, respectively. All relapses but one happened within 5 years from FU1. Univariate analysis comparing excellent, indeterminate and biochemical incomplete with structural incomplete responses at the end of the follow-up, identified tumour size ($p < .001$), T status (<0.001), positive lymph nodes (N) ($p < .01$), multifocality ($p < .004$), need of additional radioactive iodine

(RAI) (p < .0001) and first DRS status (p < .0003) as risk factors of recurrence. In the multivariate analysis, only RAI remained statistically significant (p < .02). Comparison between excellent and indeterminate with biochemical and structural incomplete responses, identified tumour size (p < .0004), T (p < .01), N (p < .0001), bilaterality (p < .03), first DRS status (p < .0001) and RAI (p < .001) as recurrence risk factors. T (p < .01) and first DRS (p < .0006) were confirmed in the multivariate analysis. CONCLUSIONS: Patients with DTC classified as low- or intermediate-risk of recurrence with excellent response to treatment at FU1 rarely develop structural disease and this occurs almost exclusively in the first 5 years. Initial DRS status is an accurate tool for determining the risk of recurrence.
PubMed-ID: 39038163
DOI: 10.1111/cen.15111

Management of Indeterminate Thyroid Nodules: A Model Comparing Surgery, Molecular Testing, and Observation.
Otolaryngol Head Neck Surg, 171(5):1349-54.
A. Welschmeyer, M. Kligerman and J. Noel. 2024.
OBJECTIVE: Optimal management of indeterminate nodules remains a controversial area of endocrine surgery. The purpose of this study is to compare observation, molecular testing, and immediate thyroid surgery for the management of Bethesda Classes III and IV nodules in patients age 50 to 90 years. STUDY DESIGN: A decision analysis was performed from April 22, 2021, to September 29, 2023, using a Markov model constructed with TreeAgePro 2023. Model variables and ranges were selected based on literature review data. SETTING: TreeAgePro. METHODS: A 1-way sensitivity analysis was performed to evaluate the age threshold at which each management pathway, immediate thyroid surgery, additional molecular testing, or observation, would be favored. A Monte Carlo probabilistic sensitivity analysis was performed 5 times with model patients assigned starting ages of 50, 60, 70, 80, and 90 years to assess how age at diagnosis would impact model results. Outcomes were measured with quality-adjusted life-years and accounted for perioperative complications including permanent recurrent laryngeal nerve injury, permanent hypoparathyroidism, and medical complications. RESULTS: In the study models, molecular testing was more beneficial than surgery and observation across all ages. The age threshold at which observation became more beneficial than surgery as the next best option was 83.1 years. However, the clinical difference between all 3 treatment algorithms was relatively minimal. CONCLUSIONS: Decision-making regarding indeterminate thyroid nodules is complex. Given the clinically similar results across all 3 treatment algorithm, this study reinforces that treatment modalities should be individually tailored and based on shared physician-patient decision making.
PubMed-ID: 39189296
DOI: 10.1002/ohn.958

Synergy of Nodal Factors in Predicting Recurrence After Treatment of N1b Papillary Thyroid Carcinoma.
J Clin Endocrinol Metab, 109(12):3137-45.
K. Xian, S. Xu, H. Huang, C. Xing, X. Wang, S. Liu and J. Liu. 2024.
BACKGROUND: Nodal factors are important predictors of prognosis for papillary thyroid carcinoma (PTC), but their synergistic effect is not well understood. We aimed to explore their synergy in predicting recurrence of clinical N1b (cN1b) PTC. METHODS: Patients who underwent surgery for cN1b PTC from 2013 to 2017 were enrolled. The association between nodal factors and recurrence was assessed using Cox proportional hazards regression models. Interaction and stratified analyses were conducted according to significant nodal factors. RESULTS: Of 1067 cN1b PTC patients included, all nodal factors (bilateral metastasis, largest dimension > 3 cm, micro and gross extranodal extension (mENE, gENE), number of metastatic lymph nodes [MLN], lymph node yield [LNY], and ratio LNR]) were significantly associated with all site and nodal recurrence in the univariate analysis (all P < .05). Multivariate analyses revealed largest dimension > 3 cm, gENE and LNR > 0.21 were associated with elevated both all site (hazard ratio [HR] [95% CI], 2.58 [1.67-4.00], 1.87 [1.26-3.01], 1.68 [1.11-2.42], all P < .01) and nodal recurrences (HR [95% CI], 2.63 [1.67-4.13], 1.90 [1.15-3.12], 1.76 [1.17-2.66], all P < .01). LNR and gENE had interactive effect (all site recurrence: P for interaction = .009; nodal recurrence: P for interaction = .02). LNR was significantly associated with recurrence in patients without gENE (HR [95% CI], all site recurrence: 2.41 [1.50-3.87]; nodal recurrence: 2.51 [1.52-4.14], all P < .001), while when gENE appeared, LNR was no longer associated with recurrence (HR [95% CI], all site recurrence: 0.81 [0.43-1.54], P = .53; nodal recurrence: 0.85 [0.43-1.67], P = .64). CONCLUSION: Nodal factors have synergistic effect in predicting recurrence in cN1b PTC patients. Increasing lymph nodes harvest may only decrease recurrence in patients without gENE, while not in gENE patients.
PubMed-ID: 38748619
DOI: 10.1210/clinem/dgae329

Parathyroids

Meta-Analyses

Cohort review of patients with parathyroid cancer in End Stage Renal Disease (ESRD).
Langenbecks Arch Surg, 409(1):300.
V. Zheng, J. Lee and R. Parameswaran. 2024.
BACKGROUND AND HYPOTHESIS: Parathyroid carcinoma (PTTC) is a rare malignant endocrine tumor seen in up to 1-2% of all cases of primary hyperparathyroidism. However, incidence of parathyroid carcinoma in renal hyperparathyroidism is a rare phenomenon. We aimed to evaluate the outcomes of PTTC in renal hyperparathyroidism published in the literature. METHODS: Cohort review of parathyroid cancer cases reported in Medline (via PubMed), COCHRANE and EMBASE between the period 1985 - 2023 in patients with renal hyperparathyroidism. RESULTS: A total of 48 patients (20 M: 28F), with a mean age of 49.8 (+/- 11.7 SD: range 20-75) years. Dialysis vintage was for a period of 8.9 (+/- 7.2; range 6 months to 40 years). The mean preoperative values were as follows: serum corrected calcium-2.87 IQR 2.56-3.01), PTH - 221.8 (IQR 86.6 -257.2 pmol/L) and serum phosphate - 2.07 (IQR 1.72-2.28) mmol/L. Preoperative imaging was in the form of ultrasound of the neck in 21 of 48 (44%), MIBI scan in 27/48 (56%), contrast enhanced computerized tomography in 14/48 (29%) and MRI neck in 1/48 (2%). The mean size of the cancer was 2.7 (+/- 1.35) cm and weight of the gland ranged between 0.9 to 4.98 g. 18/48 (37%) patients underwent a total parathyroidectomy and 30/48 (63%) had subtotal parathyroidectomy. En bloc excision of the tumour along with the thyroid along and central compartment lymph nodes was only performed in 12/48 (25%), of whom 9 (19%) had it performed at index surgery, whereas in the rest was done for persistent or recurrent disease. After a mean follow up of 34 months, 14 (29%) had local recurrence, 1 (2%) had distant metastasis to the skeletal system, and 12 (25%) to the lungs. Cohort mortality was 6 (13%) due to refractory hypercalcemia. CONCLUSIONS: Parathyroid carcinoma in renal hyperparathyroidism is rare but when encountered, en bloc excision with parathyroidectomy provides the best chance of cure. Recurrences can be difficult to treat but may be needed to treat intractable hypercalcaemia.
PubMed-ID: 39377972
DOI: 10.1007/s00423-024-03496-5

Randomized controlled trials

- None -

Consensus Statements/Guidelines

Primary hyperparathyroidism in adults-(Part II) surgical management and postoperative follow-up: 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), 101(5):516-30.
J. A. Miller, J. Gundara, S. Harper, M. Herath, S. K. Ramchand, S. Farrell, J. Serpell, K. Taubman, J. Christie, C. M. Girgis, H. G. Schneider, R. Clifton-Bligh, A. J. Gill, S. M. C. De Sousa, R. W. Carroll, F. Milat and M. Grossmann. 2024.
OBJECTIVE: To develop evidence-based recommendations to guide the surgical management and postoperative follow-up of adults with primary hyperparathyroidism. 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 eight key questions. RESULTS: Diagnostic imaging does not determine suitability for surgery but can guide the planning of surgery in suitable candidates. First-line imaging includes ultrasound and either parathyroid 4DCT or scintigraphy, depending on local availability and expertise. Minimally invasive parathyroidectomy is appropriate in most patients with concordant imaging. Bilateral neck exploration should be considered in those with discordant/negative imaging findings, multi-gland disease and genetic/familial risk factors. Parathyroid surgery, especially re-operative surgery,

has better outcomes in the hands of higher volume surgeons. Neuromonitoring is generally not required for initial surgery but should be considered for re-operative surgery. Following parathyroidectomy, calcium and parathyroid hormone levels should be re-checked in the first 24 h and repeated early if there are risk factors for hypocalcaemia. Eucalcaemia at 6 months is consistent with surgical cure; parathyroid hormone levels do not need to be re-checked in the absence of other clinical indications. Longer-term surveillance of skeletal health is recommended. CONCLUSIONS: This position statement provides up-to-date guidance on evidence-based best practice surgical and postoperative management of adults with primary hyperparathyroidism.
PubMed-ID: 34927274
DOI: 10.1111/cen.14650

Other Articles

Correlation Between Near-Infrared Autofluorescence Properties and Sestamibi Uptakes of Parathyroid Glands in Primary Hyperparathyroidism.
Otolaryngol Head Neck Surg, 171(5):1341-8.
E. Akgun, A. Ibrahimli, M. Rahman, C. Griffith and E. Berber. 2024.
OBJECTIVE: Near-infrared autofluorescence (NIRAF) characteristics of parathyroid glands in primary hyperparathyroidism (pHPT) vary, with unclarity regarding the underlying mechanism. Similarly, (99m)Tc-sestamibi uptake in diseased parathyroid glands is variable. There is a suggestion that oxyphilic cell content may influence both imaging modalities. This study aims to analyze the relationship between NIRAF imaging characteristics, (99m)Tc-sestamibi uptake, and cellular composition in pHPT. STUDY DESIGN: Retrospective analysis of an Institutional Review Board-monitored prospective database. SETTING: Single tertiary referral center. METHODS: NIRAF characteristics of parathyroid glands of patients with pHPT between 2019 and 2024 were compared with (99m)Tc-sestamibi scan findings from a prospective database. Using third-party software, brightness intensity and heterogeneity index (HI) of the glands were calculated. A subgroup of parathyroid glands obtained from consecutive patients with pHPT in 2020 to 2021 underwent histological analysis. RESULTS: A total of 428 patients with 638 diseased parathyroid glands were analyzed. Forty-seven percent of the glands showed an uptake on (99m)Tc-sestamibi scans. The brightness intensity of the NIRAF signals from parathyroid glands that were seen versus not seen on sestamibi was 2.1 versus 2.3 (P = .002) and HI 0.18 versus 0.17 (P = .35), respectively. On multivariate analysis, low autofluorescence intensity, high gland volume, and single adenoma were associated with detectability on (99m)Tc-sestamibi scan (P < .0001). Intraglandular adipose tissue content was lower in diseased glands that were detected on (99m)Tc-sestamibi scans (0% vs 5%, P < .0001). CONCLUSION: Our findings indicate an inverse relationship between autofluorescence intensity and detectability on (99m)Tc-sestamibi scans and a lack of correlation between different cell types and autofluorescence properties.
PubMed-ID: 39154258
DOI: 10.1002/ohn.948

Intraoperative radio-guided localization of parathyroid adenomas using 3D freehand SPECT technology.
Updates Surg, 76(6):2343-50.
S. Anesidis, I. Akrida, M. Michalaki, D. Apostololpoulos, N. Papathanasiou, N. Benetatos, C. Kalogeropoulou, K. Panagopoulos and I. Maroulis. 2024.
Parathyroidectomy for primary hyperparathyroidism (PHPT) could have poor outcomes, even with accurate preoperative localization of the adenomas, because their intraoperative localization can be challenging. Freehand single photon emission computed tomography (fhSPECT) is a new technique for radio-guided intraoperative navigation. Its use during parathyroidectomy could be useful and such data are limited. We herein present our experience on the feasibility of fhSPECT for intraoperative detection of abnormal parathyroid glands. We retrospectively reviewed the clinical data of 55 patients (30-77 years old) with PHPT due to parathyroid adenomas, that were subjected to parathyroidectomy from 12/2017 to 7/2022. In average, 111 +/- 74 MBq of Tc-99 m Sestamibi were injected intravenously, approximately 2 h before the operation and fhSPECT was used to generate 3D images during parathyroidectomy. Measurements of PTH and calcium levels were performed preoperatively, postoperatively and 4-6 months after the procedure. FhSPECT successfully identified the parathyroid adenoma in all the patients. It took 3 min (median time) for fhSPECT to detect at least one radioactive spot in all patients. The mean duration of the operation was 66.6 +/- 7.3 min. Forty-nine patients out of 55 had solitary and 6/55 had multiple adenomas, whereas 6/55 had ectopic abnormal parathyroid glands. None of the patients had persistent hyperparathyroidism during follow-up. To the best of our knowledge, this is the largest series of patients

with PHPT that underwent fhSPECT assisted parathyroidectomy. Our data suggest that this navigation system is helpful in identifying parathyroid adenomas intraoperatively.
PubMed-ID: 38517662
DOI: 10.1007/s13304-024-01819-1

Same-day parathyroidectomy for primary hyperparathyroidism -an over 20-year practice.
World J Surg, 48(12):2899-906.
C. A. Annesi, A. Gillis, J. M. Fazendin, B. Lindeman and H. Chen. 2024.
INTRODUCTION: There has been a shift in recent years toward same-day parathyroidectomies due to the decrease in mutual costs with few significant differences in postoperative morbidity or mortality. We sought to determine if demographics, preoperative patient risk factors, or comorbidities were associated with a patient's likelihood of having same-day or inpatient surgery. MATERIALS AND METHODS: A prospective database of parathyroid operations from 2001 to 2022 (n = 2948 patients) was reviewed for surgeries completed for primary hyperparathyroidism. Patients were categorized as same-day or inpatient surgery; demographics, risk factors, and co-morbidities were examined and differences across practice patterns during the 21-year period were studied and also analyzed in a subset of patients from 2013 to 2022. RESULTS: In a recent subset of patients from 2013 to 2022, patients having inpatient surgery were more likely to be Black and use anticoagulation or antiplatelet therapy. Multivariable regression confirmed increased odds of aging and black patients requiring inpatient parathyroidectomy. Compared to 2001-2003, there was a significantly increased proportion of patients undergoing same-day surgery; compared to 2010-2012, there was a similar proportion of patients undergoing outpatient surgery between 2013 and 2018, and there was an increased proportion from 2019 through 2022. CONCLUSION: Same-day parathyroidectomies have been shown to be safe and has become the typical practice for high-volume parathyroid surgeons over the last decade. Complications such as postoperative hematoma or hypocalcemia were previously shown to be incompletely mitigated by increased LOS or inpatient surgery, although demographics are considered to increase the odds of inpatient parathyroidectomy.
PubMed-ID: 39174347
DOI: 10.1002/wjs.12319

Parathyroidectomy and the Development of New Depression Among Adults With Primary Hyperparathyroidism.
JAMA Surg, 159(12):1375-82.
L. D. Delaney, A. Furst, H. Day, K. Arnow, R. M. Cisco, E. Kebebew, M. E. Montez-Rath, M. K. Tamura and C. D. Seib. 2024.
IMPORTANCE: Primary hyperparathyroidism (PHPT) is a common endocrine disorder associated with neuropsychiatric symptoms. Although parathyroidectomy has been associated with improvement of preexisting depression among adults with PHPT, the effect of parathyroidectomy on the development of new depression is unknown. OBJECTIVE: To determine the effect of early parathyroidectomy on the incidence of new depression among adults with PHPT compared with nonoperative management. DESIGN, SETTING, AND PARTICIPANTS: Analyzed data included observational national Veterans Affairs data from adults with a new diagnosis of PHPT from 2000 through 2019 using target trial emulation with cloning, a biostatistical method that uses observational data to emulate a randomized clinical trial. New depression rates were compared between those treated with early parathyroidectomy vs nonoperative management using an extended Cox model with time-varying inverse probability censoring weighting, adjusted for patient demographics, comorbidities, and depression risk factors. Eligible adults with a new biochemical diagnosis of PHPT, excluding those with past depression diagnoses, residing in an assisted living/nursing facility, or with Charlson Comorbidity Index score higher than 4 were included. These data were analyzed January 4, 2023, through June 15, 2023. EXPOSURE: Early parathyroidectomy (within 1 year of PHPT diagnosis) vs nonoperative management. MAIN OUTCOME: New depression, including among subgroups according to patient age (65 years or older; younger than 65 years) and baseline serum calcium (11.3 mg/dL or higher; less than 11.3 mg/dL). RESULTS: The study team identified 40 231 adults with PHPT and no history of depression of whom 35896 were male (89%) and the mean (SD) age was 67 (11.3) years. A total of 3294 patients underwent early parathyroidectomy (8.2%). The weighted cumulative incidence of depression was 11% at 5 years and 18% at 10 years among patients who underwent parathyroidectomy, compared with 9% and 18%, respectively, among nonoperative patients. Those treated with early parathyroidectomy experienced no difference in the adjusted rate of new depression compared with nonoperative management (hazard ratio, 1.05; 95% CI, 0.94-1.17). There was also no estimated effect of early parathyroidectomy on new depression in subgroup analyses based on patient age or serum calcium. CONCLUSIONS: In this study, there was no difference in the incidence of new depression among adults with PHPT treated with early parathyroidectomy vs nonoperative management, which is relevant to preoperative discussions about the benefits and risks of operative treatment.
PubMed-ID: 39230896

DOI: 10.1001/jamasurg.2024.3509
PMCID: PMC11375523

A retrospective database analysis of pediatric parathyroidectomies from the United Kingdom registry of endocrine and Thyroid Surgeons.
World J Surg, 48(10):2463-70.
Y. Embury-Young, L. Brennan, S. Jackson, S. Aspinall, M. Stechman, S. Balasubramanian, D. Kim and H. Ishii. 2024.
INTRODUCTION: The United Kingdom Registry of Endocrine and Thyroid Surgery (UKRETS) holds the largest database of pediatric parathyroidectomy cases globally. There are currently no quoted acceptable cure or complication rates in the literature. METHODS: This retrospective database analysis evaluates the efficacy and safety of targeted parathyroidectomy (tPTx) and bilateral neck exploration (BNE) in first-time parathyroidectomy for pediatric primary hyperparathyroidism (PHPT) through analysis of the UKRETS database (1995-2022). Pre-, intra- and postoperative outcomes were assessed and analyzed. RESULTS: 168 cases underwent parathyroidectomy; 25 (15%) familial and 143 (85%) sporadic PHPT. 69% were female with a mean age of 10 years (Range 0-17). BNE was the most common operative approach (61%; n = 103/168). The most frequently used imaging modality was US (80%; n = 135/168). Mean number of glands excised in familial cases was three compared to one gland in sporadic cases ($p < 0.05$). Familial cases had a significantly higher rate of postoperative hypocalcemia (32% vs. 9%, $p < 0.05$) and all were BNE. Cure rate was 96.9% (n = 127/131), with differences in cure rates that did not reach statistical significance (sporadic 98.2% vs. familial 90.5%, $p = 0.06$). Preoperative localization (image-positive or negative) made no difference to cure rates in either familial (90% vs. 91%, $p = 0.94$) or sporadic (97.5% vs. 100%, $p = 0.4$) cases. CONCLUSIONS: This analysis demonstrates that first-time pediatric parathyroidectomy for PHPT is safe and effective. Familial cases have a higher rate of postoperative hypocalcemia; therefore, parents should be informed of this when consented. Targeted parathyroidectomy is safe and effective in both sporadic and familial cases, as long as there is positive preoperative imaging.
PubMed-ID: 39297799
DOI: 10.1002/wjs.12329

Role of thymectomy in surgical treatment of renal hyperparathyroidism.
Am J Surg, 237:115864.
M. Y. Guo, M. Pillar, N. Manhas and A. Melck. 2024.
INTRODUCTION: The role for routine thymectomy in patients with secondary or tertiary hyperparathyroidism (SHPT, THPT) is unclear. We aim to compare rates of recurrence and complications in patients who underwent subtotal parathyroidectomy with and without thymectomy. METHODS: Patients who underwent surgery for renal HPT at a tertiary endocrine surgery center between 2010 and 2022 were reviewed. Presence of parathyroid tissue in resected tissue was identified through pathology reports. A multivariate logistic regression was used to compare baseline characteristics, recurrence rates and complications between those who did and did not undergo thymectomy. RESULTS: Of 107 patients who underwent subtotal parathyroidectomy, 29 (27.1 %) underwent concomitant thymectomy. Recurrence occurred in 15 patients (14 %). Thymectomy did not affect recurrence (OR: 0.33, 95%CI: 0.06-1.28, $p = 0.14$), but was associated with permanent hypoparathyroidism (OR: 4.62, 95%CI: 1.67-13.18, $p = 0.003$). Fewer parathyroid specimens increased the odds of thymectomy ($p = 0.04$). Parathyroid glands were found in 6 thymectomy samples (20.7 %). CONCLUSION: Thymectomy at the time of subtotal parathyroidectomy for renal HPT was not associated with disease recurrence, but increased likelihood of permanent hypoparathyroidism.
PubMed-ID: 39147637
DOI: 10.1016/j.amjsurg.2024.115864

Trabecular bone score norms in Asian-Indians and associations with serum 25(OH)D and parathyroid hormone.
Clin Endocrinol (Oxf), 101(6):614-22.
V. Mannar, A. Vishal, S. Saha, M. Kalaivani, D. Kandasamy and R. Goswami. 2024.
OBJECTIVE: There is limited information on population-specific norms of trabecular-bone-score (TBS) and its associated factors. Here, we provide norms of TBS in Asian-Indians and its relationship with serum 25-hydroxyvitamin D [25(OH)D] and intact-parathyroid hormone (iPTH). PARTICIPANTS AND MEASUREMENTS: TBS, bone-mineral-density (BMD), and vertebral-fractures (VFs) were assessed using dual-energy X-ray absorptiometry in 923 healthy Asian-Indians (aged 20-60 years). Serum 25(OH)D, iPTH, T4/TSH,, glycosylated-haemoglobin (HbA1c) were measured and associations with TBS assessed using multivariable linear regression. Subjects with BMD Z-score </= -2.0 or >/=2.0 at any sites, VFs, TSH > 10.0 or <0.05 microIU/ml, blood-glucose >11.1 mmol/L or HbA1c > 8.0% were excluded for generating Asian-Indian norms. RESULTS: TBS norms were generated in 744 healthy Asian-Indians (M:F,389:385). The cut-offs generated for 'normal',

'partially-degraded', and 'degraded' TBS were >1.305, 1.204-1.305 and <1.204, respectively. Mean TBS was lower in females than males (p < .001). There was 75% congruency in TBS categories between Asian-Indian and existing norms. Specificity (97.8 vs. 77.9%, p < .001) and diagnostic-accuracy (97.8% vs. 78.4%, p < .001) of TBS to detect osteoporosis were higher with Asian-Indian norms. The sensitivity of 'partially-degraded' TBS to diagnose osteopenia was also higher with Asian-Indian norms. In multivariable regression, gender, body-mass-index (BMI), BMD-L(1)-L(4), serum PTH, daily dietary-calorie intake and calcium intake were associated with TBS. Though 25(OH)D inversely correlated with PTH, 25(OH)D was not associated with TBS. CONCLUSION: This study provides norms for TBS in Asian-Indians with gender-specific differences. Increasing age and higher BMI were associated with lower TBS. Associations of TBS with circulating PTH and/or 25(OH)D need confirmation in further studies.
PubMed-ID: 39113278
DOI: 10.1111/cen.15122

Establishing the diagnosis of normocalcaemic primary hyperparathyroidism.
Am J Surg, 236:115825.
R. Mihai. 2024.
PubMed-ID: 38987067
DOI: 10.1016/j.amjsurg.2024.115825

24-hour Urine Calcium Predicts Reduced Fracture Incidence and Improved Bone Mineral Density After Surgery for Primary Hyperparathyroidism.
J Clin Endocrinol Metab, 109(12):e2273-e82.
M. Nilsson, K. E. Akesson, M. Thier, E. Nordenstrom, M. Almquist and A. Bergenfelz. 2024.
CONTEXT: Contemporary patients with primary hyperparathyroidism are diagnosed with milder disease than previously. Clinical and biochemical factors predictors with an impact on fracture incidence and bone mineral density after surgery have not been firmly established. OBJECTIVE: To investigate predictors of fracture incidence and bone mineral density preoperatively and after surgery for primary hyperparathyroidism (pHPT). DESIGN: Prospectively collected surgical cohort with matched population controls. Data were cross-linked with the Swedish National Patient Register, the Prescribed Drug Register, and the Cause of Death Register. SETTING: Tertiary referral center. PATIENTS OR OTHER PARTICIPANTS: Seven hundred nine patients with successful parathyroidectomy for pHPT and 2112 controls matched on sex, age, and municipality were included in the study. MAIN OUTCOME MEASURES: Fracture incidence, absolute change, and >/=2.77% increase in bone mineral density of femoral neck, L2-L4, and distal third of radius at 1-year follow-up. RESULTS: Patients with pHPT had an increased fracture incidence before surgery but not after pHPT surgery. Fracture incidence after surgery was inversely related to preoperative 24-hour urine calcium (incidence rate ratio for the highest tertile 220- mg/d 0.29, 95% confidence interval 0.11-0.73). Serum and 24-hour urine calcium, parathyroid hormone, osteocalcin, and adenoma weight were all associated with bone mineral density recovery after surgery. CONCLUSION: Twenty-four-hour urine calcium is the most important biochemical variable to predict a decreased fracture incidence and improved bone mineral density after surgery for pHPT.
PubMed-ID: 38412311
DOI: 10.1210/clinem/dgae106
PMCID: PMC11570390

Near-infrared autofluorescence pattern in parathyroid gland adenoma.
Surg Endosc, 38(11):6930-7.
L. Rossi, A. De Palma, P. Papini, M. Chicas Vasquez, F. Cetani, C. E. Ambrosini and G. Materazzi. 2024.
BACKGROUND: Parathyroid gland (PG) surgery is often challenging due to the small size and indistinct nature of these glands. The introduction of intraoperative near-infrared autofluorescence (NIRAF) has shown promise in localizing parathyroid tissue. However, the NIRAF features of parathyroid adenomas remain unclear. The aim of this study is to assess the NIRAF pattern of parathyroid adenomas. METHODS: Patients who underwent surgery for primary hyperparathyroidism at the University Hospital of Pisa, Endocrine Surgery Unit, between December 2021 and February 2022 were enrolled in this study. Intraoperative NIRAF patterns of suspected parathyroid adenomas were evaluated, with particular attention given to the presence of a bright cap. RESULTS: A retrospective study was conducted on 11 patients with primary hyperparathyroidism who underwent parathyroidectomy at our institution. Histopathological examination of the 15 resected specimens confirmed 14 parathyroid adenomas (12 chief cell parathyroid adenomas, 1 oxyphil cell parathyroid adenoma, and 1 mixed cell parathyroid adenoma) and one schwannoma. All adenomas exhibited a

heterogeneous NIRAF pattern, distinct from the homogeneous pattern observed in the schwannoma. A bright cap was identified in 9 out of 14 (64.3%) parathyroid adenomas (all chief cell adenomas). On the contrary, all 9 macroscopically normal PGs identified during surgery presented an homogeneous pattern. CONCLUSION: Our findings support the integration of NIRAF into parathyroid surgical procedures. The heterogeneous NIRAF pattern observed in parathyroid adenomas, often accompanied by a bright cap, offers a promising intraoperative diagnostic tool to differentiate hyperfunctioning from normal parathyroid tissue. Larger-scale randomized trials are warranted to further validate these findings.
PubMed-ID: 39382656
DOI: 10.1007/s00464-024-11314-8
PMCID: PMC11525238

Clinical utility of untimed spot urine sampling in measuring calcium creatinine clearance in the diagnostic work-up of PTH-dependent hypercalcaemia.
Clin Endocrinol (Oxf), 101(3):203-5.
E. Sharma, C. Boot, J. Ramsingh, P. Truran, R. Bliss, A. James and Y. Mamoojee. 2024.
PubMed-ID: 39004955
DOI: 10.1111/cen.15116

A new approach for perioperative parathyroid hormone (PTH) measurement to establish cure in patients with primary hyperparathyroidism.
Langenbecks Arch Surg, 409(1):285.
B. Sperotto, N. Meurer, A. Meyer, P. Ahmad-Nejad, N. Bosing, N. Lange, C. Dotzenrath and P. F. Alesina. 2024.
PURPOSE: In this study, we analyse the possibility to omit pre-incision PTH measurement since we routinely measure it at the time of pre-surgery ambulatory admission. METHODS: A total of 435 patients were enrolled. All patients with pHPT included underwent pre-surgical PTH level assessment as part of the pre-admission preparation to surgery. Intraoperative PTH was routinely assessed after induction of the anaesthesia (pre-incision PTH) and 15 min after resection of the enlarged gland(s) (post-excision PTH). Moreover, calcium and PTH levels were routinely assessed on the first postoperative day. Cure was defined as an intraoperative drop of > 50% or into normal range on first post-operative day. RESULTS: The median value of the preoperative and pre-incision PTH were both 127 pg/ml (p = ns). Thirty-two patients (7.3%) exhibited a not appropriate drop of post-excision PTH level. Nevertheless, nineteen of them (59.3%) showed a satisfying PTH drop on 1st POD. Ten patients (2.3%) experienced a persistent disease with six achieving cure through reoperation. Additionally, three patients (0.6%) showed normalization of calcium and PTH values during the follow-up. Three patients, apparently deemed cured after an adequate PTH-drop on the day of surgery, showed persistence. Cure rate at primary surgery was 98.4%. Accuracy of our simplified protocol is 99.3%. CONCLUSION: Pre-incision PTH is not superior to preoperative PTH blood test and can be omitted without compromising the sensitivity of cure prediction. One blood sample 15 min after resection, along with the postoperative PTH value on the day after surgery, is sufficient to predict the surgical outcome bearing the cost of a very low reoperation rate.
PubMed-ID: 39302485
DOI: 10.1007/s00423-024-03472-z

An Open-label Phase 2 Study of Eneboparatide, a Novel PTH Receptor 1 Agonist, in Hypoparathyroidism.
J Clin Endocrinol Metab, 109(9):2199-209.
I. Takacs, E. Mezosi, A. Soto, P. Kamenicky, L. Figueres, M. A. Galvez Moreno, S. Lemoine, F. Borson-Chazot, I. Capel, T. Ouldrouis, N. Lucas, S. Allas, M. Sumeray, M. Ovize and M. Mannstadt. 2024.
CONTEXT: Hypoparathyroidism is a rare disorder characterized by a deficiency in PTH resulting in hypocalcemia, hyperphosphatemia, and hypercalciuria. Eneboparatide is an investigational peptide agonist of the PTH1 receptor for the treatment of chronic hypoparathyroidism (HP). OBJECTIVE: To evaluate the efficacy, safety, and tolerability of eneboparatide in HP patients. DESIGN: Open-label, phase 2 study. PARTICIPANTS: Twenty-eight patients (21 women, 7 men), mean age (range): 58 years (28-72), with HP were enrolled into 2 consecutive cohorts (C1, n = 12 and C2, n = 16). INTERVENTION: Following an optimization period, daily subcutaneous injections of eneboparatide were administered for 3 months at a 20 microg/day (C1) or 10 microg/day (C2) starting dose. Conventional therapy was progressively removed, and eneboparatide could be titrated up to 60 microg (C1) or 80 microg (C2). MAIN OUTCOMES: Proportion of patients achieving independence from conventional therapy, albumin-adjusted serum calcium (ADsCa), 24-h urine calcium (uCa), serum bone turnover markers (serum carboxy-terminal telopeptide of type I collagen and procollagen 1 intact N-terminal propeptide), bone mineral density (BMD), and adverse events (AEs). RESULTS: After 3 months, >/= 88% of patients

achieved independence from conventional therapy while mean ADsCa was maintained within target range (7.8-9 mg/dL). Eneboparatide induced a rapid and sustained reduction of mean 24-hour uCa, even among patients with hypercalciuria. Bone turnover markers slightly increased, and BMD remained unchanged, consistent with progressive resumption of physiologic bone turnover. Eneboparatide was well tolerated with no serious AEs. CONCLUSION: Eneboparatide allowed independence from conventional therapy and maintenance of serum calcium within a target range while normalizing uCa excretion and producing a balanced resumption of bone turnover.
PubMed-ID: 38449442
DOI: 10.1210/clinem/dgae121

Primary Hyperparathyroidism-"Overtones" May Be Overblown.
JAMA Surg, 159(12):1382.
M. W. Yeh. 2024.
PubMed-ID: 39230929
DOI: 10.1001/jamasurg.2024.3519

Higher risk of incident diabetes among patients with primary hyperparathyroidism.
Clin Endocrinol (Oxf), 101(6):605-13.
Y. Zhang, H. Wu, A. Yang, Y. H. N. N, X. Zhang, E. S. H. Lau, E. W. K. Chow, A. P. S. Kong, E. Y. K. Chow, J. C. N. Chan, A. O. Y. Luk and R. C. W. Ma. 2024.
OBJECTIVES: There is relatively scarce data regarding the association between primary hyperparathyroidism (PHPT) and incident diabetes in large population-based longitudinal studies. We aimed to evaluate the risk of incident diabetes in individuals with and without PHPT and investigate the association between serum calcium concentrations and the risk of incident diabetes in patients with PHPT. METHODS: We included 2749 PHPT patients and 13,745 age, sex and index year matched non-PHPT individuals during 2000-2019. We used Cox regression models to compare the risk of incident diabetes in individuals with and without PHPT, and the risk of incident diabetes in PHPT patients with serum calcium concentration above and below the median value. The association between serum calcium concentrations and the risk of incident diabetes was examined by restricted cubic spline analyses in patients with PHPT. RESULTS: During a median follow-up time of 5.17 years (IQR 2.17, 9.58), 433 patients (15.75%) with PHPT and 2110 individuals (15.35%) without PHPT developed diabetes, respectively. Patients with PHPT had a higher incidence rate of diabetes compared to non-PHPT individuals (27.60 [95% CI 25.00, 30.30] vs. 23.90 [95% CI 22.80, 24.90] per 1000 person-years, log-rank test p = .007]. Crude Cox regression model showed PHPT was associated with a 15% higher risk of incident diabetes (HR 1.15, 95%CI 1.04, 1.28). In patients with PHPT, a 44% higher risk of incident diabetes was found in patients with serum calcium concentrations above the median value (2.63 mmol/L), compared to those below the median value (HR 1.44, 95%CI 1.08, 1.90). Restricted cubic spline analyses confirmed a positive linear association between serum calcium concentrations and the risk of incident diabetes in those with PHPT (p-value for nonlinear = .751) CONCLUSIONS: Patients with PHPT had a higher risk of incident diabetes compared to non-PHPT individuals. A positive linear association was found between serum calcium concentrations and the risk of incident diabetes in patients with PHPT.
PubMed-ID: 39038182
DOI: 10.1111/cen.15118

ASO Author Reflections: Distant Metastatic Parathyroid Carcinoma: Risk Factors, Patterns, and Outcomes.
Ann Surg Oncol, 31(10):6893-4.
T. Zhao, W. Yang, R. Shen, Q. Chen, M. Jin, H. Gu, H. Shen, Q. Wang, J. Wang, X. Liu, D. Feng, L. Zhao, G. An and B. Wei. 2024.
PubMed-ID: 38922544
DOI: 10.1245/s10434-024-15680-4

Risk Factors of Distant Metastatic Parathyroid Carcinoma and Insights into Therapeutic Perspectives.
Ann Surg Oncol, 31(10):6865-74.
T. Zhao, W. Yang, R. Shen, Q. Chen, M. Jin, H. Gu, H. Shen, Q. Wang, J. Wang, X. Liu, D. Feng, L. Zhao, G. An and B. Wei. 2024.
BACKGROUND: Distant metastatic parathyroid carcinoma (DM-PC) is a rare but often lethal entity with limited data about prognostic indicators. We sought to investigate the risk factors, patterns, and outcomes of DM-PC. METHODS: In this observational cohort study, 126 patients who underwent surgery for PC at a tertiary referral center from 2010 to 2023 were enrolled, among whom 38 had DMs. Univariate and multivariate Cox regression analyses were used to assess the

effects of prognostic factors on DM. RESULTS: The cumulative incidence of DM was 14.1%, 33.8%, and 66.9% at 5, 10, and 20 years in the duration of disease course, respectively. DM-PC patients suffered a worse 5-year overall survival of 37.1% compared with 89.8% in the non-DM patients ($p < 0.001$). DM-PC patients also suffered more previous operations ($p < 0.001$), higher preoperative serum calcium ($p<0.001$) and parathyroid hormone (PTH) levels ($p < 0.001$), lower frequencies of R0 resection ($p < 0.001$), higher rates of pathological vascular invasion ($p = 0.020$), thyroid infiltration ($p = 0.027$), extraglandular extension ($p = 0.001$), upper aerodigestive tract (UAT) invasion ($p < 0.001$), and lymph node metastasis ($p < 0.001$). Multivariate Cox regression revealed that non-R0 resection (HR 6.144, 95% CI 2.881-13.106, $p < 0.001$), UAT invasion (HR 3.718, 95% CI 1.782-7.756, $p < 0.001$), and higher preoperative PTH levels (HR 1.001, 95% CI 1.000-1.001, $p = 0.012$) were independent risk factors of DM. CONCLUSIONS: Upper aerodigestive tract invasion and higher preoperative PTH levels might be risk factors for possible metastatic involvement of PC. R0 resection and closer surveillance should be considered in such cases to minimize the risk of DM and to optimize patient care.
PubMed-ID: 38879674
DOI: 10.1245/s10434-024-15611-3

Adrenals

Meta-Analyses

The impact of adrenocortical carcinoma hormone secreting status as a predictor of poor survival: a systematic review and meta-analysis.
Langenbecks Arch Surg, 409(1):316.
C. Nastos, D. Papaconstantinou, A. Paspala, N. Pararas, A. Vryonidou, A. Pikouli, E. Chronopoulou, A. Lechou, M. Peppa and E. Pikoulis. 2024.
PURPOSE: Adrenocortical carcinoma (ACC) poses a significant challenge in healthcare due to its aggressive nature and rarity. Prior reports suggest a poorer prognosis associated with hormone-secreting neoplasms. This study aims to assess the impact of ACC hormonal status on patients' oncologic survival. METHODS: A comprehensive literature search of the Medline, Embase, Web of Science, CINAHL, CENTRAL and clinicaltrials.gov databases was undertaken. Utilized data involved Hazard Ratios derived from multivariable analysis in order to minimize exposure to confounding bias. Included studies were subsequently meta-analyzed using a Random effects model. RESULTS: Twelve studies incorporating 4483 patients were included in the quantitative analysis. Hormonally active ACCs comprised 48% of the entire pooled patient cohort and were found to be associated with significantly worse Overall Survival (HR 1.57, 95% Confidence Interval 1.39-1.78, $p < 0.001$). Disease-Free Survival was comparably impacted (HR 1.32, 95% CI 1.11-1.57, $p < 0.001$). Furthermore, cortisol secreting ACCs specifically, were also found to be associated with a 48% increase in the hazard of death or disease recurrence. Interstudy statistical heterogeneity was minimal among evaluated outcomes. CONCLUSIONS: Hormone-producing ACCs exhibit a poorer prognosis compared to non-secreting counterparts, with a 57% increased risk of death and a 32% increased risk of recurrence. These findings support the hypothesis that hormone production signifies an adverse tumor-specific feature, particularly when leading to hypercortisolemia, indicating an aggressive disease phenotype.
PubMed-ID: 39432022
DOI: 10.1007/s00423-024-03507-5

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Benefits of transitioning from transperitoneal laparoscopic to retroperitoneoscopic adrenalectomy-a single center experience.
Gland Surg, 13(11):1977-85.
J. Feka, B. Soliman, M. Arikan, T. Binter, L. Hargitai, C. Scheuba and P. Riss. 2024.
BACKGROUND: Since 2017, switching from laparoscopic transabdominal adrenalectomy (LTA), posterior retroperitoneoscopic adrenalectomy (RPA) is used as standard procedure in this institution. Aim of this retrospective study was to compare both techniques regarding operative time, length of stay and safety of the procedures. METHODS: All patients operated in our institution for adrenal tumors were prospectively documented in the EUROCRINE-database and retrospectively analyzed. Sex, age, body mass index (BMI), indication, operative time, conversion and complication rates, hospital stay and tumor-size were analyzed by Z-score, chi-square test, t-test, Mann-Whitney U test and Pearson correlation. RESULTS: A total of 105 RPAs and 132 LTAs were performed in an 8-year period. No difference was seen in

age, sex and tumor localization. Adenoma (n=113) and pheochromocytoma (n=64) were the most common histopathological findings. Compared to the LTA group, the RPA group had significantly shorter operative time with a median of 50 (15-380) vs. 125 (25-420) min (P<0.001) and shorter hospital stay with a median of 3 vs. 9 days (P<0.001). The decrease of the median operative time in RPA group, visualizing the learning curve of the procedure, was from 60 min (2017) to 45 min (2020). Four conversions from RPA to open adrenalectomy had to be performed due to bleeding or adhesions, whereas 9 LTA procedures had to be converted due to bleeding (n=2), unclear anatomy (n=1), adhesions (n=1), difficult access (n=1) or planned conversion (n=4). CONCLUSIONS: RPA could be safely introduced with reduced operative times and shorter length of hospital stay compared to LTA.
PubMed-ID: 39678401
DOI: 10.21037/gs-24-286
PMCID: PMC11635560

ASO Author Reflections: Continued Refinement of Perioperative Protocols to Predict Secondary Adrenal Insufficiency After Unilateral Adrenalectomy.
Ann Surg Oncol, 31(12):8146-7.
S. Johnson, S. Dream and T. S. Wang. 2024.
PubMed-ID: 39068314
DOI: 10.1245/s10434-024-15900-x

Cushing syndrome from an ACTH-producing pheochromocytoma or paraganglioma: structured review of 94 cases.
Endocr Relat Cancer, 31(11)
D. Kishlyansky, A. A. Leung, J. L. Pasieka, A. Mahajan and G. A. Kline. 2024.
Adrenocorticotropic hormone-producing pheochromocytomas/paragangliomas are rare neuroendocrine tumors that co-secrete excess catecholamines and adrenocorticotropic hormone, resulting in Cushing syndrome (CS). This review aims to summarize important patient characteristics, investigations, and outcomes in all cases reported in the English literature. A literature search was conducted to identify all English-language case reports and case series describing adrenocorticotropic hormone-producing pheochromocytomas/paragangliomas. Relevant characteristics were systematically recorded. Cases that did not provide definitive evidence of an adrenocorticotropin (ACTH)-producing pheochromocytoma/paraganglioma were excluded. Our search strategy identified 93 published cases that met the inclusion criteria. We additionally reported one patient for a total of 94 cases. Details related to patient characteristics, laboratory data, and outcomes were commonly underreported. The median age was 47 years, and females accounted for 72% of cases. A cushingoid appearance was reported in 82% of patients, and hypertension in 86%. Infections were reported in 23% of patients. Urinary metanephrines were elevated at least three-fold above normal in 74% of cases. ACTH levels were high in 88% of patients and inappropriately normal in 12%. The median 24-hour urinary cortisol was 21-fold the upper limit of normal. Adrenalectomy was performed in nearly all patients, with 88% achieving a cure for both catecholamine and glucocorticoid excess. A total of 11 patients died. Metastases were uncommon (6%). Adrenocorticotropic hormone-producing pheochromocytomas/paragangliomas are associated with considerable morbidity and mortality. It should be considered in the diagnostic workup of all patients with ectopic CS. Surgical cure is achieved in most patients, and infections are the leading cause of peri-operative mortality.
PubMed-ID: 39283908
DOI: 10.1530/ERC-24-0029

Paediatric phaeochromocytoma and paraganglioma: A clinical update.
Clin Endocrinol (Oxf), 101(5):446-54.
M. A. Nazari, A. Jha, M. J. M. Kuo, M. Patel, T. Prodanov, J. S. Rosenblum, S. Talvacchio, A. Derkyi, K. Charles and K. Pacak. 2024.
Paediatric phaeochromocytomas and paragangliomas (PPGLs), though rare tumours, are associated with significant disability and death in the most vulnerable of patients early in their lives. However, unlike cryptogenic and insidious disease states, the clinical presentation of paediatric patients with PPGLs can be rather overt, allowing early diagnosis, granted that salient findings are recognized. Additionally, with prompt and effective intervention, prognosis is favourable if timely intervention is implemented. For this reason, this review focuses on four exemplary paediatric cases, succinctly emphasizing the now state-of-the-art concepts in paediatric PPGL management.
PubMed-ID: 37515400
DOI: 10.1111/cen.14955

Contralateral Suppression in Adrenal Venous Sampling Predicts Clinical and Biochemical Outcome in Primary Aldosteronism.
J Clin Endocrinol Metab, 109(9):2282-93.
J. Okubo, P. Frudit, A. Cavalcante, A. A. W. Maciel, T. C. Freitas, B. Pilan, G. F. C. Fagundes, N. L. Queiroz, M. A. M. Stumpf, V. C. M. Souza, E. Z. Kawahara, T. S. Goldbaum, M. A. A. Pereira, V. F. Calsavara, F. M. A. Coelho, V. Srougi, F. Y. Tanno, J. L. Chambo, L. A. Bortolotto, L. F. Drager, M. Fragoso, A. C. Latronico, B. B. Mendonca, F. C. Carnevale and M. Q. Almeida. 2024.
CONTEXT: The role of hormone parameters at adrenal venous sampling (AVS) in predicting clinical and biochemical outcomes remains controversial. OBJECTIVE: To investigate the impact of hormone parameters at AVS under cosyntropin stimulation on lateralization and on complete biochemical and clinical outcomes. METHODS: We retrospectively evaluated 150 sequential AVS under cosyntropin infusion. The bilateral successful cannulation rate was 83.3% (n = 140), 47.9% bilateral and 52.1% unilateral. The lateralization index, aldosterone/cortisol ratio (A/C) in the dominant adrenal vein (AV), and relative aldosterone secretion index (RASI = A/C in AV divided by A/C in inferior vena cava) were assessed. The contralateral suppression (CS) percentage was defined by (1 - nondominant RASI) * 100. RESULTS: A nondominant RASI <0.5 (CS >50%) had 86.84% sensitivity and 92.96% specificity to predict contralateral lateralization. An A/C ratio in dominant AV >5.9 (74.67% sensitivity and 80% specificity) and dominant RASI >4.7 (35.21% sensitivity and 88.06% specificity) had the worst performance to predict ipsilateral lateralization. Complete biochemical and clinical cure was significantly more frequent in the patients with CS >50% [98.41% vs 42.86% (P < .001) and 41.94% vs 0% (P < .001)]. CS correlated with high aldosterone at diagnosis (P < .001) and low postoperative aldosterone levels at 1 month (P = .019). Postoperative biochemical hypoaldosteronism was more frequent in patients with CS >50% (70% vs 16.67%, P = .014). In multivariable analysis, a CS >50% was associated with complete biochemical cure [odds ratio (OR) 125, 95% confidence interval (CI) 11.904-5000; P = .001] and hypertension remission (OR 12.19, 95% CI 2.074-250; P = .023). CONCLUSION: A CS >50% was an independent predictor of complete clinical and biochemical cure. Moreover, it can predict unilateral primary aldosteronism and postoperative biochemical hypoaldosteronism. Our findings underscore the usefulness of CS for clinical decision-making.
PubMed-ID: 38442744
DOI: 10.1210/clinem/dgae142

Diagnosis and management of urinary bladder paragangliomas: A Sino-American-European retrospective observational study.
Clin Endocrinol (Oxf), 101(3):234-42.
Y. Pang, J. Zhang, J. Jiang, C. Pamporaki, M. Li, N. Bechmann, L. Meuter, Y. Wei, H. Huang, S. Huang, X. Yu, M. Robledo, M. J. Soria, D. Zhong, S. Xu, H. Timmers, J. F. Langenhuijsen, X. Chen, W. Deng, T. Deutschbein, H. Remde, L. Wang, H. Yao, B. Yan, A. M. A. Berends, M. N. Kerstens, Y. Jiang, J. Crona, N. Xu, H. Cai, Y. Wen, A. Wang, J. Wu, Z. Zhang, J. Ning, F. Cheng, X. Chen, J. Wang, B. Xie, D. Chen, Y. Liu, L. Liu, K. Pacak, G. Eisenhofer and J. W. M. Lenders. 2024.
OBJECTIVE: Paragangliomas of the urinary bladder (UBPGLs) are rare neuroendocrine tumours and pose a diagnostic and surgical challenge. It remains unclear what factors contribute to a timely presurgical diagnosis. The purpose of this study is to identify factors contributing to missing the diagnosis of UBPGLs before surgery. DESIGN, PATIENTS AND MEASUREMENTS: A total of 73 patients from 11 centres in China, and 51 patients from 6 centres in Europe and 1 center in the United States were included. Clinical, surgical and genetic data were collected and compared in patients diagnosed before versus after surgery. Logistic regression analysis was used to identify clinical factors associated with initiation of presurgical biochemical testing. RESULTS: Among all patients, only 47.6% were diagnosed before surgery. These patients were younger (34.0 vs. 54.0 years, p < .001), had larger tumours (2.9 vs. 1.8 cm, p < .001), and more had a SDHB pathogenic variant (54.7% vs. 11.9%, p < .001) than those diagnosed after surgery. Patients with presurgical diagnosis presented with more micturition spells (39.7% vs. 15.9%, p = .003), hypertension (50.0% vs. 31.7%, p = .041) and catecholamine-related symptoms (37.9% vs. 17.5%, p = .012). Multivariable logistic analysis revealed that presence of younger age (<35 years, odds ratio [OR] = 6.47, p = .013), micturition spells (OR = 6.79, p = .007), hypertension (OR = 3.98, p = .011), and sweating (OR = 41.72, p = .013) increased the probability of initiating presurgical biochemical testing. CONCLUSIONS: Most patients with UBPGL are diagnosed after surgery. Young age, hypertension, micturition spells and sweating are clues in assisting to initiate early biochemical testing and thus may establish a timely presurgical diagnosis.
PubMed-ID: 38606576
DOI: 10.1111/cen.15058

Kidney Function in Patients With Adrenal Adenomas: A Single-Center Retrospective Cohort Study.
J Clin Endocrinol Metab, 109(9):e1750-e8.

L. Rahimi, A. Kittithaworn, R. Gregg Garcia, J. Saini, P. Dogra, E. J. Atkinson, S. J. Achenbach, A. Kattah and I. Bancos. 2024.
CONTEXT: Patients with nonfunctioning adrenal adenomas (NFA) and mild autonomous cortisol secretion (MACS) demonstrate an increased risk of chronic kidney disease (CKD); however, factors associated with CKD are unknown. OBJECTIVE: We aimed to identify the factors associated with CKD and assess the effect of adrenalectomy on kidney function in patients with NFA or MACS. METHODS: A single-center cohort study of patients with NFA and MACS, 1999 to 2020, was conducted. MACS was diagnosed based on post dexamethasone suppression test (DST) cortisol greater than or equal to 1.8 mcg/dL. Age, sex, dysglycemia, hypertension, therapy with statin, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker were included in the multivariable analysis. Outcomes included estimated glomerular filtration rate (eGFR) at the time of diagnosis with MACS or NFA and postadrenalectomy delta eGFR. RESULTS: Of 972 patients, 429 (44%) had MACS and 543 (56%) had NFA. At the time of diagnosis, patients with MACS had lower eGFR (median 79.6 vs 83.8 mL/min/1.73 m2; P < .001) than patients with NFA. In a multivariable analysis, factors associated with lower eGFR were older age, hypertension, and higher DST. In 204 patients (MACS: 155, 76% and NFA: 49, 24%) treated with adrenalectomy, postadrenalectomy eGFR improved in both groups starting at 18 months up to 3.5 years of follow-up. Factors associated with increased eGFR were younger age, lower preadrenalectomy eGFR, and longer follow-up period. CONCLUSION: DST cortisol is an independent risk factor for lower eGFR in patients with adrenal adenomas. Patients with both MACS and NFA demonstrate an increase in eGFR post adrenalectomy, especially younger patients with lower eGFR pre adrenalectomy.
PubMed-ID: 38157409
DOI: 10.1210/clinem/dgad765
PMCID: PMC11318994

SDHB-Associated Pheochromocytomas: What is Their Clinical Behavior?
Ann Surg Oncol, 31(13):9007-13.
T. Szabo Yamashita, A. Tame-Elorduy, C. M. Skefos, J. M. Varghese, M. A. Habra, S. B. Fisher, P. H. Graham, E. G. Grubbs, S. G. Waguespack, C. Jimenez and N. D. Perrier. 2024.
INTRODUCTION: Germline pathogenic variants in succinate dehydrogenase subunit B (SDHB) cause paraganglioma/pheochromocytoma syndrome type 4 (PGL-4). SDHB-associated pheochromocytomas (PCC) are thought to be rare and little data exist about their clinical behavior. PATIENTS AND METHODS: Retrospective review of patients treated (1993-2023) at a tertiary cancer center for SDHB-associated PCC. Clinical and demographic variables were retrieved to characterize disease-free survival, disease progression, and overall survival. RESULTS: In total, 90 SDHB-carriers were identified, 18% had PCC (n = 16). Median age at diagnosis of was 40 (19-76) years, 50% (n = 8) of patients were male, 25% (n = 4) had distant metastasis (DM) at diagnosis, and 13% (n = 2) had synchronous PGL. No patients had bilateral disease, and 94% of patients underwent surgery as initial treatment with a curative intent in 75%. Overall, 64% of patients underwent open resection. Recurrence occurred in 77% of patients (n = 10), 75% in minimally invasive surgery (MIS) versus 77% open, p = 0.63. Bone was the most common site of DM (100%, n = 13). Metaidobenzyleguanidine (MIBG) imaging was performed in 69% of patients, 91% of which were positive. Median time from surgery until recurrence was 36 months (1-295 months). Radiation therapy was the most common adjuvant treatment (44%) followed by Iobenguane I-131 (31%) and systemic therapy (31%). Median follow-up time was 56 months (1-408 months). Overall, 33% of patients were alive, 19% of patients were disease-free, and 50% of the patients with DM had stable disease at last follow-up. CONCLUSIONS: Overall, 18% of germline SDHB mutation-carriers were diagnosed with PCC, all of which were unilateral. SDHB-associated PCC was associated with advanced and recalcitrant disease and was often MIBG positive. More studies are needed to better understand the clinical behavior of PCC in PGL-4.
PubMed-ID: 39382746
DOI: 10.1245/s10434-024-16120-z

Robot-assisted laparoscopic adrenalectomy: Extended application in children.
Eur J Surg Oncol, 50(12):108627.
K. Taghavi, M. Glenisson, K. Loiselet, V. Fiorenza, M. Cornet, C. Capito, N. Vinit, A. Pire, S. Sarnacki and T. Blanc. 2024.
BACKGROUND: Minimally invasive surgery for paediatric adrenal tumours has evolved, but robot-assisted laparoscopic adrenalectomy (RALA) in children remains poorly studied. The current prospective study aims to demonstrate the safety and efficacy of RALA in treating children with adrenal tumours. METHODS: A prospective institutional analysis of children presenting with neuroblastic and endocrine tumours treated with RALA was undertaken over a six year-period. For each child, clinical parameters were collected relating to diagnosis, surgery and outcomes. RESULTS: A total 50 RALA were performed; 23 for unilateral neuroblastic tumours (87 % neuroblastomas) and 27 for endocrine tumours. Eight neuroblastic tumours (35 %) had image-defined risk factors (all due to tumour invading the renal pedicle). Median length

of stay was two days. Resection margins were macroscopically clear in all cases. After median follow-up of 2.9 years (1.6-3.9), two children are under treatment for metastatic relapse (high-risk disease) and three died due to refractory disease. Sixteen children had endocrine tumours: pheochromocytoma (n = 13), or bilateral nodular adrenocortical hyperplasia with Cushing's syndrome (n = 14). One child required non-emergent conversion, and one complication occurred (grade IIIb) after median follow-up of 3.3 years (1.0-5.7). CONCLUSIONS: The current study is the largest reported experience in the literature and confirms the safety and effectiveness of RALA in carefully selected children with adrenal tumours. Through an iterative process and in the setting of a dedicated paediatric robotic surgical team indications have been clarified and extended. The current study confirms RALA has particularly utility in patients with severe disease (IDRF + metastatic neuroblastomas) or genetic predisposition syndromes.
PubMed-ID: 39214030
DOI: 10.1016/j.ejso.2024.108627

NET

Meta-Analyses

Management of advanced high grade gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs): comprehensive review of the current literature.
Endocr Relat Cancer, 31(10)
A. Mohamed, M. Trybula, S. L. Asa, T. R. Halfdanarson and M. B. Sonbol. 2024.
The classification and management of neuroendocrine neoplasms (NENs) arising in the tubular gastrointestinal (GI) tract and pancreas have significantly evolved over the last decades. In the latest WHO classification published in 2022, NENs are separated regardless of their primary origin into two main groups: well-differentiated neuroendocrine tumors (NETs) and poorly differentiated neuroendocrine carcinomas (NECs). The substantial changes in the grading system changed the definition of grade 3 to include high-grade well-differentiated NETs (G3-NETs), and poorly differentiated NECs (-NECs). Although these two subgroups are considered high grades with Ki-67 >20%, they have different genomic profiles, prognosis, and clinical behavior, which critically influence their treatment strategies. The available clinical trial data to guide therapy of these high-grade subgroups are extremely limited, which impacts their management. In this review, we will summarize the current advances in the multidisciplinary approach for the management of high-grade gastroenteropancreatic NENs (GEP-NENs) including G3-NETs and NECs.
PubMed-ID: 39133180
DOI: 10.1530/ERC-24-0025

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Preoperative Prediction of Lymph Node Metastases in Nonfunctional Pancreatic Neuroendocrine Tumors Using a Combined CT Radiomics-Clinical Model.
Ann Surg Oncol, 31(12):8136-45.
T. M. Ahmed, Z. Zhu, M. Yasrab, A. Blanco, S. Kawamoto, J. He, E. K. Fishman, L. Chu and A. A. Javed. 2024.
BACKGROUND: PanNETs are a rare group of pancreatic tumors that display heterogeneous histopathological and clinical behavior. Nodal disease has been established as one of the strongest predictors of patient outcomes in PanNETs. Lack of accurate preoperative assessment of nodal disease is a major limitation in the management of these patients, in particular those with small (< 2 cm) low-grade tumors. The aim of the study was to evaluate the ability of radiomic features (RF) to preoperatively predict the presence of nodal disease in pancreatic neuroendocrine tumors (PanNETs). PATIENTS AND METHODS: An institutional database was used to identify patients with nonfunctional PanNETs undergoing resection. Pancreas protocol computed tomography was obtained, manually segmented, and RF were extracted. These were analyzed using the minimum redundancy maximum relevance analysis for hierarchical feature selection. Youden index was used to identify the optimal cutoff for predicting nodal disease. A random forest prediction model was trained using RF and clinicopathological characteristics and validated internally. RESULTS: Of the 320 patients included in the study, 92 (28.8%) had nodal disease based on histopathological assessment of the surgical specimen. A radiomic signature based on ten selected RF was developed. Clinicopathological characteristics predictive of nodal disease included tumor grade and size. Upon internal validation the combined radiomics and clinical feature model demonstrated adequate performance (AUC 0.80) in identifying nodal disease. The model accurately identified nodal disease in 85% of patients with small tumors

(< 2 cm). CONCLUSIONS: Non-invasive preoperative assessment of nodal disease using RF and clinicopathological characteristics is feasible.
PubMed-ID: 39179862
DOI: 10.1245/s10434-024-16064-4

Surgical management of pancreatic neuroendocrine tumors - An EYSAC and E-AHPBA international survey of current practice.
Eur J Surg Oncol, 50(10):108544.
A. Brandl, D. Lundon, A. K. Siriwardena, D. Sochorova, W. Ceelen, M. Besselink, K. Soreide and S. Stattner. 2024.
INTRODUCTION: Pancreatic neuroendocrine tumors (pNET) exhibit a wide spectrum of clinical behavior, which makes their assessment and management quite challenging. The purpose of this study was to comprehensively assess the existing treatment landscape for patients with pNET. MATERIALS AND METHODS: The study was conducted with the support of the ESSO-EYSAC Research Academy in collaboration with the E-AHPBA. An online survey was distributed via email and social media to surgical networks across Europe and beyond (September 1-30, 2023). RESULTS: Overall, 155 complete responses were obtained. A specialized NET tumor board was present at the institutions of 94 (61 %) of the study participants. The most frequently applied guidelines were from ENETS (n = 97; 63 %), NCCN (n = 74; 48 %), and ESMO (n = 53; 34 %). For resectability, similar criteria as in pancreatic ductal adenocarcinoma were used by 111 (72 %) participants, even though 116 (75 %) participants believed that pNET/pNEC should have their own resectability criteria. Most respondents used somatostatin analogues (n = 126; 81 %) and chemotherapy (n = 85; 55 %) as neoadjuvant treatments, followed by molecularly targeted agents (n = 45; 29 %) and PRRT (n = 37; 24 %). Only 17 (11 %) participants agreed/strongly agreed that the management of pNET/pNEC is sufficiently addressed in surgical education programs. CONCLUSION: This international survey highlighted areas for improvement in the care of pNET, namely the lack of pNET-specific resectability criteria and educational programs addressing pNET management.
PubMed-ID: 39059195
DOI: 10.1016/j.ejso.2024.108544

Long-term clinical and radiological outcomes of endoscopic ultrasound-guided radiofrequency ablation of benign insulinomas.
Clin Endocrinol (Oxf), 101(5):485-90.
Z. Debraine, I. Borbath, P. Deprez, F. Bosly, D. Maiter and R. M. Furnica. 2024.
OBJECTIVE: In recent years, endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) has emerged as an alternative nonsurgical treatment for pancreatic neuroendocrine tumours. The aim of our study was to assess the long-term follow-up of patients treated with EUS-RFA for a sporadic insulinoma in our centre in terms of efficacy, safety and risk of recurrence. DESIGN, PATIENTS AND MEASUREMENTS: We retrospectively analysed the data of 11 patients with an insulinoma treated by EUS-RFA in our tertiary centre between June 2018 and April 2022. Clinical and biological, as well as imaging, follow-up was planned at 3, 6, 12 months and then annually. RESULTS: In our series, there were nine women and two men with a median age of 65 years. All tumours were sporadic, with a mean size of 11 mm. The procedure allowed an immediate and complete symptomatic and biological remission in all patients without notable complications. Complete radiological resolution of the tumour after ablation was observed in seven patients, and persistence of an asymptomatic tumour residue was observed in four patients. During the mean follow-up period of 26 months, two patients presented a significant but asymptomatic increase of the tumour residue; a second EUS-RFA session was performed in one patient and the other patient is being closely monitored. CONCLUSIONS: EUS-RFA treatment of benign insulinomas provides a long-term complete clinical resolution of hypoglycaemia. A long-term follow-up is essential if residual tumour persists after initial EUS-RFA treatment.
PubMed-ID: 37859570
DOI: 10.1111/cen.14981

Subgrading of G2 Pancreatic Neuroendocrine Tumors as 2A (Ki67 3% to < 10%) Versus 2B (10% to </= 20%) Identifies Behaviorally Distinct Subsets in Keeping with the Evolving Management Protocols.
Ann Surg Oncol, 31(10):7001-11.
O. C. Eren, P. Bagci, S. Balci, N. Ohike, B. Saka, C. Sokmensuer, C. B. Leblebici, Y. Xue, M. D. Reid, A. M. Krasinskas, D. Kooby, S. K. Maithel, J. Sarmiento, J. D. Cheng, O. C. Taskin, Y. Kapran, Z. C. Tarcan, C. Luchini, A. Scarpa, O. Basturk and N. V. Adsay. 2024.
BACKGROUND: Grade 1/2 PanNETs are mostly managed similarly, typically without any adjunct treatment with the belief that their overall metastasis rate is low. In oncology literature, Ki67-index of 10% is increasingly being used as the cutoff in

stratifying patients to different protocols, although there are no systematic pathology-based studies supporting this approach. METHODS: Ki67-index was correlated with clinicopathologic parameters in 190 resected PanNETs. A validation cohort (n = 145) was separately analyzed. RESULTS: In initial cohort, maximally selected rank statistics method revealed 12% to be the discriminatory cutoff (close to 10% rule of thumb). G2b cases had liver/distant metastasis rate of almost threefold higher than that of G2a and showed significantly higher frequency of all histopathologic signs of aggressiveness (tumor size, perineural/vascular invasion, infiltrative growth pattern, lymph node metastasis). In validation cohort, these figures were as striking. When all cases were analyzed together, compared with G1, the G2b category had nine times higher liver/distant metastasis rate (6.1 vs. 58.5%; p < 0.001) and three times higher lymph node metastasis rate (20.5 vs. 65.1%; p < 0.001). CONCLUSIONS: G2b PanNETs act very similar to G3, supporting management protocols that regard them as potential therapy candidates. Concerning local management, metastatic behavior in G2b cases indicate they may not be as amenable for conservative approaches, such as watchful waiting or enucleation. This substaging should be considered into diagnostic guidelines, and clinical trials need to be devised to determine the more appropriate management protocols for G2b (10% to </= 20%) group, which shows liver/distant metastasis in more than half of the cases, which at minimum warrants closer follow-up.
PubMed-ID: 38955993
DOI: 10.1245/s10434-024-15632-y
PMCID: PMC11413052

Invited Editorial: Long-Term Survival Outcomes After Minimally Invasive Surgery for Ileal Neuroendocrine Tumors.
Ann Surg Oncol, 31(9):5487-8.
A. Gustafson and S. M. Sadowski. 2024.
PubMed-ID: 38839670
DOI: 10.1245/s10434-024-15563-8

Larger Tumor Size and Elevated Serum Chromogranin A Levels Predict Metastatic Disease on DOTATATE Imaging in Patients with Gastroenteropancreatic Neuroendocrine Tumors.
Ann Surg Oncol, 31(10):6875-82.
A. Labora, T. Shimizu, A. Moore, A. Premji, W. R. Armstrong, K. Y. Chen, J. Link, C. S. Chan, M. S. Allen-Auerbach and T. R. Donahue. 2024.
PURPOSE: DOTATATE PET/CT (DOTATATE) is superior to conventional imaging in detecting metastasis for gastroenteropancreatic neuroendocrine tumors (GEP-NETs). However, limited availability, high-cost, and additive radiation exposure necessitate guidelines for its use. This study seeks to investigate the relationship between clinical characteristics and metastasis on DOTATATE. METHODS: This was a retrospective analysis of 815 patients who underwent DOTATATE at UCLA from 2014 to 2022. After applying inclusion and exclusion criteria, the study cohort consisted of 163 patients with pathologically diagnosed GEP-NETs, who either underwent primary tumor resection within 1-year prior, or had not undergone resection at the time of DOTATATE imaging. The presence of metastasis was determined using DOTATATE. Fisher's exact test, chi-squared test, and Mann-Whitney test were conducted to compare intergroup difference. Multivariate analysis was performed to identify clinical characteristics associated with metastasis on DOTATATE. RESULTS: Of patients with GEP-NETs, 40.5% (n = 66) were diagnosed with metastases by using DOTATATE. Those with metastatic disease were more likely to exhibit a larger primary tumor size (median 3.4 vs. 1.2, cm, P < 0.001), elevated serum chromogranin A level (CgA, median 208 vs. 97, mg/ml, P = 0.005), and higher tumor grade (P < 0.001). Primary tumor size >/=2 cm and serum CgA level >/=150 ng/mL for metastatic disease had a sensitivity and specificity of 64% and 89%, and 72% and 59%, respectively. Multivariate analysis demonstrated that primary tumor size (>/=2/<2, cm, odds ratio [OR] 47.90, P < 0.001), tumor functionality (functional/nonfunctional, adjusted OR 10.17 P = 0.008), serum CgA level (>/=150/<150, ng/ml, OR 6.25, P = 0.005), and tumor grade G2 (G2/G1, OR 9.6, P < 0.001) were independently associated with metastases on DOTATATE. CONCLUSIONS: Among patients with GEP-NETs, primary tumor size >/=2 cm, serum CgA level >/=150 ng/mL, and tumor grade G2 are associated with an increased risk of metastases on DOTATATE, and these predictors may be helpful to identify patients where DOTATATE is indicated for complete staging.
PubMed-ID: 38909116
DOI: 10.1245/s10434-024-15538-9

Surgery for pancreatic neuroendocrine tumors during the COVID-19 pandemic: a retrospective cohort from a high-volume center.
Updates Surg, 76(5):1827-32.
S. Paiella, L. Landoni, M. De Pastena, G. Elio, F. Casciani, S. Cingarlini, M. D'Onofrio, G. Maistri, I. Ciatti, M. Tuveri, M. V.

Davi, C. Luchini, K. Donadello, G. Manzini, G. Malleo and R. Salvia. 2024.
During the COVID-19 pandemic, pancreatic surgery for pancreatic neuroendocrine tumors (PNETs) with surgical indications was postponed or canceled. Patients with PNET patients who underwent pancreatic surgery during the COVID-19 restriction period (3 years) were compared with a similar cohort of patients who underwent surgery in the previous 3 years. Data on patients' characteristics, waiting time, and surgical and pathology outcomes were evaluated. During the study period, 370 patients received surgery for PNETs, 205 (55%) during the first period, and 165 (45%) during the pandemic. A lengthening of the waiting list (182 [IQR 100-357] vs. 60 [40-88] days, $p < 0.001$) and increased use of anti-tumor medical treatments (any therapy, peptide receptor radionuclide therapy, and somatostatin analogs; all $p < 0.001$) was found. During the pandemic, surgery occurred after a median of 381 days [IQR 200-610] from diagnosis (vs. 103 [IQR 52-192] of the pre-COVID-19 period, $p < 0.001$). No statistically significant differences in tumor size and grading distribution were found between the two periods (both $p > 0.05$), yet only a modest increase of the median Ki67 values in cases operated during the pandemic (4% vs. 3%, $p = 0.03$). Lastly, these latter patients experienced less major postoperative complications (13% vs. 24%, $p = 0.007$). During COVID-19, the surgical waiting list of PNET patients was drastically extended, and bridge therapies were preferred. This did not result in more advanced cases at final pathology. PRRT and SSA are valid alternative therapies for PNETs when surgery is not feasible.
PubMed-ID: 39033485
DOI: 10.1007/s13304-024-01942-z
PMCID: PMC11455720

General

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Analysis of Opioid Prescribing Trends Following Thyroidectomy and Parathyroidectomy Before and After the 2021 American Academy of Otolaryngology-Head and Neck Surgery Opioid Prescribing Clinical Practice Guidelines.
Otolaryngol Head Neck Surg, 171(6):1690-6.
R. E. Africa, B. J. McKinnon, O. M. Coblens, V. J. Ranasinghe and S. Shabani. 2024.
OBJECTIVE: To evaluate the trends in opioid and nonopioid prescribing for thyroidectomy and parathyroidectomy before and after the publication of guidelines by the American Academy of Otolaryngology-Head and Neck Surgery in April 2021. STUDY DESIGN: Retrospective. SETTING: Eighty-three health care organizations in the United States that contribute to the TriNetX database. METHODS: Deidentified patient data were retrieved from the TriNetX. Patients who were prescribed either opioids or nonopioid analgesic within 1 to 5 days following thyroid surgery and parathyroidectomy were included. Evaluation of the prescription trends was performed by interrupted time series analysis in Statistical Analysis System 9.4 with significance set at P < .05 to assess trends before and after the new opioid prescription guidelines. RESULTS: For thyroid surgery, there was an immediate effect of the guideline change indicated by a 3.3% decrease in the opioid prescription trend (P = .03) and a significant increase in nonopioid use of overtime by 0.13% every 3 months (P < .0001). The opioid prescription trend following parathyroidectomy significantly decreased over time by 0.28% every 3 months (P < .0001), while the nonopioid prescription trend increased by 0.14% (P < .0001). CONCLUSION: There was an associated immediate reduction in the opioid prescribing trend for thyroidectomy, but the change was not sustained overtime. There was an associated decrease in the opioid prescribing trend for parathyroidectomy, but not immediately after the initial publication of the prescription guidelines. LEVEL OF EVIDENCE: Level III.
PubMed-ID: 39413345
DOI: 10.1002/ohn.1008

SDHA-related phaeochromocytoma and paraganglioma: review and clinical management.
Endocr Relat Cancer, 31(10)
A. I. Kaplan, T. Dwight, C. Luxford, D. E. Benn and R. J. Clifton-Bligh. 2024.
Phaeochromocytomas and paragangliomas (collectively termed PPGL) are rare yet highly heritable neuroendocrine tumours, with over one-third of cases associated with germline pathogenic variants (PVs) in numerous genes. PVs in the succinate dehydrogenase subunit-A gene (SDHA) were initially implicated in hereditary PPGL in 2010, and SDHA has since become an important susceptibility gene accounting for up to 2.8% of cases. However, it remains poorly understood, particularly regarding the clinical nature of SDHA PPGL, rates of recurrence and metastasis, and the nature of metastatic disease. We present a narrative review of SDHA-related PPGL, covering pathophysiology, relevance to current clinical practice, and considerations for clinical genetics. We analyse a pool of 107 previously reported cases of SDHA-associated PPGL to highlight the spectrum of SDHA-related PPGL. Our analysis demonstrates that SDHA PPGL occurs across a wide age range (11-81 years) and affects men and women equally. SDHA PPGL typically presents as single tumours (91%),

usually occurring in the head and neck (46%) or abdomen (43%, including 15% with phaeochromocytomas). Metastatic disease was reported in 25.5% of cases, with bone (82%) and lymph nodes (71%) being the most common sites of metastasis, often identified many years after the initial diagnosis. A family history of SDHA-related neoplasia was rare, reported in only 4% of cases. Understanding the clinical nature and risks associated with SDHA PVs is essential for facilitating the optimal management of patients and their families.
PubMed-ID: 39133175
DOI: 10.1530/ERC-24-0111
PMCID: PMC11466202