EUROPEAN SOCIETY OF ENDOCRINE SURGEONS

ESES Review of Recently Published Literature

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

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

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Journals covered

Journal	IF2021	Journal	IF2021
Acta Cytol	3.000	J Bone Miner Res	6.390
Am J Kidney Dis	11.072	J Clin Endocrinol Metab	6.134
Am J Nephrol	4.605	J Clin Oncol	50.717
Am J Surg	3.125	J Endocrinol	4.669
Am Surgeon	1.002	J Endocrinol Invest	5.467
Ann Surg	13.787	J Nephrol	4.393
Ann Surg Oncol	4.339	J Nucl Med	11.082
ANZ J Surg	2.025	J Surg Oncol	2.885
Br J Surg	11.122	Lancet	202.731
Cancer	6.921	Langenbecks Arch Surg	2.895
Chirurg	0.920	Laryngoscope	2.970
Clin Endocrinol Oxf	3.523	N Engl J Med	176.079
Clin Nucl Med	10.782	Nat Rev Endocrinol	47.564
Curr Opin Oncol	3.915	Nat Rev Clin Oncol	65.011
Endocr Relat Cancer	5.900	Nephrol Dial Transplant	7.186
Endocr Rev	25.261	Neuroendocrinology	5.135
Eur Arch Otorhinolaryngol	3.236	Oncologist	5.837
Eur J Endocrinol	6.558	Otolaryngol Head Neck Surg	5.591
Eur J Surg Oncol	4.037	Surg Clin North Am	3.537
Gland Surg	2.160	Surg Endosc	3.453
Head Neck	3.821	Surg Laparosc Endosc Percutan Tech	1.455
Horm Metab Res	2.788	Surg Oncol	2.388
JAMA Otolaryngol Head Neck Surg	8.961	Surg Oncol Clin N Am	2.402
JAMA Surg	16.681	Surgery	4.348
Int J Cancer	7.316	Thyroid	6.506
J Am Coll Surg	6.532	Updates In Surgery	2.692
J Am Soc Nephrol	14.978	World J Surg	3.282
J Bone Miner Metab	2.976		

Journal names are links to the journal's homepage!, IF2021: Impact factor 2021

Thyroid

Meta-Analyses

Ultrasound-guided thermal ablation for papillary thyroid microcarcinoma: A systematic review.
Clin Endocrinol (Oxf), 98(3):296-305.
Z. Chen, W. Zhang and W. He. 2023.
OBJECTIVE: Thyroidectomy is the first-line treatment for papillary thyroid microcarcinoma (PTMC), but often involves aggressive overtreatment. Thermal ablation (TA) has been gradually used for the treatment of recurrent PTMC. However, it is not recommended for the treatment of primary PTMC according to the Korean and Italian guidelines. Therefore, this systematic review aimed to analyse the indications, efficacy, and safety of TA in the treatment of PTMC. DESIGN: Systematic review. PATIENTS AND MEASUREMENTS: A search strategy was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. A total of 27 articles were included in this study until January 2022. RESULTS: According to current guidelines and studies, we divided the indications of TA for PTMC into six primary and three secondary indications. Laser ablation (LA) has the advantages of a small needle, accurate output energy and precision ablation, and it is safe to important organs around the lesion. The patients recover quickly after radiofrequency ablation (RFA), with no major complications, recurrence, or lymph node metastasis. The volume reduction rate after RFA was the highest, followed by microwave ablation and LA, and the improvement in patient quality of life after TA was significantly better than after thyroidectomy. CONCLUSIONS: TA is an effective alternative method for surgery in the treatment of low-risk PTMC and has the advantages of being minimally invasive, economical, having less bleeding and having a high postoperative quality of life.
PubMed-ID: 36471482
http://dx.doi.org/10.1111/cen.14857

The efficacy of adjuvant radioactive iodine after reoperation in patients with persistent or recurrent differentiated thyroid cancer: a systematic review.
Langenbecks Arch Surg, 408(1):21.
J. Raghupathy, B. K. J. Tan, H. Song, A. Z. Q. Chia, Y. Z. Tan, S. P. Yang and R. Parameswaran. 2023.
OBJECTIVE: The effectiveness of adjuvant radioiodine (RAI) after reoperation in patients with persistent or recurrent differentiated thyroid cancer (DTC) is controversial. Although various organizations recognize that strong evidence for the use of RAI is lacking, they continue to recommend the use of adjuvant RAI therapy for select groups of patients. This is concerning as RAI therapy has potential side effects such as gastrointestinal symptoms, bone marrow suppression, and gonadal damage. METHODS: Four electronic databases were systematically searched for randomized trials or observational studies that examined the outcomes of adjuvant RAI after reoperation for recurrent DTC, among patients of any age. The baseline characteristics, treatment response, disease progression, and overall survival of these studies were synthesized and reported. A meta-analysis of the use of RAI on progression-free survival was also performed. RESULTS: Six observational studies, comprising a combined cohort of 437 patients who underwent reoperation, were included from 1212 records. Adjuvant RAI after reoperation in recurrent DTC was not associated with longer progression-free or overall survival. There was also no association of RAI with excellent structural or biochemical treatment response, lower thyroglobulin levels, nor a lower rate of second recurrence or distant metastases. CONCLUSIONS: Adjuvant RAI after reoperation in recurrent DTC was not associated with improved cancer or treatment-related outcomes. However, as the included studies were of inadequate quality, there is an urgent need for randomized trials and well-analyzed cohort studies. Physicians should exercise clinical judgment to prescribe adjuvant RAI for only selected, high-risk patients.
PubMed-ID: 36635455
http://dx.doi.org/10.1007/s00423-022-02747-7

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Comparison of Lobectomy vs Total Thyroidectomy for Intermediate-Risk Papillary Thyroid Carcinoma With Lymph Node Metastasis.
JAMA Surg, 158(1):73-9.
S. Xu, H. Huang, Y. Huang, J. Qian, X. Wang, Z. Xu, S. Liu and J. Liu. 2023.
IMPORTANCE: Surgical treatment of patients with papillary thyroid cancer (PTC) by either lobectomy or total thyroidectomy (TT) has long been a topic of debate, especially for patients with intermediate-risk PTC. OBJECTIVE: To compare recurrence-free survival (RFS) for patients with PTC and lymph node metastasis after lobectomy vs TT. DESIGN, SETTING, AND PARTICIPANTS: This retrospective cohort study included a review of patients with PTC treated from January 1, 2000, to December 31, 2017. Propensity score matching (PSM) was performed between patients treated with lobectomy and TT. This study involved a single institute in a cancer referral center. Enrolled were adult patients (aged 18-75 years) with unilateral PTC and ipsilateral clinical lateral neck metastasis (cN1b). Patients with the following characteristics were excluded: a lymph node yield less than 20, primary tumor size greater than 4 cm, gross extrathyroidal extension, metastatic lymph node size greater than 3 cm, and distant metastasis. Data analysis was performed from April 1 to April 30, 2022. EXPOSURES: Lobectomy and TT. MAIN OUTCOMES AND MEASURES: The primary outcome was the association between extent of surgery and RFS, assessed using Cox proportional hazards regression models. RESULTS: A total of 946 patients with PTC (mean [SD] age, 37.0 [12.1] years, 630 female individuals [66.6%]) were analyzed. Lobectomy (624 [66.0%]) was negatively correlated with the frequencies of older age (>/=65 years, 17 [2.7%]), female sex (393 [63.0%]), multifocality (132 [21.2%]), minor extrathyroidal extension (259 [41.5%]), number of metastatic lymph nodes (median [range], 9 [6-14] nodes), and radioactive iodine ablation (0). After PSM with treatment period and potential prognostic factors (age, sex, primary tumor size, multifocality, minor extrathyroidal extension, number of lymph node metastases and lymph node ratio), 265 pairs of patients were available for analysis. After a median (range) follow-up of 60 (9-150) months in the lobectomy group and 58 (8-161) months in the TT group, 21 (7.9%) and 17 (6.4%) structural recurrences were identified in the lobectomy and TT groups, respectively. Lobectomy was not associated with significantly compromised 5-year RFS rate (lobectomy, 92.3% vs TT, 93.7%; adjusted hazard ratio, 1.10; 95% CI, 0.58-2.11; P = .77). Power analysis indicated that the test had 90% power to detect a more than 4.9% RFS difference. No significant difference in RFS was observed between patients treated with TT and radioactive iodine ablation (n = 75) and their counterparts (adjusted hazard ratio, 0.59; 95% CI, 0.14-2.41; P = .46). CONCLUSIONS AND RELEVANCE: Results of this cohort study suggest that patients with PTC and lymph node metastasis had a similar RFS after lobectomy vs those who had TT. If radioactive iodine ablation is not going to be performed, lobectomy may be an effective alternative option.
PubMed-ID: 36449303
http://dx.doi.org/10.1001/jamasurg.2022.5781

Artificial Intelligence for Pre-operative Diagnosis of Malignant Thyroid Nodules Based on Sonographic Features and Cytology Category.
World J Surg, 47(2):330-9.
K. Jassal, A. Koohestani, A. Kiu, A. Strong, N. Ravintharan, M. Yeung, S. Grodski, J. W. Serpell and J. C. Lee. 2023.
BACKGROUND: Current diagnosis and classification of thyroid nodules are susceptible to subjective factors. Despite widespread use of ultrasonography (USG) and fine needle aspiration cytology (FNAC) to assess thyroid nodules, the interpretation of results is nuanced and requires specialist endocrine surgery input. Using readily available pre-operative data, the aims of this study were to develop artificial intelligence (AI) models to classify nodules into likely benign or malignant and to compare the diagnostic performance of the models. METHODS: Patients undergoing surgery for thyroid nodules between 2010 and 2020 were recruited from our institution's database into training and testing groups. Demographics, serum TSH level, cytology, ultrasonography features and histopathology data were extracted. The training group USG images were re-reviewed by a study radiologist experienced in thyroid USG, who reported the relevant features and supplemented with data extracted from existing reports to reduce sampling bias. Testing group USG features were extracted solely from existing reports to reflect real-life practice of a non-thyroid specialist. We developed four AI models based on classification algorithms (k-Nearest Neighbour, Support Vector Machine, Decision Tree, Naive Bayes) and evaluated their diagnostic performance of thyroid malignancy. RESULTS: In the training group (n = 857), 75% were female

and 27% of cases were malignant. The testing group (n = 198) consisted of 77% females and 17% malignant cases. Mean age was 54.7 +/- 16.2 years for the training group and 50.1 +/- 17.4 years for the testing group. Following validation with the testing group, support vector machine classifier was found to perform best in predicting final histopathology with an accuracy of 89%, sensitivity 89%, specificity 83%, F-score 94% and AUROC 0.86. CONCLUSION: We have developed a first of its kind, pilot AI model that can accurately predict malignancy in thyroid nodules using USG features, FNAC, demographics and serum TSH. There is potential for a model like this to be used as a decision support tool in under-resourced areas as well as by non-thyroid specialists.
PubMed-ID: 36336771
http://dx.doi.org/10.1007/s00268-022-06798-1

Facility Volume as a Prognosticator of Survival in Locally Advanced Papillary Thyroid Cancer.
Laryngoscope, 133(2):443-50.
A. Abiri, J. C. Pang, K. Roman, K. Goshtasbi, J. L. Birkenbeuel, E. C. Kuan, T. Tjoa and Y. M. Haidar. 2023.
OBJECTIVES: To evaluate the influence of facility case-volume on survival in patients with locally advanced papillary thyroid cancer (PTC), and to identify prognostic case-volume thresholds for facilities managing this patient population. STUDY DESIGN: Retrospective database study. METHODS: The 2004-2017 National Cancer Database was queried for patients receiving definitive surgery for locally advanced PTC. Using K-means clustering and multivariable Cox proportional-hazards (CPH) regression, two groups with distinct spectrums of facility case-volumes were generated. Multivariable CPH regression and Kaplan-Meier analysis assessed for the influence of facility case-volume and the prognostic value of its stratification on overall survival (OS). RESULTS: Of 48,899 patients treated at 1304 facilities, there were 34,312 (70.2%) females and the mean age was 48.0 +/- 16.0 years. Increased facility volume was significantly associated with reduced all-cause mortality (HR 0.996; 95% CI, 0.992-0.999; p = 0.008). Five facility clusters were generated, from which two distinct cohorts were identified: low (LVF; <27 cases/year) and high (HVF; >/=27 cases/year) facility case-volume. Patients at HVFs were associated with reduced mortality compared to those at LVFs (HR 0.791; 95% CI, 0.678-0.923, p = 0.003). Kaplan-Meier analysis of propensity score-matched N0 and N1 patients demonstrated higher OS in HVF cohorts (all p < 0.001). CONCLUSIONS: Facility case-volume was an independent predictor of improved OS in locally advanced PTC, indicating a possible survival benefit at high-volume medical centers. Specifically, independent of a number of sociodemographic and clinical factors, facilities that treated >/=27 cases per year were associated with increased OS. Patients with locally advanced PTC may, therefore, benefit from referrals to higher-volume facilities. LEVEL OF EVIDENCE: 4 Laryngoscope, 133:443-450, 2023.
PubMed-ID: 35822421
http://dx.doi.org/10.1002/lary.30280

A multicenter evaluation of near-infrared autofluorescence imaging of parathyroid glands in thyroid and parathyroid surgery.
Surgery, 173(1):132-7.
L. Sehnem, Jr., S. I. Noureldine, S. Avci, G. Isiktas, M. Elshamy, Y. Saito, A. H. A. Ahmed, H. T. Tierney, L. N. Trinh, A. S. Karcioglu, A. Y. Cheung, M. Otremba, V. Krishnamurthy, K. Heiden, J. Jin, J. Shin, A. Siperstein, M. Zafereo, R. P. Tufano, G. W. Randolph, E. Kebebew, M. Milas, Q. Y. Duh and E. Berber. 2023.
BACKGROUND: The usefulness of incorporating near-infrared autofluorescence into the surgical workflow of endocrine surgeons is unclear. Our aim was to develop a prospective registry and gather expert opinion on appropriate use of this technology. METHODS: This was a prospective multicenter collaborative study of patients undergoing thyroidectomy and parathyroidectomy at 7 academic centers. A questionnaire was disseminated among 24 participating surgeons. RESULTS: Overall, 827 thyroidectomy and parathyroidectomy procedures were entered into registry: 42% of surgeons found near-infrared autofluorescence useful in identifying parathyroid glands before they became apparent; 67% correlated near-infrared autofluorescence pattern to normal and abnormal glands; 38% of surgeons used near-infrared autofluorescence, rather than frozen section, to confirm parathyroid tissue; and 87% and 78% of surgeons reported near-infrared autofluorescence did not improve the success rate after parathyroidectomy or the ability to find ectopic glands, respectively. During thyroidectomy, 66% of surgeons routinely used near-infrared autofluorescence to rule out inadvertent parathyroidectomy. However, only 36% and 45% felt near-infrared autofluorescence decreased inadvertent parathyroidectomy rates and improved ability to preserve parathyroid glands during central neck dissections, respectively. CONCLUSION: This survey study identified areas of greatest potential use for near-infrared autofluorescence, which can form the basis of future objective trials to document the usefulness of this technology.
PubMed-ID: 36511281
http://dx.doi.org/10.1016/j.surg.2022.07.057

Parathyroid hormone-driven algorithms after thyroid surgery: Not one-size-fits-all.
Head Neck, 45(3):595-603.
S. Samargandy, J. Wadie, H. Msallak, A. Chiodo, W. El Masri, B. Hubbard, D. Enepekides, K. Higgins, A. Assal, R. Fine, R. Fung, E. Nicholas, V. Beadle and A. Eskander. 2023.
BACKGROUND: Underreported variation in parathyroid hormone (PTH) assays exists. Using quality improvement methods, we aimed to develop an institution-specific PTH-based protocol to predict hypocalcemia after thyroidectomy. METHODS: We retrospectively reviewed patients who underwent total/completion thyroidectomy. A receiver operating curve (ROC) determined postoperative PTH cut-offs predictive of hypocalcemia. The stakeholders developed PTH-driven calcium management guidelines. Post-implementation outcomes were prospectively measured. RESULTS: Pre-implementation, 95 patients were assessed. PTH </=1.5 pmol/L (14.1 pg/ml) predicted hypocalcemia (96%sensitivity), and >/=2.8 pmol/L (26.4 pg/ml) predicted normocalcemia (99%specificity) (area under curve = 0.97, SEM = 0.018). PTH on the day of and morning after surgery were identically predictive. Post-implementation, 64 patients were assessed. Hypocalcemia occurred with PTH >2.8 pmol/L in 2 cases (3.1%). Calcium over-prescribing decreased from 13.7% to 3.1% (p = 0.06). Length of stay (LOS) > 2 nights decreased from 13% to 3.1% (p = 0.05). CONCLUSION: A PTH-driven calcium management protocol post-thyroidectomy effectively reduces unnecessary calcium replacement and LOS. Given the variability in PTH assays, each institution may need to use individual cut-offs.
PubMed-ID: 36571430
http://dx.doi.org/10.1002/hed.27272

Long-term predictive value of highly sensitive thyroglobulin measurement.
Clin Endocrinol (Oxf), 98(4):622-8.
L. R. Bogershausen, L. Giovanella, T. Stief, M. Luster and F. A. Verburg. 2023.
OBJECTIVE: To examine the predictive value of unremarkable nonstimulated highly sensitive thyroglobulin (hsTg) measurement with regard to the results of stimulated thyroglobulin (Tg) measurement, diagnostic whole-body scintigraphy, recurrence and differentiated thyroid cancer (DTC)-related death. DESIGN, PATIENTS AND MEASUREMENTS: We retrospectively analysed the data of all 461 (410 without anti-Tg-antibodies [TgAbs], 51 with) DTC patients who were referred to our department for treatment and follow-up care of differentiated thyroid cancer from 2004 onwards, and in whom at least one posttreatment Tg value was measured in our hospital at least 3 months after I-131 ablation. RESULTS: In the group of TgAb-negative patients, 2.0% of patients with an unstimulated Tg < 0.1 ng/ml showed a stimulated Tg >/= 1.0 ng/ml, whereas this happened in 77.6% with an unstimulated Tg >/= 0.1 but <1.0 ng/ml. An unstimulated hsTg >/= 0.1 ng/ml had a sensitivity specificity positive and negative predictive value of 90.0%, 94.1%, 77.6% and 97.6%, respectively, for a stimulated Tg >/= 1.0 ng/ml. In TgAb-positive patients, this was 75%, 97%, 75% and 97%, respectively. An unstimulated Tg >/= 0.1 ng/ml did not significantly discriminate with regard to the risk of DTC-related death (p = .06), but >/=1.0 ng/ml did (p = .012), as did a stimulated Tg >/= 1.0 ng/ml (p = .029). Excluding patients with distant metastases at diagnosis nullifies this significance. CONCLUSION: Except for patients with distant metastases, both TgAb negative and TgAb positive patients with an undetectable nonstimulated hsTg measurement have a very good prognosis. The high net present value of unstimulated hsTg testing means that further diagnostic procedures can be omitted in such patients.
PubMed-ID: 36263618
http://dx.doi.org/10.1111/cen.14837

Just a Little Bit of Anaplastic Thyroid Cancer?
Ann Surg Oncol, 30(1):10-1.
E. Kebebew. 2023.
PubMed-ID: 36271305
http://dx.doi.org/10.1245/s10434-022-12703-w

Current Controversies in Low-Risk Differentiated Thyroid Cancer: Reducing Overtreatment in an Era of Overdiagnosis.
J Clin Endocrinol Metab, 108(2):271-80.
T. M. Ullmann, M. Papaleontiou and J. A. Sosa. 2023.
CONTEXT: Low-risk differentiated thyroid cancer (DTC) is overdiagnosed, but true incidence has increased as well. Owing to its excellent prognosis with low morbidity and mortality, balancing treatment risks with risks of disease progression can be challenging, leading to several areas of controversy. EVIDENCE ACQUISITION: This mini-review is an overview of controversies and difficult decisions around the management of all stages of low-risk DTC, from diagnosis through treatment and follow-up. In particular, overdiagnosis, active surveillance vs surgery, extent of surgery, radioactive iodine

(RAI) treatment, thyrotropin suppression, and postoperative surveillance are discussed. EVIDENCE SYNTHESIS: Recommendations regarding the diagnosis of DTC, the extent of treatment for low-risk DTC patients, and the intensity of posttreatment follow-up have all changed substantially in the past decade. While overdiagnosis remains a problem, there has been a true increase in incidence as well. Treatment options range from active surveillance of small tumors to total thyroidectomy followed by RAI in select cases. Recommendations for long-term surveillance frequency and duration are similarly broad. CONCLUSION: Clinicians and patients must approach each case in a personalized and nuanced fashion to select the appropriate extent of treatment on an individual basis. In areas of evidential equipoise, data regarding patient-centered outcomes may help guide decision-making.
PubMed-ID: 36327392
http://dx.doi.org/10.1210/clinem/dgac646

What are the Parameters as to When to Re-Operate on Patients with Recurrent Well Differentiated Thyroid Cancer?
Laryngoscope, 133(1):4-5.
A. Y. Xiao, J. E. Miller and M. A. St John. 2023.
PubMed-ID: 35567408
http://dx.doi.org/10.1002/lary.30209

Learning curve of transoral robotic thyroidectomy.
Surg Endosc, 37(1):535-43.
K. H. Kim, Y. B. Ji, C. M. Song, E. Kim, K. N. Kim and K. Tae. 2023.
BACKGROUND: Transoral thyroidectomy has superior cosmesis and better postoperative voice outcomes than conventional thyroidectomy. However, it usually requires a steep learning curve and longer operative time. The transoral robotic thyroidectomy (TORT) learning curve has not been well investigated. This study aimed to evaluate the TORT learning curve and factors affecting operative time. METHODS: We retrospectively studied 173 consecutive patients who underwent TORT with or without central neck dissection from July 2017 to August 2021. We assessed the TORT learning curve using operative time, complication rate, and surgical success (procedure conversion) rate. The operative time and surgical success rate learning curves were calculated using the cumulative summation (CUSUM) method. Additionally, we analyzed factors affecting operative time in TORT. RESULTS: Total thyroidectomy operative time was significantly longer than those of lobectomy and isthmusectomy ($p < 0.001$). In correlation analysis, a significantly positive correlation was observed between body mass index (BMI) and operative time ($R(2) = 0.04$, $p = 0.025$). The TORT learning curve was 52 cases in the CUSUM operative time analysis. In the CUSUM surgical success rate chart, the turning point was the 55th case. Complication and procedure conversion rates were significantly decreased after the learning curve. CONCLUSIONS: The CUSUM learning curve of TORT was about 52-55 cases, and the operative time, total complication rate, and procedure conversion decreased significantly after the learning curve. The operative time was associated with the extent of thyroidectomy and BMI.
PubMed-ID: 36002679
http://dx.doi.org/10.1007/s00464-022-09549-4

Ultrasound Follow-Up of Benign Thyroid Nodules: A Scoping Review.
Thyroid, 33(4):420-7.
R. Chou, T. Dana, S. E. Mayson, E. S. Cibas, C. Durante, C. C. Solorzano, S. J. Mandel and L. A. Orloff. 2023.
Background: For cytologically benign thyroid nodules with very low to intermediate suspicion ultrasound patterns, optimal ultrasound follow-up intervals and outcomes of discontinuing follow-up are unclear. Methods: Ovid MEDLINE, Embase, and Cochrane Central were searched through August 2022 for studies comparing different ultrasound follow-up intervals and discontinuation versus continuation of ultrasound follow-up. The population was patients with cytologically benign thyroid nodules and very low to intermediate suspicion ultrasound patterns, and the primary outcome was missed thyroid cancers. Utilizing a scoping approach, we also included studies that were not restricted to very low to intermediate suspicion ultrasound patterns or evaluated additional outcomes such as thyroid cancer-related mortality rate, nodule growth, and subsequent procedures. Quality assessment was performed, and evidence was synthesized qualitatively. Results: One retrospective cohort study (n = 1254; 1819 nodules) compared different first follow-up ultrasound intervals for cytologically benign thyroid nodules. There was no difference between >4- versus 1- to 2-year intervals to first follow-up ultrasound in the likelihood of malignancy (0.4% [1/223] vs. 0.3% [2/715]), and no cancer-related deaths occurred. Follow-up ultrasound at >4 years was associated with increased likelihood of >/=50% nodule growth (35.0% [78/223] vs. 15.1% [108/715]), repeat fine needle aspiration (19.3% [43/223] vs. 5.6% [40/715]), and thyroidectomy (4.0% [9/223] vs. 0.8% [6/715]). The study did not describe ultrasound patterns or control for confounders, and analyses were based on

interval to first follow-up ultrasound only. Other methodological limitations were not controlling for variability in follow-up duration and unclear attrition. The certainty of evidence was very low. No study compared discontinuation of ultrasound follow-up versus continuation. Conclusions: This scoping review found that evidence comparing different ultrasound follow-up intervals in patients with benign thyroid nodules is limited to one observational study, but suggests that the subsequent development of thyroid malignancies is very uncommon regardless of follow-up interval. Longer follow-up may be associated with more repeat biopsies and thyroidectomies, which could be related to more interval nodule growth that meets thresholds for further evaluation. Research is needed to clarify optimal ultrasound follow-up intervals for low to intermediate suspicion cytologically benign thyroid nodules and outcomes of discontinuing ultrasound follow-up for very low suspicion nodules.
PubMed-ID: 36800900
http://dx.doi.org/10.1089/thy.2022.0692

Cost comparison between open thyroid lobectomy and radiofrequency ablation for management of thyroid nodules.
Head Neck, 45(1):59-63.
J. R. Miller, V. Tanavde, C. Razavi, A. Saraswathula, J. O. Russell and R. P. Tufano. 2023.
BACKGROUND: There is an increasing array of treatment options for addressing clinically significant thyroid nodules, including radiofrequency ablation (RFA). While effective, the cost compared to alternative approaches has not been well elucidated. METHODS: This study involved a retrospective chart review, focusing on variable direct cost (VDC) of each procedure, from April 2016 to January 2020. We analyzed costs for 53 open lobectomies and 16 RFA procedures. RESULTS: Cost effectiveness depended on the simulated cost of the RFA probe. In comparison to open lobectomy, the VDC to perform RFA was $597 (19%) cheaper when the simulated probe cost was $1500 and $403 (13%) more expensive for a probe cost of $2500. Statistical significance was achieved for both these differences. CONCLUSIONS: If cost per RFA probe can be less than $2100-the break-even dollar amount between open lobectomy and RFA-there would be considerable cost savings for treating thyroid nodules.
PubMed-ID: 36200695
http://dx.doi.org/10.1002/hed.27213

Is There Any Reliable Predictor of Functional Recovery Following Post-thyroidectomy Vocal Fold Paralysis?
World J Surg, 47(2):429-36.
L. Revelli, P. Gallucci, M. R. Marchese, N. Voloudakis, S. Di Lorenzo, C. Montuori, L. D'Alatri, F. Pennestri, C. De Crea and M. Raffaelli. 2023.
BACKGROUND: Predicting definitive outcomes of post-thyroidectomy vocal fold paralysis (VFP) is challenging. We aimed to identify reliable predictors based on intraoperative neuromonitoring (IONM) and flexible fiberoptic laryngostroboscopy (FFL) findings. METHODS: Among 1172 thyroid operations performed from April to December 2021, all patients who exhibited vocal fold paralysis (VFP) at post-operative laryngoscopy were included. IONM data, including type of loss of signal (LOS), were collected. Patients underwent FFL, with arytenoid motility assessment, at 15, 45 and 120 days post-operatively. Patients were divided into two groups: those who recovered vocal fold motility (VFM) by the 120th post-operative day (recovery group) and those who did not (non-recovery group). RESULTS: Fifty-nine VFP cases (5.0% of total patients) met the inclusion criteria. Eight patients were lost at follow-up and were excluded. Overall, 9 patients were included in the non-recovery group (0.8% of total patients) and 42 in the recovery group. Among various predictive factors, only arytenoid fixation (AF) at the 15th post-operative day and Type I LOS were significant predictors for no VFM recovery ($p = 0.007$, RR = 9.739, CI:1.3-72.3 and $p = 0.001$, RR = 9.25, CI:2.2-39.3 for AF and Type I injury, respectively). The combination of type of LOS and arytenoid motility at the 15th post-op day yielded satisfactory predictive values for the progression of transient VFP to permanent. CONCLUSIONS: Arytenoid motility at the 15th post-op day and type II LOS are associated with recovery of VFM. Type of LOS and FFL could be included in the follow-up protocols of patients with VFP to reliably predict clinical outcomes.
PubMed-ID: 36222871
http://dx.doi.org/10.1007/s00268-022-06765-w

Longitudinal experience of patients with post-thyroidectomy vocal cord paralysis.
Am J Surg, 225(4):685-9.
A. Chiu, C. Damico, K. Bach, N. Arroyo, R. Sippel and D. O. Francis. 2023.
BACKGROUND: Prior studies of post-thyroidectomy vocal cord paralysis (VCP) present static and limited evaluations. We comprehensively assessed the experience of patients with VCP post-thyroidectomy over 1 year. METHODS: Voice Handicap Index (VHI), Eating Assessment Tool (EAT-10), 12-Item Short Form Survey (SF-12), and qualitative interviews

were assessed preoperatively, and 2-weeks, 6-weeks, 6-months, and 1-year postoperatively. OUTCOMES: 7 of 44 patients (15.9%) had postoperative VCP. Compared to those without complication, mean VHI scores for VCP patients increased significantly from baseline at 2-weeks (27.9 point increase vs 1.6, $p < 0.01$) and 6-weeks (26.3 vs. -0.3, $p < 0.01$) postoperative. There were no significant differences between groups in SF-12 or EAT-10 scores at any point. Qualitative interviews showed that both groups noted bothersome voice symptoms at 2-weeks; however, by 6-weeks, only VCP patients noted voice symptoms negatively affecting their life. CONCLUSION: While both patients with and without VCP reported subjective voice symptoms immediately postoperatively, those with VCP had worse quantitative measures. Understanding the longitudinal experience of VCP can help providers tailor counseling for these patients.
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http://dx.doi.org/10.1016/j.amjsurg.2022.10.005

Extent of Surgery for Follicular Thyroid Carcinoma.
Laryngoscope, 133(4):993-9.
N. Kethidi, S. Vedula, D. Shihora, R. Patel and R. C. W. Park. 2023.
OBJECTIVES: To examine the association between the extent of surgery and overall survival in follicular thyroid cancer (FTC) patients. STUDY DESIGN: Retrospective analysis of the National Cancer Database (NCDB). METHODS: Patients who underwent surgical intervention for FTC from 2004 to 2015 were selected. Patients were >18 years old, with tumor size 1-4 cm, no other malignancies, and >0 follow up time. Patients were divided into two cohorts based on extent of surgery: lobectomy (>/=1 lobe resected) and thyroidectomy (total or near total resection). Pearson's chi-squared analysis was used to compare cohorts. Kaplan-Meier survival and Cox hazards models were utilized to determine overall survival between two cohorts with $p < 0.05$ used for significance. RESULTS: A total of 6871 patients were identified with FTC, of which 1507 patients underwent lobectomy and 5364 patients underwent total thyroidectomy. There were no significant differences in patient demographics, comorbidity index, local spread, or tumor grade. Patients undergoing lobectomy had mean survival of 12.94 versus 12.71 years for those undergoing thyroidectomy. Extent of surgery was not associated with a significant difference in survival (5 years OS = 96% in lobectomy and 95.5% in total thyroidectomy, $p = 0.08$). Stratification by tumor grade resulted in no significant difference in survival between lobectomy and thyroidectomy. CONCLUSION: Survival time was not significantly different in patients with more extensive resection of FTC. LEVEL OF EVIDENCE: 3 Laryngoscope, 133:993-999, 2023.
PubMed-ID: 36317788
http://dx.doi.org/10.1002/lary.30441

Thyroid-Stimulating Hormone, Age, and Tumor Size are Risk Factors for Progression During Active Surveillance of Low-Risk Papillary Thyroid Microcarcinoma in Adults.
World J Surg, 47(2):392-401.
Y. Ito, A. Miyauchi, M. Fujishima, T. Noda, T. Sano, T. Sasaki, T. Kishi and T. Nakamura. 2023.
BACKGROUND: Active surveillance (AS) of low-risk papillary thyroid microcarcinoma (PTMC) was initiated at Kuma Hospital in 1993 and is gradually spreading worldwide. We assessed the effect of thyroid-stimulating hormone (TSH) levels on PTMC enlargement in patients on AS. METHODS: We enrolled 2705 patients with cytologically diagnosed PTMC who had undergone AS between January 2005 and July 2019. Patients with Graves disease were excluded. The median AS period was 5.5 years (range 1.0-15.7 years). Tumor enlargement was defined as a size increase >/=3 mm. Chi-square test, Kaplan-Meier method, log-rank test, Cox proportional hazard, and logistic regression were used to compare variables. RESULTS: Ninety-two patients (3.4%) experienced tumor enlargement; the 5-, 10-, and 15-year enlargement rates were 3.0%, 5.5%, and 6.2%, respectively. Young age (<40 years, $p < 0.001$), large tumor size (>/=9 mm, $p = 0.017$), and high detailed TSH score (>/=3, higher than the lower normal limit, $p = 0.011$) were significant factors relating to tumor enlargement in the multivariate analysis. In a subset of patients aged <40 years, a low detailed TSH score (<3) was an independent factor against tumor enlargement ($p = 0.039$). Only 22 patients (0.8%) experienced novel lymph node metastasis; the 5-, 10-, and 15-year node metastasis rates were very low, at 0.9%, 1.1%, and 1.1%, respectively. CONCLUSIONS: Young patients with PTMC are more likely to experience tumor growth. Mild TSH suppression to achieve a low normal range may prevent carcinoma enlargement; however, prospective studies are needed to draw more reliable conclusions.
PubMed-ID: 36182976
http://dx.doi.org/10.1007/s00268-022-06770-z

The Prognostic Impact of Extent of Vascular Invasion in Follicular Thyroid Carcinoma.
World J Surg, 47(2):412-20.
D. Leong, A. J. Gill, J. Turchini, M. Waller, R. Clifton-Bligh, A. Glover, M. Sywak and S. Sidhu. 2023.

BACKGROUND: Encapsulated angioinvasive follicular thyroid carcinoma (EAFTC) is associated with an increased risk of distant metastasis and reduced survival compared to minimally invasive follicular thyroid carcinoma (MIFTC). There is controversy regarding the extent of surgery and adjuvant radioactive iodine therapy for angioinvasive follicular thyroid carcinoma when stratified by number of foci of angioinvasion. METHODS: All follicular thyroid carcinoma cases from 1990-2018 were identified from a thyroid cancer database. Primary outcomes were distant metastasis-free survival (DMFS) and disease-specific survival (DSS) with factors of interest being age, gender, tumour size, treatment, foci of angioinvasion and histological subtype. RESULTS: A total of 292 cases were identified; 139 MIFTC, 141 EAFTC and 12 widely invasive follicular thyroid carcinoma (WIFTC). Over a follow-up period of 6.25 years, DMFS was significantly reduced ($p < 0.001$) with 14.2% (EAFTC) and 50% of WIFTC developing metastasis. The risk of metastasis in EAFTC with >/= 4 foci of angioinvasion was 31.7% (HR = 5.89, p = 0.004), 6.3% for EAFTC with < 4 foci of angioinvasion (HR = 1.74, p = 0.47), compared to 3.6% MIFTC. Age >/= 50 years (HR = 4.24, p = 0.005) and tumour size (HR = 1.27, p = 0.014) were significantly associated with increased risk of distant metastasis. DSS was reduced significantly ($p < 0.001$), with 7.8% EAFTC patients dying of disease. For EAFTC patients, DSS was 96.8% for < 4 foci and 82.6% for >/= 4 foci of angioinvasion (p = 0.003). CONCLUSION: EAFTC is at increased risk of distant metastasis related to the extent of angioinvasion. Tumours with < 4 foci of angioinvasion should be considered for a total thyroidectomy, particularly in older patients.
PubMed-ID: 36031639
http://dx.doi.org/10.1007/s00268-022-06696-6

Impact of Age on Prognosis in Papillary Thyroid Carcinoma: How Should Age be Incorporated into the Treatment Strategy?
World J Surg, 47(3):674-81.
K. Sugino, K. Matsuzu, M. Nagahama, W. Kitagawa, A. Suzuki, C. Tomoda, K. Y. Hames, J. Akaishi, C. Masaki, K. Yoshioka, Y. Saito and K. Ito. 2023.
BACKGROUND: Age has been recognized as one of the strong prognostic indicators for thyroid cancer. However, treatment strategies for papillary thyroid cancer (PTC) are usually determined only by the extent of disease progression, without considering the patient's age. The aim of this study was to investigate how the surgical strategy for PTC should take into account patient age. METHODS: To exclude the effect of treatment strategy, 837 patients treated with uniform treatment strategies (hemithyroidectomy without radioiodine therapy) between 1986 and 1995 were the subjects of this study. Using a Cox proportional hazard model, clinical risk factors related to disease-specific survival (DSS), disease-free survival (DFS), and distant metastasis-free survival (DMFS) were analyzed. A receiver-operating characteristic (ROC) curve analysis was performed to identify the optimal cutoff points. RESULTS: Significant risk factors related to DSS and DMFS were age, extrathyroidal extension (ETE), and numbers of metastatic lymph nodes (NMLNs), but age was not significantly related to DFS. The 20-year DSS and DMFS rates were fair in patients without ETE regardless of age or NMLNs. However, in patients with ETE, DSS and DMFS rates were significantly worse in elderly patients than in young patients. ROC curve analysis showed that the optimal cutoff age was 48 years for discriminating DSS in patients with ETE. CONCLUSION: Regardless of age, PTC patients without ETE are candidates for a treatment strategy not using RAI, and more aggressive treatment may be recommended for elderly PTC patients with ETE.
PubMed-ID: 36445452
http://dx.doi.org/10.1007/s00268-022-06843-z

Anaplastic Transformation of Differentiated Thyroid Carcinoma.
Laryngoscope, 133(2):437-42.
A. C. Yu, A. Y. Han, D. A. Cronkite, D. Sajed and M. A. St John. 2023.
OBJECTIVES: Anaplastic thyroid carcinoma (ATC) is a rare but highly aggressive form of thyroid cancer. Increasingly, patients with ATC present with concurrent foci of well-differentiated thyroid carcinoma (WDTC); however, the significance of these pathologic findings remains unclear. The objective of this study is to determine whether the presence of WDTC within anaplastic tumors is a prognosticator of survival. METHODS: A retrospective cohort study of all cases of biopsy-proven ATC managed at a tertiary care academic medical center from 2002 to 2020 was performed. Mean age at diagnosis, median survival time, and locations of distant metastases were assessed. The impact of clinical markers such as presence of differentiation, demographic variables, and oncologic information on overall survival was also determined via univariate and multivariate analysis. RESULTS: Forty-five patients were included in this study. The mean age at diagnosis was 69.1 years. Median survival time was 6.1 months after diagnosis. The most common location of distant metastases was the lung (40%). The presence of limited areas of WDTC in patients with predominantly anaplastic thyroid tumors was not significantly associated with improved outcomes (p = 0.509). Smaller tumor size and use of chemotherapy in ATC patients were significantly associated with prolonged survival (p = 0.026 and 0.010, respectively). CONCLUSIONS: Clinical

outcomes for ATC remain poor. The presence of foci of differentiation within anaplastic thyroid tumors does not appear to improve overall survival-the anaplastic component evidently drives outcomes. Further studies into novel therapies are needed to improve survival in ATC. LEVEL OF EVIDENCE: 4 Laryngoscope, 133:437-442, 2023.
PubMed-ID: 35779253
http://dx.doi.org/10.1002/lary.30277

Usefulness of ICG Angiography-Guided Thyroidectomy for Preserving Parathyroid Function.
World J Surg, 47(2):421-8.
P. Moreno-Llorente, A. Garcia-Barrasa, M. Pascua-Sole, S. Videla, A. Otero and J. L. Munoz-de Nova. 2023.
INTRODUCTION: Hypoparathyroidism is the most frequent complication after total thyroidectomy and, when permanent, it becomes a severe chronic disease. We assessed the usefulness of indocyanine green (ICG) angiography-guided thyroidectomy to reduce the postoperative hypocalcemia. METHODS: Prospective study with two consecutive cohorts of patients who underwent total thyroidectomy: historical control group (CG) and angiography-guided thyroidectomy group (AG). In all patients, ICG-angiography was performed at the end of the surgery to predict immediate parathyroid gland (PG) function. In the AG, ICG-angiography was also done after PG identification to show their vascular supply. We compared the rate of postoperative hypocalcemia (calcium supplementation needed due to hypocalcemia symptoms or calcium levels < 1.8 mmol/L on the first postoperative day) and permanent hypocalcemia (need of calcium +/- vitamin D supplementation 12 months after thyroidectomy). RESULTS: We included 120 consecutive patients (84 CG; 36 AG). Thyroid cancer was the most common diagnostic (63.1% CG-69.4% AG; p = 0.646) and central neck dissection was also frequent (54.8% CG-64.3% AG; p = 0.468). The AG developed a lower rate of postoperative (26.2-5.6%; p = 0.011) and permanent hypocalcemia (11.9-0%; p = 0.032). The OR for permanent hypocalcemia was 0.673 (95% CI 0.591-0.766). A significant higher rate of well vascularized PG at the end of the surgery (score 2) in the AG (39.2-52.9%; p = 0.018) was also seen. CONCLUSION: ICG angiography-guided thyroidectomy is a useful tool to identify PG vascularization, allowing a better PG preservation and a significant decrease in hypocalcemia rates.
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http://dx.doi.org/10.1007/s00268-022-06683-x

Varying impact of patient age on the rising rate of pediatric thyroid cancer: Analysis of NCDB database (2004-2017).
Am J Surg, 225(3):532-6.
H. H. Zhao, C. Pickney, A. L. Sarode, A. Kim-Mackow and S. M. Wilhelm. 2023.
Pediatric thyroid carcinoma is on the rise. We sought to better characterize patient factors associated with this and evaluate for trends based on age groups. Additionally, we examined surgical management over time, and whether it aligns with recommendations made by the American Thyroid Association. Using the National Cancer Database (NCDB), we examined cases of thyroid cancer from 2004 to 2017, ages 1-18 years. We subdivided this cohort by age group: those <10y, 10-15y, and >15y. NCDB query yielded 5,814 cases. The annual proportion of total cases ranged from 3% to 8% for <10y, 31%-40% for 10-15y, and 52%-66% for >15y. 80-90% of cases in all age groups did indeed receive total thyroidectomy which is consistent with ATA guidelines. Our results verify an overall increase in pediatric thyroid cancer cases, occurring mostly in the 10-18 years old age range with the largest year-to-year increases in the >15y group.
PubMed-ID: 36473736
http://dx.doi.org/10.1016/j.amjsurg.2022.11.030

Incidence of Vocal Cord Paralysis in Medullary Thyroid Cancer.
Laryngoscope, 133(4):890-4.
V. Drozdowski, D. Martini and S. Charous. 2023.
OBJECTIVE: Medullary thyroid cancer (MTC) is a neuroendocrine tumor that comprises 3-5% of all thyroid cancers in the United States. Vocal cord paralysis (VCP) may be due to involvement of the recurrent laryngeal nerve (RLN) preoperatively, or nerve sacrifice during surgery. The purpose of this study was to demonstrate the incidence of VCP in MTC and evaluate whether VCP has an impact on overall survival. METHODS: This was a retrospective chart review of patients with MTC treated at Loyola University Medical Center from 2007 to 2021. Information on demographics, cancer diagnosis and treatment, laboratory data, and survival were collected. RESULTS: A total of 79 patients were included in our study. 47 (59.5%) patients were female. The average age at the time of diagnosis was 51.3 years (SD 13.58). VCP was identified in 13 out of 79 (16.5%) patients. There were 71 patients with at least 1-year follow-up with median (Q1, Q3) years of 7.2 (3.9, 11.0). Those with VCP within 1 year had 7.2 (95% CI: 2.3, 22.7) times the risk of death compared to those without (p < 0.001). CONCLUSION: MTC is a rare thyroid cancer, however, its incidence is on the rise. Our study suggests that the incidence of VCP in these patients appears to be higher than seen in other thyroid malignancies, and VCP is

associated with a statistically significant negative impact on survival. LEVEL OF EVIDENCE: 3 Laryngoscope, 133:890-894, 2023.
PubMed-ID: 35833484
http://dx.doi.org/10.1002/lary.30297

Long-Term Outcomes After Lobectomy for Patients with High-Risk Papillary Thyroid Carcinoma.
World J Surg, 47(2):382-91.
I. Sugitani, H. Kazusaka, A. Ebina, W. Shimbashi, K. Toda and K. Takeuchi. 2023.
BACKGROUND: Guidelines universally recommend total thyroidectomy for high-risk papillary thyroid carcinoma (PTC). However, in Japan, thyroid-conserving surgery had been widely applied for such patients until recently. We investigated long-term outcomes for this strategy. METHODS: A prospectively recorded database was retrospectively analyzed for 368 patients who had undergone curative surgery for high-risk PTC without distant metastasis between 1993 and 2013. High-risk PTC was defined for tumors showing tumor size > 4 cm, extrathyroidal extension, or large nodal metastasis >/= 3 cm. RESULTS: Median age was 59 years and 243 patients were female. Mean duration of follow-up was 12.7 years. Lobectomy was conducted for 207 patients (LT group) and total or near-total thyroidectomy for 161 patients (TT group). The frequency of massive extrathyroidal invasion and large nodal metastasis was lower in the LT group than in the TT group. After propensity score matching, no significant differences were seen between groups for overall survival, cause-specific survival or distant recurrence-free survival. In the overall cohort, multivariate analysis identified age >/= 55 years, large nodal metastasis, tumor size > 4 cm and massive extrathyroidal invasion as significantly associated with cause-specific survival, whereas extent of thyroidectomy was not. CONCLUSIONS: For patients with high-risk PTC without distant metastasis, curative surgery with lobectomy showed almost identical oncological outcomes compared to total thyroidectomy. The benefits of total thyroidectomy for high-risk PTC should be reevaluated in the future prospective studies.
PubMed-ID: 35972533
http://dx.doi.org/10.1007/s00268-022-06705-8

Risk staging with prophylactic unilateral central neck dissection in low-risk papillary thyroid carcinoma.
Eur J Surg Oncol, 49(3):568-74.
D. M. Hartl, A. Al Ghuzlan, S. Bidault, I. Breuskin, J. Guerlain, E. Girard, E. Baudin, L. Lamartina and J. Hadoux. 2023.
OBJECTIVE: Current guidelines favor thyroid lobectomy for intrathyroidal cT1bT2cN0 papillary thyroid carcinoma. Prophylactic neck dissection (PND) is not recommended for these low-risk tumors due to the lack of high-level evidence on improvement in outcomes, but the information from PND may be used for staging. The aim of this study was to evaluate the rate of upstaging with ipsilateral PND. MATERIALS AND METHODS: Retrospective study of patients with intrathyroidal unifocal cT1bT2cN0 papillary thyroid carcinoma from 2008 to 2021. All patients underwent total thyroidectomy and PND. Tumors were classified as low or intermediate risk based on the information from pathological analysis of the primary tumor and then from adding the analysis of the lymph nodes. The difference between the tumor-only and the PND-added risk staging was evaluated. RESULTS: Three hundred three patients (241 women, median age 45, median tumor size 17 mm) were included. Microscopic extrathyroidal extension was found in 23.4%, aggressive histology in 6.6%, vascular invasion in 29.3%, and lymph node metastases in 37.3%. One hundred ten patients (36.3%) were intermediate-risk based on the primary tumor. An additional 26 (8.6%) were upstaged to intermediate-risk based on the ipsilateral PND and 2% based on the contralateral PND. Kaplan-Meier 10-year event-free survival in tumors upstaged with ipsilateral PND was not statistically different from intermediate-risk tumors based on the primary tumor characteristics (92% versus 90.9%, Log Rank p = 0.943). CONCLUSIONS: Ipsilateral PND upstaged low-risk cT1bT2cN0 patients to intermediate risk in only 8.6% of cases, and contralateral PND in an additional 2%. Routinely performing PND may not be warranted.
PubMed-ID: 36411174
http://dx.doi.org/10.1016/j.ejso.2022.11.007

Prognostic Utility of Tumor Stage versus American Thyroid Association Risk Class in Thyroid Cancer.
Laryngoscope, 133(1):205-11.
A. Abiri, J. Pang, K. R. Prasad, K. Goshtasbi, E. C. Kuan, W. B. Armstrong, Y. M. Haidar and T. Tjoa. 2023.
OBJECTIVE: To evaluate the prognostic strengths of American Joint Committee on Cancer (AJCC) staging and American Thyroid Association (ATA) risk classification in well-differentiated thyroid cancer (DTC), and their implications in guiding medical decision-making and epidemiological study designs. METHODS: The 2004-2017 National Cancer Database was queried for DTC patients. Cox proportional hazards (CPH) and Kaplan-Meier analyses modeled patient mortality and overall survival, respectively. Each CPH model was evaluated by its concordance index, measure of explained randomness

(MER), Akaike information criterion (AIC), and area under receiver operating characteristic curve (AUC). RESULTS: Overall, 134,226 patients were analyzed, with an average age of 48.1 +/- 15.1 years (76.9% female). Univariate CPH models using AJCC staging demonstrated higher concordance indices, MERs, and AUCs than those using ATA risk classification (all p < 0.001). Multivariable CPH models using AJCC staging demonstrated higher concordance indices (p = 0.049), MERs (p = 0.046), and AUCs (p = 0.002) than those using ATA risk classification. The AICs of multivariable AJCC staging and ATA risk models were 7.564 x 10(4) and 7.603 x 10(4) , respectively. AJCC stage I tumors were associated with greater overall survival than those classified as ATA low risk, whereas AJCC stages II-III and stage IV tumors demonstrated worse survival than ATA intermediate- and high-risk tumors, respectively (all p < 0.001). CONCLUSION: AJCC staging may be a more predictive system for patient survival than ATA risk. The prognostic utility of these two systems converges when additional demographic and clinical factors are considered. AJCC staging was found to classify patients across a wider range of survival patterns than the ATA risk stratification system. LEVEL OF EVIDENCE: 4 Laryngoscope, 133:205-211, 2023.
PubMed-ID: 35716358
http://dx.doi.org/10.1002/lary.30252

A retrospective study of papillary thyroid carcinoma: Hashimoto's thyroiditis as a protective biomarker for lymph node metastasis.
Eur J Surg Oncol, 49(3):560-7.
Y. Wang, J. Zheng, X. Hu, Q. Chang, Y. Qiao, X. Yao and X. Zhou. 2023.
PURPOSE: There is approximately 10%-50% of papillary thyroid carcinoma (PTC) patients with Hashimoto's thyroiditis (HT). In this research, we sought to better understand the role of HT in PTC progression as well as lymph node metastasis. METHODS: It is a retrospective and cross-sectional study, and 4131 PTC patients who underwent thyroidectomy were finally enrolled. Chi-square test, univariate and multivariate logistic regression analyses were employed to evaluate both the risk factors and the critical roles of HT during PTC metastasis. RESULT: In this cohort, 1555 patients (37.6%) were diagnosed with HT. According to multivariate analysis, male sex, high levels of TG and TPOAb, tumor extrathyroidal extension, maximum diameter >1 cm, and multifocality were independent risk factors for both central lymph node metastasis (CLNM) and lateral lymph node metastasis (LLNM). In addition, age <55 years and smoking were risk factors for CLNM, while CLNM was one of the risk factors for LLNM. Furthermore, HT was suggested a valuable protective factor for both CLNM and LLNM. In patients with HT, the total number of central lymph nodes was higher, while the positive rate was lower. Compared with those without HT, age and sex did not predict CLNM and LLNM in patients with HT. CONCLUSION: HT is considered a protective factor for both CLNM and LLNM in PTC. For patients with HT, surgeons should pay more attention to the preservation of parathyroid gland and the protection of recurrent laryngeal nerve due to less lymph node metastasis. Otherwise, radical operation is highly recommended.
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http://dx.doi.org/10.1016/j.ejso.2022.11.014

Ferroptosis Inducers in Thyroid Cancer.
World J Surg, 47(2):371-81.
K. R. Sekhar, S. Cyr and N. Baregamian. 2023.
PURPOSE: Papillary thyroid carcinoma (PTC) progression imparts reduced patient survival. Tumor resistance and progression can be influenced by Glutathione (GSH) metabolism. Glutathione peroxidase 4 (GPX4) regulates GSH oxidation to prevent lipid peroxidation of cell membranes during increased oxidative stress and regulates ferroptosis cell death pathway in tumor cells. This study examines the differential ferroptosis effects by GPX4 inhibitors in thyroid cancer cell and 3-D spheroid in vitro models. MATERIALS AND METHODS: We examined differential effects of GPX4 inhibitors on PTC cells (K1, MDA-T32, MDA-T68) with BRAF and RAS mutations, and TERT promoter and PIK3CA co-mutations. The effects of GPX4 inhibitors on ferroptosis activation, proliferation, oxidative stress, and activation of signaling pathways were assessed by Western blot, total (GSH) and oxidized glutathione (GSSG) levels, ROS induction, RT-qPCR, migration, and proliferation assays. RESULTS: GPX4 inhibitors induced ferroptosis, rising ROS, GSH depletion, arrested tumor cell migration, increased DNA damage, suppressed mTOR pathway and DNA repair response in PTC cells in vitro. Differential responses to DNA damage and GPX4 levels were observed between 3-D PTC spheroids and thyroid cancer cells in a monolayer model. CONCLUSION: Effective GPX4 inhibition with various inhibitors induced a robust but differential activation of ferroptosis in monolayer thyroid tumor cell and 3-D PTC spheroid models. Our study is the first of its kind to determine the differential effects of GPX4 inhibitors on thyroid cancer cells with diverse mutational signatures. We have identified a novel mechanism of action of GPX4 inhibition in preclinical in vitro models of thyroid cancer that can be further exploited for therapeutic benefit in advanced therapy-resistant thyroid cancers.

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http://dx.doi.org/10.1007/s00268-022-06738-z

Delays in Surgery for Differentiated Thyroid Carcinomas: How Long Is Reasonable, and What Questions Remain?
J Clin Endocrinol Metab, 108(2):e23-e4.
J. M. Broekhuis and B. C. James. 2023.
PubMed-ID: 36317658
http://dx.doi.org/10.1210/clinem/dgac641

Surgical management of T1/T2 node-negative papillary thyroid cancer with tall cell histology: Is lobectomy enough?
Surgery, 173(1):246-51.
R. S. R. Woods, C. W. R. Fitzgerald, C. Valero, J. Lopez, L. G. T. Morris, M. A. Cohen, R. J. Wong, S. G. Patel, R. A. Ghossein, R. M. Tuttle, A. R. Shaha, J. P. Shah and I. Ganly. 2023.
BACKGROUND: The tall cell variant of papillary thyroid carcinoma has traditionally been treated more aggressively than classic papillary thyroid carcinoma. However, this may not be justified in patients with T1/T2 tall cell variant node-negative tumors. METHODS: We evaluated well-differentiated thyroid cancers treated surgically between 1985 and 2015 at our institution. We compared patients undergoing lobectomy for node-negative T1/T2 tall cell variant tumors with the same cohort with classic papillary thyroid carcinoma. Patients who underwent early planned completion thyroidectomy were excluded. Tall cell variant tumors were defined as those with >/=30% tall cells. Survival and recurrence outcomes were determined by the Kaplan-Meier method and groups compared using the log-rank test. RESULTS: Thyroid lobectomy was performed for T1/T2 N0X disease in 70 (15%) tall cell cases and 429 (23%) classic papillary thyroid carcinoma cases. There was no significant difference in 10-year overall survival (P = .56) or locoregional recurrence-free probability (P = .52). Disease-specific survival and local or central nodal recurrence-free probability were 100% in both groups. In 9 papillary thyroid carcinoma cases, subsequent contralateral lobe tumors developed, and in 5, lateral neck metastases developed. No recurrences were seen in the tall cell group. CONCLUSION: T1 node-negative tumors with tall cell histology can be satisfactorily managed with thyroid lobectomy, with equivalent oncological outcomes to classic papillary thyroid carcinoma.
PubMed-ID: 36257862
http://dx.doi.org/10.1016/j.surg.2022.05.045

Is Lobectomy as Effective as Total Thyroidectomy in Treating Patients With Intermediate-Risk Papillary Thyroid Carcinoma With Lateral Lymph Node Metastasis?
JAMA Surg, 158(1):80.
M. B. Mulder and Q. Y. Duh. 2023.
PubMed-ID: 36449317
http://dx.doi.org/10.1001/jamasurg.2022.5790

Robotic versus endoscopic transoral thyroidectomy in papillary thyroid cancer: A comparative analysis of surgical outcomes in 240 consecutive patients.
Head Neck, 45(4):827-37.
J. H. Lee, H. J. Choi, J. W. Woo and E. J. Jung. 2023.
BACKGROUND: This study compared the surgical outcomes of transoral endoscopic thyroidectomy vestibular approach (TOETVA) and transoral robotic thyroidectomy (TORT) in papillary thyroid cancer (PTC). METHODS: The TOETVA and TORT groups comprised 119 and 121 patients between November 2016 and May 2022. Clinico-surgical outcomes and operation times were retrospectively reviewed. RESULTS: The TORT group showed a higher number of retrieved central compartment lymph nodes, shorter hospital stays, and lower pain score after 48 h than the TOETVA group. No significant difference was observed in the other postoperative complications, including permanent vocal cord palsy. Total operation, working space creation, and endoscopic or robotic surgery times of the TORT group were longer than those of the TOETVA group. CONCLUSIONS: TORT and TOETVA are feasible and safe. TORT may have some advantages, such as central compartment node dissection, shorter hospital stays, and pain score after 48 h in PTC, despite a longer operative time.
PubMed-ID: 36606489
http://dx.doi.org/10.1002/hed.27295

Surgeon Thyroidectomy Case Volume Impacts Disease-free Survival in the Management of Thyroid Cancer.
Laryngoscope, 133 Suppl 4(S4):S1-S15.
A. Eskander, C. W. Noel, R. Griffiths, J. D. Pasternak, K. Higgins, D. Urbach, D. P. Goldstein, J. C. Irish and R. Fu. 2023.
OBJECTIVES: To assess the association between surgeons thyroidectomy case volume and disease-free survival (DFS) for patients with well-differentiated thyroid cancer (WDTC). A secondary objective was to assess a surgeon volume cutoff to optimize outcomes in those with WDTC. We hypothesized that surgeon volume will be an important predictor of DFS in patients with WDTC after adjusting for hospital volume and sociodemographic and clinical factors. METHODS: In this retrospective population-based cohort study, we identified WDTC patients in Ontario, Canada, who underwent thyroidectomy confirmed by both hospital-level and surgeon-level administrative data between 1993 and 2017 (N = 37,233). Surgeon and hospital volumes were calculated based on number of cases performed in the year prior by the physician and at an institution performing each case, respectively and divided into quartiles. A multilevel hierarchical Cox regression model was used to estimate the effect of volume on DFS. RESULTS: A crude model without patient or treatment characteristics demonstrated that both higher surgeon volume quartiles ($p < 0.001$) and higher hospital volume quartiles ($p < 0.001$) were associated with DFS. After controlling for clustering and patient/treatment covariates and hospital volume, moderately low (18-39/year) and low (0-17/year) volume surgeons (hazard ratios [HR]: 1.23, 95% confidence interval [CI]: 1.09-1.39 and HR: 1.34, 95% CI: 1.17-1.53 respectively) remained an independent statistically significant negative predictor of DFS. CONCLUSION: Both high-volume surgeons and hospitals are predictors of better DFS in patients with WDTC. DFS is higher among surgeons performing more than 40 thyroidectomies a year. LEVEL OF EVIDENCE: 3 Laryngoscope, 133:S1-S15, 2023.
PubMed-ID: 35796293
http://dx.doi.org/10.1002/lary.30276

The Effects of Chronic Steroid Use on Postoperative Complications Following Thyroidectomy.
World J Surg, 47(4):995-1002.
E. S. Koh, F. R. Chen, S. Chen, T. Quan, K. L. Leung and J. Yang. 2023.
BACKGROUND: Patients undergoing thyroidectomy are sometimes on chronic steroids for underlying disease. This study examined the postoperative risk profile of thyroidectomy patients on chronic steroids. METHODS: Patients in the National Surgical Quality Improvement Program (NSQIP) database who underwent thyroidectomy were sorted by presence or absence of chronic steroid use. Clinicodemographics, comorbidities, and postoperative complications were recorded and compared between the two. Univariate and multivariate analyses compared the groups and calculated odds ratios (OR). RESULTS: We identified 42,857 patients. 41,903 (97.8%) patients were not on chronic steroids, while 954 (2.2%) were. Most underwent total thyroidectomy (18,748, 43.75%) or total lobectomy (16,323, 38.09%). Following univariate and multivariate analyses, patients on chronic steroids had increased risk of postoperative bleeding and transfusions (OR = 0.375, p = 0.046, 95% CI 0.223-0.988), open wound infection (OR = 0.226, $p < 0.001$, 95% CI 0.117-0.437), pulmonary embolism (OR = 0.312, p = 0.034, 95% CI 0.106-0.918), and ventilator use > 48 h (OR = 0.401, $p < 0.008$, 95% CI 0.205-0.785). CONCLUSIONS: Chronic steroid use prior to thyroidectomy is an independent risk factor for multiple postoperative complications, namely postoperative bleeding and transfusions, open wound infection, pulmonary embolism, and ventilator use over 48 h. Patients on chronic steroids should be medically optimized before thyroidectomy to reduce the risk of potentially life-threatening complications.
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http://dx.doi.org/10.1007/s00268-023-06903-y

Surgical resources in advanced thyroid cancer treatment with aerodigestive tract invasion.
Surg Oncol, 46:101863.
E. Mercader-Cidoncha, L. Zarain-Obrador, J. M. Lasso and C. Simon-Adiego. 2023.
BACKGROUND: Despite papillary thyroid cancer (PTC) excellent prognosis, 10-15% of patients may present aggressive local behaviour. We present two cases with different aerodigestive tract invasion partners in which two reconstructions were used, out of all the surgical resources we have planned preoperatively [1-4]. METHODS: Case 1: 57-year-old woman with asymmetric goitre and a 60mm nodule (Bethesda-VI). CT showed suspected involvement of aero-digestive tract. Endobronchial ultrasound (EBUS) showed no tracheal invasion. Per oral endoscopic-US confirmed transmural oesophageal involvement. Surgery included total thyroidectomy(left recurrent laryngeal nerve was sacrificed), bilateral central and left lateral lymph node dissection, oesophageal partial resection and reconstruction with free radial flap. Case 2: 75-year-old male with cervical mass and haemoptysis. US showed a 62 mm nodule (Bethesda-VI). PET-CT showed tracheal invasion(bronchoscopy confirmatory). Per oral endoscopic-US showed no transmural oesophageal involvement. Surgery included total thyroidectomy (right recurrent laryngeal nerve was sacrificed), bilateral central lymph node dissection,

tracheal resection and extra-mucosal oesophageal resection. RESULTS: First patient required tracheostomy. She presented a self-limiting salivary fistula. She was discharged after 6 weeks with good oral intake and tracheostomy closed. Pathology report showed multifocal papillary thyroid cancer(tall cells, 70mm),micro-metastatic lymph node involvement. Afterwards, radioiodine ablation was performed. Six months after surgery there was no evidence of structural disease and analysis showed Tg 1 mug/L. Second patient developed nosocomial pneumonia and was discharged after 3 weeks. Pathology report showed papillary thyroid cancer (insular growth, 52 mm), bilateral neck central lymph nodes involvement, transmural tracheal infiltration, free margins. Radioiodine ablation is pending. CONCLUSIONS: Surgical treatment of advanced/invasive PTC offers good results in terms of survival and quality of life. Adequate pre-surgical planning, which includes multiple surgical resources, and a multidisciplinary team approach are required.
PubMed-ID: 36542909
http://dx.doi.org/10.1016/j.suronc.2022.101863

Chronology of Thyroid Cancer.
World J Surg, 47(2):288-95.
A. Miyauchi. 2023.
INTRODUCTION: The basic nature of cancer includes unlimited growth, invasion, and metastasis. The TNM staging system is very simple and popular. It indicates the degree of the anatomical spread of the disease but does not include tumor growth. Collins reported that human tumors grow exponentially, which can be expressed in doubling time. PATIENTS AND METHODS: We found that in patients with medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC) serum calcitonin and thyroglobulin levels changed exponentially over time, respectively, and that doubling times of these values were very strong prognostic factors. Doubling time has two major limitations. Doubling rate resolves these limitations. Using doubling rate, we performed kinetic analyses on tumor volume during active surveillance of micro-PTC. RESULTS: Our kinetic studies on patients with biochemically persistent disease revealed that 17% of MTC and 51% of PTC showed decrease in serum tumor marker levels over time. During active surveillance of micro-PTC, 17% of the patients showed clear decrease in their tumor volume. The evidences currently available are limited. However, our data indicate the following: Growth slowdown and regression are very common phenomena in the natural history of micro-PTC, clinical PTC in young and middle-aged patients, and hereditary MTC. The biologic characteristics of cancers of the same name, such as PTC, are diverse and vary widely with age. CONCLUSIONS: Doubling time and doubling rate are very powerful tools to provide the most appropriate management for the patients with thyroid cancers. Knowing the natural history of thyroid cancer is essential for the best disease management of thyroid cancer.
PubMed-ID: 36153411
http://dx.doi.org/10.1007/s00268-022-06741-4

Developing and validating a multivariable machine learning model for the preoperative prediction of lateral lymph node metastasis of papillary thyroid cancer.
Gland Surg, 12(1):101-9.
J. Huang, Z. Li, Q. Zhong, J. Fang, X. Chen, Y. Zhang and Z. Huang. 2023.
BACKGROUND: At present, preoperative diagnosis of lateral cervical lymph node metastasis (LLNM) in patients with papillary thyroid carcinoma (PTC) mostly depends on the training and expertise of ultrasound doctors. A machine-learning model for predicting LLNM accurately before PTC surgery may help to determine the scope of surgery and reduce unnecessary surgical trauma. METHODS: The data of patients with primary PTC who underwent thyroidectomy with lateral cervical lymph node surgery at Beijing Tongren Hospital between July 2009 and June 2021 were retrospectively analyzed. All patients had complete ultrasonic examination, clinical data, and definite pathology diagnosis of lymph nodes. LLNM was confirmed by postoperative pathology. The patients were randomly divided into a training set (155 cases) and a test set (98 cases) at a ratio of 6:4. Eleven parameters, including patient demographics, ultrasound results, and tumor-related conditions, were collected, and a prediction model was established using the support vector machine (SVM) algorithm. Several other machine-learning algorithms were also used to establish models for comparison. The accuracy, precision, recall, F1-score, sensitivity, specificity, Cohen's kappa value, and area under the receiver operating characteristic curve (AUC) were used to evaluate model performance. RESULTS: A total of 87 males and 156 females were included in the study, aged 14-80 years. One hundred and four patients of them had LLNM and 139 did not have LLNM. The pandas Python library was used for the statistical analysis, and the Spearman coefficient was used to analyze the correlation between each parameter and the prediction index. The SVM model performed the best among all the models. Its accuracy, precision, recall, F1-score, sensitivity, specificity, Cohen's kappa value, and AUC were 90.8%, 91.0%, 90.8%, 90.8%, 87.5%, 94.0%, 81.6%, and 91.0%, respectively. CONCLUSIONS: This model can enable surgeons to improve the accuracy of ultrasonography in predicting LLNM without additional examination, thus avoiding missing positive lateral

cervical lymph nodes and reducing the sequelae caused by unnecessary lateral neck dissection.
PubMed-ID: 36761483
http://dx.doi.org/10.21037/gs-22-741

Parathyroids

Meta-Analyses

- None -

Randomized controlled trials

Evaluating the clinical and mechanistic effects of eplerenone and amiloride monotherapy, and combination therapy with cinacalcet, in primary hyperparathyroidism: A placebo-controlled randomized trial.
Clin Endocrinol (Oxf), 98(4):516-26.
W. W. Parksook, M. Heydarpour, J. M. Brown, A. Turchin, M. Mannstadt and A. Vaidya. 2023.
OBJECTIVES: Human physiology and epidemiology studies have demonstrated complex interactions between the renin-angiotensin-aldosterone system, parathyroid hormone and calcium homeostasis. Several of these studies have suggested that aldosterone inhibition may lower parathyroid hormone (PTH) levels. The objective of this study was to assess the effect of 4 weeks of maximally tolerated mineralocorticoid receptor antagonist therapy with eplerenone on PTH levels in patients with primary hyperparathyroidism (P-HPT) when compared to amiloride and placebo. We also investigated the synergistic effect of these interventions when combined with cinacalcet for an additional 2 weeks. DESIGN: Randomized, double-blinded, three parallel-group, placebo-controlled trial. PATIENTS: Patients with P-HPT. RESULTS: Most patients were women (83%) and White (76%). Maximally tolerated doses of eplerenone and amiloride induced significant reductions in blood pressure and increases in renin and aldosterone production; however, despite these physiologic changes, neither intervention induced significant changes in PTH or calcium levels when compared to the placebo. Both eplerenone and amiloride therapy induced significant reductions in procollagen type 1 N-terminal propeptide levels when compared to placebo. When cinacalcet therapy was added, PTH and calcium levels were markedly reduced in all groups; however, there was no significant difference in PTH or serum calcium reductions between groups. CONCLUSIONS: Although maximally tolerated therapy with eplerenone and amiloride induced expected changes in renin, aldosterone and blood pressure, there were no meaningful changes in PTH or serum calcium levels in P-HPT patients. These results suggest that inhibition of aldosterone action does not have a clinically meaningful role in medical therapy for P-HPT.
PubMed-ID: 36316798
http://dx.doi.org/10.1111/cen.14840

Consensus Statements/Guidelines

- None -

Other Articles

Microencapsulation of parathyroid cells via electric field and non-surgical transplantation approach.
J Endocrinol Invest,
O. Karabiyik Acar, H. Basoglu, M. Kegin, G. D. Nozhatzadeh, E. Hacihasanoglu, A. A. Tuncer, F. Sahin, G. Torun Kose and E. Aysan. 2023.
PURPOSE: Hypoparathyroidism is a rare disease with low PTH, mostly seen as a consequence of neck surgery. Current management is the prescription of calcium and vitamin D, but the definitive treatment is parathyroid allotransplantation, which frequently triggers an immune response, thus cannot achieve the expected success. To overcome this problem, encapsulation of allogeneic cells is the most promising method. By optimizing the standard alginate cell encapsulation technique with parathyroid cells under high-voltage application, the authors reduced the size of parathyroid-encapsulated beads and evaluated these samples in vitro and in vivo. METHODS: Parathyroid cells were isolated, and standard-sized alginate macrobeads were prepared without any electrical field application, while microbeads in smaller sizes (< 500 microm), by the application of 13 kV. Bead morphologies, cell viability, and PTH secretion were evaluated in vitro for four

weeks. For the in vivo part, beads were transplanted into Sprague-Dawley rats, and after retrieval, immunohistochemistry and PTH release were evaluated in addition to the assessment of cytokine/chemokine levels. RESULTS: The viability of parathyroid cells in micro- and macrobeads did not differ significantly. However, the amount of in vitro PTH secretion from microencapsulated cells was significantly lower than that from macroencapsulated cells, although it increased throughout the incubation period. Immunohistochemistry of PTH staining in both of the encapsulated cells identified as positive after retrieval. CONCLUSION: Contrary to the literature, a minimal in vivo immune response was developed for alginate-encapsulated parathyroid cells, regardless of bead size. Our findings suggest that injectable, micro-sized beads obtained using high-voltage may be a promising method for a non-surgical transplantation approach.
PubMed-ID: 36976484
http://dx.doi.org/10.1007/s40618-023-02075-7

Environmental Chemicals and their Association with Hyperparathyroidism.
World J Surg, 47(2):296-303.
J. L. McMullin, J. Codner, S. G. Patel, J. Sharma, X. Hu, D. P. Jones, C. J. Weber and N. D. Saunders. 2023.
BACKGROUND: The incidence of hyperparathyroidism has increased in the USA. The previous work from our institution detected environmental chemicals (EC) within hyperplastic parathyroid tumors. The National Health and Nutrition Examination Survey (NHANES) is a program designed to assess the health status of people in the USA and includes measurements of EC in serum. Our aim was to determine which EC are associated with elevated parathyroid hormone (PTH) and calcium levels within NHANES. METHODS: NHANES was queried from 2003-2016 for our analysis with calcium. A separate subgroup was queried from 2003-2006 that included PTH levels. Subjects with elevated calcium, and elevated PTH and normal Vitamin D levels were identified. Wilcoxon rank sum tests were used to analyze levels of EC in those with elevated calcium, and those with elevated PTH in the subgroup. All EC with $p < 0.05$ were then included in separate multivariate models adjusting for serum vitamin D and creatinine for PTH and albumin for calcium. RESULTS: There were 51,395 subjects analyzed, and calcium was elevated in 2.1% (1080) of subjects. Our subgroup analysis analyzed 14,681 subjects, and PTH was elevated without deficient Vitamin D in 9.4% (1,377). Twenty-nine different polychlorinated biphenyls and the organochlorine pesticides hexachlorobenzene, transnonachlor, oxychlordane, and p,p'-dichlorodiphenyldichloroethylene (DDE) were found to be associated with elevated calcium and separately with elevated PTH (all $p < 0.05$). CONCLUSION: In NHANES, 33 ECs were found to be associated with elevated calcium as well as elevated PTH levels on our subgroup analysis. These chemicals may lead us toward a causal link between environmental factors and the development of hyperparathyroidism and should be the focus of future studies looking at chemical levels within specimens.
PubMed-ID: 36161354
http://dx.doi.org/10.1007/s00268-022-06759-8

C(11) choline PET/CT succeeds when conventional imaging for primary hyperparathyroidism fails.
Surgery, 173(1):117-23.
S. Saha, R. A. Vierkant, G. B. Johnson, A. Parvinian, R. A. Wermers, T. Foster, T. McKenzie, B. Dy and M. Lyden. 2023.
BACKGROUND: Focused parathyroidectomy in primary hyperparathyroidism is possible with accurate preoperative localization. A growing body of data exists regarding the role of radio-labeled C(11) choline positron emission tomography/computed tomography. In cases of nonlocalized disease, it may be a useful adjunct to ultrasound, (123)I/(99)Tc-sestamibi (I-123 sestamibi), or 4-dimensional computed tomography imaging. METHODS: Patients who received a neck and chest limited coverage C(11) choline positron emission tomography/computed tomography for evaluation of primary hyperparathyroidism from 2017 to 2021 at a single institution were retrospectively reviewed. We assessed the sensitivity, positive predictive value, and false negative rate. We also compared these rates to the standard modalities of ultrasound, I-123 sestamibi, 4-dimensional computed tomography, and examined concordance rates. RESULTS: We identified 43 patients, of whom 33 had a positive C(11) choline positron emission tomography/computed tomography finding. This cohort of patients had failed to localize on multiple standard imaging modalities. Twenty-five patients proceeded to surgery, 72% of whom were reoperative cases. Twenty (80%) achieved an intraoperative cure. Analysis showed that C(11) choline positron emission tomography/computed tomography achieved a sensitivity of 64% (95% confidence interval 47%-82%) and positive predictive value of 72% (95% confidence interval 54%-90%). There were 5/25 (20%) false positive positron emission tomography C(11) choline results found to be lymph nodes, normal parathyroid, and 1 recurrent laryngeal nerve neuroma. CONCLUSION: C(11) choline positron emission tomography/computed tomography is a useful adjunct for parathyroid localization in a complex population of patients who have failed standard localization techniques including ultrasound, I-123 sestamibi, or 4-dimensional computed tomography and/or prior operations. Although routine inclusion of C(11) choline positron emission

tomography/computed tomography imaging may not be necessary, it may aid in preoperative localization in the reoperative setting.
PubMed-ID: 36229257
http://dx.doi.org/10.1016/j.surg.2022.08.024

Primary hyperparathyroidism after radioactive iodine therapy: Is it a distinct clinical entity?
Am J Surg, 225(1):180-3.
I. Bobanga, J. Jin, S. Wilhelm, A. Sarode, C. E. Alvarado, A. ElSherif and C. R. McHenry. 2023.
BACKGROUND: Radioactive iodine (RAI) treatment is considered a rare cause of primary hyperparathyroidism (pHPT). METHOD: A multi-institutional retrospective review of patients with pHPT who underwent parathyroidectomy from 1990 to 2020 was completed to evaluate the prevalence and latency time for development of RAI-associated pHPT and determine clinical differences in pHPT patients with or without prior RAI treatment. RESULTS: 1929 patients with sporadic pHPT underwent parathyroidectomy; 48 (2.5%) had prior RAI treatment and 1881 (97.5%) did not. RAI treatment was for thyrotoxicosis in 43 (90%) patients. Average latency was 24 years (3-59 years) and inversely correlated with age. Patients with prior RAI treatment had lower preoperative calcium and PTH levels ($p < 0.0001$). No significant differences were observed in age, symptoms, pathology, ectopic glands and cure rate. CONCLUSION: RAI is a potential causative factor for pHPT, accounting for 2.5% of sporadic pHPT. RAI-associated pHPT may be a less severe form of sporadic pHPT and latency inversely correlates with age.
PubMed-ID: 35934557
http://dx.doi.org/10.1016/j.amjsurg.2022.07.024

Parathyroidectomy for Normocalcemic Primary Hyperparathyroidism Improves Bone Mineral Density Regardless of Postoperative Parathyroid Hormone Levels.
World J Surg, 47(3):830-1.
M. S. Lui and N. D. Perrier. 2023.
PubMed-ID: 36622434
http://dx.doi.org/10.1007/s00268-022-06877-3

Surgery for primary hyperparathyroidism in Germany, Switzerland, and Austria: an analysis of data from the EUROCRINE registry.
Langenbecks Arch Surg, 408(1):150.
L. Hargitai, T. Clerici, T. J. Musholt, P. Riss and E. council. 2023.
PURPOSE: EUROCRINE is an endocrine surgical register documenting diagnostic processes, indication for surgical treatment, surgical procedures, and outcomes. The purpose was to analyse data for PHPT in German speaking countries regarding differences in clinical presentation, diagnostic workup, and treatment. METHODS: All operations for PHPT performed from 07/2015 to 12/2019 were analysed. RESULTS: Three thousand two hundred ninety-one patients in Germany (9 centres; 1762 patients), Switzerland (16 centres; 971 patients) and Austria (5 centres; 558 patients) were analysed. Hereditary disease was seen in 36 patients in Germany, 16 patients in Switzerland and 8 patients in Austria. In sporadic disease before primary operation, PET-CT showed the highest sensitivity in all countries. In re-operations, CT and PET-CT achieved the highest sensitivities. The highest sensitivity of IOPTH was seen in Austria (98.1%), followed by Germany (96.4%) and Switzerland (91.3%). Operation methods and mean operative time reached statistical significance ($p<0.05$). Complication rates are low. Overall, 656 (19.9%) patients were asymptomatic; the remainder showed bone manifestations, kidney stones, fatigue and/or neuropsychiatric symptoms. CONCLUSION: Early postoperative normocalcaemia ranged between 96.8 and 97.1%. Complication rates are low. PET-CT had the highest sensitivity in all three countries in patients undergoing primary operation as well as in Switzerland and Austria in patients undergoing re-operation. PET-CT could be considered a first-line preoperative imaging modality in patients with inconclusive ultrasound examination. The EUROCRINE registry is a beneficial and comprehensive data source for outcome analysis of endocrine procedures on a supranational level.
PubMed-ID: 37055669
http://dx.doi.org/10.1007/s00423-023-02819-2

Making the Cut: Parathyroidectomy Before or After Kidney Transplantation?
World J Surg, 47(2):319-29.
R. Wang, F. Saad, M. C. McLeod, C. Kew, G. Agarwal, K. Wille, J. E. Locke, H. Chen and S. Ong. 2023.
BACKGROUND: Hyperparathyroidism is common in patients with end-stage kidney disease and may persist after kidney

transplantation (KT). Parathyroidectomy (PTx) is curative, but whether PTx should be performed before or after KT remains controversial. There is concern that PTx can adversely affect renal allograft function if performed post-KT and result in persistent hypocalcemia. This study evaluated outcomes and postoperative complications of PTx before and after KT at our institution. METHODS: We performed a retrospective review of patients at our center (1/2012-2/2019) who had PTx either pre-KT or post-KT. Data on patient demographics, surgical outcomes, and postoperative complications of PTx were collected. RESULTS: Ninety-eight patients were included in this study, with 23 patients undergoing PTx before KT and 75 after KT. The length of follow-up after KT was 67.7 +/- 25.5 months. In post-KT PTx patients, 30-day allograft function was unchanged after PTx. Calcium oxalate and phosphate crystals were less common on allograft biopsies in pre-KT PTx patients (10.0% vs. 34.8%, p = 0.038). Patients in the pre-KT group required more calcium supplementation after PTx than the post-KT group (p < 0.001). At one-year post-PTx, 17 (19.1%) patients required > 1000 mg elemental calcium per day and 7 (7.9%) patients required > 2000 mg/day. There was no difference in surgical success or postoperative complications between the two groups. CONCLUSIONS: Parathyroidectomy before or after kidney transplantation does not adversely affect allograft function. The incidence of persistent hypocalcemia was low. Parathyroidectomy is safe and effective either before or after kidney transplantation.
PubMed-ID: 36239741
http://dx.doi.org/10.1007/s00268-022-06757-w

Educational Review: Intraoperative Parathyroid Fluorescence Detection Technology in Thyroid and Parathyroid Surgery.
Ann Surg Oncol, 30(2):973-93.
T. C. St Amour, M. S. Demarchi, G. Thomas, F. Triponez, C. M. Kiernan and C. C. Solomicronrzano. 2023.
BACKGROUND: Accurate parathyroid gland (PG) identification is a critical yet challenging component of cervical endocrine procedures. PGs possess strong near-infrared autofluorescence (NIRAF) compared with other tissues in the neck. This property has been harnessed by image- and probe-based near-infrared fluorescence detection systems, which have gained increasing popularity in clinical use for their ability to accurately aid in PG identification in a rapid, noninvasive, and cost-effective manner. All NIRAF technologies, however, cannot differentiate viable from devascularized PGs without the use of contrast enhancement. Here, we aim to provide an overview of the rapid evolution of these technologies and update the surgery community on the most recent advancements in the field. METHODS: A PubMed literature review was performed using the key terms "parathyroid," "near-infrared," and "fluorescence." Recommendations regarding the use of these technologies in clinical practice were developed on the basis of the reviewed literature and in conjunction with expert surgeons' opinions. RESULTS: The use of near-infrared fluorescence detection can be broadly categorized as (1) using parathyroid NIRAF to identify both healthy and diseased PGs, and (2) using contrast-enhanced (i.e., indocyanine green) near-infrared fluorescence to evaluate PG perfusion and viability. Each of these approaches possess unique advantages and disadvantages, and clinical trials are ongoing to better define their utility. CONCLUSIONS: Near-infrared fluorescence detection offers the opportunity to improve our collective ability to identify and preserve PGs intraoperatively. While additional work is needed to propel this technology further, we hope this review will be valuable to the practicing surgeon.
PubMed-ID: 36481865
http://dx.doi.org/10.1245/s10434-022-12807-3

Intrathyroidal parathyroid adenomas: Scoping review on clinical presentation, preoperative localization, and surgical treatment.
Head Neck, 45(3):706-20.
S. V. Gowrishankar, R. Bidaye, T. Das, V. Majcher, B. Fish, R. Casey and L. Masterson. 2023.
Intrathyroidal parathyroid adenomas (IPAs) are a rare cause of primary hyperparathyroidism. They are often difficult to localize preoperatively and intraoperatively, making diagnosis and treatment challenging. Current data on IPAs are sparse and fragmented in the literature. This makes it difficult to compare the effectiveness of different imaging and surgical techniques. To address this issue, this scoping review maps the literature on IPAs, focusing on four domains: clinical presentation, current localization methods, different surgical techniques, and histopathological features. A search of MEDLINE, Embase, and the Cochrane Library was conducted, with 19 studies meeting the inclusion criteria. The characteristics of IPAs on ultrasound, fine-needle aspiration, CT, MRI, sestamibi-based techniques, and selective venous sampling are summarized. Emerging imaging modalities, including autofluorescence, are introduced. Surgical methods and intraoperative factors that correlate with high success rates for removal are highlighted. This review also identifies gaps in knowledge to guide further research into this area.
PubMed-ID: 36563301
http://dx.doi.org/10.1002/hed.27287

Effects of parathyroidectomy on kidney function in patients with primary hyperparathyroidism: Results of a prospective study.
Surgery, 173(1):146-53.
S. Frey, M. Wargny, C. Blanchard, C. Caillard, S. Hadjadj, B. Cariou, L. Figueres and E. Mirallie. 2023.
BACKGROUND: Altered glomerular filtration rate is a controversial indication for parathyroidectomy in patients with primary hyperparathyroidism. The objective of this study was to evaluate the estimated glomerular filtration rate change 12 months after parathyroidectomy for primary hyperparathyroidism according to preoperative kidney function. METHOD: Patients who underwent parathyroidectomy for primary hyperparathyroidism between 2016 and 2021 (n = 381) were enrolled in a monocentric prospective cohort. Patients without 1-year follow-up or with missing data were excluded (n = 135, 35%). Patients were dichotomized according to their baseline estimated glomerular filtration rate: <60 mL/min (group 1) and >/=60 mL/min (group 2). Parameters were measured before and then at 6 and 12 months after parathyroidectomy. RESULTS: Out of 246 included patients, 27 (11%) were assigned to group 1 and 219 (89%) to group 2. The mean baseline estimated glomerular filtration rate was 46.8 +/- 11.5 and 87.3 +/- 14.7 mL/min in groups 1 and 2, respectively. Group 1 patients were older (P = .0006) and had a higher median serum parathyroid hormone level (P = .021). At 6 months postoperative, 224 patients (91%) were normocalcemic. The estimated glomerular filtration rate raw change after parathyroidectomy was significantly higher in group 1 than in group 2 (4.2 +/- 7.8 vs -2.2 +/- 9.1 mL/min, P = .0004). In group 1, 13/27 patients (48%) improved their chronic kidney disease stage after parathyroidectomy, including 6/13 (46%) with postoperative estimated glomerular filtration rate >/=60 mL/min, whereas 2/27 (7%) worsened. The baseline estimated glomerular filtration rate <60 mL/min and elevated serum calcium level were associated with postoperative estimated glomerular filtration rate improvement in multivariable analysis (P = .0023 and .039, respectively). CONCLUSION: Parathyroidectomy for primary hyperparathyroidism is more likely to improve kidney function in patients with preoperative estimated glomerular filtration rate <60 mL/min. These results strengthen the current guidelines for surgery.
PubMed-ID: 36167701
http://dx.doi.org/10.1016/j.surg.2022.05.038

Hyperparathyroid crisis: Characteristics and outcomes.
Am J Surg, 225(3):477-80.
A. Muntaser, A. Thelen, A. R. Sehgal and C. R. McHenry. 2023.
BACKGROUND: Hyperparathyroid crisis (HPTC) is a potentially lethal condition characterized by severe symptomatic hypercalcemia with calcium levels >/=14 mg/dl. We sought to determine the rate of HPTC and how it differs from hyperparathyroidism (HPT) without crisis (HPTWC). METHODS: A retrospective review of patients with surgically treated HPT from 1990 to 2022 was completed. RESULTS: HPTC occurred in 18 (2.4%) of 783 with primary HPT. Patients with HPTC had higher preoperative calcium and parathyroid hormone levels, lower postoperative calcium levels, larger gland weights and higher rates of ectopic glands, carcinoma, recurrence and mortality compared to patients with HPTWC (all p < 0.05). CONCLUSIONS: HPTC is a rare condition manifested by severe HPT that is associated with a higher rate of recurrence and mortality compared to HPTWC. HPTC is associated with larger parathyroid glands that are more often ectopic and malignant.
PubMed-ID: 36307336
http://dx.doi.org/10.1016/j.amjsurg.2022.10.028

Pediatric primary hyperparathyroidism: Surgical pathology and long-term outcomes in sporadic and familial cases.
Am J Surg, 225(4):699-702.
T. Szabo Yamashita, H. Gudmundsdottir, T. R. Foster, M. L. Lyden, B. M. Dy, P. J. Tebben and T. McKenzie. 2023.
BACKGROUND: Primary Hyperparathyroidism (PHPT) is rare in pediatric patients. Data regarding surgical outcomes are scarce. METHODS: Single-center retrospective review (1994-2020) of patients </=21 years undergoing surgery for PHPT. RESULTS: 66 patients were identified (61% female, 17 +/- 3 years). 71% of patients were symptomatic at diagnosis. 32% of patients had known familial syndromes, most commonly MEN-1. 23% of patients without a known mutation had genetic testing, 22% positive. 56% of the total and 19% of the familial cohort underwent focused exploration. Single gland disease was found in 19% of familial vs 85% of sporadic cases, p < 0.00001. Persistence was 9%, all in the sporadic group, p = 0.11. Recurrence was 15%: 38% in the familial vs 2% in the sporadic groups, p=0.0004. Time to recurrence was 59 months (Q1-38, Q3-95), familial 61 vs 124 months sporadic, p=0.001. CONCLUSION: Pediatric PHPT is frequently sporadic, although 5% of apparent sporadic cases are secondary to syndromes. Familial cases have higher rates of recurrence, requiring closer follow-up.

PubMed-ID: 36270819
http://dx.doi.org/10.1016/j.amjsurg.2022.10.018

A 15-year experience: intraoperative parathyroid hormone assay for the management of primary hyperparathyroidism in a UK endocrine surgical unit.
Langenbecks Arch Surg, 408(1):120.
N. Patel, C. Whittet, D. Zhao, J. Rees, M. J. Stechman and D. M. Scott-Coombes. 2023.
PURPOSE: This study aims to evaluate the outcomes of first-time parathyroidectomy for primary hyperparathyroidism using intraoperative PTH (IOPTH) assay in the light of the UK National Institute for Health and Care Excellence (NICE) guidelines for the management of primary hyperparathyroidism. METHOD: This is a retrospective cohort analysis of a prospectively maintained database of endocrine surgery in a tertiary centre. Preoperative radiological localisation (concordance and accuracy), intraoperative PTH parameters and adjusted serum calcium at minimum 6-month follow-up were analysed. The accuracy of IOPTH to predict post-operative normocalcaemia and the number needed to treat (NNT) within the cohort when IOPTH was utilised were determined. Differences between groups were evaluated with Chi-squared and Fisher's exact test. RESULTS: Between January 2004 and September 2018, 849 patients (75.4% women), median age 64 years (IQR 54-72), were analysed. The median preoperative adjusted serum calcium was 2.80mmol/l (IQR 2.78-2.90), and the median preoperative PTH was 14.20pmol/l (IQR 10.70-20.25). The overall first-time cure (normocalcaemia) rate was 96.4%. The sensitivity, specificity, positive predictive value and negative predictive values of IOPTH were 96.8%, 83.2%, 97.6% and 78.8%, respectively, with an accuracy of 95.1%. For patients with concordant scans (48.3%), a targeted approach without IOPTH would have achieved a cure rate of 94.1% compared with 98.0% using IOPTH ($p<0.01$) CONCLUSION: The use of IOPTH assay significantly improved the rate of normocalcaemia at 6 months. The low NNT to benefit from IOPTH, particularly those patients with a single positive scan, and the inevitable reduction in the potential costs incurred from failure and reoperation justify its utilisation.
PubMed-ID: 36920573
http://dx.doi.org/10.1007/s00423-023-02848-x

The importance of hypophosphatemia in the clinical management of primary hyperparathyroidism.
J Endocrinol Invest,
H. Duger, H. Bostan, U. Gul, B. Ucan, S. Hepsen, D. Sakiz, P. Akhanli, E. Cakal and M. Kizilgul. 2023.
AIM: The levels of serum phosphorus (P) are low or low-normal in primary hyperparathyroidism (PHPT), and there is an inverse relationship between the levels of parathormone (PTH) and P. However, when considering the diagnostic and surgical indication criteria of PHPT, serum P levels are generally ignored. The aim of this study was to retrospectively evaluate the association of serum P levels with the clinical outcomes of PHPT. MATERIALS AND METHODS: A retrospective evaluation was made of the data of 424 consecutive patients (370 females, 54 males) with PHPT who presented at our centre. RESULTS: The mean age of the study population was 57 +/- 11.68 years. The mean P was 2.57 +/- 0.53 mg/dl. Asymptomatic disease was determined in 199 (47%) patients. Male patients had significantly lower levels of P. Symptomatic patients and patients with renal stones, vitamin D < 20 microg/l, calcium level >/= 11.2 mg/dl, 24 h urinary calcium > 400 mg/day, or hypomagnesemia, were seen to have significantly lower levels of P ($p < 0.05$). Hypophosphatemia (hypoP) was found in 202 of 424 patients (47%), and these patients had a higher rate of symptomatic disease (63% to 44%, $p < .0001$). Of the 61 (88%) patients with moderate hypoP, 54 (88%) had at least one of the surgical criteria. A statistically significant increase in the incidence of hypoP was determined in symptomatic and male patients. In the patients with hypoP, serum PTH and urine calcium levels were found to be higher, and lumbar T-scores and serum vitamin D levels were lower. The patients with hypoP had higher rates of renal stones and osteoporosis ($p < 0.05$). CONCLUSIONS: The current study results show that hypoP is associated with a higher risk of osteoporosis and renal stones in PHPT patients. Even if patients are asymptomatic, moderate hypoP may be associated with poor outcomes of PHPT. Therefore, moderate hypoP may be a new criterion for parathyroidectomy, regardless of hypercalcemia level.
PubMed-ID: 36929458
http://dx.doi.org/10.1007/s40618-023-02064-w

Adrenals

Meta-Analyses

Open Versus Laparoscopic Surgery in the Management of Adrenocortical Carcinoma: A Systematic Review and Meta-analysis.
Ann Surg Oncol, 30(2):994-1005.
H. Nakanishi, S. Miangul, R. Wang, J. El Haddad, N. El Ghazal, F. A. Abdulsalam, R. H. Matar, C. A. Than, B. E. Johnson and H. Chen. 2023.
BACKGROUND: Laparoscopic surgery is considered a standard treatment for benign adrenal tumors; however, no consensus has been reached on the optimal resection technique for adrenocortical carcinomas. This study aims to evaluate the safety and efficacy of laparoscopic surgery and open surgery in the management of adrenocortical carcinoma. METHODS: The Cochrane, Embase, PubMed, Scopus, and Web of Science databases were searched for articles from inception to May 2022, by two independent reviewers using the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. The review was registered prospectively on the PROSPERO database (CRD42022316050). RESULTS: From 183 studies screened, 11 studies met the eligibility criteria, with a total of 1617 patients with adrenocortical carcinoma undergoing either laparoscopic surgery (n = 472) or open surgery (n = 1145). Open surgery demonstrated a lower rate of positive resection margin compared with laparoscopic surgery (odds ratio [OR] 1.52, 95% confidence interval [CI] 1.10-2.10; I(2) = 0%). Additionally, open surgery had more favorable overall survival (OR 0.56, 95% CI 0.44-0.72; I(2) = 0%) and recurrence-free rates (OR 0.60, 95% CI 0.42-0.85; I(2) = 38%) than laparoscopic surgery at 3 years. Hospital stay was shorter for laparoscopic surgery than open surgery (mean difference - 2.49 days, 95% CI - 2.95 to - 2.04; I(2) = 45%). CONCLUSIONS: Open surgery should still be considered the standard operative approach; however, laparoscopic surgery could be regarded as an effective and safe operation for selected adrenocortical carcinoma cases with appropriate laparoscopic expertise. Further randomized controlled studies with tumor stage- and resection margin-dependent survival analysis are necessary to ascertain the safety and efficacy of the treatment.
PubMed-ID: 36344710
http://dx.doi.org/10.1245/s10434-022-12711-w

Efficacy and Safety of Tyrosine Kinase Inhibitors in Patients with Metastatic Pheochromocytomas/Paragangliomas.
J Clin Endocrinol Metab, 108(3):755-66.
Y. Zhou, Y. Cui, D. Zhang and A. Tong. 2023.
CONTEXT: Tyrosine kinase inhibitors (TKIs) can be used to treat locally unresectable or distantly metastatic pheochromocytomas/paragangliomas (PPGLs), such as sunitinib, according to the National Comprehensive Cancer Network guidelines in 2022. However, the precise effect of different TKIs in metastatic PPGLs is still unclear. OBJECTIVE: The aim of this meta-analysis is to assess the efficacy and safety of TKIs in metastatic PPGLs. METHODS: The PubMed, Cochrane Library, Scopus, Clinical Trial, and Embase databases were searched by synonyms of 48 TKIs and metastatic PPGLs from inception up to August 2022. Outcomes were tumor response or survival data and the incidence of adverse events (AEs) after treatment. The MIONRS scale and the JBI's tools for case series were used for interventional and observational studies to assess risk of bias, respectively. The combined effects with fixed- or random-effect models, the combined median with the weighted median of medians method and their 95% CIs were reported. RESULTS: A total of 7 studies with 160 patients were included. Tumor responses in metastatic PPGLs in 5 studies with available data showed the pooled proportion of partial response (PR), stable disease, and disease control rate (DCR) of, respectively, 0.320 (95% CI 0.155-0.486), 0.520 (95% CI 0.409-0.630), and 0.856 (95% CI 0.734-0.979). The combined median progressive-free survival in 6 studies was 8.9 months (95% CI 4.1-13.5) and the proportion of those who discontinued due to AEs in 5 studies was 0.143 (95% CI 0.077-0.209). CONCLUSION: This meta-analysis suggests that patients with metastatic PPGLs can benefit from TKI therapy with PR and DCR up to more than 30% and 80%. However, because of restricted studies, larger clinical trials should be performed in the future.
PubMed-ID: 36383456
http://dx.doi.org/10.1210/clinem/dgac657

Exclusion Tests in Unilateral Primary Aldosteronism (ExcluPA) Study.
J Clin Endocrinol Metab, 108(2):496-506.
R. Zhu, T. Shagjaa, G. Rossitto, B. Caroccia, T. M. Seccia, D. Gregori and G. P. Rossi. 2023.
CONTEXT: Determining the diagnostic accuracy of "exclusion" tests for primary aldosteronism (PA) compared to the

aldosterone to renin ratio (ARR) is fundamental to avoid invasive subtyping in false-positive patients at screening. OBJECTIVE: To assess the accuracy of exclusion tests for PA using the diagnosis of unilateral PA as reference. METHODS: PubMed, EMBASE, Web of Science, and Cochrane Library databases were searched for studies published from January 1, 1970, to December 31, 2021, meeting tight quality criteria. Data were extracted following the PRISMA methodology. We performed a two-stage meta-analysis that entailed an exploratory and a validation phase based on a "golden" or "gold" diagnostic standard, respectively. Pooled specificity, negative likelihood ratio, diagnostic odds ratio, and summary area under the ROC curve (sAUROC) were calculated to analyze the accuracy of exclusion tests. RESULTS: A meta-analysis of 31 datasets comprising a total of 4242 patients fulfilling the predefined inclusion criteria found that pooled accuracy estimates (sAUROC) did not differ between the ARR (0.95; 95% CI, 0.92-0.98), the captopril challenge test (CCT) (0.92; 95% CI, 0.88-0.97), and the saline infusion test (SIT) (0.96; 95% CI, 0.94-0.99). Solid information could not be obtained for the fludrocortisone suppression test and the furosemide upright test, which were assessed in only 1 study each. CONCLUSION: The apparently high diagnostic accuracy of the CCT and the SIT was due to the selection of patients with an elevated ARR and thus a high pretest probability of unilateral PA; however, neither test furnished a diagnostic gain over the ARR. Therefore, the systematic use of these exclusion tests in clinical practice is not justified by available evidence.
PubMed-ID: 36373399
http://dx.doi.org/10.1210/clinem/dgac654

Randomized controlled trials

Do multiple types of confirmatory tests improve performance in predicting subtypes of primary aldosteronism?
Clin Endocrinol (Oxf), 98(4):473-80.
H. Kaneko, H. Umakoshi, T. Fukumoto, N. Wada, T. Ichijo, S. Sakamoto, T. Watanabe, Y. Ishihara, T. Tagami, M. Ogata, N. Iwahashi, M. Yokomoto-Umakoshi, Y. Matsuda, R. Sakamoto and Y. Ogawa. 2023.
OBJECTIVE: The clinical practice guideline for primary aldosteronism (PA) places a high value on confirmatory tests to sparing patients with false-positive results in case detection from undergoing adrenal venous sampling (AVS). However, it is unclear whether multiple types of confirmatory tests are more useful than a single type. To evaluate whether the machine-learned combination of two confirmatory tests is more useful in predicting subtypes of PA than each test alone. DESIGN: A retrospective cross-sectional study in referral centres. PATIENTS: This study included 615 patients with PA randomly assigned to the training and test data sets. The participants underwent saline infusion test (SIT) and captopril challenge test (CCT) and were subtyped by AVS (unilateral, n = 99; bilateral, n = 516). MEASUREMENTS: The area under the curve (AUC) and clinical usefulness using decision curve analysis for the subtype prediction in the test data set. RESULTS: The AUCs for the combination of SIT and CCT, SIT alone and CCT alone were 0.850, 0.813 and 0.786, respectively, with no significant differences between them. The AUC for the baseline clinical characteristics alone was 0.872, whereas the AUCs for these combined with SIT, combined with CCT and combined with both SIT and CCT were 0.868, 0.854 and 0.855, respectively, with no significant improvement in AUC. The additional clinical usefulness of the second confirmatory test was unremarkable on decision curve analysis. CONCLUSIONS: Our data suggest that patients with positive case detection undergo one confirmatory test to determine the indication for AVS.
PubMed-ID: 36415024
http://dx.doi.org/10.1111/cen.14854

Consensus Statements/Guidelines

- None -

Other Articles

Cardiac Changes and Their Reversal Following Curative Surgery in Pheochromocytoma: PheoCard Prospective Cohort Study.
World J Surg, 47(2):304-11.
K. M. M. Vishvak Chanthar, R. Khanna, G. Agarwal, S. R. Rout, A. Kapoor, M. Sabaretnam, G. Chand, A. Mishra, A. Agarwal

and S. K. Mishra. 2023.
BACKGROUND: Pheochromocytoma and paraganglioma (PPGL) are catecholamine producing tumors of chromaffin cell origin, known to cause varied cardiovascular manifestations from hypertension to myocardial infarction. This study sought to objectively evaluate the cardiac changes in PPGL patients and their reversal following curative surgery. METHODS: The PheoCard study was registered in ClinicalTrials.gov (NCT05082311) and involved 35 consecutive PPGL patients managed as per standard protocol involving alpha blockade followed by curative surgery. They underwent detailed cardiac evaluation using 2D-echocardiography and speckle tracking echocardiography at the time of diagnosis, 7-10 days after alpha blockade, and at 7 days, 3 months, and 6 months after surgical removal. Age- and gender-matched essential hypertensives and healthy individuals (10 in each group) served as two control groups. RESULTS: Patients with PPGLs had significantly higher mean blood pressure, left ventricle end-diastolic dimension and volume (LVEDD, LVEDV), left ventricle end-systolic volume (LVESV), septal wall thickness, LV hypertrophy, lower mean LV ejection fraction (LVEF), early diastolic mitral annular velocity (E/A), decreased amplitude of LV longitudinal strain, and increased circumferential strain ($p < 0.001$) when compared with the control groups at baseline. After alpha blockade, there was marked reduction in the mean LVEDD, LVEDV, LVESV, and normalization of E/A ratio ($p < 0.001$) in the PPGL patients. Following curative surgery (normalization of fractionated urinary metanephrines at 7-10 days post-operatively), there was early improvement in all echocardiographic parameters and it continued to improve even at 6 months after surgery. There was marked improvement in the global longitudinal strain as seen on serial speckle tracking echocardiography with recovery of most of the segments of LV depicting the reversal of subclinical endocardial dysfunction ($p < 0.001$). CONCLUSION: PPGL patients despite normal systolic function have subclinical LV diastolic dysfunction which is reversed after curative surgery. TRIAL REGISTRATION: ClinicalTrials.gov NCT05082311.
PubMed-ID: 36210362
http://dx.doi.org/10.1007/s00268-022-06731-6

Label-Free Enhancement of Adrenal Gland Visualization Using Near-Infrared Autofluorescence for Surgical Guidance.
World J Surg, 47(2):350-60.
G. Thomas, C. M. Kiernan, P. A. Willmon, E. Haugen, A. N. Luckenbaugh, D. A. Barocas, N. Baregamian, A. Mahadevan-Jansen and C. C. Solomicronrzano. 2023.
BACKGROUND: During adrenalectomy, surgeons have traditionally relied on their subjective visual skills to distinguish adrenal glands (AGs) from retroperitoneal fat and surrounding structures, while ultrasound and exogenous contrast agents have been employed for intraoperative AG visualization, all of which have their limitations. We present a novel label-free approach that uses near-infrared autofluorescence (NIRAF) detection, which demonstrates potential for enhanced intraoperative AG visualization and efficient tumor resection during adrenalectomies. METHODS: Patients undergoing adrenalectomy or nephrectomy were enrolled for this feasibility study. NIRAF emitted beyond 800 nm was detected in vivo from AGs and surrounding tissues during open adrenalectomies or nephrectomies. NIRAF was also measured ex vivo in excised AGs following robotic adrenalectomies. NIRAF images of tissues were captured using near-infrared (NIR) camera systems, whereas NIRAF intensities were recorded concurrently using fiber-optic probe-based NIR devices. Normalized NIRAF intensities (expressed as mean +/- standard error) were analyzed and compared. RESULTS: Among the 55 enrolled patients, NIRAF intensity was elevated significantly for AGs versus retroperitoneal fat and other structures. NIR images of AGs also revealed a distinct demarcation of NIRAF between adrenal cortex and other periadrenal structures. NIRAF intensity in AGs was decreased markedly in malignant adrenal tumors, while benign adrenal cortical tumors and healthy adrenal cortex exhibited the strongest NIRAF levels. CONCLUSIONS: Our preliminary findings indicate that NIRAF detection could be a promising label-free technology to enhance intraoperative AG visualization and holds immense potential for effective tumor demarcation during cortical-sparing adrenalectomies or adrenal-conserving surgeries.
PubMed-ID: 36184672
http://dx.doi.org/10.1007/s00268-022-06755-y

Adrenocortical carcinoma with venous tumor invasion: is there a role for mini-invasive surgery?
Langenbecks Arch Surg, 408(1):17.
A. Olivero, K. Liu, E. Checchucci, L. Liu, L. Ma, G. Wang, G. Mantica, S. Tappero, D. Amparore, M. Sica, C. Fiori, Q. Huang, S. Niu, B. Wang, X. Ma, X. Hou, F. Porpiglia, C. Terrone and X. Zhang. 2023.
OBJECTIVE: This study aims to investigate early oncologic outcomes in patients with adrenocortical carcinoma (ACC) with venous invasion (VI) treated using both open and mini-invasive approaches. PATIENTS AND MATERIALS: We conducted a retrospective analysis of 4 international referral center databases, including all the patients undergoing adrenalectomy for ACC with VI from January 2007 to March 2020. According to CT scan or MRI, the tumor thrombus was classified into four

levels: (1) adrenal vein invasion; (2) renal vein invasion; (3) infra-hepatic Inferior vena cava (IVC); and (4) retro-hepatic IVC. In addition, we divided our patients into patients who had undergone open surgery and mini-invasive surgery. RESULTS: We identified 20 patients with a median follow-up of 12 months. The median tumor size was 110mm. ENSAT stage was II in 4 patients, III in 13 patients, and IV in 3 patients. Tumor thrombus extended in the adrenal vein (n=5), renal vein (n=1), infra-hepatic IVC (n=9), or into the retro-hepatic IVC (n=5). Ten patients were treated with a mini-invasive approach. The patient treated with an open approach reported a more aggressive disease. The two groups did not differ in surgical margins, surgical time, blood losses, complications, and length of stay. The prognosis resulted worse in the patient undergoing open. Kaplan-Meier analysis indicated a difference in OS for the patients stratified by ENSAT stage (Log-rank p=0.011); we also reported a difference in DFS for patients stratified for thrombus extension (p=0.004) and ENSAT stage (p<0.001). CONCLUSION: The DFS of patients with VI from ACC is influenced by the staging and the extension of the venous invasion; the staging influences the OS. The mini-invasive approach seems feasible in selected patients; however, further studies investigating the oncological outcomes are needed. A mini-invasive approach for adrenal tumors with venous invasion is an explorable option in very selected patients.
PubMed-ID: 36625975
http://dx.doi.org/10.1007/s00423-023-02765-z

Near-Infrared Autofluorescence to Improve Visualization During Adrenal Surgery: A New Frontier for Interdisciplinary Collaboration.
World J Surg, 47(2):361-2.
J. A. Miller. 2023.
PubMed-ID: 36350364
http://dx.doi.org/10.1007/s00268-022-06820-6

Pheochromocytoma: A Story of Broken Hearts.
World J Surg, 47(2):312-3.
E. J. Kuo and J. A. Lee. 2023.
PubMed-ID: 36175649
http://dx.doi.org/10.1007/s00268-022-06751-2

Recurrent Disease in Patients With Sporadic Pheochromocytoma and Paraganglioma.
J Clin Endocrinol Metab, 108(2):397-404.
M. Li, T. Prodanov, L. Meuter, M. N. Kerstens, N. Bechmann, A. Prejbisz, H. Remde, H. Timmers, S. Nolting, S. Talvacchio, A. M. A. Berends, S. Fliedner, M. Robledo, J. W. M. Lenders, K. Pacak, G. Eisenhofer and C. Pamporaki. 2023.
CONTEXT: Long-term follow-up has been recommended for patients with pheochromocytoma or paraganglioma (PPGL) due to potential for recurrent disease. However, the need to follow patients with sporadic PPGL has recently become controversial. OBJECTIVE: To investigate the prevalence of recurrence among patients with sporadic compared with hereditary PPGL and to identify predictors of recurrence for sporadic disease. METHODS: This multicenter study included retrospective data from 1127 patients with PPGL. In addition to sex and age at primary tumor diagnosis, clinical information included location, size, and catecholamine phenotype of primary tumors, genetic test results, and subsequent development of recurrent and/or metastatic disease. Patients with sporadic PPGL were defined as those with negative genetic test results. RESULTS: Prevalence of recurrence among patients with sporadic PPGL (14.7%) was lower ($P < 0.001$) than for patients with pathogenic variants that activate pseudohypoxia pathways (47.5%), but similar to those with variants that activate kinase pathways (14.9%). Among patients with sporadic recurrent PPGL, 29.1% and 17.7% were respectively diagnosed at least 10 and 15 years after first diagnosis. Multivariable regression analysis showed that a noradrenergic/dopaminergic phenotype (HR 2.73; 95% CI, 1.553-4.802; $P < 0.001$), larger size (HR 1.82; 95% CI, 1.113-2.962; $P = 0.017$) and extra-adrenal location (HR 1.79; 95% CI, 1.002-3.187; $P = 0.049$) of primary tumors were independent predictors of recurrence in sporadic PPGL. CONCLUSION: Patients with sporadic PPGL require long-term follow-up, as supported by the 14.7% prevalence of recurrent disease, including recurrences at more than 10 years after first diagnosis. The nature of follow-up could be individualized according to tumor size, location, and biochemical phenotype.
PubMed-ID: 36190922
http://dx.doi.org/10.1210/clinem/dgac563

Genotype-Phenotype Correlations and Clinical Outcomes in 155 Cases of Pheochromocytoma and Paraganglioma.
World J Surg, 47(3):690-8.
H. Wang, A. J. Papachristos, A. J. Gill, R. Clifton-Bligh, A. M. Aniss, A. Glover, M. Sywak and S. B. Sidhu. 2023.
BACKGROUND: Pheochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumours, often associated with germline mutations that influence the disease biology and clinical course. We aimed to describe the genotypic and phenotypic characteristics of a consecutive series of PPGL patients and correlate mutation status with clinical outcomes. METHODS: We performed a retrospective cohort study of all PPGL patients who presented to a tertiary referral centre between March 2005 and February 2022. Genotypic, phenotypic and follow-up data were analysed. RESULTS: A total of 140 patients were included. Of these, 94 (67%) patients underwent genetic testing and a mutation was detected in 36 (38%) patients. Mutation presence was associated with younger age, smaller tumour size and bilateral adrenal tumours. Disease recurrence occurred at a median time of 5.4 (IQR 2.8-11.0) years after treatment in 21 (15%) patients, of which 14 (67%) had a mutation in a susceptibility gene. Recurrence pattern was influenced by mutation type; higher local recurrence risk for SDHA, SDHB, and MEN2B disease, and higher metastatic risk for SDHB, VHL and MEN2A disease. Recurrence occurred in three (3%) patients with mutation absence. Multivariate analysis revealed that age </=40 years and mutation presence were associated with increased risk of disease recurrence. CONCLUSIONS: Genotypic characteristics strongly influence disease presentation and recurrence risk, which may occur more than 5 years after initial treatment. Routine genetic testing of PPGL patients is warranted given the high prevalence of mutations, allowing for prognostication and tailored follow-up. In the presence of germline mutations, follow-up should be life-long.
PubMed-ID: 36550325
http://dx.doi.org/10.1007/s00268-022-06862-w

Differences in intraoperative and surgical outcomes between normotensive pheochromocytomas and sympathetic paragangliomas (PPGLs) and hypertensive PPGLs: results from the PHEO-RISK STUDY.
J Endocrinol Invest, 46(4):805-14.
M. Araujo-Castro, I. Garcia Sanz, C. Minguez Ojeda, M. Calatayud, F. Hanzu, M. Mora, A. Vicente, C. Blanco Carrera, P. De Miguel Novoa, M. D. C. Lopez Garcia, L. Manjon-Miguelez, P. Rodriguez de Vera, M. Del Castillo Tous, R. Barahona San Millan, M. Recasens, M. Tome Fernandez-Ladreda, N. Valdes, P. Gracia Gimeno, C. Robles Lazaro, T. Michalopoulou, C. Alvarez Escola, R. Garcia Centeno and C. Lamas. 2023.
PURPOSE: To compare the intraoperative and surgical outcomes of normotensive pheochromocytomas and sympathetic paragangliomas (PPGLs), hypertensive PPGLs and non-PPGL adrenal lesions. METHODS: This a retrospective multicenter cohort study of patients with PPGLs from 18 tertiary hospitals. A control group of histologically confirmed adrenocortical adenomas (non-PPGL group) was selected to compare intraoperative and surgical outcomes with of the normotensive PPGLs. RESULTS: Two hundred and ninety-six surgeries performed in 289 patients with PPGLs were included. Before surgery, 209 patients were classified as hypertensive PPGLs (70.6%) and 87 as normotensive PPGLs. A higher proportion of normotensive PPGLs than hypertensive PPGLs did not receive alpha presurgical blockade (P = 0.009). When we only considered those patients who received presurgical alpha blockers (200 hypertensive PPGLs and 76 normotensive PPGLs), hypertensive PPGLs had a threefold higher risk of intraoperative hypertensive crisis (OR 3.0 [95% 1.3-7.0]) and of hypotensive episodes (OR 2.9 [95% CI 1.2-6.7]) than normotensive PPGLs. When we compared normotensive PPGLs (n = 76) and non-PPGLs (n = 58), normotensive PPGLs had a fivefold higher risk of intraoperative complications (OR 5.3 [95% CI 1.9-14.9]) and a six times higher risk of postoperative complications (OR 6.1 [95% CI 1.7-21.6]) than non-PPGLs. CONCLUSION: Although the risk of intraoperative hypertensive and hypotensive episodes in normotensive PPGLs is significantly lower than in hypertensive PPGLs, normotensive PPGLs have a greater risk of intraoperative and postoperative complications than non-PPGL adrenal lesions. Therefore, it is recommended to follow the standard of care for presurgical and anesthetic management of PPGLs also in normotensive PPGLs.
PubMed-ID: 36323983
http://dx.doi.org/10.1007/s40618-022-01954-9

Laparoscopic versus robotic adrenalectomy in severely obese patients.
Surg Endosc, 37(2):1107-13.
G. Isiktas, S. N. Avci, O. Erten, O. Ergun, V. Krishnamurthy, J. Shin, A. Siperstein and E. Berber. 2023.
BACKGROUND: Over the last 20 years, the prevalence of severe obesity (body mass index >/= 35 kg/m(2)) has almost doubled. This condition increases the challenge of laparoscopic adrenalectomy (LA) by creating problems with instrument reach, adequate exposure, and visualization. The aim was to compare perioperative outcomes of laparoscopic versus robotic adrenalectomy (RA) in severely obese patients. METHODS: This was an institutional review board-approved retrospective study. Prospectively collected clinical parameters of patients who underwent LA versus RA between 2000

and 2021 at a single center were compared using Mann-Whitney U, ANOVA, Chi-square, and multivariate regression analysis. Continuous data are expressed as median (interquartile range). RESULTS: For lateral transabdominal (LT) adrenalectomies, skin-to-skin operative time (OT) [164.5 (71.0) vs 198.8 (117.0) minutes, p = 0.006] and estimated blood loss [26.2 (15.0) vs 72.6 (50.0) ml, p = 0.010] were less in RA versus LA group, respectively. Positive margin rate, hospital stay and 90-day morbidity were similar between the groups (p = NS). For posterior retroperitoneal (PR) approach, operative time and perioperative outcomes were similar between LA and RA groups. Multivariate analysis demonstrated robotic versus laparoscopic technique (p = 0.006) to be an independent predictor of a shorter OT. CONCLUSION: There was a benefit of robotic over the laparoscopic LT adrenalectomy regarding OT and estimated blood loss. Although limited by the small sample size, there was no difference regarding perioperative outcomes between RA and LA performed through a PR approach.
PubMed-ID: 36123544
http://dx.doi.org/10.1007/s00464-022-09594-z

Adrenal incidentaloma and evaluation of mass size alone as an indication for adrenalectomy: experience in a UK tertiary-care hospital.
Br J Surg, 110(4):518-9.
M. M. Gabriel, O. Prankerd Smith, J. Saada and N. A. Burgess. 2023.
PubMed-ID: 36935400
http://dx.doi.org/10.1093/bjs/znad063

Node-by-node diagnosis for multiple ipsilateral nodules by segmental adrenal venous sampling in primary aldosteronism.
Clin Endocrinol (Oxf), 98(4):487-95.
H. Tannai, K. Makita, Y. Koike, H. Kubo, K. Nakai, Y. Yamazaki, Y. Tsurutani, J. Saito, S. Matsui, Y. Kakuta, H. Sasano and T. Nishikawa. 2023.
OBJECTIVES: In patients with primary aldosteronism (PA), multiple adrenocortical nodules may be present on the surgical side. The aim of this study was to clarify the pathological diagnosis and the node-by-node diagnostic capability of segmental adrenal venous sampling (sAVS). DESIGN: Retrospective study. PATIENTS: A total of 162 patients who underwent adrenalectomy following sAVS were studied. MEASUREMENTS: Multiple nodules on the surgical side were extracted while referring to contrast-enhanced computed tomography images. We also performed a detailed histopathological analysis of the resected specimens from patients undergoing sAVS, which included immunohistochemistry for CYP11B2. RESULTS: In 11 (6.8%) patients, two to three nodules were detected on the surgical side. All patients were diagnosed by sAVS with at least one aldosterone-producing adenoma (APA) for localized aldosterone elevation in tributaries. Seven patients showed a lateralization index value of >/=4 after ACTH stimulation. Histopathologically and clinically, two patients had two or three CYP11B2-positive APAs, and the other nine patients both APAs and non-APAs. The positive predictive value of the most suspected APA, that is, the drainer that showed the highest aldosterone level by sAVS, was 11/11 (100%, 95% confidence interval [CI]: 71.5%-100%), while that for the second and third suspected APA was 3/7 (42.9%, 95% CI: 9.9%-81.6%), and they were significantly different (p = .01). Further, the positive predictive value of non-APA was 4/4 (100%, 95% CI: 39.8%-100%). CONCLUSIONS: The sAVS could correctly diagnose the aldosterone production in multiple ipsilateral adrenal nodules.
PubMed-ID: 36471563
http://dx.doi.org/10.1111/cen.14858

Pheochromocytoma recurrence in hereditary disease: does a cortical-sparing technique increase recurrence rate?
Surgery, 173(1):26-34.
A. S. Shirali, U. Clemente-Gutierrez, B. L. Huang, M. S. Lui, Y. J. Chiang, C. Jimenez, S. B. Fisher, P. H. Graham, J. E. Lee, E. G. Grubbs and N. D. Perrier. 2023.
BACKGROUND: Posterior retroperitoneoscopic adrenalectomy is an appealing approach for patients with hereditary pheochromocytoma and lends well to cortex preservation. We sought to examine pheochromocytoma recurrence in patients with hereditary pheochromocytoma in the era of posterior retroperitoneoscopic adrenalectomy and evaluate the predictors of recurrence. METHODS: Patients with hereditary pheochromocytoma who underwent adrenalectomy for pheochromocytoma between 1995 and 2020 with biochemical cure and follow-up >1 year were identified. Recurrence was defined as plasma metanephrines above the upper limit of normal with radiographic evidence of disease in the ipsilateral adrenal bed. RESULTS: Seventy-eight hereditary pheochromocytoma patients (median age = 32.4 years; 60.3% women) underwent 114 adrenalectomies for pheochromocytoma. Of these patients, 40 had multiple endocrine neoplasia

type 2A (51.3%), 10 had multiple endocrine neoplasia type B (12.8%), 17 had von Hippel-Lindau disease (21.8%), and 11 had neurofibromatosis type 1 (14.1%). Thirty-eight adrenalectomies (33.3%) were performed before the introduction of posterior retroperitoneoscopic adrenalectomy and 76 (66.7%) after. Cortical-sparing technique was performed in 62 (54.4%) adrenalectomies, with no difference in its use before and after posterior retroperitoneoscopic adrenalectomy introduction (P > .05). During a median follow-up of 80.7 months (interquartile range 43.4-151.2), 12 ipsilateral recurrences (10.5%) were identified. There was no difference in recurrence before and after the introduction of posterior retroperitoneoscopic adrenalectomy or by surgical technique or approach of the entire cohort (P > .05). Recurrence was more common in those with RET M918T mutation (23.5% vs 8.2%; P = .05). Patients with RET M918T mutations had a shorter recurrence-free survival (P = .013). On multivariate analysis, only RET M918T mutation was independently associated with an increased recurrence risk (hazard ratio = 4.30; 95% confidence interval, 1.26-14.66; P = .019). CONCLUSION: The introduction of posterior retroperitoneoscopic adrenalectomy did not influence the recurrence rate after adrenalectomy for hereditary pheochromocytoma patients. Patients with a RET M918T germline mutation are at increased risk for pheochromocytoma recurrence and may benefit from initial total adrenalectomy.
PubMed-ID: 36229248
http://dx.doi.org/10.1016/j.surg.2022.05.003

Phenoxybenzamine is no longer the standard agent used for alpha blockade before adrenalectomy for pheochromocytoma: A national study of 552 patients.
Surgery, 173(1):19-25.
E. J. Kuo, L. Chen, J. D. Wright, C. M. McManus, J. A. Lee and J. H. Kuo. 2023.
BACKGROUND: Phenoxybenzamine has been the standard agent for blockade before adrenalectomy for pheochromocytoma. However, high cost and limited availability have hampered its use. This study investigated whether other agents have supplanted the use of phenoxybenzamine as the first-line agent for alpha blockade in pheochromocytoma. METHODS: We performed a retrospective analysis of patients in the IBM MarketScan Database who underwent adrenalectomy for pheochromocytoma (2008-2019). Patients were categorized as having been blocked with phenoxybenzamine, selective alpha blockers, calcium channel blockers and/or beta blockers, or none of the above. The outcomes included prescription costs, perioperative costs, and length of stay. RESULTS: A total of 552 patients were identified; 58.7% were female, and the median age was 49 (interquartile range 40-57) years. In total, 291 (52.7%) patients were blocked with phenoxybenzamine, 114 (20.7%) with selective alpha blockers, 42 (7.6%) with only calcium channel blockers and/or beta blockers, and 76 (13.8%) with none. The proportion of patients blocked with phenoxybenzamine decreased from 71.0% in 2008 to 21.2% in 2019. The proportion of patients blocked with selective alpha blockers increased from 6.5% in 2008 to 42.4% and in 2019. The median cost of phenoxybenzamine increased from $722 (interquartile range $441-$1,514) in 2008 to $9,616 (interquartile range $5,049-$16,373) in 2019 (P < .001). Length of stay (2 [interquartile range 1-4] days vs 2 [interquartile range 0-3] days) and total perioperative costs ($24,250 [interquartile range $17,462-$33,849] vs $22,098 [interquartile range $16,341-$29,178] between phenoxybenzamine and selective alpha blocker groups were similar. CONCLUSION: There has been a significant shift away from phenoxybenzamine for preoperative blockade before resection of pheochromocytoma. Selective alpha blockers and calcium channel blockers are increasingly used, likely due to reduced costs, without compromised length of stay or intensive care unit admission.
PubMed-ID: 36167697
http://dx.doi.org/10.1016/j.surg.2022.05.039

Adrenal venous sampling for lateralization of cortisol hypersecretion in patients with bilateral adrenal masses.
Clin Endocrinol (Oxf), 98(2):177-89.
P. C. Johnson, S. M. Thompson, D. Adamo, C. J. Fleming, I. Bancos, T. J. McKenzie, J. Cheville, W. F. Young and J. C. Andrews. 2023.
OBJECTIVE: The objective of this study was to evaluate the role of adrenal venous sampling (AVS) in guiding the management of patients with corticotropin (ACTH)-independent glucocorticoid secretory autonomy and bilateral adrenal masses. DESIGN AND PATIENTS: A cohort with 25 patients underwent AVS and surgical management. MEASUREMENTS: Cortisol was measured from the adrenal veins (AVs) and inferior vena cava (IVC). AV/IVC cortisol ratio and cortisol lateralization ratio (CLR) (dominant AV cortisol concentration divided by the nondominant AV cortisol concentration) were calculated. Posthoc receiver-operating characteristic curves were generated to determine the specificity of revised AV/IVC cortisol ratio and CLR in differentiating unilateral from bilateral disease. RESULTS: Patients underwent unilateral (n = 21) or bilateral (n = 4) adrenalectomy. The mean AV/IVC cortisol ratio for unilateral adrenalectomy was 12.1 +/- 9.6 (dominant) and 4.7 +/- 3.8 (contralateral) with a mean CLR of 3.6 +/- 3.5. The mean AV/IVC cortisol ratio for bilateral adrenalectomy was 7.5 +/- 2.1, with a mean CLR of 1.1 +/- 0.6. At a mean follow-up of 22 months, one patient who underwent unilateral

adrenalectomy for the predicted bilateral disease developed recurrent mild autonomous cortisol secretion. Posthoc analyses demonstrated a specificity of 95%-100% for unilateral disease with AV/IVC cortisol ratio >9 for one side, <2.0 for the opposite side and a CLR > 2.3. The specificity was 80%-90% for bilateral disease with AV/IVC cortisol ratio >5.1 bilaterally and a CLR < 1.1. CONCLUSIONS: Among patients with bilateral adrenal masses and ACTH-independent autonomous cortisol secretion, AVS can distinguish between unilateral and bilateral disease with high specificity and may guide surgical management.
PubMed-ID: 36263687
http://dx.doi.org/10.1111/cen.14833

Unilateral Adrenalectomy for Primary Aldosteronism Due to Bilateral Adrenal Disease Can Result in Resolution of Hypokalemia and Amelioration of Hypertension.
World J Surg, 47(2):314-8.
T. Szabo Yamashita, O. A. Shariq, T. R. Foster, M. L. Lyden, B. M. Dy, W. F. Young, Jr., I. Bancos and T. J. McKenzie. 2023.
BACKGROUND: Bilateral idiopathic hyperaldosteronism (IHA) is responsible for 60% of primary aldosteronism (PA) cases. Medical management is standard of care for IHA. Unilateral adrenalectomy (UA) with the intent of debulking total aldosterone production as a palliative measure remains controversial. METHODS: Single-center retrospective review (2010-2020) of patients undergoing UA with a diagnosis of PA due to IHA (lateralization index [LI] on adrenal venous sampling [AVS] < 4). Demographic, pre-operative, intra-operative, and post-operative variables were assessed. Hypertensive regimens were converted to the WHO Defined Daily Dose (DDD). RESULTS: Twenty-four patients were identified, 14, 58% male and mean age 52 +/- 10 years. Preoperative hypokalemia was present in 22, 92% of patients. Median number of antihypertensives taken was 3 (interquartile range [IQR], 2-4) and median DDD was 4 (IQR, 3-5.3). Median lateralization index on AVS was 3.52 (range, 1.19-3.88). All operations were performed in minimally invasive fashion. There were no conversions to open procedure, ICU admissions, or post-operative complications. Median follow-up was 10.5 months (range, 1-145 months). Hypokalemia resolved in 17, 76% of patients at last follow-up. Post-operative median number of antihypertensives taken was 1 (IQR, 1-3) and median DDD was 2 (IQR, 0.5-2.75) from 4, P = 0.003. Three (%) patients required continuation of mineralocorticoid receptor antagonists post-operatively. Blood pressure control improved in 65% of patients. CONCLUSION: Unilateral adrenalectomy in the setting of bilateral hyperaldosteronism can improve blood pressure control and stabilize potassium levels in selected patients. Further prospective studies in larger cohorts will be necessary to further define the role of unilateral adrenalectomy in the setting of PA due to bilateral adrenal disease.
PubMed-ID: 36207420
http://dx.doi.org/10.1007/s00268-022-06780-x

The new robotic platform Hugo RAS for lateral transabdominal adrenalectomy: a first world report of a series of five cases.
Updates Surg, 75(1):217-25.
M. Raffaelli, P. Gallucci, N. Voloudakis, F. Pennestri, R. De Cicco, G. Arcuri, C. De Crea and R. Bellantone. 2023.
Robotic assisted surgery is the most rapidly developing field of minimally invasive surgery. Its wide diffusion has led to the development and standardization of robotic-assisted approaches also for adrenalectomy. In this study, we present the first five robotic-assisted lateral transabdominal adrenalectomies performed with the new Hugo RAS system (Medtronic, Minneapolis, MN, USA). After an official training course of the surgical team, five consecutive patients scheduled for unilateral adrenalectomy, underwent robotic-assisted operations in our institution. Patients that were candidates for partial adrenalectomy were excluded. A description of the operating theatre, robotic arms and docking setup is provided. Four female and one male patient underwent lateral transabdominal adrenalectomy, three for lesions on the left side and two on the right. Median lesion size was 3.9 cm (range: 30-90) and preoperative diagnosis was Cushing's syndrome in three patients, an adrenal cystic lesion and a pheochromocytoma. The median docking time was 5 min (range: 5-8) and the median console time was 55 min (range: 29-108). Procedures were performed without intraoperative complications and no conversions or additional ports were needed. System's function and docking were uneventful. Based on our initial experience, adrenalectomy with the Hugo system is feasible. This study provides technical notes for other centres that wish to perform robotic-assisted adrenalectomies with the Hugo RAS as well as general information and our preliminary insights on this new platform.
PubMed-ID: 36333563
http://dx.doi.org/10.1007/s13304-022-01410-6

Mitotane With or Without Cisplatin and Etoposide for Patients with a High Risk of Recurrence in Stages 1-3 Adrenocortical Cancer After Surgery.
Ann Surg Oncol, 30(2):680-2.
A. L. Sarvestani, S. N. Gregory, M. E. Teke, M. Terzolo, A. Berruti, J. M. Hernandez and M. A. Habra. 2023.
PubMed-ID: 36305989
http://dx.doi.org/10.1245/s10434-022-12725-4

Higher SUV(max) on FDG-PET is associated with shorter survival in adrenocortical carcinoma.
Am J Surg, 225(2):309-14.
S. M. Wrenn, A. L. Moore, H. J. Shah, J. A. Barletta, A. Vaidya, K. L. Kilbridge, G. M. Doherty, H. A. Jacene and M. A. Nehs. 2023.
BACKGROUND: Adrenocortical carcinoma (ACC) is an aggressive, rare malignancy. 2-deoxy-2-[18F]-fluoro-d-glucose positron emission tomography (FDG-PET) assesses tumor metabolism and glucose utilization. We hypothesized that higher maximum standard uptake value (SUV(max)) is associated with decreased survival. METHODS: We performed a retrospective analysis of patients with ACC. Included patients (n = 26) had an FDG-PET scan available with a documentable SUV(max). Patients were dichotomized into "High" (>/=8.4, n = 12) and "Low" (<8.4, n = 14) SUV(max). Univariate analysis and survival analysis were performed to compare groups. RESULTS: Demographics between groups were equivalent. The high SUV(max) cohort demonstrated lower survival (median 479 days or 15.7 months) compared to the low group (median 1490 days or 48.6 months, p = .01). Log-Rank curve confirmed differences in survival (p = .007). CONCLUSIONS: Higher SUV(max) was associated with significantly worse survival in ACC and may reflect a more aggressive phenotype. FDG-PET may provide clinically useful information to determine prognosis and treatment. Further studies should prospectively evaluate using FDG-PET/CT in ACC.
PubMed-ID: 36137821
http://dx.doi.org/10.1016/j.amjsurg.2022.08.020

Prognostic value of contralateral suppression on kidney function after surgery in patients with primary aldosteronism.
Clin Endocrinol (Oxf), 98(3):306-14.
N. Voss, S. Morup, C. Clausen, C. L. Feltoft, J. V. Jepsen, M. Hornum, M. Andreassen and J. Krogh. 2023.
BACKGROUND AND OBJECTIVE: Adrenalectomy for primary aldosteronism (PA) has been associated with decreased kidney function after surgery. It has been proposed that elimination of excess aldosterone unmasks an underlying failure of the kidney function. Contralateral suppression (CLS) is considered a marker of aldosterone excess and disease severity, and the purpose of this study was to assess the hypothesis that CLS would predict change in kidney function after adrenalectomy in patients with PA. DESIGN AND PATIENTS: Patients with PA referred for adrenal venous sampling (AVS) between May 2011 and August 2021 and who were subsequently offered surgical or medical treatment were eligible for the current study. RESULTS: A total of 138 patients were included and after AVS 85/138 (61.6%) underwent adrenalectomy while 53/138 (38.4%) were treated with MR-antagonists. In surgically treated patients the estimated glomerular filtration rate (eGFR) was reduced by 11.5 (SD: 18.5) compared to a reduction of 5.9 (SD: 11.5) in medically treated patients (p = .04). Among surgically treated patients, 59/85 (69.4%) were classified as having CLS. After adrenalectomy, patients with CLS had a mean reduction in eGFR of 17.5 (SD: 17.6) compared to an increase of 1.8 (SD: 12.8) in patients without CLS (p < .001). The association between CLS and change in kidney function remained unchanged in multivariate analysis. Post-surgery, 16/59 (27.1%) patients with CLS developed hyperkalemia compared to 2/26 (7.7%) in patients without CLS (p = .04). CONCLUSION: This retrospective study found that CLS was a strong and independent predictor of a marked reduction of eGFR and an increased risk of hyperkalemia after adrenalectomy in patients with PA.
PubMed-ID: 36263597
http://dx.doi.org/10.1111/cen.14836

Approach to the Patient With Adrenal Hemorrhage.
J Clin Endocrinol Metab, 108(4):995-1006.
Y. S. Elhassan, C. L. Ronchi, P. Wijewickrama and S. E. Baldeweg. 2023.
Adrenal hemorrhage is an uncommon, underrecognized condition that can be encountered in several clinical contexts. Diagnosing adrenal hemorrhage is challenging due to its nonspecific clinical features. Therefore, it remains a diagnosis that is made serendipitously on imaging of acutely unwell patients rather than with prospective clinical suspicion. Adrenal hemorrhage can follow abdominal trauma or appear on a background of predisposing conditions such as adrenal tumors, sepsis, or coagulopathy. Adrenal hemorrhage is also increasingly reported in patients with COVID-19 infection and in the context of vaccine-induced immune thrombocytopenia and thrombosis. Unexplained abdominal pain with hemodynamic

instability in a patient with a predisposing condition should alert the physician to the possibility of adrenal hemorrhage. Bilateral adrenal hemorrhage can lead to adrenal insufficiency and potentially fatal adrenal crisis without timely recognition and treatment. In this article, we highlight the clinical circumstances that are associated with higher risk of adrenal hemorrhage, encouraging clinicians to prospectively consider the diagnosis, and we share a diagnostic and management strategy.
PubMed-ID: 36404284
http://dx.doi.org/10.1210/clinem/dgac672

NET

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Testing the Use of Chemotherapy After Surgery for High-Risk Pancreatic Neuroendocrine Tumors.
Ann Surg Oncol, 30(3):1302-4.
C. E. Ryan, A. Saif, F. Rocha, P. Philip, J. M. Hernandez, S. Ahmad and H. Soares. 2023.
PubMed-ID: 36474095
http://dx.doi.org/10.1245/s10434-022-12906-1

Overall Survival in Patients with Stage IV Pan-NET Eligible for Liver Transplantation.
World J Surg, 47(2):340-7.
J. Kjaer, S. Smith, P. Hellman, P. Stalberg, J. Crona, S. Welin and O. Norlen. 2023.
BACKGROUND: The use of liver transplantation (LT) in patients with stage IV neuroendocrine pancreatic tumors (pan-NET) is under debate. Previous studies report a 5-year survival of 27-53% after LT in pan-NET and up to 92.7% in patients with mixed NETs. This study aimed to determine survival rates of patients with stage IV pan-NET meeting criteria for LT while only subjected to multimodal treatment. METHODS: Medical records of patients with pan-NET diagnosed from 2000 to 2021 at a tertiary referral center were evaluated for eligibility. Patients without liver metastases, who did not undergo primary tumor surgery, age > 75 years and with grade 3 tumors were excluded. The patients were divided into groups; all included patients, patients meeting the Milan, the United Network for Organ Sharing (UNOS) or the European Neuroendocrine Tumor Society (ENETS) criteria for LT. Kaplan-Meier survival analysis was used to calculate overall survival. RESULTS: Out of 519 patients with pan-NET, 41 patients were included. Mean follow-up time was 5.4 years. Overall survival was 9.3 years (95% CI 6.8-11.7), and 5-year survival was 64.7% (95% CI 48.2-81.2). Patients meeting the Milan, ENETS and UNOS criteria for LT had a 5-year survival of 64.9% (95% CI 32.2-97.6), 85.7% (95% CI 59.8-100.0) and 55.4% (95% CI 26.0-84.8), respectively. CONCLUSIONS: In patients with stage IV pan-NET, grade 1 and 2, with no extra abdominal disease, 5-year survival was 64.7% (95% CI 48.2-81.2). As these survival rates exceed previously published series of LT for pan-NET, the evidence base for this treatment is very weak.
PubMed-ID: 36175647
http://dx.doi.org/10.1245/s10434-022-12906-1

Hemicolectomy versus appendectomy for patients with appendiceal neuroendocrine tumours 1-2 cm in size: a retrospective, Europe-wide, pooled cohort study.
Lancet Oncol, 24(2):187-94.
C. Nesti, K. Brautigam, M. Benavent, L. Bernal, H. Boharoon, J. Botling, A. Bouroumeau, I. Brcic, M. Brunner, G. Cadiot, M. Camara, E. Christ, T. Clerici, A. K. Clift, H. Clouston, L. Cobianchi, J. B. Cwikla, K. Daskalakis, A. Frilling, R. Garcia-Carbonero, S. Grozinsky-Glasberg, J. Hernando, V. Hervieu, J. Hofland, P. Holmager, F. Inzani, H. Jann, P. Jimenez-Fonseca, E. Kacmaz, D. Kaemmerer, G. Kaltsas, B. Klimacek, U. Knigge, A. Kolasinska-Cwikla, W. Kolb, B. Kos-Kudla, C. A. Kunze, S. Landolfi, S. La Rosa, C. L. Lopez, K. Lorenz, M. Matter, P. Mazal, C. Mestre-Alagarda, P. M. Del Burgo, E. van Dijkum, K. Oleinikov, L. A.

Orci, F. Panzuto, M. Pavel, M. Perrier, H. M. Reims, G. Rindi, A. Rinke, M. Rinzivillo, X. Sagaert, I. Satiroglu, A. Selberherr, A. R. Siebenhuner, M. E. T. Tesselaar, M. J. Thalhammer, E. Thiis-Evensen, C. Toumpanakis, T. Vandamme, J. G. van den Berg, A. Vanoli, M. F. van Velthuysen, C. Verslype, S. A. Vorburger, A. Lugli, J. Ramage, M. Zwahlen, A. Perren and R. M. Kaderli. 2023.

BACKGROUND: Awareness of the potential global overtreatment of patients with appendiceal neuroendocrine tumours (NETs) of 1-2 cm in size by performing oncological resections is increasing, but the rarity of this tumour has impeded clear recommendations to date. We aimed to assess the malignant potential of appendiceal NETs of 1-2 cm in size in patients with or without right-sided hemicolectomy. METHODS: In this retrospective cohort study, we pooled data from 40 hospitals in 15 European countries for patients of any age and Eastern Cooperative Oncology Group performance status with a histopathologically confirmed appendiceal NET of 1-2 cm in size who had a complete resection of the primary tumour between Jan 1, 2000, and Dec 31, 2010. Patients either had an appendectomy only or an appendectomy with oncological right-sided hemicolectomy or ileocecal resection. Predefined primary outcomes were the frequency of distant metastases and tumour-related mortality. Secondary outcomes included the frequency of regional lymph node metastases, the association between regional lymph node metastases and histopathological risk factors, and overall survival with or without right-sided hemicolectomy. Cox proportional hazards regression was used to estimate the relative all-cause mortality hazard associated with right-sided hemicolectomy compared with appendectomy alone. This study is registered with ClinicalTrials.gov, NCT03852693. FINDINGS: 282 patients with suspected appendiceal tumours were identified, of whom 278 with an appendiceal NET of 1-2 cm in size were included. 163 (59%) had an appendectomy and 115 (41%) had a right-sided hemicolectomy, 110 (40%) were men, 168 (60%) were women, and mean age at initial surgery was 36.0 years (SD 18.2). Median follow-up was 13.0 years (IQR 11.0-15.6). After centralised histopathological review, appendiceal NETs were classified as a possible or probable primary tumour in two (1%) of 278 patients with distant peritoneal metastases and in two (1%) 278 patients with distant metastases in the liver. All metastases were diagnosed synchronously with no tumour-related deaths during follow-up. Regional lymph node metastases were found in 22 (20%) of 112 patients with right-sided hemicolectomy with available data. On the basis of histopathological risk factors, we estimated that 12.8% (95% CI 6.5 -21.1) of patients undergoing appendectomy probably had residual regional lymph node metastases. Overall survival was similar between patients with appendectomy and right-sided hemicolectomy (adjusted hazard ratio 0.88 [95% CI 0.36-2.17]; p=0.71). INTERPRETATION: This study provides evidence that right-sided hemicolectomy is not indicated after complete resection of an appendiceal NET of 1-2 cm in size by appendectomy, that regional lymph node metastases of appendiceal NETs are clinically irrelevant, and that an additional postoperative exclusion of metastases and histopathological evaluation of risk factors is not supported by the presented results. These findings should inform consensus best practice guidelines for this patient cohort. FUNDING: Swiss Cancer Research foundation.

PubMed-ID: 36640790
http://dx.doi.org/10.1016/S1470-2045(22)00750-1

General

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

Update on the clinical management of multiple endocrine neoplasia type 1.
Clin Endocrinol (Oxf), 97(4):409-23.
C. R. C. Pieterman and G. D. Valk. 2022.
This review provides an overview of novel insights in the clinical management of patients with Multiple Endocrine Neoplasia Type 1, focusing on the last decade since the last update of the MEN1 guidelines. With regard to Diagnosis: Mutation-negative patients with 2/3 main manifestations have a different clinical course compared to mutation-positive patients. As for primary hyperparathyroidism: subtotal parathyroidectomy is the initial procedure of choice. Current debate centres around the timing of initial parathyroidectomy as well as the controversial topic of unilateral clearance in young patients. For duodenopancreatic neuroendocrine tumours (NETs), the main challenge is accurate and individualized risk stratification to enable personalized surveillance and treatment. Thymus NETs remain one of the most aggressive MEN1-related tumours. Lung NETs are more frequent than previously thought, generally indolent, but rare aggressive cases do occur. Pituitary adenomas are most often prolactinomas and nonfunctioning microadenomas with an excellent prognosis and good response to therapy. Breast cancer is recognized as part of the MEN1 syndrome in women and periodical screening is advised. Clinically relevant manifestations are already seen at the paediatric age and initiating screening in the second decade is advisable. MEN1 has a significant impact on quality of life and US data show a significant financial burden. In conclusion, patient outcomes have improved, but much is still to be achieved. For care tailored to the needs of the individual patient and improving outcomes on an individual basis, studies are now needed to define predictors of tumour behaviour and effects of more individualized interventions.
PubMed-ID: 35319130
http://dx.doi.org/10.1111/cen.14727

Other Articles

A practical guide to genetic testing in endocrinology.
Clin Endocrinol (Oxf), 97(4):388-99.
L. Izatt, M. M. Owens, H. Pierce, S. Wilcox and S. M. Park. 2022.
Rapid advances in sequencing technology have led to significant improvements in genomic analysis, resulting in increased understanding of the molecular basis of many endocrine conditions. Genomic testing for rare disease is being integrated into everyday clinical practice, as the importance of confirming a genetic diagnosis earlier in a patient's pathway helps direct their clinical care and specialized management. In England, the new nationally commissioned Genomic Medicine Service has started to deliver testing for rare and inherited disease and cancer somatic tissue via seven Genomic Laboratory Hubs. The range of genetic tests, technology employed and eligibility criteria for patient testing are all defined in the National Genomic Test Directory. This review provides practical guidance on how to access genomic testing for endocrine disease, how to interpret and relay results, and details how genetic counselling can help integrate results into ongoing care of the individual and their family. This article discusses general principles as well as specifics related to the process of genomic testing in England. We illustrate mainstream genetic testing with a clinical scenario involving an individual with inherited endocrine neoplasia, followed by a generic description of the different steps involved, including

informed consent to proceed to diagnostic testing. Most genetic tests analyse multiple genes simultaneously by next-generation sequencing, and variant interpretation may yield not only pathogenic explanatory results, but also ambiguous outcomes, with variants of unknown significance or incidental findings. Delivery of results and posttest genetic counselling are therefore key components of integrating genetic testing into routine endocrine care.
PubMed-ID: 34528717
http://dx.doi.org/10.1111/cen.14596

Total thyroidectomy is more cost-effective than radioactive iodine as an alternative to antithyroid medication for Graves' disease.
Surgery, 173(1):193-200.
E. Z. Ma, J. H. Kuo, R. Malek, D. J. Turner, J. A. Olson, Jr., J. F. Slejko, C. D. Mullins and Y. Hu. 2023.
BACKGROUND: Patients with Graves' disease treated with radioactive iodine report worse quality of life than those treated by thyroidectomy. However, radioactive iodine is often selected due to lower risk of complications and lower cost. The objective of this study was to estimate the cost-effectiveness of radioactive iodine versus total thyroidectomy for treatment of Graves' disease. METHODS: A Markov decision-analytic model was created to simulate clinical outcomes and costs of medication-refractory Graves' disease treated with radioactive iodine or total thyroidectomy. Complication rates and utilities were derived from published data. Costs were extracted from national Medicare reimbursement rates. We conducted 1-way, 2-way, and probabilistic sensitivity analyses to identify factors that influence cost-effectiveness and reflect uncertainty in model parameters. The willingness-to-pay threshold was set at $100,000/quality-adjusted life-years. RESULTS: Total thyroidectomy yielded 23.6 quality-adjusted life-years versus 20.9 quality-adjusted life-years for radioactive iodine. The incremental cost-effectiveness ratio was $2,982 per quality-adjusted life-years, indicating that surgery is highly cost-effective relative to radioactive iodine. Surgery was more cost effective than radioactive iodine in 88.2% of model simulations. Sensitivity analyses indicate that the model outcomes are driven predominantly by posttreatment quality of life, with contributing effects from rates of treatment complications and the impact of these complications on quality of life. CONCLUSION: For patients with Graves' disease who either cannot tolerate or are refractory to antithyroid drugs, thyroidectomy is more cost-effective than radioactive iodine. Future research should validate reported differences in quality of life between these 2 treatment modalities.
PubMed-ID: 36208983
http://dx.doi.org/10.1016/j.surg.2022.06.044

Thyroid hormone replacement following lobectomy: Long-term institutional analysis 15 years after surgery.
Surgery, 173(1):189-92.
H. Barranco, J. Fazendin, B. Lindeman, H. Chen and K. M. Ramonell. 2023.
BACKGROUND: The decision to pursue lobectomy versus total thyroidectomy is highly individualized. The rate of thyroid hormone replacement therapy after lobectomy varies considerably (15%-48%) and studies are limited by short-term follow-up. We sought to assess long-term thyroid hormone replacement therapy-requirement for lobectomy. METHODS: Patients undergoing lobectomy from January 2005 to July 2010 at an academic institution were reviewed. Demographic, laboratory, pathology, and thyroid hormone replacement therapy use were compared. RESULTS: In total, 235 patients were included. The rate of thyroid hormone replacement therapy after lobectomy was 46.8% (110/235). The majority were female (84.7%), with a mean age of 52 +/- 1 years, 97% with benign pathology, and the median duration of follow-up was 7.2 years. Among the 110 thyroid hormone replacement therapy, the mean postoperative thyroid stimulating hormone level 9.08 +/- 0.96m IU/L and the time to thyroid hormone replacement therapy-initiation was 621 days; 24% started therapy >/=2 years after surgery. There was no difference in age, sex, or malignancy. Hashimoto thyroiditis was diagnosed in 21.8% patients who underwent thyroid hormone replacement therapy versus 8.0% of those without thyroid hormone replacement therapy (odds ratio 3.2; 95% confidence interval, 1.43-6.79; P < .001). On multivariate analysis, only Hashimoto thyroiditis was independently associated with thyroid hormone replacement therapy use (odds ratio 2.88; 95% confidence interval, 1.3-6.6; P = .012). CONCLUSION: With long-term follow-up, nearly 50% of patients who underwent lobectomy for benign disease required thyroid hormone replacement therapy and nearly one-quarter of these patients not starting until >/=2 years after surgery. Therefore, patients who undergo thyroid lobectomy should be counseled appropriately and thyroid function followed for a minimum of 2 years.
PubMed-ID: 36202649
http://dx.doi.org/10.1016/j.surg.2022.06.044