



ESES Review of Recently Published Literature

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

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Journals covered

Journal	IF2022	Journal	IF2022
Acta Cytol	1.8	J Bone Miner Res	6.2
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Am J Nephrol	4.2	J Clin Oncol	45.3
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J Bone Miner Metab	3.3		

Journal names are links to the journal's homepage!, IF2022: [Impact factor](#)

Thyroid

Meta-Analyses

Bilateral axillo-breast approach robotic thyroidectomy (BABA-RT) versus transoral robotic thyroidectomy (TORT): a systematic review and meta-analysis.

Updates Surg, 75(5):1277-87.

E. Albazee, A. Abdelaziz, R. Alabduhadi, D. I. Alkandari, A. Abduljabbar, S. Sulaiman, M. Alnifise, J. Ameen, H. Magzoub, K. Alomar, S. A. Maghdi and A. Abu-Zaid. 2023.

The aim of this study is to conduct a systematic review and meta-analysis of all comparative studies that evaluated the surgical outcomes between bilateral axillo-breast approach-robotic thyroidectomy (BABA-RT) and transoral robotic thyroidectomy (TORT). The Cochrane Central Register of Controlled Trials, PubMed, Scopus, and Web of Science databases were screened until July 2022. The Risk of Bias in Non-Randomized Studies for Interventions (ROBINS-I) tool was used to evaluate study quality. The data were summarized as mean difference (MD) or risk ratio (RR) with 95% confidence interval (CI) in a fixed-effects or random-effects model. Five comparative observational studies met the inclusion criteria comprising 923 patients (TORT = 408 and BABA-RT = 515). The study quality varied and included low (n = 4) and moderate (n = 1) risk of bias. There was no significant difference between both groups regarding the mean operative time (MD = 19.98 min, 95% CI [-11.33, 51.28], p = 0.21), mean hospital stay (MD = -0.14 days, 95% CI [-0.66, 0.38], p = 0.60), mean number of retrieved lymph nodes (MD = 0.42, 95% CI [-0.16, 0.99], p = 0.16), and rate of recurrent laryngeal nerve injury (RR = 0.39, 95% CI [0.13, 1.19], p = 0.10). However, the TORT group had significantly reduced mean postoperative pain score (MD = -0.39, 95% CI [-0.51, -0.26], p < 0.001) and lower rate of hypocalcemia (RR = 0.08, 95% CI [0.02, 0.26], p < 0.001) than the BABA-RT group. TORT and BABA-RT have comparable surgical outcomes. Both methods are largely safe and effective when patients are carefully chosen. However, TORT appears to offer better results regarding postoperative pain and hypocalcemia. Further clinical trials with extended follow-up periods are needed to confirm our findings.

PubMed-ID: [37193851](#)

DOI: [10.1007/s13304-023-01539-y](#)

Total vs less than total thyroidectomy for benign multinodular non-toxic goiter: an updated systematic review and meta-analysis.

Langenbecks Arch Surg, 408(1):200.

S. Bharath, S. K. Yadav, D. Sharma, C. K. Jha, A. Mishra, S. K. Mishra and S. Shekhar. 2023.

BACKGROUND: We have performed an updated meta-analysis of randomized controlled trials (RCT) comparing total thyroidectomy (TT) with less than total thyroidectomy (LTT) for benign multinodular non-toxic goiter (BMNG).

OBJECTIVES: The objective was to evaluate the effects and outcomes of TT as compared to LTT. **METHODS:** Eligibility criteria: RCTs comparing TT vs LTT. **INFORMATION SOURCES:** PubMed, Embase, Cochrane Library and online registers were searched for articles comparing TT with LTT. **Risk of bias:** Articles were assessed for risk of bias using the Cochrane's revised tool to assess risk of bias in randomized trials (RoB 2 tool). **SYNTHESIS OF RESULTS:** The main summary measures were risk difference using a random effects model. **RESULTS:** Five randomized controlled trials were included in the meta-analysis. Recurrence rate was lower for TT compared to LTT. Adverse events like temporary or permanent recurrent laryngeal nerve (RLN) palsy and permanent hypoparathyroidism were similar in both groups except for the rate of temporary hypoparathyroidism which was lower in the LTT group. **DISCUSSION:** All studies had unclear risk of bias for blinding of the participants and personnel and high risk of bias for certain selective reporting. This meta-analysis did not show any clear benefit or harm of either procedure (TT vs LTT) for goiter recurrence and re-operation rates (for both recurrence and incidental thyroid cancer). However, re-operation for goiter recurrence was significantly higher in the LTT group based on a single RCT. Evidence suggests increased rates of temporary hypoparathyroidism with TT but there was no difference in the rate of RLN palsy and permanent hypoparathyroidism between the two methods. The overall quality of evidence was low to moderate.

PubMed-ID: [37204607](#)

DOI: [10.1007/s00423-023-02941-1](#)

Locoregional strategies to decrease postoperative pain and neck discomfort after open thyroidectomy: A scoping review.

Head Neck, 45(7):1841-55.

A. Sanabria, C. Betancourt, C. Chiesa-Estomba, A. Coca-Pelaz, E. Florek, O. Guntinas-Lichius, F. Lopez, A. A. Makitie, I. J. Nixon, G. Randolph, A. Rinaldo, J. P. Rodrigo, A. R. Shaha, R. P. Tufano, M. Zafereo and A. Ferlito. 2023. Adequate pain control enhances patients' quality of life and allows a quick return to normal activities. Current pain management practices may contribute to the crisis of opioid addiction. We summarize the evidence that evaluates locoregional interventions to decrease pain and neck discomfort after thyroidectomy. We designed a scoping review. The search strategy was made in the Pubmed/MEDLINE and EMBASE database. We included only systematic reviews and RCTs that compared two or more strategies. Forty-nine publications including 5045 patients fulfilled criteria. Sore throat frequency is higher for endotracheal intubation and topical administration of anesthetic before intubation decreases this. Pre-incisional infiltration of the surgical wound decreases postoperative pain. Bilateral superficial plexus nerve block decreases analgesic requirements during and after thyroidectomy. Wound massage and neck exercises decrease postoperative discomfort. Locoregional interventions significantly impact postoperative pain and may reduce opioid use and improve patient outcomes.

PubMed-ID: [37163465](#)

DOI: [10.1002/hed.27392](#)

Randomized controlled trials

- None -

Consensus Statements/Guidelines

Thyroglobulin and thyroglobulin antibody: an updated clinical and laboratory expert consensus.

Eur J Endocrinol, 189(2):R11-R27.

L. Giovannella, F. D'Aurizio, A. Algeciras-Schimmich, R. Gorges, P. Petranovic Ovcaricek, R. M. Tuttle, W. E. Visser, F. A. Verburg, hsTg and G. TgAb Consensus Working. 2023.

OBJECTIVE: Thyroglobulin measurement is the cornerstone of modern management of differentiated thyroid cancer, with clinical decisions on treatment and follow-up based on the results of such measurements. However, numerous factors need to be considered regarding measurement with and interpretation of thyroglobulin assay results. DESIGN: The present document provides an integrated update to the 2013 and 2014 separate clinical position papers of our group on these issues. METHODS: Issues concerning analytical and clinical aspects of highly-sensitive thyroglobulin measurement will be reviewed and discussed based on an extensive analysis of the available literature. RESULTS: Thyroglobulin measurement remains a highly complex process with many pitfalls and major sources of interference, especially anti-thyroglobulin antibodies, need to be assessed, considered and, when necessary, dealt with appropriately. CONCLUSIONS: Our expert consensus group formulated 53 practical, graded recommendations for guidance on highly-sensitive thyroglobulin and TgAb in laboratory and clinical practice, especially valuable where current guidelines do not offer sufficient guidance.

PubMed-ID: [37625447](#)

DOI: [10.1093/ejendo/lvad109](#)

Use of liothyronine (T3) in hypothyroidism: Joint British Thyroid Association/Society for endocrinology consensus statement.

Clin Endocrinol (Oxf), 99(2):206-16.

R. Ahluwalia, S. E. Baldeweg, K. Boelaert, K. Chatterjee, C. Dayan, O. Okosieme, J. Priestley, P. Taylor, B. Vaidya, N. Zammitt and S. H. Pearce. 2023.

Persistent symptoms in patients treated for hypothyroidism are common. Despite more than 20 years of debate, the use of liothyronine for this indication remains controversial, as numerous randomised trials have failed to show a benefit of treatment regimens that combine liothyronine (T3) with levothyroxine over levothyroxine monotherapy. This consensus statement attempts to provide practical guidance to clinicians faced with patients who have persistent symptoms during thyroid hormone replacement therapy. It applies to non-pregnant adults and is focussed on care delivered within the UK National Health Service, although it may be relevant in other healthcare environments. The statement emphasises several key clinical practice points for patients dissatisfied with treatment for hypothyroidism. Firstly, it is important to establish a diagnosis of overt hypothyroidism; patients with persistent symptoms during thyroid hormone replacement but with no clear biochemical evidence of overt hypothyroidism should first have a trial without thyroid hormone replacement. In

those with established overt hypothyroidism, levothyroxine doses should be optimised aiming for a TSH in the 0.3-2.0 mU/L range for 3 to 6 months before a therapeutic response can be assessed. In some patients, it may be acceptable to have serum TSH below reference range (e.g. 0.1-0.3 mU/L), but not fully suppressed in the long term. We suggest that for some patients with confirmed overt hypothyroidism and persistent symptoms who have had adequate treatment with levothyroxine and in whom other comorbidities have been excluded, a trial of liothyronine/levothyroxine combined therapy may be warranted. The decision to start treatment with liothyronine should be a shared decision between patient and clinician. However, individual clinicians should not feel obliged to start liothyronine or to continue liothyronine medication provided by other health care practitioners or accessed without medical advice, if they judge this not to be in the patient's best interest.

PubMed-ID: [37272400](#)

DOI: [10.1111/cen.14935](#)

Other Articles

Ultrasound-Guided Ethanol Ablation as a Primary Treatment for Thyroglossal Duct Cyst: Feasibility, Characteristics, and Outcomes.

Otolaryngol Head Neck Surg, 168(6):1381-8.

D. Ahn, J. H. Kwak, G. J. Lee and J. H. Sohn. 2023.

OBJECTIVES: To evaluate the feasibility, characteristics, and outcomes of ultrasound-guided ethanol ablation (US-EA) as a primary treatment for thyroglossal duct cysts (TGDCs). **STUDY DESIGN:** Prospective case series. **SETTING:** Single center study. **METHODS:** The inclusion criteria were as follows: (i) patients with TGDC aged ≥ 18 years, (ii) benign TGDC in imaging and cytological examinations, and (iii) patients' need for nonsurgical scarless treatment. US-EA was used as the primary treatment strategy. The primary outcome variables were the volume reduction rate (VRR) and cosmetic score at the last follow-up. **RESULTS:** We enrolled 28 patients with TGDC. The median TGDC volume at baseline was 6.7 mL. The median procedure time of the US-EA was 6.5 minutes. The median volumes of the cyst aspirate and injected ethanol were 4.0 and 2.0 mL, respectively. Overall, 18, 8, and 2 patients underwent 1, 2, and 3 treatment sessions, respectively. There were no complications. The median VRR was 96.2%, and the treatment success rate was 96.4%. The World Health Organization cosmetic score decreased from 4 (baseline) to 1 (after treatment) in all patients. The subjective grade for cosmetic satisfaction was satisfactory or highly satisfactory in all patients. The VRR, treatment success rate, and the number of treatment sessions did not differ as functions of the characteristics of the TGDC, including the initial volume, septation, debris, or viscosity of the cyst fluid. **CONCLUSION:** US-EA was feasible, safe, and effective in patients with TGDC. Therefore, US-EA can be used as a primary treatment for TGDC, evading general anesthesia and surgical scar.

PubMed-ID: [36939631](#)

DOI: [10.1002/ohn.231](#)

Transoral Thyroidectomy: Initial Results of the European TOETVA Study Group.

World J Surg, 47(5):1201-8.

M. Arikan, P. Riss and T. S. G. European. 2023.

BACKGROUND: The aim of this study was to evaluate a new surgical technique by the European Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) Study Group. **METHODS:** This study included 391 patients (47 [(12%)] male and 344 [(88%)] female) who had undergone endoscopic thyroid or parathyroid surgery via the vestibular approach between February 2016 and May 2022 at nine centers. The data were analyzed with regard to complications, surgery time and specimen retrieval. **RESULTS:** Overall, 376 (96.2%) TOETVA and 15 (3.8%) transoral endoscopic parathyroidectomy vestibular approach interventions were performed with an average surgery time of 145 (+/- 61.2) minutes and 509 nerves at risk. The specimens were retrieved via a transoral vestibular and retroauricular approach in 66 (16.9%) patients and via a transaxillary approach in 8 (2%). Benign histology including Grave's disease was identified in 272 (69.6%) patients, 1 (0.3%) presented noninvasive follicular thyroid neoplasms with papillary-like nuclear features, and 103 (26.3%) showed differentiated thyroid carcinoma. Solitary parathyroid adenoma were removed in 15 (3.8%) patients. Conversion to open surgery was necessary in 13 (3.3%) and revision had to be performed in 2 (0.5%) patients. Transient recurrent laryngeal nerve palsy (RLNP) was present in 18 (4.6%) and permanent RLNP in 2 (0.5%) patients. Fifteen (3.8%) patients experienced transient hypoparathyroidism after thyroidectomy. No case of permanent hypoparathyroidism was observed. Postoperative surgical site infection occurred in 1 (0.3%) patient. Despite a higher rate of sensory and motor disorders and

skin discoloration at discharge, permanent disorders were present in only 3 (0.8%) and 16 (4.1%) patients, respectively. CONCLUSION: Our results show that transoral endoscopic surgery, performed by experienced endocrine surgeons, is a safe alternative to conventional thyroid surgery.

PubMed-ID: [36799993](#)

DOI: [10.1007/s00268-023-06932-7](#)

PMCID: PMC10070222

Levothyroxine absorption test: A therapeutic strategy for improving medication adherence.

Clin Endocrinol (Oxf), 98(5):741-2.

B. Barbar, S. Hossen, R. Quinton, A. James, P. Perros, S. Pearce, C. Napier, E. Gan, A. Mitchell and Y. H. Mamoojee. 2023.

PubMed-ID: [36854622](#)

DOI: [10.1111/cen.14902](#)

Risk factors for recurrent disease in small papillary thyroid cancers - a Swedish register-based study.

Langenbecks Arch Surg, 408(1):162.

H. Bayadsi, C. Nylen, M. Sandstrom, J. Angelsten, M. Sund and J. Hennings. 2023.

AIMS: To study the correlation between clinicopathological risk factors and the risk for intervention-requiring cancer recurrence in patients with small papillary thyroid cancers (sPTCs). MATERIALS AND METHODS: Records for 397 patients with sPTC (T1 \leq 20mm) were obtained from the Scandinavian Quality Register for Thyroid, Parathyroid and Adrenal Surgery (SQRTPA) between 2010 and 2016. Follow-up time was at least 5 years. Data regarding intervention-requiring cancer recurrence were obtained from patient medical records and analysed regarding lymph node (LN) status (N0, N1a and N1b) and recurrence. RESULTS: Age was significantly lower in the N1a and N1b groups compared to N0 (45 vs. 40.5 vs. 49 years, respectively; $p = 0.002$). Tumour size was smaller in the N1a group compared to N1b group (9 vs. 11.8 mm; $p < 0.01$). The mean number of metastatic LNs at initial surgery was higher in the N1b compared to N1a group (6.6 vs. 3; $p = 0.001$), and in the recurrent compared to the non-recurrent group (7 versus 3.9; $p < 0.01$). The recurrence rate was higher in the N1b group than the N1a and N0 groups (25% vs. 2.4% vs. 1.4%, respectively; $p = 0.001$). CONCLUSIONS: Lymph node stage N1b at diagnosis, and having five or more metastatic nodes, are strong risk factors for cancer recurrence and decreased disease-free survival in sPTC. The management of patients with sPTC should include thorough lymph node mapping for optimal treatment and individual risk stratification.

PubMed-ID: [37099203](#)

DOI: [10.1007/s00423-023-02905-5](#)

PMCID: PMC10133060

In Graves' disease, thyroid autoantibodies and ultrasound features correlate with distinctive histological features.

J Endocrinol Invest, 46(8):1695-703.

A. Brancatella, L. Torregrossa, N. Viola, D. Sgro, M. Casula, F. Basolo, G. Materazzi, M. Marino, C. Marcocci, F. Santini and F. Latrofa. 2023.

PURPOSE: Laboratory, imaging, and pathological features of Graves' disease (GD), although well characterized, have been barely correlated each other. Aim of the study was to link laboratory and ultrasound characteristics of GD with its pathological features. METHODS: We correlated laboratory and ultrasound data at the time of diagnosis in 28 consecutive GD patients who underwent thyroidectomy with their pathological features, i.e., lymphocytic infiltration and follicular hyperplasia (both classified as mild or severe). RESULTS: Thyroid volume correlated positively with the levels of FT4 ($P = 0.002$, $r(2) = 0.42$), FT3 ($P = 0.011$, $r(2) = 0.22$), autoantibodies to thyroglobulin (TgAbs) ($P = 0.016$, $r(2) = 0.32$), autoantibodies to thyroid peroxidase (TPOAbs) ($P = 0.011$, $r(2) = 0.34$) and the extent of lymphocytic infiltration ($P = 0.006$ comparing mild to severe lymphocytic infiltration) but not with the levels of autoantibodies to the thyrotropin receptor (TRAbs) and to follicular hyperplasia. Compared to subjects with mild lymphocytic infiltration, those with severe lymphocytic infiltration showed higher levels of TgAbs (316 vs 0.0 IU/mL, $P < 0.0001$) and TPOAbs (295 IU/mL vs 14 IU/mL, $P < 0.0001$) and similar levels of TRAbs (7.5 vs 13 IU/mL, $P = 0.68$). Compared to patients with mild, those with severe follicular hyperplasia had similar levels of TgAbs (76 vs 30 IU/mL, $P = 0.31$) and TPOAbs (251 IU/mL vs 45 IU/mL, $P = 0.26$) but higher levels of TRAbs (39 vs 7.2 IU/mL, $P < 0.001$). CONCLUSION: In GD, TgAbs and TPOAbs levels correlate with the extent of lymphocytic infiltration, TRAbs levels with the degree of follicular hyperplasia. Thyroid volume, the main factor influencing the severity of hyperthyroidism, is related to lymphocytic infiltration and not to follicular hyperplasia.

PubMed-ID: [36840841](#)

DOI: [10.1007/s40618-023-02044-0](#)

PMCID: PMC10348939

Thyroid cancer.

Lancet, 401(10387):1531-44.

D. W. Chen, B. H. H. Lang, D. S. A. McLeod, K. Newbold and M. R. Haymart. 2023.

The past 5-10 years have brought in a new era in the care of patients with thyroid cancer, with the introduction of transformative diagnostic and management options. Several international ultrasound-based thyroid nodule risk stratification systems have been developed with the goal of reducing unnecessary biopsies. Less invasive alternatives to surgery for low-risk thyroid cancer, such as active surveillance and minimally invasive interventions, are being explored. New systemic therapies are now available for patients with advanced thyroid cancer. However, in the setting of these advances, disparities exist in the diagnosis and management of thyroid cancer. As new management options are becoming available for thyroid cancer, it is essential to support population-based studies and randomised clinical trials that will inform evidence-based clinical practice guidelines on the management of thyroid cancer, and to include diverse patient populations in research to better understand and subsequently address existing barriers to equitable thyroid cancer care.

PubMed-ID: [37023783](#)

DOI: [10.1016/S0140-6736\(23\)00020-X](#)

Clinical characteristics and long-term outcomes for parapharyngeal metastases of well-differentiated thyroid cancer during (131) I therapy and follow-up.

Clin Endocrinol (Oxf), 99(1):92-102.

X. Z. Deng, Y. F. Shi, C. T. Shen, H. J. Song, J. Wang, Y. B. Fan, Q. Y. Luo and Z. L. Qiu. 2023.

OBJECTIVE: Parapharyngeal metastases (PPM) are rarely observed in patients with well-differentiated thyroid cancer (WDTC). Radioiodine ((131) I) therapy has been the main treatment for metastatic and recurrent DTC after thyroidectomy. This study was performed to evaluate the clinicopathological features and long-term outcomes associated with survival of patients with PPM at the end of follow-up. DESIGN: In total, 14,984 consecutive patients with DTC who underwent (131) I therapy after total or near-total thyroidectomy from 2004 to 2021 were retrospectively reviewed. Therapeutic efficacy was evaluated using the Response Evaluation Criteria in Solid Tumours v1.1 and logistic regression analysis. The disease status was determined using dynamic risk stratification. Disease-specific survival (DSS) was assessed using the Kaplan-Meier method and a Cox proportional hazards model. PATIENTS: Seventy-five patients with PPM from WDTC were enrolled in this study. Their median age at the initial diagnosis of PPM was 40.2 +/- 14.1 years, and the patients comprised 32 men and 43 women (male:female ratio, 1.00:1.34). Of the 75 patients, 43 (57.33%) presented with combined distant metastases. Fifty-seven (76.00%) patients had (131) I avidity and 18 had non-(131) I avidity. At the end of follow-up, 22 (29.33%) patients showed progressive disease. Sixteen of the 75 patients died; of the remaining 59 patients, 6 (8.00%) had an excellent response, 6 (8.00%) had an indeterminate response, 10 (13.33%) had a biochemical incomplete response, and 37 (49.33%) had a structural incomplete response. Multivariate analysis confirmed that age at initial PPM diagnosis, the maximal size of PPM, and (131) I avidity had significant effects on progressive disease of PPM lesions ($p = .03$, $p = .02$, and $p < .01$, respectively). The 5- and 10-year DSS rates were 98.49% and 62.10%, respectively. Age of ≥ 55 years at initial diagnosis of PPM and the presence of concomitant distant metastasis were independently associated with a poor prognosis ($p = .03$ and $p = .04$, respectively). CONCLUSION: The therapeutic effect for PPM was closely associated with (131) I avidity, age at initial PPM diagnosis, and maximal size of PPM at the end of follow-up. Age of ≥ 55 years at initial diagnosis of PPM and the presence of concomitant distant metastasis were independently associated with poor survival.

PubMed-ID: [37029081](#)

DOI: [10.1111/cen.14916](#)

Retroauricular Single-Site Endoscopic Thyroidectomy-A Balanced Endoscopic Approach for Thyroid Excision.

JAMA Surg, 158(5):548-9.

F. Dong, A. Yang and D. Ouyang. 2023.

This article discusses how retroauricular single-site endoscopic thyroidectomy is performed and compares it with transaxillary, transareolar, retroauricular hairline, and transoral endoscopic thyroidectomy vestibular approaches.

PubMed-ID: [36753130](#)

DOI: [10.1001/jamasurg.2022.7723](#)

A quantitative assessment of the number of disease foci in papillary thyroid cancer.

Eur J Surg Oncol, 49(7):1141-6.

N. Evans Harding, R. Simo, L. Li, P. Maniam, R. Adamson, A. Hay, B. Conn, M. Lyall and I. J. Nixon. 2023.

AIM: Multifocality is a frequent feature of papillary thyroid carcinoma (PTC). Its prognostic value is controversial although national guidelines recommend treatment intensification if present. However, multifocality is not a binary but discrete variable. This study aimed to examine the association between increasing number of foci and risk of recurrence following treatment. METHODS: 577 patients with PTC were identified with median follow-up of 61 months. Number of foci were taken from pathology reports. Log-rank test was used to assess significance. Multivariate analysis was performed and Hazard Ratios were calculated. RESULTS: Of 577 patients, 206(35%) had multifocal disease and 36(6%) recurred. 133(23%), 89(15%) and 61(11%) had 3+, 4+ or 5+ foci respectively. The 5-year RFS stratified by number of foci was 95%v93% for 2+foci ($p = 0.616$), 95%v96% for 3+foci ($p = 0.198$) and 89%v96% for 4+foci ($p = 0.022$). The presence of 4 foci was associated with an over 2-fold risk of recurrence (HR 2.296, 95% CI 1.106-4.765, $p = 0.026$) although this was not independent of TNM staging. Of the 206 multifocal patients, 31(5%) had 4+foci as their sole risk factor for treatment intensification. CONCLUSION: Although multifocality per se does not confer worse outcome in PTC, finding 4+foci is associated with worse outcome and could therefore be appropriate as a cut-off for treatment intensification. In our cohort, 5% of patients had 4+foci as a sole indication for treatment intensification, suggesting that such a cut off could impact clinical management.

PubMed-ID: [37024371](#)

DOI: [10.1016/j.ejso.2022.11.592](#)

Surgical Treatment of Hyperthyroidism Can Be Performed Safely Before a Euthyroid State is Achieved.

Thyroid, 33(6):691-6.

J. Fazendin, P. Zmijewski, A. Allahwasaya, C. McLeod, R. Akhund, A. Gillis, K. Ramonell, J. Porterfield, H. Chen and B. Lindeman. 2023.

Background: The 2016 American Thyroid Association guidelines recommend that hyperthyroid patients should be euthyroid before thyroidectomy. This recommendation is based on low-quality evidence. In this retrospective cohort study, we compare peri- and post-operative outcomes of patients with hyperthyroidism who were controlled versus uncontrolled at the time of thyroidectomy. Methods: A retrospective cohort study was performed on 275 hyperthyroidism patients at a single institution from December 2015 to November 2022. Patients were defined as hyperthyroid if they had a diagnosis of hyperthyroidism with at least one suppressed thyrotropin (TSH). Patients were considered uncontrolled if triiodothyronine or thyroxine (T4) was elevated immediately before surgery. Patient demographics, perioperative data, and postoperative outcomes were compared with Chi-square and Wilcoxon Rank Sum tests, as appropriate. Results: Of the 275 patients, 84.3% were women and 51.3% were uncontrolled at time of surgery. Controlled patients had higher median [interquartile range] TSH (0.4 [0.0, 2.4] mIU/L vs. 0.0 [0.0, 0.0] mIU/L, $p < 0.001$) and lower free T4 (fT4) (0.9 [0.7, 1.1] ng/dL vs. 3.1 [1.9, 4.4] ng/dL, $p < 0.001$), respectively. Uncontrolled patients were more likely to be diagnosed with Grave's disease (85.1% vs. 67.9%, $p < 0.001$) and to undergo surgery due to medication intolerance (12.1% vs. 6%) or history of thyroid storm (6.4% vs. 1.5%) ($p = 0.008$). Uncontrolled patients were also more likely to take a larger number of preoperative medications (2.3 vs. 1.4, $p < 0.001$). No patient in either group experienced thyroid storm precipitated by surgery. Controlled patients had shorter operative times (7.3% vs. 19.8% < 1 hour, $p < 0.014$) and decreased median estimated blood loss (15.0 [5.0, 30.0] mL vs. 20.0 [10.0, 50.0] mL, $p = 0.002$). Both groups experienced similar, low rates of postoperative complications, apart from an increase in temporary hypocalcemia in the uncontrolled group (13.4% vs. 4.7%, $p = 0.013$). Conclusion: Our study is the largest to date examining the postoperative outcomes of patients with uncontrolled hyperthyroidism who undergo thyroidectomy. Our results affirm that thyroidectomy in actively thyrotoxic patients is safe and will not precipitate thyroid storm.

PubMed-ID: [37253173](#)

DOI: [10.1089/thy.2022.0392](#)

Nomograms for Prediction of High-Volume Lymph Node Metastasis in Papillary Thyroid Carcinoma Patients.

Otolaryngol Head Neck Surg, 168(5):1054-66.

J. W. Feng, J. Ye, G. F. Qi, L. Z. Hong, J. Hu, F. Wang, S. Y. Liu and Y. Jiang. 2023.

OBJECTIVE: The coexistence rate between chronic lymphocytic thyroiditis (CLT) and papillary thyroid carcinoma (PTC) is quite high. Whether CLT influences metastatic lymph nodes remains uncertain. High-volume lymph node metastasis is recommended as an unfavorable pathological feature. We aimed to investigate risk factors for high-volume central lymph node metastasis (CLNM) and lateral lymph node metastasis (LLNM) in PTC patients. STUDY DESIGN: Retrospective cohort study. SETTING: Changzhou First People's Hospital. METHODS: Clinicopathological characteristics of 1094 PTC patients who underwent surgery in our center from January 2019 to November 2021 were analyzed. RESULTS: The number of metastatic lymph nodes in the central compartment and lateral compartment were lower in the CLT group. We demonstrated that age, BRAF V600E, shape, and the number of foci were risk factors for high-volume CLNM in patients

with CLT. For patients without CLT, sex, age, tumor size, number of foci, and margin were risk factors for high-volume CLNM. Tumor size, number of foci, location, and CLNM were all risk factors for high-volume LLNM in patients with or without CLT. Body mass index was only associated with high-volume LLNM in CLT patients. All the above factors were incorporated into nomograms, which showed perfect discriminative ability. CONCLUSION: Separate predictive systems should be used for CLT and non-CLT patients for a more accurate clinical assessment of lymph node status. Our nomograms of predicting high-volume CLNM and LLNM could facilitate risk-stratified management of PTC recurrence and treatment decisions.

PubMed-ID: [36856043](#)

DOI: [10.1002/ohn.161](#)

ASO Visual Abstract: Racial and Ethnic Disparities in Appropriate Thyroid Cancer Treatment, Before and After the Release of the 2015 American Thyroid Association Guidelines.

Ann Surg Oncol, 30(5):2940-1.

S. P. Ginzberg, J. M. Soegaard Ballester, C. J. Wirtalla, K. H. Morales, D. A. Pryma, S. J. Mandel, R. R. Kelz and H. Wachtel. 2023.

PubMed-ID: [36840865](#)

DOI: [10.1245/s10434-023-13241-9](#)

Racial and Ethnic Disparities in Appropriate Thyroid Cancer Treatment, Before and After the Release of the 2015 American Thyroid Association Guidelines.

Ann Surg Oncol, 30(5):2928-37.

S. P. Ginzberg, J. M. Soegaard Ballester, C. J. Wirtalla, K. H. Morales, D. A. Pryma, S. J. Mandel, R. R. Kelz and H. Wachtel. 2023.

BACKGROUND: The 2015 American Thyroid Association (ATA) guidelines reduced the recommended extent of therapy for low-risk thyroid cancers. Little is known about the impact of these changes on overall treatment patterns and on previously described racial/ethnic disparities in guideline-concordant care. This study aimed to assess trends in thyroid cancer care before and after release of the 2015 guidelines, with particular attention to racial/ethnic disparities.

METHODS: Patients with well-differentiated thyroid cancer were identified from the National Cancer Database (2010-2018). An interrupted time series design was used to assess trends in treatment before and after the 2015 guidelines. Appropriateness of surgical and radioactive iodine (RAI) treatment was determined based on the ATA guidelines, and the likelihood of receiving guideline-concordant treatment was compared between racial/ethnic groups. RESULTS: The study identified 309,367 patients (White 74%, Black 8%, Hispanic 9%, Asian 6%). Between 2010 and 2015, the adjusted probability of appropriate surgery was lower for Black (- 2.1%; $p < 0.001$), Hispanic (- 1.0%; $p < 0.001$), and Asian (- 2.1%; $p < 0.001$) patients than for White patients. After 2015, only Hispanic patients had a lower probability of undergoing appropriate surgical therapy (- 2.6%; $p = 0.040$). Similarly, between 2010 and 2015, the adjusted probability of receiving appropriate RAI therapy was lower for the Hispanic (- 3.6%; $p < 0.001$) and Asian (- 2.4%; $p < 0.001$) patients than for White patients. After 2015, the probability of appropriate RAI therapy did not differ between groups. CONCLUSIONS: Between 2010 and 2015, patients from racial/ethnic minority backgrounds were less likely than White patients to receive appropriate surgical and RAI therapy for thyroid cancer. After the 2015 guidelines, racial/ethnic disparities in treatment improved.

PubMed-ID: [36749501](#)

DOI: [10.1245/s10434-023-13158-3](#)

ASO Author Reflections: Achieving Equity in Thyroid Cancer Treatment-More Work Ahead.

Ann Surg Oncol, 30(5):2938-9.

S. P. Ginzberg and H. Wachtel. 2023.

PubMed-ID: [36765004](#)

DOI: [10.1245/s10434-023-13216-w](#)

Large goiters and postoperative complications: does it really matter?

Langenbecks Arch Surg, 408(1):213.

J. Gomez-Ramirez, P. C. Heras, R. A. Jimenez, L. D. J. Saez, E. Y. Pineda, C. Z. Syro and C. F. Campo. 2023.

INTRODUCTION: Thyroidectomy is one of the most commonly performed surgical procedures worldwide. Although the mortality rate is currently approaching 0%, the incidence of complications in such a frequent surgery is not insignificant. The most frequent are postoperative hypoparathyroidism, recurrent injury, and asphyxial hematoma. The size of the

thyroid gland has traditionally been considered one of the most important risk factors, but there is currently no study that analyzes it independently. The objective of this study is to analyze whether the size of the thyroid gland is an isolated risk factor for the development of postoperative complications. PATIENTS AND METHOD: A prospective review of all patients who underwent total thyroidectomy at a third-level hospital between January 2019 and December 2021 was conducted. The thyroid volume was calculated preoperatively using ultrasound and, together with the weight of the definitive piece, was correlated with the development of postoperative complications. RESULTS: One hundred twenty-one patients were included. When analyzing the incidence of complications based on the quartiles of weight and glandular volume, there were no significant differences in the incidence of transient or permanent hypoparathyroidism in any of the groups. No differences were found in terms of recurrent paralysis. No fewer parathyroid glands were visualized intraoperatively in patients with larger thyroid glands, nor did the number of them accidentally removed during surgery increase. In fact, a certain protective trend was observed with regard to the number of glands visualized and glandular size or in the relationship between thyroid volume and accidental gland removal, with no significant differences. CONCLUSION: The size of the thyroid gland has not been shown to be a risk factor for the development of postoperative complications, contrary to what has traditionally been considered.

PubMed-ID: [37247029](#)

DOI: [10.1007/s00423-023-02959-5](#)

Diagnosis and treatment of primary thyroid lymphoma from a surgical perspective: a multi-institutional study.

Langenbecks Arch Surg, 408(1):206.

C. Gonzalez-Sanchez, M. P. Salvador-Egea, E. Gluckmann-Maldonado, A. Rios, J. Martin-Fernandez, J. I. Perez-Garcia, F. Garcia-Lorenzo, B. Flores-Pastor, J. Gomez-Ramirez, J. Ortega-Serrano, S. Ros-Lopez, J. Villar-Del-Moral, D. Morales-Garcia, M. T. Gutierrez-Rodriguez, J. Domenech-Calvet, J. M. Nuno-Vazquez-Garza and G. Franch-Arcas. 2023.

PURPOSE: Surgery of primary thyroid lymphoma (PTL) has been mostly limited to diagnostic work-up. This study aimed to further study its potential role. METHODS: This was a retrospective study from a multi-institutional registry of PTL patients. Clinical, diagnostic work-up (fine needle aspiration, FNA; core needle biopsy, CoreNB), contribution of surgery (open surgical biopsy, OpenSB; thyroidectomy), histology subtype, and outcome data were evaluated. RESULTS: Some 54 patients were studied. Diagnostic work-up included FNA in 47 patients, CoreNB in 11, and OpenSB in 21. CoreNB yielded the best sensitivity (90.9%). Thyroidectomy was performed in 14 patients with other diagnosis (incidental PTL), in 4 for diagnosis and in 4 for elective treatment of PTL. Incidental PTL was associated with not performed FNA nor CoreNB (OR 52.5; P = 0.008), mucosa-associated lymphoid tissue (MALT) subtype (OR 24.3; P = 0.012), and Hashimoto's thyroiditis (OR 11.1; P = 0.032). Lymphoma-related death (10 cases) mostly occurred within the first year after diagnosis and was associated with diffuse large B-cell (DLBC) subtype (OR 10.3; P = 0.018) and older patients (OR 1.08 for every 1-year increase; P = 0.010). There was a trend towards lower mortality rate in patients receiving thyroidectomy (2/22 versus 8/32, P = 0.172). CONCLUSION: Incidental PTL accounts for most of thyroid surgery cases and are associated with incomplete diagnostic work-up, Hashimoto's thyroiditis and MALT subtype. CoreNB appears to be the best tool for diagnosis. Most of PTL deaths occurred during the first year after diagnosis and mostly related to systemic treatment. Age and DLBC subtype are poor prognostic factors.

PubMed-ID: [37221304](#)

DOI: [10.1007/s00423-023-02945-x](#)

The Tyrosine Kinase Inhibitor Lenvatinib Inhibits Anaplastic Thyroid Carcinoma Growth by Targeting Pericytes in the Tumor Microenvironment.

Thyroid, 33(7):835-48.

A. Iesato, S. Li, P. M. Sadow, M. Abbasian, A. Nazarian, J. Lawler and C. Nucera. 2023.

Background: Anaplastic thyroid carcinoma (ATC) is a rapidly fatal cancer with a median survival of a few months. Enhanced therapeutic options for durable management of ATC will rely on an understanding of genetics and the role of the tumor microenvironment. The prognosis for patients with ATC has not improved despite more detailed scrutiny of underlying tumor genetics. Pericytes in the microenvironment play a key evasive role for thyroid carcinoma (TC) cells. Lenvatinib improves outcomes in patients with radioiodine-refractory well-differentiated TC. In addition to the unclear role of pericytes in ATC, the effect and mechanism of lenvatinib efficacy on ATC have not been sufficiently elucidated. Design: We assessed pericyte enrichment in ATC. We determined the effect of lenvatinib on ATC cell growth cocultured with pericytes and in a xenograft mouse model from human BRAF(WT/V600E)-ATC-derived cells coimplanted with pericytes. Results: ATC samples were significantly enriched in pericytes compared with normal thyroid samples. BRAF(WT/V600E)-ATC-derived cells were resistant to lenvatinib treatment shown by a lack of suppression of MAPK and Akt pathways. Moreover, lenvatinib increased CD47 protein (thrombospondin-1 [TSP-1] receptor) levels over time vs. vehicle. TSP-1 levels were

downregulated upon lenvatinib at late vs. early time points. Critically, ATC cells, when cocultured with pericytes, showed increased sensitivity to this therapy and ultimately decreased number of cells. The coimplantation in vivo of ATC cells with pericytes increased ATC growth and did not downregulate TSP-1 in the microenvironment in vivo. Conclusions and Implications: Pericytes are enriched in ATC samples. Lenvatinib showed inhibitory effects on BRAF(WT/V600E)-ATC cells in the presence of pericytes. The presence of pericytes could be crucial for effective lenvatinib treatment in patients with ATC. Degree of pericyte abundance may be an attractive prognostic marker in assessing pharmacotherapeutic options. Effective durable management of ATC will rely on an understanding not only of genetics but also on the role of the tumor microenvironment.

PubMed-ID: [37171127](#)

DOI: [10.1089/thy.2022.0597](#)

PMCID: PMC10354711

Patient-Reported Outcomes in Patients with Low-Risk Papillary Thyroid Carcinoma: Cross-Sectional Study to Compare Active Surveillance and Immediate Surgery.

World J Surg, 47(5):1190-8.

H. Kazusaka, I. Sugitani, K. Toda, M. Sen, M. Saito, R. Nagaoka and Y. Yoshida. 2023.

BACKGROUND: This cross-sectional study compared patient-reported outcomes of low-risk papillary thyroid carcinoma (PTC, T1N0M0) between patients who underwent active surveillance (AS) and those who received immediate surgery, METHODS: Using the State-Trait Anxiety Inventory, Short-Form 36 version 2, and a visual analog scale for neck symptoms, 249 patients under AS and 32 patients underwent immediate surgery were compared. To match the difference in time from the onset of treatment to the survey, we conducted propensity score matching. We also investigated factors affecting anxiety in patients under AS in multiple linear regression analysis. RESULTS: In the entire group, patients under AS had significantly longer time from the onset to the survey than patients underwent immediate surgery (7.9 vs. 4.0 years). After matching, AS group showed significantly better trait anxiety and mental component summary (MCS) compared to surgery group, while surgery group showed better role-social component summary. AS group also had significantly better MCS than the Japanese norm-based score. Surgery group displayed worse neck symptoms than AS group. Among AS group, trait anxiety and time from the onset were significant predictors of state anxiety. Compared with the group with < 5 years since starting AS, the group with \geq 5 years of follow-up showed a significantly better state anxiety only in patients with better trait anxiety. CONCLUSIONS: Low-risk PTC patients under AS showed better trait anxiety and mental health than surgery group. After a certain period, the anxiety of patients under AS seems to be improved, especially in patients with better trait anxiety.

PubMed-ID: [36282283](#)

DOI: [10.1007/s00268-022-06786-5](#)

Body weight change trajectories following the treatment of hyperthyroidism: A prospective cohort study.

Clin Endocrinol (Oxf), 98(5):738-40.

A. Kyriacou, A. A. Syed, N. Sawicka-Gutaj, M. Picolos, P. Economides and A. Kyriacou. 2023.

PubMed-ID: [36574980](#)

DOI: [10.1111/cen.14873](#)

Aggressive Subtypes of Papillary Thyroid Carcinoma Smaller Than 1 cm.

J Clin Endocrinol Metab, 108(6):1370-5.

J. S. Lee, J. S. Lee, H. J. Yun, S. M. Kim, H. Chang, Y. S. Lee, H. S. Chang and C. S. Park. 2023.

CONTEXT: Tumor size is important in determining the range of surgery in papillary thyroid carcinomas (PTCs), especially those smaller than 1 cm. OBJECTIVE: We aimed to analyze the features of small PTCs with aggressive subtypes based on histological characteristics. METHODS: In this retrospective study, we reviewed the medical records of 11 570 patients with PTCs smaller than or equal to 1 cm who underwent thyroidectomy between January 2009 and December 2016. Aggressive subtypes included diffuse sclerosing, solid, tall cell, columnar cell, and hobnail subtypes. RESULTS: Among the 11 570 patients with PTCs smaller than or equal to 1 cm, 177 aggressive PTC subtypes were identified. Propensity score matching revealed 110 tumors (62.1%) with extrathyroidal extension of aggressive PTC subtypes and 451 (51.1%) nonaggressive PTC subtypes (95% CI, 0.41-0.80; $P < .001$). Metastatic central and lateral neck lymph nodes constituted 3.06 +/- 3.67 and 3.81 +/- 5.39 of aggressive PTC subtypes and 1.22 +/- 2.14 and 2.85 +/- 3.79 of nonaggressive PTC subtypes, respectively (central neck nodes: 95% CI, 1.42-2.26; $P < .001$; lateral neck nodes: 95% CI, 2.9-5.90; $P < .001$). Seven patients with aggressive PTC subtypes (3.95%) and 12 with nonaggressive PTC subtypes (1.7%) exhibited recurrence. CONCLUSION: Aggressive subtypes of small PTC tumors smaller than or equal to 1 cm exhibited more extrathyroidal

extension and neck node metastasis. This study suggests that surgeons should consider the aggressive subtypes as important factors when deciding the range of surgery in PTCs smaller than 1 cm.

PubMed-ID: [36546348](#)

DOI: [10.1210/clinem/dgac739](#)

PMCID: PMC10188299

A Prospective Study of Electromyographic Amplitude Changes During Intraoperative Neural Monitoring for Open Thyroidectomy.

World J Surg, 47(8):1971-7.

T. Lian, D. Leong, K. Ng, S. Bajenov and M. Sywak. 2023.

BACKGROUND: Intraoperative nerve monitoring (IONM) of the vagus and recurrent laryngeal nerve (RLN) enables prediction of postoperative nerve function. The underlying mechanism for loss of signal (LOS) in a visually intact nerve is poorly understood. The correlation of intraoperative electromyographic amplitude changes (EMG) with surgical manoeuvres could help identify mechanisms of LOS during conventional thyroidectomy. **METHODS:** A prospective study of consecutive patients undergoing thyroidectomy was performed with intermittent IONM using the NIM Vital nerve monitoring system. The ipsilateral vagus and RLN was stimulated, and vagus nerve signal amplitude recorded at five time points during thyroidectomy (baseline, after mobilisation of superior pole, medialisation of the thyroid lobe, before release at Ligament of Berry, end of case). RLN signal amplitude was recorded at two time points; after medialisation of the thyroid lobe (R1), and end of case (R2). **RESULTS:** A total of 100 consecutive patients undergoing thyroidectomy were studied with 126 RLN at risk. The overall rate of LOS was 4.0%. Cases without LOS demonstrated a highly significant vagus nerve median percentage amplitude drop at medialisation of the thyroid lobe (- 17.9 +/- 53.1%, $P < 0.001$), and end of case (- 16.0 +/- 47.2%, $P < 0.001$) compared to baseline. RLN had no significant amplitude drop at R2 compared to R1 ($P = 0.207$). **CONCLUSIONS:** A significant reduction in vagus nerve EMG amplitude at medialisation of the thyroid and the end of case compared to baseline indicates that stretch injury or traction forces during thyroid mobilisation are the most likely mechanism of RLN impairment during conventional thyroidectomy.

PubMed-ID: [37005926](#)

DOI: [10.1007/s00268-023-07000-w](#)

PMCID: PMC10310560

ASO Visual Abstract: Perineural Invasion in Papillary Thyroid Cancer-A Rare Indicator of Aggressive Disease.

Ann Surg Oncol, 30(6):3578-9.

J. Limberg, Y. J. Lee-Saxton, C. E. Egan, A. AlAnazi, I. Easthausen, D. Stefanova, A. Stamatiou, T. Beninato, R. Zarnegar, T. Scognamiglio, T. J. Fahey, 3rd and B. M. Finnerty. 2023.

PubMed-ID: [37052824](#)

DOI: [10.1245/s10434-023-13412-8](#)

Perineural Invasion in Papillary Thyroid Cancer: A Rare Indicator of Aggressive Disease.

Ann Surg Oncol, 30(6):3570-7.

J. Limberg, Y. J. Lee-Saxton, C. E. Egan, A. AlAnazi, I. Easthausen, D. Stefanova, A. Stamatiou, T. Beninato, R. Zarnegar, T. Scognamiglio, T. J. Fahey, 3rd and B. M. Finnerty. 2023.

BACKGROUND: Perineural invasion (PNI) is associated with aggressive tumor behavior, increased locoregional recurrence, and decreased survival in many carcinomas. However, the significance of PNI in papillary thyroid cancer (PTC) is incompletely characterized. **METHODS:** Patients diagnosed with PTC and PNI from 2010-2020 at a single, academic center were identified and matched using a 1:2 scheme to patients without PNI based on gross extrathyroidal extension (ETE), nodal metastasis, positive margins, and tumor size (+/-4 cm). Mixed and fixed effects models were used to analyze the association of PNI with extranodal extension (ENE)-a surrogate marker of poor prognosis. **RESULTS:** In total, 78 patients were included (26 with PNI, 52 without PNI). Both groups had similar demographics and ultrasound characteristics preoperatively. Central compartment lymph node dissection was performed in most patients (71%, $n = 55$), and 31% ($n = 24$) underwent a lateral neck dissection. Patients with PNI had higher rates of lymphovascular invasion (50.0% vs. 25.0%, $p = 0.027$), microscopic ETE (80.8% vs. 44.0%, $p = 0.002$), and a larger burden [median 5 (interquartile range [IQR] 2-13) vs. 2 (1-5), $p = 0.010$] and size [median 1.2 cm (IQR 0.6-2.6) vs. 0.4 (0.2-1.4), $p = 0.008$] of nodal metastasis. Among patients with nodal metastasis, those with PNI had an almost fivefold increase in ENE [odds ratio [OR] 4.9 (95% confidence interval [CI] 1.5-16.5), $p = 0.008$] compared with those without PNI. More than a quarter (26%) of all patients had either persistent or recurrent disease over follow-up (IQR 16-54 months). **CONCLUSIONS:** PNI is a rare, pathologic finding that is associated with ENE in a matched cohort. Additional investigation into PNI as a prognostic feature in PTC is warranted.

PubMed-ID: [36897419](#)

DOI: [10.1245/s10434-023-13307-8](#)

Thyroid Lobectomy for Low-Risk 1-4 CM Papillary Thyroid Cancer is not Associated with Increased Recurrence Rates in the Dutch Population with a Restricted Diagnostic Work-Up.

World J Surg, 47(5):1211-8.

J. F. Lin, P. M. Rodriguez Schaap, M. J. H. Metman, E. J. M. Nieveen van Dijkum, C. Dickhoff, T. P. Links, S. Kruijff and A. F. Engelsman. 2023.

INTRODUCTION: The 2015 American Thyroid Association guidelines recommend to de-escalate treatment such as Thyroid lobectomy instead of total thyroidectomy for 1-4 cm papillary thyroid cancer (PTC). Dutch guidelines endorse restricted work-up for thyroid incidentalomas recommending only fine needle aspiration in case of a 'palpable thyroid nodule'. This diagnostic work-up algorithm may result in the identification of less indolent PTCs and may lead to a patient population with relatively more aggressive PTCs. This study aims to retrospectively analyze recurrence rates of low-risk 1-4 cm PTC in the Netherlands. METHODS: From the national cancer registry, patients with low-risk 1-4 cm PTC between 2005 and 2015 were included for analysis. Disease free survival (DFS) and overall survival were compared between patients who underwent TT +/- RAI and TL without RAI. Post-hoc propensity score analysis was performed correcting for age, sex, T-stage, and N-stage. RESULTS: In total 901 patients were included, of which 711 (78.9%) were females, with a median follow-up of 7.7 years. TT was performed in 893 (94.8%) patients. Recurrence occurred in 23 (2.6%) patients. Multivariable analysis showed no significant correlation between extent of surgery and DFS ($p = 0.978$), or overall survival ($p = 0.590$). After propensity score matching, multivariable analysis showed no significant difference on extent of surgery and recurrence. CONCLUSION: Low-risk PTC patients with 1-4 cm tumor who underwent TL showed similar recurrence rates as those who underwent TT +/- adjuvant RAI, which suggests that TL can be sufficient in treating low-risk 1-4 cm PTC, possibly reducing morbidity of these patients in the Netherlands.

PubMed-ID: [36303039](#)

DOI: [10.1007/s00268-022-06813-5](#)

PMCID: PMC10070212

The influence of papillary features on the risk of malignancy in thyroid nodules diagnosed as atypia of undetermined significance or follicular lesion of undetermined significance.

Am J Surg, 225(5):857-60.

A. Mashat, R. Hilzenrat, H. Masoudi, B. Walker and S. M. Wiseman. 2023.

BACKGROUND: The objective of this study was to assess the risk of malignancy in thyroid lesions that were diagnosed as AUS/FLUS when using a novel cytology subclassification system that is based on the presence or absence of papillary features. METHODS: AUS/FLUS case cytology was re-reviewed and subclassified into minor or major concern groups based upon the absence or presence of papillary features, respectively. The risk of malignancy (ROM) was calculated and compared between the two groups. Inter-pathologist agreement in case subclassification was also measured. RESULTS: The minor concern group had a 12.6% associated ROM, while the major concern group had a significantly higher ROM (58.4%), ($P < 0.001$). Based on 108 cases, the inter-pathologist agreement in case subclassification was 79%, and the kappa value was 0.47. CONCLUSIONS: The identification of papillary features significantly increases the ROM in thyroid lesions with an AUS/FLUS diagnosis.

PubMed-ID: [36872125](#)

DOI: [10.1016/j.amjsurg.2023.02.019](#)

Long-Term Outcomes of Active Surveillance and Immediate Surgery for Adult Patients with Low-Risk Papillary Thyroid Microcarcinoma: 30-Year Experience.

Thyroid, 33(7):817-25.

A. Miyauchi, Y. Ito, M. Fujishima, A. Miya, N. Onoda, M. Kihara, T. Higashiyama, H. Masuoka, S. Kawano, T. Sasaki, M. Nishikawa, S. Fukata, T. Akamizu, M. Ito, E. Nishihara, M. Hisakado, K. Kosaka, M. Hirokawa and T. Hayashi. 2023.

Background: It has been 30 years since the initiation of active surveillance (AS) for adult patients with low-risk papillary thyroid microcarcinoma (PTMC). This study compared the long-term oncological outcomes of patients who underwent AS or immediate surgery (IS). Methods: This is a retrospective review of extended follow-up data from patients enrolled in a single-center, prospective observational study in Japan. In total, 5646 patients diagnosed with low-risk PTMC at Kuma Hospital between 1993 and 2019 were enrolled in this study. Of these, 3222 patients underwent AS (AS group), whereas 2424 underwent IS (IS group). The patients were followed up regularly, at least once per year. Descriptive outcome data were presented according to the treatment group. Results: In the AS group, 124 patients (3.8%) had tumor enlargement of

>/=3 mm, and the 10- and 20-year enlargement rates were 4.7% and 6.6%, respectively. Novel lymph node metastases occurred in 27 patients (0.8%), and the 10- and 20-year nodal metastasis occurrence rates were 1.0% and 1.6%, respectively. In the IS group, 13 patients (0.5%) experienced lymph node recurrence postoperatively, and the 10- and 20-year nodal recurrence rates were 0.4% and 0.7%, respectively. Eighteen (1.4%) of the 1327 patients who underwent hemithyroidectomy experienced recurrence in the residual thyroid. The rate of lymph node metastasis was significantly higher in the AS group than in the IS group (1.1% vs. 0.4% and 1.7% vs. 0.7% at 10 and 20 years, respectively; $p = 0.009$), but the differences were small. However, the proportion of patients who underwent one or more and two or more surgeries was significantly higher in the IS group than in the AS group (100% vs. 12.3% and 1.07% vs. 0.09%, $p < 0.01$). Distant metastatic recurrence was observed in one patient after AS and conversion surgery and another after IS; however, they were alive (18.4 and 18.8 years after diagnosis, respectively). None of the patients in this study died of thyroid carcinoma. Conclusions: Long-term oncological outcomes of patients with PTMC generally did not differ clinically significantly between those undergoing AS and IS. AS is a viable initial management option for patients with low-risk PTMC.

PubMed-ID: [37166389](#)

DOI: [10.1089/thy.2023.0076](#)

PMCID: PMC10354707

A Comparison of Outcomes in Medullary Thyroid Carcinoma Patients With and Without a Preoperative Diagnosis: A Multicenter Retrospective Cohort Study.

Thyroid, 33(5):578-85.

K. Oleinikov, E. Yaakov, A. Mizrahi, D. Hirsch, N. Hirshoren, G. Bachar, E. Robenshtok, C. Benbassat, K. Atlan, I. Mizrahi, B. Nisman, O. Twito, S. Grozinsky-Glasberg and H. Mazeh. 2023.

Background: Cytological limitations pose a challenge to preoperative diagnosis of medullary thyroid carcinoma (MTC) and therefore, a significant subset of patients is only diagnosed postoperatively. The objective of this study was to investigate the impact of knowledge of a preoperative MTC diagnosis on disease management and outcomes. Methods: Multicenter, retrospective, cohort study of MTC patients treated in Israel from January 2000 to June 2021. We compared cohorts of patients according to the presence or absence of a preoperative MTC diagnosis. Results: Ninety-four patients with histologically confirmed MTC were included (mean age 56.2 +/- 14.3 years, 43% males). Fifty-three patients (56%) had a preoperative MTC diagnosis (preop-Dx group), and 41 (44%) were confirmed only postoperatively (no-Dx group). The extent of surgical resection, including completion procedures, was as follows: total thyroidectomy in 83% versus 100% ($p = 0.002$), central lymph node dissection (LND) in 46% versus 98% ($p < 0.001$), ipsilateral lateral LND in 36% versus 79% ($p < 0.001$), and contralateral lateral LND in 17% versus 28% (NS), in the no-Dx versus the preop-Dx group, respectively. Pathology confirmed a smaller median tumor size of 16 +/- 17.4 mm versus 23 +/- 14.0 mm ($p = 0.09$), a higher proportion of micro-MTC (size </=10 mm) 32% versus 15% ($p = 0.03$), and a higher rate of co-occurrence of follicular cell-derived carcinoma 24% versus 4% ($p = 0.003$), in the no-Dx compared to the preop-Dx group, respectively. The rates of extrathyroidal and extranodal tumor extension were not significantly different between the groups. At the last follow-up, the biochemical cure was attained in 55% [CI 0.38-0.71] compared to 64% [CI 0.50-0.77] of the no-Dx and the preop-Dx group, respectively ($p = 0.41$). After the exclusion of patients with micro-MTC, biochemical cure was more commonly achieved in the preop-Dx group (33% [CI 0.14-0.52] vs. 62% [CI 0.46-0.77], $p = 0.04$). Preop-Dx patients had improved overall survival compared to the no-Dx group (log-rank $p = 0.04$) over a median follow-up of 82 months (interquartile range [IQR] 30-153). Conclusions: Preoperatively, the diagnosis of MTC is often missed. An accurate preoperative diagnosis of MTC may enable guideline-concordant surgical treatment and ultimately contribute to an overall survival benefit in MTC patients.

PubMed-ID: [36792935](#)

DOI: [10.1089/thy.2022.0424](#)

ASO Visual Abstract: Selection Criteria for Completion Thyroidectomy in Follicular Thyroid Carcinoma Using Primary Tumor Size and TERT Promoter Mutational Status.

Ann Surg Oncol, 30(5):2926-7.

H. Park, J. Heo, C. S. Ki, J. H. Shin, Y. L. Oh, Y. I. Son, J. S. Kim, S. W. Kim, J. H. Chung, T. Y. Kim, T. H. Kim and J. H. Kim. 2023.

PubMed-ID: [36715856](#)

DOI: [10.1245/s10434-023-13146-7](#)

Selection Criteria for Completion Thyroidectomy in Follicular Thyroid Carcinoma Using Primary Tumor Size and TERT Promoter Mutational Status.

Ann Surg Oncol, 30(5):2916-25.

H. Park, J. Heo, C. S. Ki, J. H. Shin, Y. L. Oh, Y. I. Son, J. S. Kim, S. W. Kim, J. H. Chung, T. Y. Kim, T. H. Kim and J. H. Kim. 2023. BACKGROUND: A stepwise surgical approach with hemithyroidectomy and completion thyroidectomy was used to achieve definite characterization of follicular thyroid carcinoma (FTC). Choosing appropriate candidates for completion thyroidectomy has been controversial. OBJECTIVE: The aim of this study was to clarify the selection criteria for completion thyroidectomy using telomerase reverse transcriptase (TERT) promoter mutation. METHODS: A total of 87 FTC patients who had information about TERT promoter mutation from August 1995 to November 2020 were investigated. The cumulative risk of initial distant metastasis, disease recurrence, and cancer-specific death according to primary tumor size in each of the World Health Organization (WHO) 2017 classifications were calculated. RESULTS: Of the 87 patients, 8 (9.2%) had initial distant metastasis and 15 (17.2%) had persistent disease or developed structural recurrence. The threshold diameter for initial distant metastasis, disease recurrence, and cancer-specific death was 2 cm in minimally invasive FTC (MI-FTC) with mutant TERT (M-TERT) and in encapsulated angioinvasive FTC (EA-FTC) with M-TERT, while that in MI-FTC with wild-type TERT (WT-TERT) and EA-FTC with WT-TERT was 4 cm. The cumulative risk of initial distant metastasis, disease recurrence, and cancer-specific death according to primary tumor size in each WHO 2017 classification was significantly different only in patients with WT-TERT ($p = 0.001$, $p = 0.019$, and $p = 0.005$, respectively). CONCLUSIONS: The data suggest 2 cm as a critical threshold diameter for performance of completion thyroidectomy in MI-FTC with M-TERT and EA-FTC with M-TERT. TERT promoter mutational status can help select candidates for completion thyroidectomy.

PubMed-ID: [36637642](#)

DOI: [10.1245/s10434-022-13089-5](#)

PMCID: PMC9838536

What Is the Role of Laryngeal Reinnervation Surgery for Adults With Unilateral Vocal Fold Paralysis?

Laryngoscope, 133(6):1277-8.

P. Pillutla, K. Meenan and D. K. Chhetri. 2023.

Vocal cord paralysis can cause a hoarse voice and has many treatment options, including reinnervation of the vocal cords. Some patients have been shown to get the most benefit from reinnervation surgery. This article reviews available evidence for reinnervation surgery in adults.

PubMed-ID: [36757023](#)

DOI: [10.1002/lary.30614](#)

PMCID: PMC10175114

Clinical Evolution of Sporadic Medullary Thyroid Carcinoma With Biochemical Incomplete Response After Initial Treatment.

J Clin Endocrinol Metab, 108(8):e613-e22.

A. Prete, C. Gambale, L. Torregrossa, R. Ciampi, C. Romei, T. Ramone, L. Agate, V. Bottici, V. Cappagli, E. Molinaro, G. Materazzi, R. Elisei and A. Matrone. 2023.

CONTEXT: The clinical response after surgery is a determinant in the management of patients with medullary thyroid carcinoma (MTC). In case of excellent or structural incomplete response, the follow-up strategies are well designed. Conversely, in case of biochemical incomplete response (BiR) the management is not clearly defined. OBJECTIVE: This work aimed to evaluate the overall and per-site prevalence of structural disease detection in sporadic MTC patients with BiR and to assess the predictive value of various clinical, biochemical, and genetic features. METHODS: We evaluated data of 599 consecutive patients surgically treated for sporadic MTC (2000-2018) and followed-up at the endocrine unit of the University Hospital of Pisa. RESULTS: After a median of 5 months from surgery, 145 of 599 (24.2%) patients were classified as BiR. Structural disease was detected in 64 of 145 (44.1%), after a median time of 3.3 years. In 73.6%, structural disease was detected at a single site, prevalently cervical lymph nodes. Among several others, at the time of first evaluation after surgery, only basal calcitonin (bCTN) and stage IVa/b were independent predictive factors. Also, structural disease was more frequent in patients with shorter CTN doubling time and somatic RET mutation. CONCLUSION: In sporadic MTC patients with BiR, the risk of detection of structural disease was about 50% at 10 years. Higher bCTN levels and staging predicted the risk of detecting structural disease. According to these findings, stricter follow-up should be reserved for MTC with BiR and elevated values of bCTN and to those with an advanced stage. Long follow-up should be considered for all BiR patients since 50% of them develop structural disease within 10 years.

PubMed-ID: [36722192](#)

DOI: [10.1210/clinem/dgad061](#)

Outcomes of Thyroidectomy During the COVID-19 Pandemic: A NSQIP Analysis.

World J Surg, 47(6):1373-8.

G. Romero-Velez, S. I. Noureldine, T. A. Burneikis, P. Bletsis, M. Parmer and A. Siperstein. 2023.

BACKGROUND: The coronavirus disease 19 (COVID-19) has had a profound impact on our healthcare system. Surgery in particular faced significant challenges related to allocation of resources and equitable patient selection, resulting in a delay in non-emergent procedures. We sought to study the impact of the COVID-19 pandemic on patient outcomes after thyroidectomy. **METHODS:** This was a cross-sectional study using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database that included all thyroidectomies from 2018 to 2020. The primary outcome evaluated was surgical outcomes during 2020, the first year of the pandemic, compared to years preceding the pandemic. Factors associated with adverse postoperative outcomes during the study period were included in a multivariate analysis. **RESULTS:** The volume of thyroidectomy procedures in 2020 decreased 16.4% when compared to the preceding years. During 2020, there was a significant increase in mortality (0.14% vs. 0.07%, $p = 0.03$), unplanned intubation (0.45% vs. 0.27%, $p < 0.01$) and cardiac arrest (0.11% vs. 0.03%, $p < 0.01$), while other complications remained stable. Undergoing surgery in 2020 remained as a risk factor for mortality in a multivariate analysis (OR 2.4 95% CI 1.3-4.4). **CONCLUSION:** The first year of the COVID-19 pandemic had a significant impact on outcomes after thyroidectomy resulting in increased mortality. As the world recovers, there will likely be an increase number of patients seeking care who were unable to obtain it during the pandemic. Close attention should be placed on the outcomes which were altered during the pandemic.

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DOI: [10.1007/s00268-023-06997-4](https://doi.org/10.1007/s00268-023-06997-4)

PMCID: PMC10054183

Effect of postoperative radiotherapy for patients with differentiated thyroid cancer.

Clin Endocrinol (Oxf), 98(6):803-12.

H. Ryu, H. G. Wu, K. E. Lee, E. J. Chung, S. H. Ahn, Y. J. Park and H. S. Choi. 2023.

OBJECTIVE: We evaluated the efficacy and safety of postoperative radiotherapy (PORT) for differentiated thyroid cancer (DTC) with high risk features. **MATERIALS AND METHODS:** This retrospective study analyzed 187 patients treated for DTC from 1985 to 2019. DTC referred to nonanaplastic thyroid cancer originating from follicular cells. PORT was defined as the administration of external beam radiation to the thyroid and regional lymph nodes following surgery for initially diagnosed DTC. The patients were included in the analysis if they received PORT or exhibited any of the following features: (a) pT4 or pN1b according to the 8th American Joint Committee on Cancer, (b) poorly differentiated thyroid cancer (PDTC), or (c) unfavourable variants such as anaplastic foci and etc. After 1:1 propensity matching, a total of 108 patients were analyzed according to PORT receipt. The median follow-up duration of the matched group was 10.4 years. **RESULTS:** After matching, most of the variables became balanced, but the PORT group still had more PDTC and DTC with anaplastic foci. Radioactive iodine (RAI) was less frequently administered in the PORT group. PORT yielded a significantly higher 5-year locoregional recurrence free survival (LRFS) than the No PORT group (5-year LRFS 86.1% vs. 72.7%, $p = 0.022$), but the 10-year cancer specific survival (CSS) was similar between them (97.8% vs. 85.9%, $p = 0.122$). The multivariable analysis indicated that PORT was a favourable prognostic factor (Hazard ratio 0.3, 95% Confidence interval 0.1-0.8, $p = 0.02$) for LRFS, but not for CSS. Among 133 patients without PORT for initial disease, 39 of them received salvage surgery followed by salvage PORT. No severe toxicity after PORT was reported. **CONCLUSION:** PORT reduced locoregional recurrence in DTC patients without severe toxicity. PORT can be an effective and safe treatment to improve locoregional control in DTC with high risk features. However, further study is warranted to identify those who can benefit from PORT.

PubMed-ID: [36535908](https://pubmed.ncbi.nlm.nih.gov/36535908/)

DOI: [10.1111/cen.14865](https://doi.org/10.1111/cen.14865)

Features of mixed medullary thyroid tumors: An NCDDB analysis of clinicopathologic characteristics and survival.

Am J Surg, 226(1):53-8.

G. Sandilos, J. Lou, M. V. Butchy, J. P. Gaughan, L. Reid, F. R. Spitz, T. Beninato and M. D. Moore. 2023.

BACKGROUND: Mixed medullary-papillary thyroid carcinoma (MMPTC) and mixed medullary-follicular thyroid carcinoma (MMFTC) are rare variants with little known regarding behavior and prognosis. **METHODS:** Using the National Cancer Database (NCDDB), demographics, clinicopathologic features, treatment, and overall survival (OS) from patients with MMPTC and MMFTC were compared to more prevalent subtypes. **RESULTS:** There were 296,101 patients: 421 MMPTC (0.14%), 133 MMFTC (0.04%), 263,140 PTC (88.87%), 24,208 FTC (8.18%) and 8,199 MTC (2.77%). Compared to PTC, MMPTC and MMFTC patients were older ($p < 0.001$) with a higher Charlson-Deyo comorbidity index ($p < 0.001$). Mixed

tumors exhibited lower rates of nodal disease but more distant metastases compared to PTC ($p < 0.001$). MMPTC demonstrated lower estimated 10-year OS than PTC and FTC (76.04% vs 89.04% and 81.95%, $p < 0.001$), yet higher than MTC (70.29%, $p < 0.001$). MMFTC had a worse OS compared to all groups (63.32%, $p < 0.001$). CONCLUSION: Patients with MMFTC had significantly worse OS compared to DTC, portending a worse prognosis.

PubMed-ID: [36775791](#)

DOI: [10.1016/j.amjsurg.2023.02.006](#)

ASO Visual Abstract: Diffuse Sclerosing Papillary Thyroid Carcinoma-Clinicopathological Characteristics and Prognostic Implications in Comparison with Classic and Tall Cell Papillary Thyroid Cancer.

Ann Surg Oncol, 30(8):4771-2.

D. W. Scholfield, C. W. Fitzgerald, B. Alzumaili, A. Eagan, B. Xu, G. Martinez, R. M. Tuttle, A. R. Shaha, J. P. Shah, R. J. Wong, S. G. Patel, R. A. Ghossein and I. Ganly. 2023.

PubMed-ID: [37219658](#)

DOI: [10.1245/s10434-023-13661-7](#)

Diffuse Sclerosing Papillary Thyroid Carcinoma: Clinicopathological Characteristics and Prognostic Implications Compared with Classic and Tall Cell Papillary Thyroid Cancer.

Ann Surg Oncol, 30(8):4761-70.

D. W. Scholfield, C. W. Fitzgerald, B. Alzumaili, A. Eagan, B. Xu, G. Martinez, R. M. Tuttle, A. R. Shaha, J. P. Shah, R. J. Wong, S. G. Patel, R. A. Ghossein and I. Ganly. 2023.

BACKGROUND: The clinical behaviour and oncologic outcome of diffuse sclerosing papillary thyroid carcinoma (DS-PTC) is poorly understood. The objectives of this study were to compare the clinicopathological characteristics and oncological outcomes of DS-PTC to classic PTC (cPTC) and tall cell PTC (TC-PTC). METHODS: After institutional review board approval, 86 DS-PTC, 2,080 cPTC, and 701 TC-PTC patients treated at MSKCC between 1986 and 2021 were identified.

Clinicopathological characteristics were compared by using chi-square test. Kaplan-Meier and log rank were used to compare recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS). DS-PTC patients were propensity matched to cPTC and TC-PTC patients for further comparison. RESULTS: DS-PTC patients were younger with more advanced disease than cPTC and TC-PTC ($p < 0.05$). Lymphovascular invasion (LVI), extranodal extension, and positive margins were more common in DS-PTC ($p < 0.02$). Propensity matching confirmed more aggressive histopathological features in DS-PTC. The median number of metastatic lymph nodes was significantly greater and DS-PTC metastases were RAI avid. DS-PTC 5-year RFS was 50.4% compared with 92.4% in cPTC and 88.4% in TC-PTC ($p < 0.001$). Multivariate analysis confirmed DS-PTC as an independent prognostic factor of recurrence. Ten-year DSS for DS-PTC was 100% compared with 97.1% in cPTC and 91.1% in TC-PTC. Differentiated high-grade, thyroid carcinoma DS had more advanced T-stage and worse 5-year RFS than DS-PTC. CONCLUSIONS: DS-PTC presents with more advanced clinicopathological features than cPTC and TC-PTC. Large-volume nodal metastases and LVI are characteristic features. Almost half of patients develop recurrence despite aggressive initial management. Despite this, with successful salvage surgery DSS is excellent.

PubMed-ID: [37154968](#)

DOI: [10.1245/s10434-023-13589-y](#)

PMCID: PMC10751659

Incremental value of magnification and indocyanine green for parathyroid preservation in thyroid surgery.

Head Neck, 45(7):1753-60.

K. Shaphaba, A. Thakar, P. Sakthivel, K. Sikka, C. A. Singh, R. Kumar, A. Chandran and R. Goswami. 2023.

BACKGROUND: To assess the promise of surgical magnification and of intraoperative indocyanine green (ICG) assisted near-infrared fluorescence (NIRF) in improving parathyroid identification and viability assessment during thyroidectomy. METHODS: Prospective comparative study. Parathyroid gland identification sequentially assessed by naked eye, surgical microscopy, and by NIRF imaging following ICG administration (5 mg/IV). Parathyroid perfusion/vitality reassessed end-surgery by ICG-NIRF. RESULTS: An expected total of 104 parathyroid glands were assessed in 35 patients (17 total-thyroidectomy, 18 hemi-thyroidectomy). 54/104 (51.9%) were identified by naked eye, and sequentially greater numbers identified by microscope magnification ($n = 61$; 58.7%; $p = 0.33$), and by ICG-NIRF ($n = 72$; 69.2%; $p = 0.01$). ICG-NIRF detected additional parathyroid glands in 16/35 patients (45.7%). Confident identification of at least one parathyroid remained unachieved in 5/35 by naked eye, in 4/35 by microscopic magnification, and in no patient by ICG-NIRF. ICG-NIRF indicated end-of-surgery devascularization in 12/72 glands and informed decisions regarding gland implantation. CONCLUSION: Significantly greater parathyroid glands are identified and preserved with surgical magnification and with

ICG-NIRF. Both techniques merit routine adoption for thyroidectomy.

PubMed-ID: [37144335](#)

DOI: [10.1002/hed.27387](#)

Radioactive Iodine Therapy Decreases the Recurrence of Intermediate-Risk PTC With Low Thyroglobulin Levels.

J Clin Endocrinol Metab, 108(8):2033-41.

T. Tian, Z. Qi, S. Huang, H. Wang and R. Huang. 2023.

CONTEXT: Whether radioactive iodine therapy (RAIT) is necessary for intermediate-risk papillary thyroid cancer (PTC) after total thyroidectomy is still lacking reliable evidence, especially for patients with low postoperative thyroglobulin (Tg) levels. OBJECTIVE: This study conducted a propensity score matching (PSM) analysis to investigate whether RAIT is effective in reducing the recurrence of intermediate-risk PTC with low Tg levels. METHODS: In total, 1487 patients with intermediate-risk PTC with unstimulated Tg \leq 1 ng/mL or stimulated Tg \leq 10 ng/mL after total thyroidectomy were enrolled retrospectively. The clinicopathological characteristics were compared between the non-RAIT and RAIT groups before and after PSM (1:4 matching). The impact of RAIT on biochemical recurrence and structural recurrence was evaluated. RESULTS: Overall, 1349 (90.7%) patients underwent RAIT, and 138 (9.3%) did not. After a median follow-up time of 51 months, 30 patients presented with recurrence, including 11 structural and 19 biochemical recurrences. After PSM, the non-RAIT group had a higher rate of structural recurrence (5/138 vs 5/552, $P = .046$) and biochemical recurrence (6/138 vs 4/552, $P = .005$) than the RAIT group. Multivariate analysis showed that not receiving RAIT was an independent risk factor for structural recurrence (hazard ratio [HR] 10.572, 95% CI 2.439-45.843, $P = .002$) and biochemical recurrence (HR 16.568, 95% CI 3.670-74.803, $P < .001$). Kaplan-Meier analysis showed that the non-RAIT group had more unfavorable recurrence-free survival (structural and biochemical, all $P < .05$). CONCLUSION: RAIT could decrease the recurrence risk of intermediate-risk PTC in patients with unstimulated Tg \leq 1 ng/mL or stimulated Tg \leq 10 ng/mL. Further prospective randomized studies are needed to confirm these findings.

PubMed-ID: [36715264](#)

DOI: [10.1210/clinem/dgad045](#)

Clinical value of molecular markers as diagnostic and prognostic tools to guide treatment of thyroid cancer.

Clin Endocrinol (Oxf), 98(6):753-62.

P. Valderrabano, M. Eszlinger, P. Stewardson and R. Paschke. 2023.

OBJECTIVE: Advances in our understanding of the molecular biology of thyroid tumours is being rapidly translated into their clinical management. This review summarizes the current use of molecular testing in thyroid tumours, focusing on their usefulness as diagnostic and prognostic tools to guide treatment with consideration of present limitations. DESIGN: Considerations about molecular testing applications for the diagnosis and treatment of thyroid tumours are divided into four sections/roles: (1) evaluating cytologically indeterminate thyroid nodules; (2) guiding extent of surgery in indeterminate thyroid nodules; (3) completing histological characterization of thyroid tumours and (4) identifying actionable mutations in advanced progressive thyroid cancers. RESULTS: Genomic testing can improve the presurgical malignancy risk assessment in indeterminate thyroid nodules. However, a prior in-depth analysis of institutional quality and outcomes of sonographical, cytological and histological characterization of thyroid tumours is necessary. Presently, it remains uncertain whether knowing the molecular profile of a cytologically indeterminate thyroid nodule might be advantageous to modify the extent of initial surgery. Molecular characterization of thyroid tumours can be a valuable adjunct to morphological diagnosis in some challenging cases, such as in low-risk follicular cell-derived neoplasms, or rare tumours. Finally, as selective kinase inhibitors are available, molecular testing in locally advanced/metastatic progressive thyroid cancers should also be integrated into the institutional clinical management pathway to improve outcomes and limit toxicity. CONCLUSIONS: Molecular testing needs to be implemented into the local evidence-based clinical management thyroid nodule/cancer pathways to improve its diagnostic and prognostic value and to optimize cost-effectiveness.

PubMed-ID: [36715016](#)

DOI: [10.1111/cen.14882](#)

Thyroid surgery in the elderly: a surgical cohort.

Langenbecks Arch Surg, 408(1):254.

F. Van den Eynde, K. Van Den Heede, N. Brusselaers and S. Van Slycke. 2023.

PURPOSE: The need for thyroid surgery in the elderly is rising due to an ageing population, the liberal use of imaging studies, and the increasing prevalence of thyroid nodules and cancer with age. Data on surgical outcomes in this population are scarce and conflicting, but essential to assess safety of short-stay surgery. This study aims to compare

surgical outcomes by age. METHODS: All consecutive patients undergoing thyroid surgery from January 2010 to July 2021 in a large tertiary referral centre for endocrine surgery were included in this surgical cohort. The indication for surgery, surgical morbidity (hypocalcaemia, bleeding, recurrent laryngeal nerve (RLN) palsy), and length of hospital stay were assessed in three age groups (young: 18-64y, older: 65-74y, and the elderly: 75 years and older). RESULTS: A total of 2,030 patients (1,499 young, 370 older, and 161 elderly) were included. The indication for surgery was significantly different, with the main indications in the elderly being multinodular goitre (70.2% vs. 47.7% in young patients) and thyroid cancer (9.9% vs. 7.0%). Reintervention for bleeding was more often required in the older (4.6%) and the elderly (2.5%) patients (vs. 1.4%). There was no difference in the proportion of hypocalcaemia or RLN palsy. The length of hospital stay was significantly longer in the elderly (length of stay longer than one day 43.5% vs. 9.8%). CONCLUSION: Thyroid surgery in patients aged 75 years and older is a safe procedure with morbidity comparable to younger patients. However, the risk of reintervention for bleeding is higher, rendering ambulatory surgery not advisable. TRIAL REGISTRATION: Researchregistry6182 on October 29(th) 2020, retrospectively registered. PubMed-ID: [37386199](https://pubmed.ncbi.nlm.nih.gov/37386199/) DOI: [10.1007/s00423-023-02982-6](https://doi.org/10.1007/s00423-023-02982-6)

Redifferentiation of Differentiated Thyroid Cancer: Clinical Insights from a Narrative Review of Literature.

Thyroid, 33(6):674-81.

D. Van Nostrand, I. Veytsman, K. Kulkarni, L. Heimlich and K. D. Burman. 2023.

Background: Patients who have metastatic differentiated thyroid cancer (mDTC) frequently have negative diagnostic and/or post-therapy radioiodine scans. As a result, (131)I therapy is frequently no longer considered a therapeutic option for these patients. However, with the knowledge of genomic alterations of patients with mDTC, the use of selected agents in specific patient groups may be used with the intention to re-establish (131)I uptake (i.e., redifferentiation) and additional (131)I therapy. The objectives of this narrative review are to present definitions of related terminology, a brief overview of the molecular mechanisms of redifferentiating agents, and a narrative review of the literature for redifferentiation in patients who have radioiodine refractory mDTC. Summary: We searched multiple electronic databases and reviewed the relevant English-language literature reported after 2010. Fourteen articles were included in this narrative review. Conclusions: Preliminary data suggest that select agents may offer potential for re-establishing (131)I uptake in selected patients with radioiodine refractory mDTC (e.g., negative diagnostic and/or post-therapy radioiodine scans). These agents may also enhance uptake (e.g., uptake enhancement) in patients who have (131)I uptake in mDTC on a diagnostic and/or post-therapy radioiodine scan. As a result, this may facilitate higher absorbed dose delivered (Gy (rad)) per (131)I activity administered [GBq (mCi)]. This in turn may increase the likelihood of a better therapeutic effect for the planned administered (131)I activity or a reduction in the originally planned administered (131)I activity, while achieving the same intended therapeutic effect with potentially less untoward effects. Further studies are warranted to confirm these preliminary observations and to confirm acceptable subsequent (131)I therapy responses after redifferentiation and/or uptake enhancement.

PubMed-ID: [36792922](https://pubmed.ncbi.nlm.nih.gov/36792922/)

DOI: [10.1089/thy.2022.0632](https://doi.org/10.1089/thy.2022.0632)

Diagnostic value and cost-effectiveness of FNA-CT versus FNAC for medullary thyroid carcinoma.

Clin Endocrinol (Oxf), 98(5):709-18.

M. Wang, H. Chen, Y. Wang, J. Lei and Z. Li. 2023.

OBJECTIVE: To evaluate the diagnostic performance and cost-effectiveness of calcitonin assays in fine-needle aspiration washout fluid (FNA-CT) compared to fine-needle aspiration cytology (FNAC) for medullary thyroid carcinoma (MTC). METHODS: A total of 27,404 patients from three medical centres between January 2020 and May 2022 were screened for serum calcitonin (sCT). Of whom, 223 patients met endpoints and were enrolled for analyses. Based on sCT levels, patients were divided into two groups (group 1: $10 \text{ pg/ml} < \text{sCT} \leq 100 \text{ pg/ml}$ and group 2: $\text{sCT} > 100 \text{ pg/ml}$). The diagnostic performance and cost-effectiveness of FNA-CT and FNAC were compared. RESULTS: Most patients ($N = 25,228$; 92.1%) with thyroid nodules had normal sCT levels. In group 1, 24 and 167 nodules were diagnosed as MTC and non-MTC lesions, respectively. FNA-CT showed better performance in diagnosing MTC than FNAC in terms of sensitivity (100.0% vs. 58.3%), negative predictive value (100.0% vs. 94.3%), and overall accuracy (100.0% vs. 94.7%). In group 2, 67 and 7 nodules were diagnosed as MTC and non-MTC lesions, respectively. The diagnostic performance of FNA-CT was superior to FNAC in terms of sensitivity (100.0% vs. 64.2%), negative predictive value (100.0% vs. 22.6%), and overall accuracy (100.0% vs. 67.6%). Furthermore, analysis from the decision tree model showed that FNA-CT was a cost-effective tool for diagnosing MTC lesions. CONCLUSIONS: FNA-CT can serve as an auxiliary and cost-effective approach for patients with indeterminate sCT levels to detect occult MTC lesions. FNA-CT can be recommended for patients with $\text{sCT} > 100 \text{ pg/ml}$ to overcome the

high false-negative rate of FNAC.

PubMed-ID: [36394172](#)

DOI: [10.1111/cen.14852](#)

Construction and validation of nomograms to reduce completion thyroidectomy by predicting lymph node metastasis in low-risk papillary thyroid carcinoma.

Eur J Surg Oncol, 49(8):1395-404.

R. Wang, Z. Tang, Z. Wu, Y. Xiao, J. Li, J. Zhu, X. Zhang and J. Ming. 2023.

CONTEXT: More than 5 central lymph nodes metastases (CLNM) or lateral lymph node metastasis (LLNM) indicates a higher risk of recurrence in low-risk papillary thyroid carcinoma (PTC) and may lead to completion thyroidectomy (CTx) in patients initially undergoing lobectomy. OBJECTIVE: To screen potentially high-risk patients from low-risk patients by using preoperative and intraoperative clinicopathological features to predict lymph node status. METHODS: A retrospective analysis of 8301 PTC patients in Wuhan Union Hospital database (2009-2021) was performed according to the 2015 American Thyroid Association (ATA) and 2021 National Comprehensive Cancer Network (NCCN) guidelines, respectively. Logistic regression and best subsets regression were used to identify risk factors. Nomograms were established and externally validated using the Differentiated Thyroid Cancer in China cohort. RESULTS: More than 5 CLNM or LLNM was detected in 1648 (19.9%) patients. Two predictive models containing age, gender, maximum tumor size, free thyroxine (FT4) and palpable node (all $p < 0.05$) were established. The nomogram based on NCCN criteria showed better discriminative power and consistency with a specificity of 0.706 and a sensitivity of 0.725, and external validation indicated that 76% of potentially high-risk patients could achieve preoperative conversion of surgical strategy. CONCLUSIONS: Models based on large cohorts with good predictive performance were constructed and validated. Preoperative low-risk (T1-2N0M0) patients with age younger than 40 years, male gender, large tumor size, low FT4 and palpable nodes may be at high risk of LLNM or more than 5 CLNM, and they should receive more aggressive initial therapy to reduce CTx.

PubMed-ID: [37061404](#)

DOI: [10.1016/j.ejso.2023.03.236](#)

Patient's age with papillary thyroid cancer: Is it a key factor for cervical lymph node metastasis?

Eur J Surg Oncol, 49(7):1147-53.

W. Wang, Y. Ding, C. Meng, P. Li, N. Bai and X. Li. 2023.

BACKGROUND: Age is one of the important prognostic indicators of papillary thyroid cancer (PTC). However, the distinct metastatic patterns and prognosis of age-related lymph node metastasis (LNM) are unclear. This study aims to investigate the impact of age on LNM. METHODS: We conducted two independent cohort studies to assess age-nodal disease association using logistic regression analysis and a restricted cubic splines model. A multivariable Cox regression model was utilized to test the impact of nodal disease on cancer-specific survival (CSS) after age stratification. RESULTS: For this study, we included 7572 and 36,793 patients with PTC in Xiangya and SEER cohorts, respectively. After adjustment, advanced age was linearly associated with decreasing risk of central LNM. Patients of age ≤ 18 years (OR = 4.41, $P < 0.001$) and 19-45 years (OR = 1.97, $P = 0.002$) had a higher risk of developing lateral LNM than patients of age > 60 years in both cohorts. Furthermore, CSS is significantly reduced in N1b disease ($P < 0.001$), not N1a disease, regardless of age. The incidence of high-volume LNM (HV-LNM) was significantly higher in patients of age ≤ 18 years and 19-45 years than in those of age > 60 years ($P < 0.001$), in both cohorts. In addition, CSS was compromised in patients with PTC of age 46-60 years (HR = 1.61, $P = 0.022$) and those of age > 60 (HR = 1.40, $P = 0.021$) after developing HV-LNM. CONCLUSIONS: Patient age is significantly associated with LNM and HV-LNM. Patients with N1b disease or patients with HV-LNM of age > 45 years have significantly shorter CSS. Age can, thus, be a useful guide for determining treatment strategies in PTC.

PubMed-ID: [36863913](#)

DOI: [10.1016/j.ejso.2023.02.011](#)

Identifying and Predicting Diverse Patterns of Benign Nodule Growth.

J Clin Endocrinol Metab, 108(7):e458-e63.

P. Xiang, S. Ahmadi, A. Coleman, W. West, I. Lobon, A. Bikas, I. Landa, E. Marqusee, M. Kim, E. K. Alexander and T. Pappa. 2023.

CONTEXT: The natural history of benign thyroid nodules is typically characterized by slow growth and minimal risk of malignant transformation. Available data have, to date, been unable to elucidate the diversity of benign nodule growth patterns over time nor predictive of which patients follow which pattern. OBJECTIVE: We aimed to better define the diverse patterns of benign nodule behavior and their predictors. METHODS: We prospectively studied 389 consecutive

patients with solitary, solid, cytologically benign thyroid nodules ≥ 1 cm and follow-up ultrasound for at least 4 years. Demographic, sonographic, biochemical data were collected at initial evaluation, and subsequent growth patterns were identified over the follow-up. Predictors of growth at initial evaluation and 3 years of follow-up were defined. RESULTS: The mean (+/-SD) follow-up was 7.7 (+/-2.7) years. Three distinct growth patterns were identified: A) stagnant nodules with average growth rate < 0.2 mm/year; B) slow-growing nodules with a rate 0.2 to 1.0 mm/year; and C) fast-growing nodules increasing > 1.0 mm/year. Fast-growing nodules represented 17.2% of the cohort, and were more frequent in patients younger than 50 years (OR 2.2 [1.2-4.1], $P = 0.016$), and in larger nodules (2.0-2.9 cm, OR 3.5 [1.7-7.1], $P = 0.001$; > 3.0 cm, OR 4.4 [1.8-10.4], $P = 0.001$ vs reference 1-1.9 cm). In a multiple regression model, nodule growth at 3 years at an average growth rate over 0.2 mm/year over 3 years since initial evaluation was an independent predictor of longer-term fast nodule growth, even after adjusting for age, biological sex, TSH level, and nodule size ($P < 0.001$). CONCLUSION: The natural history of benign nodule growth is diverse, with over 80% of nodules demonstrating minimal to no growth long-term. Nearly 20% of cytologically benign nodules may exhibit a fast, continued growth pattern, which can be predicted by the 3-year growth rate pattern. These findings can help inform decision making for tailored benign nodule follow-up and monitoring.

PubMed-ID: [36625198](#)

DOI: [10.1210/clinem/dgad007](https://doi.org/10.1210/clinem/dgad007)

Concerns Over Diagnostic Accuracy of Fine-Needle Biopsy in Thyroid Nodule Diagnosis.

JAMA Surg, 158(8):889.

S. Yang, M. Tan and X. Xu. 2023.

PubMed-ID: [37043212](#)

DOI: [10.1001/jamasurg.2023.0566](https://doi.org/10.1001/jamasurg.2023.0566)

Diffuse Sclerosing Papillary Thyroid Cancer: Excellent Survival Despite Frequent Nodal Metastases.

Ann Surg Oncol, 30(8):4568.

M. W. Yeh and J. X. Wu. 2023.

PubMed-ID: [37193893](#)

DOI: [10.1245/s10434-023-13603-3](https://doi.org/10.1245/s10434-023-13603-3)

Parathyroids

Meta-Analyses

- None -

Randomized controlled trials

Calcitriol supplementation before parathyroidectomy and calcium level after surgery in parathyroid adenoma patients: a randomized controlled trial.

J Endocrinol Invest, 46(5):985-90.

R. Shahriarirad, S. M. Meshkati Yazd, A. Ardekani, A. Mokhtari Ardekani, N. Moradi and S. Nasiri. 2023.

BACKGROUND: Hypocalcemia is the most common complication after parathyroidectomy, contributing to extended hospital stays and higher hospitalization costs. The present study aimed to evaluate whether preoperative Calcitriol could help reduce hypocalcemia rates. **METHOD:** In this randomized controlled trial, we included 80 patients with primary hyperparathyroidism candidates for parathyroidectomy. The intervention group received Calcitriol 0.25 microg/day 1 week before parathyroidectomy. Baseline laboratory data, parathyroid hormone level (before, during, after 5, and 10 min of operation), calcium level (6, 24, and 48 h after operation), and clinical signs and symptoms were recorded. **RESULTS:** Of the 80 participants, 40 (mean age: 53.36 +/- 12.97) were randomized to the intervention, and 40 (mean age: 52.84 +/- 12.32) to the control group. There were no statistically significant differences in age, tumor size, gender, baseline laboratory data, intra-operative PTH, and calcium level 6 and 24 h after the operation. We observed a significantly higher calcium level in the intervention group 48 h post-operation (8.57 +/- 0.30 vs. 8.33 +/- 0.38). Also, days of hospital stay and symptomatic hypocalcemia rate were significantly lower in the intervention group. **CONCLUSION:** In patients with primary hyperparathyroidism, preoperative Calcitriol may be of value in preventing post-parathyroidectomy hypocalcemia and subsequent complications.

PubMed-ID: [36459369](https://pubmed.ncbi.nlm.nih.gov/36459369/)

DOI: [10.1007/s40618-022-01963-8](https://doi.org/10.1007/s40618-022-01963-8)

Consensus Statements/Guidelines

- None -

Other Articles

Impact of Fluoro-Choline PET/CT in Reduction in Failed Parathyroid Localization in Primary Hyperparathyroidism.

World J Surg, 47(5):1231-7.

R. Aphale, N. Damle, S. Chumber, M. Khan, R. Khadgawat, Y. Dharmashaktu, S. Agarwal and C. Bal. 2023.

INTRODUCTION: Accurate localization of the pathological parathyroid gland is a prerequisite for minimally invasive surgical management of hyperparathyroidism (HPT). Poor imaging or discordance in odd situations like ectopic adenomas, parathyroid hyperplasia, syndromic HPT results in localization dilemma thus causing failed parathyroidectomy. We studied the impact of Fluoro-Choline (FCH) PET/CT imaging in reduction in localization failure of parathyroid adenoma. **MATERIALS AND METHODS:** We did a retrospective observational study (2018-2021) of HPT among which 97 patients underwent focused parathyroidectomy (FP). All patients had undergone ultrasound imaging and 99mTc-sestaMIBI scan with early SPECT/CT (MIBI). When this preliminary imaging was doubtful or negative or multiple lesions were expected, FCH PET/CT was performed. We compared the localization accuracy of MIBI scan and FCH PET/CT with surgical outcomes as reference standard. **RESULTS:** MIBI scan showed overall lesion detection rate (LDR) of 88.65% in localization of pathological parathyroid gland in 97 patients. The addition of FCH PET/CT improved the overall lesion detection to 97.9%. The overall possible localization failure was reduced from 11.34 to 2.06% with the addition of FCH PET/CT ($p < 0.05$). Out of 97 patients of FP, 87 patients showed features of parathyroid adenoma. Single hyperplastic gland was seen in 7 patients,

lipoadenoma was seen in 1 patient and 1 patient had features suggestive of parathyroiditis on histopathology. FCH PET/CT was a useful adjunct and showed significant reduction in localization failure of parathyroid adenoma.

PubMed-ID: [36599952](#)

DOI: [10.1007/s00268-022-06866-6](#)

Approach to the Patient: Management of Parathyroid Diseases Across Pregnancy.

J Clin Endocrinol Metab, 108(6):1505-13.

N. M. Appelman-Dijkstra and S. Pilz. 2023.

Taking care of patients with parathyroid disorders during pregnancy requires consideration of the physiological fundamental changes in bone and mineral metabolism occurring in these women. Diagnostic and therapeutic procedures regarding primary hyperparathyroidism (PHPT) and hypoparathyroidism significantly differ from the nonpregnant population. PHPT should preferably be cured by parathyroidectomy before pregnancy since in women with hypercalcemic PHPT, maternal and fetal pregnancy complications seem to increase according to the degree of hypercalcemia. Parathyroidectomy, if needed during pregnancy, is preferentially performed in the second trimester. Conservative treatment is recommended for milder cases and is mainly restricted to hydration, with only limited evidence regarding drug treatment. Women with hypoparathyroidism can be informed that there are no major concerns regarding disease-associated infertility and that the risk of pregnancy complications is low if the disease is properly managed. Regular active surveillance is recommended, as requirements for calcium and active vitamin D may change during the course of pregnancy in either direction, with an overall trend for rather reduced doses. Any woman suffering from parathyroid disorders during pregnancy requires further surveillance in the postpartum period and during lactation, as there is an increased risk of hypercalcemia after delivery. Newborns of mothers with parathyroid diseases should, depending on disease severity, be carefully monitored for calcium levels in the first days (to weeks) after delivery since intrauterine exposure to hyper- or hypocalcemia may impact their postnatal regulation of calcium metabolism.

PubMed-ID: [36546344](#)

DOI: [10.1210/clinem/dgac734](#)

PMCID: PMC10188304

Pre-operative Cinacalcet Administration Reduces Immediate Post-operative Hypocalcemia Following Total Parathyroidectomy in Severe Renal Hyperparathyroidism.

World J Surg, 47(8):1986-94.

M. M. Fung, D. S. Tam, D. T. Lui and B. H. Lang. 2023.

BACKGROUND: In severe renal hyperparathyroidism (RHPT), whether administering Cinacalcet before total parathyroidectomy can reduce post-operative hypocalcemia remains unclear. We compared post-operative calcium kinetics between those who took Cinacalcet before surgery (Group I) and those who did not (Group II). **METHODS:** Patients with severe RHPT (defined by PTH \geq 100 pmol/L) who underwent total parathyroidectomy between 2012 and 2022 were analyzed. Standardized peri-operative protocol of calcium and vitamin D supplementation was followed. Blood tests were performed twice daily in the immediate post-operative period. Severe hypocalcemia was defined as serum albumin-adjusted calcium $<$ 2.00 mmol/L. **RESULTS:** Among 159 patients who underwent parathyroidectomy, 82 patients were eligible for analysis (Group I, $n = 27$; Group II, $n = 55$). Demographics and PTH levels before Cinacalcet administration were comparable (Group I: 169 \pm 49 pmol/L vs Group II: 154 \pm 45, $p = 0.209$). Group I had significantly lower pre-operative PTH (77 \pm 60 pmol/L vs 154 \pm 45, $p < 0.001$), higher post-operative calcium ($p < 0.05$), and lower rate of severe hypocalcemia (33.3% vs 60.0%, $p = 0.023$). Longer duration of Cinacalcet use correlated with higher post-operative calcium levels ($p < 0.05$). Cinacalcet use for > 1 year resulted in fewer severe post-operative hypocalcemia than non-users ($p = 0.022$, OR 0.242, 95% CI 0.068-0.859). Higher pre-operative ALP independently correlated with severe post-operative hypocalcemia (OR 3.01, 95% CI 1.17-7.77, $p = 0.022$). **CONCLUSION:** In severe RHPT, Cinacalcet led to significant drop in pre-operative PTH, higher post-operative calcium levels, and less frequent severe hypocalcemia. Longer duration of Cinacalcet use correlated with higher post-operative calcium levels, and the use of Cinacalcet for > 1 year reduced severe post-operative hypocalcemia.

PubMed-ID: [37140608](#)

DOI: [10.1007/s00268-023-07030-4](#)

ASO Visual Abstract: Primary Hyperparathyroidism in Young Adult Patients.

Ann Surg Oncol, 30(7):4166.

J. A. Gasior, R. R. Kelz, G. C. Karakousis, D. L. Fraker and H. Wachtel. 2023.

PubMed-ID: [37069475](#)

DOI: [10.1245/s10434-023-13401-x](#)

ASO Author Reflections: Primary Hyperparathyroidism in Young Adults-Age Alone Does Not Predict Multi-Gland Disease.

Ann Surg Oncol, 30(7):4165.

J. A. Gasior and H. Wachtel. 2023.

PubMed-ID: [37024767](#)

DOI: [10.1245/s10434-023-13407-5](#)

Revisiting Age Criterion for Surgery in Asymptomatic Primary Hyperparathyroidism.

Otolaryngol Head Neck Surg, 169(2):309-16.

G. Horowitz, M. Leshno, E. Izkhakov, D. Halpern, N. Muhanna, Y. Greenman, O. J. Ungar, N. N. Carmel-Neidermann, L. Kampel and A. Warshavsky. 2023.

OBJECTIVE: To revisit the current age criterion (50 years) for surgical candidacy in patients diagnosed with asymptomatic primary hyperparathyroidism (PHPT). STUDY DESIGN: A predictive model relying on past publications using the electronic databases "PubMed," "Embase," "Medline," and "Google Scholar." SETTING: Hypothetical large cohort. METHODS: A Markov model was constructed, based on relevant literature, to compare 2 potential treatment algorithms for asymptomatic PHPT patients, parathyroidectomy (PTX), and observation. The various potential health states were characterized for the 2 treatment options and included potential surgical complications, end-organ deterioration, and death. A 1-way sensitivity analysis was performed to calculate the quality-adjusted life year (QALY) gains of both strategies. A Monte-Carlo simulation for 30,000 subjects was performed and cycled per annum. RESULTS: On the basis of the model's assumptions, the QALY value for the PTX strategy was 19.17 versus 17.82 for the observation strategy. The incremental QALY gains for various ages according to the sensitivity analyses for PTX in comparison to observation were: 2.84 QALY for 40-year-old patients, 2.2 QALY for 50-year-old patients, 1.81 QALY for 55-year-old patients, 1.35 QALY for 60-year-old patients, and 0.86 QALY for 65-year-old patients. The incremental QALY is below 0.5 after the age of 75 years. CONCLUSION: This study found PTX to be advantageous for asymptomatic PHPT patients older than the current age criterion of 50 years. The calculated QALY gains support a surgical approach for medically fit patients in their 50s. The current guidelines for the surgical treatment of young asymptomatic PHPT patients should be revisited by the next steering committee.

PubMed-ID: [36808632](#)

DOI: [10.1002/ohn.298](#)

Clinical characteristics of primary parathyroid adenoma and its relationship with coexisting papillary thyroid carcinoma: a clinical retrospective study.

Gland Surg, 12(5):577-85.

L. Hu, B. Qian, K. Bing, L. Mei and X. Qu. 2023.

BACKGROUND: Parathyroid adenoma (PA) is a common but relatively poorly understood endocrine tumor. A significant number of PA patients also have papillary thyroid carcinoma (PTC). The clinicopathological characteristics of PA and its relationship with PTC need further study. METHODS: The clinical data of 99 PA patients were reviewed and the clinicopathologic features of PA were analyzed. PTC occurred in 22 PA patients. The clinicopathologic features of 22 patients with PA + PTC and 77 patients with PA alone were compared. According to age, gender and thyroid surgery methods, 22 PA + PTC patients were matched with 1,123 patients with PTC alone during the same period. The pathological characteristics of the two groups of patients were compared. All data analysis was performed using SPSS23.0, variables were compared by t-test, chi square test or Mann Whitney U-test as appropriate. RESULTS: Ninety-nine PA patients (21 males, 78 females) with a median age of 51 [10-80] years were included. The preoperative parathyroid hormone (PTH) (P=0.007) and preoperative blood calcium (P=0.036) of male patients were higher than those of female patients, and the proportion of asymptomatic patients (P=0.008) and postoperative PTH level (P=0.013) were lower. The preoperative PTH level (P=0.002), preoperative blood calcium level (P=0.004), preoperative alkaline phosphatase (ALP) level (P=0.018) and postoperative PTH levels (P=0.023) in PA + PTC group were lower than those in PA group. The asymptomatic rate was higher in PTC + PA group than that in PA group (P<0.001). There was no statistical difference between PA + PTC group and PTC group in multifocal tumor, capsule invasion, lymph node metastasis (P>0.05). The lymph node metastasis rate in PA + PTC group (9/215) was significantly lower than that in PTC group (37/337) (P=0.005). CONCLUSIONS: PA exhibited the following characteristics: occurred in all age groups; more common in women but more severe in men; more located in the lower pole. The coexistence of PTC and PA did not promote the progression of PA, nor did it increase the

aggressiveness of PTC. Conversely, their co-existence may lead to early diagnosis of the disease. PA patients (22.2%) also have PTC, so surgeons should pay attention to thyroid disease to prevent the need for reoperation.

PubMed-ID: [37284718](#)

DOI: [10.21037/gc-22-635](#)

PMCID: PMC10240434

FCH-PET/CT in Primary Hyperparathyroidism With Discordant/Negative MIBI Scintigraphy and Ultrasonography.

J Clin Endocrinol Metab, 108(8):1958-67.

E. Koumakis, M. Gauthe, A. Martinino, R. Sindayigaya, T. Delbot, M. Wartski, J. Clerc, C. Roux, D. Borderie, B. Cochand-Priollet, C. Cormier and S. Gaujoux. 2023.

CONTEXT: The contribution of [18F]F-fluorocholine (FCH)-positron emission tomography (PET)/computed tomography (CT) in normocalcemic primary hyperparathyroidism (nPHPT) remains unknown. OBJECTIVE: To evaluate the sensitivity and specificity of FCH-PET/CT in a cohort of osteoporotic patients with nPHPT and discordant or negative [99mTc]Tc-sestamibi scintigraphy and ultrasonography who all underwent parathyroidectomy (PTX). DESIGN: Longitudinal retrospective cohort study in patients referred for osteoporosis with mild biological primary hyperparathyroidism. SETTING: Tertiary referral center with expertise in bone metabolism and surgical management of hyperparathyroidism. PATIENTS: Among 109 patients with PHPT analyzed, 3 groups were individualized according to total serum calcium (tCa) and ionized calcium (iCa): 32 patients with hypercalcemia (HtCa group), 39 patients with normal tCa and elevated iCa (NtCa group), and 38 patients with both normal tCa and iCa (NiCa). All patients had biochemical follow-up confirming or not the success of PTX. MAIN OUTCOME MEASURES: To evaluate the performance of FCH-PET/CT in terms of sensitivity and specificity, and to compare with first-line imaging procedures in the setting of nPHPT. RESULTS: The sensitivity of FCH-PET/CT was 67% in the hypercalcemic group, 48% in the NtCa group ($P = .05$ vs HtCa), and 33% in the NiCa group ($P = .004$ vs HtCa). Specificity ranged from 97% to 99%. FCH-PET/CT was positive in 64.3% of patients with negative conventional imaging, with biochemical resolution after PTX in 77.8% of patients. Triple negative imaging was observed in 20 patients, with PHPT resolution in 85% of these patients. CONCLUSION: This study highlights the contribution of FCH-PET/CT in a well-phenotyped cohort of normocalcemic patients with discordant or negative findings in [99mTc]Tc-sestamibi scintigraphy and ultrasonography. However, negative imaging in nPHPT does not rule out the possibility of surgical cure by an experienced surgeon.

PubMed-ID: [36750257](#)

DOI: [10.1210/clinem/dgad073](#)

Characterization of primary hyperparathyroidism based on target organ involvement: An analysis from the Indian PHPT registry.

Clin Endocrinol (Oxf), 99(2):158-64.

S. Mukherjee, A. K. Arya, S. K. Bhadada, R. Pal, S. Lohani, A. Gupta and S. D. Rao. 2023.

BACKGROUND: It has been a matter of debate for long time about the existence of two distinct phenotypes of primary hyperparathyroidism (PHPT) predisposed to either renal or skeletal manifestation. OBJECTIVE: To differentiate characteristics of symptomatic PHPT patients based on the presence of skeletal or renal involvement. DESIGN: Retrospective analysis of data from the Indian PHPT registry. PATIENTS: PHPT patients were divided into four discrete groups: asymptomatic, presenting with renal manifestations alone, skeletal manifestations alone, and both skeletal and renal manifestations. MEASUREMENTS: Clinical, biochemical, and tumour weight and histopathological characteristics of these groups were compared. RESULTS: Of the 229 eligible patients, 45 were asymptomatic, 62 had renal manifestations, 55 had skeletal manifestations, and 67 had both skeletal and renal manifestations. Patients with both skeletal and renal manifestations had higher serum calcium levels than those with isolated skeletal involvement [12.5 (11.1-13.7) mg/dL, 11.2 (10.6-12.3) mg/dL, respectively; $p < .05$]. Serum alkaline phosphatase (AP), plasma parathyroid hormone (PTH) levels, and parathyroid tumour weight were significantly higher in patients with isolated skeletal, and both skeletal and renal manifestations, compared to the other two groups. A preoperative PTH and AP level of 300 pg/mL and 152 U/L, predicted the risk of developing skeletal involvement with sensitivity and specificity of 71%, 70%, and 69%, 67%, respectively. CONCLUSIONS: We observed distinct skeletal and renal phenotypic subgroups among PHPT patients with characteristic biochemical and hormonal patterns with higher parathyroid disease burden in patients with skeletal complications compared to those with isolated renal manifestation.

PubMed-ID: [36998119](#)

DOI: [10.1111/cen.14915](#)

18F-fluorocholine PET/MRI versus ultrasound and sestamibi for the localization of parathyroid adenomas.

Langenbecks Arch Surg, 408(1):155.

M. E. Noltes, L. Rotstein, A. Eskander, W. P. Kluijffhout, P. Bongers, A. H. Brouwers, S. Kruijff, U. Metser, J. D. Pasternak and P. Veit-Haibach. 2023.

PURPOSE: Accurate preoperative localization is imperative to facilitate a minimally invasive parathyroidectomy (MIP) in primary hyperparathyroidism (pHPT). This study aims to compare the diagnostic value of standard-of-care localization techniques (ultrasound [US] and (99m)Technetium ((99m)Tc) -sestamibi scintigraphy) to [F-18]-fluorocholine positron emission tomography/magnetic resonance imaging (FCH-PET/MRI) to determine the additional clinical usefulness of PET/MRI in a Canadian cohort. **METHODS:** We conducted a prospective, appropriately powered, study to compare the diagnostic value of FCH PET/MRI to that of the US and (99m)Tc-sestamibi scintigraphy for localization of parathyroid adenomas in a patient with pHPT. The primary outcome was the per-lesion sensitivity and positive predictive value (PPV) of FCH-PET/MRI, US, and (99m)Tc-sestamibi scintigraphy. Intraoperative surgeon localization, parathormone levels, and histopathological findings were used as reference standards. **RESULTS:** Forty-one patients underwent FCH-PET/MRI of which 36 patients had parathyroidectomy. In these 36 patients, 41 parathyroid lesions were histologically confirmed as adenomas or hyperplastic glands. Per-lesion sensitivity of FCH-PET/MRI was 82.9% and of US and (99m)Tc-sestamibi scintigraphy combined at 50.0%, respectively. The sensitivity of FCH-PET/MRI was superior to that of US and (99m)Tc-sestamibi scintigraphy ($p = 0.002$). In the 19 patients in whom both US and (99m)Tc-sestamibi scintigraphy were negative, PET/MRI correctly identified the parathyroid adenoma in 13 patients (68%). **CONCLUSIONS:** FCH-PET/MRI is a highly accurate imaging modality for localization of parathyroid adenomas in a tertiary center in North America. It is a superior functional imaging modality to (99m)Tc-sestamibi scintigraphy alone and more sensitive for localization of parathyroid lesions than US and (99m)Tc-sestamibi scintigraphy combined. This imaging modality could become the most valuable preoperative localization study given its superior performance in localizing parathyroid adenomas.

PubMed-ID: [37079138](#)

DOI: [10.1007/s00423-023-02893-6](#)

Does Surgeon Volume Impact Morbidity Following Parathyroidectomy? A Study of 16,140 Parathyroidectomies from the UK Registry of Endocrine and Thyroid Surgery (UKRETS) Database.

World J Surg, 47(5):1221-30.

S. Rajan, D. Gracie and S. Aspinall. 2023.

BACKGROUND: Outcomes in endocrine surgery have been shown to improve with surgeon volume. We aimed to study the effect of surgeon volume on morbidity following parathyroidectomy. **METHODS:** UKRETS data from 2004 to 2019 was studied. Parathyroidectomies for primary hyperparathyroidism with complete data were included. Exclusion criteria were age <18 or >80 years; surgeons contributing <10 cases overall; and length of stay >28 days. Multivariable analysis was performed. Primary outcome was persistent hypercalcaemia; secondary outcomes were haemorrhage, length of stay, need for re-admission, post-operative hypocalcaemia, and need for calcium/vitamin D supplements to maintain eucalcaemia at 6 months. **RESULTS:** 153 surgeons undertook mean 22.5 (median 17, range 2-115) parathyroidectomies/year. Persistent hypercalcaemia affected 4.8% (776/16140) overall; 5.7% (71/1242) in surgeons undertaking < 10 cases/year; 5.1% (3339/6617) for 10-30 cases/year; 5.0% (270/5397) for 30-50 cases; and 3.3% (96/2884) for >50 cases/year. High-volume (>50 parathyroidectomies/year) surgeons operated 23.4% (809/3464) of negative localisation cases compared to 16.4% (2074/12676) of positive localisation cases. Persistent hypercalcaemia was almost twice as common in image negative (7.9%) compared to image-positive (4%) cases. Persistent hypercalcaemia was significantly more likely to occur in the low volume (<10 parathyroidectomies/year) group than high volume (>50 parathyroidectomies/year), regardless of image positivity ($p = 0.0006$). Surgeon volume significantly reduced persistent hypercalcaemia on multivariable analysis (OR = 0.878, 95%CI 0.842-0.914, $p < 0.001$), along with age, sex, and positive localisation. BNE and re-operation significantly increased persistent hypercalcaemia. Post-operative hypocalcaemia occurred in 3.2% (509/16040) and was reduced with increasing surgeon volume (OR = 0.951, 95%CI 0.910-0.993, $p < 0.001$). Haemorrhage and length of stay were not significantly associated with surgeon volume. **CONCLUSION:** The incidence of persistent hypercalcaemia, post-operative hypocalcaemia, and persistent hypoparathyroidism decreased with increasing surgeon volume. The relative reduction in persistent hypercalcaemia with surgeon volume was similar in image negative and positive groups, but the absolute reduction was higher in image negative cases. Restricting image negative parathyroidectomy to high-volume surgeons could be considered.

PubMed-ID: [36593341](#)

DOI: [10.1007/s00268-022-06863-9](#)

Recurrent vomiting and confusion in pregnancy: hypercalcaemia due to parathyroid adenoma.

Lancet, 402(10395):62-3.

N. Sabbah, M. Demar, F. Sogbo, M. Zappa, K. D. Alsibai, H. Amroun and P. Chanson. 2023.

PubMed-ID: [37393105](#)

DOI: [10.1016/S0140-6736\(23\)01050-4](#)

Parathyroid Autofluorescence in Pediatric Thyroid Surgery: Experience With False Positive and False Negative Results.

Otolaryngol Head Neck Surg, 169(1):185-9.

B. M. Su-Velez, G. E. Hartman, H. Seeley, L. A. Orloff, J. E. Noel and K. D. Meister. 2023.

Devices for near-infrared light stimulation of autofluorescence (NIRAF) allow for intraoperative identification of parathyroid glands with high sensitivity in adults. However, their performance in the pediatric population is unknown. In this case series with chart review at a tertiary academic children's hospital, we investigated pediatric patients undergoing thyroid surgery and concurrent use of a probe-based NIRAF device. Thirteen patients (ages 6-18 years) underwent thyroid and/or neck dissection procedures, and 2 patients had revision procedures for a total of 15 cases with the NIRAF device. Eight cases had NIRAF values that matched surgeon opinion of parathyroid tissue or histology when available. Six cases had false positive NIRAF readings (40.0%) and 1 case had false negative readings (6.7%). Compared with surgeon opinion or histology, the NIRAF device confirmed 26 of 34 parathyroid gland candidates (76.5%). These devices need further investigation in pediatric patients, whose tissues may have different autofluorescence characteristics.

PubMed-ID: [36939554](#)

DOI: [10.1002/ohn.272](#)

Persistence and Recurrence of Hypercalcemia After Parathyroidectomy Over 5 Decades (1965-2010) in a Community-based Cohort.

Ann Surg, 278(2):e309-e13.

T. Szabo Yamashita, M. Mirande, C. T. Huang, A. Kearns, R. Fyffe-Freil, R. Singh, T. Foster, G. Thompson, M. Lyden, T. McKenzie, R. A. Wermers and B. Dy. 2023.

BACKGROUND: There is limited long-term follow-up of patients undergoing parathyroidectomy. Recurrence is described as 4% to 10%. This study evaluated persistence and recurrence of hypercalcemia in primary hyperparathyroidism after parathyroidectomy. METHODS: Single-institution retrospective (1965-2010) population-based cohort from Olmsted County (MN) of patients undergoing surgery for primary hyperparathyroidism. Patients' demographic data, preoperative and postoperative laboratory values, clinical characteristics, surgical treatment, and follow-up were noted. RESULTS: A total of 345 patients were identified, 75.7% female, and median age 58.4 years [interquartile range (IQR): 17.6]. In all, 68% of patients were asymptomatic and the most common symptoms were musculoskeletal complaints (28.4%) and nephrolithiasis (25.6%). Preoperative median serum calcium was 11 mg/dL (IQR: 10.8-11.4 mg/dL), and median parathyroid hormone was 90 pg/mL (IQR: 61-169 pg/dL). Bilateral cervical exploration was performed in 38% and single gland resection in 79% of cases. Median postoperative serum calcium was 9.2 mg/dL (IQR: 5.5-11.3). Nine percent of patients presented persistence of hypercalcemia, and recurrence was found in 14% of patients. Highest postoperative median serum calcium was 10 mg/dL (IQR: 6-12.4), and median number of postoperative calcium measurements was 10 (IQR: 0-102). Postoperative hypercalcemia was identified in 37% of patient. Fifty-three percent were attributed to secondary causes, most commonly medications, 22%. Three percent of patients required treatment for postoperative hypercalcemia. Median time to recurrence and death were 12.2 and 16.7 years, respectively. CONCLUSION: Recurrent hypercalcemia after successful parathyroidectomy is higher than previously reported. Most cases are transient and often associated to other factors with only the minority requiring treatment. Long-term follow-up of serum calcium should be considered in patients after successful parathyroidectomy.

PubMed-ID: [36017920](#)

DOI: [10.1097/SLA.0000000000005688](#)

PMCID: PMC9968357

Long-term effects of primary hyperparathyroidism and parathyroidectomy on kidney function.

Eur J Endocrinol, 189(1):115-22.

C. Y. Zhu, H. X. Zhou, C. H. Tseng, O. J. Fackelmayer, P. I. Haigh, A. L. Adams and M. W. Yeh. 2023.

IMPORTANCE: Limited evidence supports kidney dysfunction as an indication for parathyroidectomy in asymptomatic primary hyperparathyroidism (PHPT). OBJECTIVE: To investigate the natural history of kidney function in PHPT and whether parathyroidectomy alters renal outcomes. DESIGN: Matched control study. SETTING: A vertically integrated health care system serving 4.6 million patients in Southern California. PARTICIPANTS: 6058 subjects with PHPT and 16 388

matched controls, studied from 2000 to 2016. EXPOSURES: Biochemically confirmed PHPT with varying serum calcium levels. MAIN OUTCOMES: Estimated glomerular filtration rate (eGFR) trajectories were compared over 10 years, with cases subdivided by severity of hypercalcemia: serum calcium 2.62-2.74 mmol/L (10.5-11 mg/dL), 2.75-2.87 (11.1-11.5), 2.88-2.99 (11.6-12), and >2.99 (>12). Interrupted time series analysis was conducted among propensity-score-matched PHPT patients with and without parathyroidectomy to compare eGFR trajectories postoperatively. RESULTS: Modest rates of eGFR decline were observed in PHPT patients with serum calcium 2.62-2.74 mmol/L (-1.0 mL/min/1.73 m²/year) and 2.75-2.87 mmol/L (-1.1 mL/min/1.73 m²/year), comprising 56% and 28% of cases, respectively. Compared with the control rate of -1.0 mL/min/1.73 m²/year, accelerated rates of eGFR decline were observed in patients with serum calcium 2.88-2.99 mmol/L (-1.5 mL/min/1.73 m²/year, P < .001) and >2.99 mmol/L (-2.1 mL/min/1.73 m²/year, P < .001), comprising 9% and 7% of cases, respectively. In the propensity score-matched population, patients with serum calcium >2.87 mmol/L exhibited mitigation of eGFR decline after parathyroidectomy (-2.0 [95% CI: -2.6 to -1.5] to -0.9 [95% CI: -1.5 to 0.4] mL/min/1.73 m²/year). CONCLUSIONS AND RELEVANCE: Compared with matched controls, accelerated eGFR decline was observed in the minority of PHPT patients with serum calcium >2.87 mmol/L (11.5 mg/dL). Parathyroidectomy was associated with mitigation of eGFR decline in patients with serum calcium >2.87 mmol/L.

PubMed-ID: [37449311](#)

DOI: [10.1093/ejendo/lvad081](#)

Adrenals

Meta-Analyses

Comparing surgical outcomes of approaches to adrenalectomy - a systematic review and network meta-analysis of randomised clinical trials.

Langenbecks Arch Surg, 408(1):180.

M. G. Davey, E. J. Ryan, N. E. Donlon, O. K. Ryan, M. Al Azzawi, M. R. Boland, M. J. Kerin and A. J. Lowery. 2023.

BACKGROUND: No randomised clinical trials (RCTs) have simultaneously compared the safety of open (OA), transperitoneal laparoscopic (TLA), posterior retroperitoneal (PRA), and robotic adrenalectomy (RA) for resecting adrenal tumours. **AIM:** To evaluate outcomes for OA, TLA, PRA, and RA from RCTs. **METHODS:** A NMA was performed according to PRISMA-NMA guidelines. Analysis was performed using R packages and Shiny. **RESULTS:** Eight RCTs with 488 patients were included (mean age: 48.9 years). Overall, 44.5% of patients underwent TLA (217/488), 37.3% underwent PRA (182/488), 16.4% underwent RA (80/488), and just 1.8% patients underwent OA (9/488). The mean tumour size was 35 mm in largest diameter with mean sizes of 44.3 mm for RA, 40.9 mm for OA, 35.5 mm for TLA, and 34.4 mm for PRA ($P < 0.001$). TLA had the lowest blood loss (mean: 50.6 ml), complication rates (12.4%, 14/113), and conversion to open rates (1.3%, 2/157), while PRA had the shortest intra-operative duration (mean: 94 min), length of hospital stay (mean: 3.7 days), lowest visual analogue scale pain scores post-operatively (mean: 3.7), and was most cost-effective (mean: 1728 euros per case). At NMA, there was a significant increase in blood loss for OA (mean difference (MD): 117.00 ml (95% confidence interval (CI): 1.41-230.00)) with similar blood loss observed for PRA (MD: - 10.50 (95% CI: - 83.40-65.90)) compared to TLA.

CONCLUSION: TLA and PRA are important contemporary options in achieving favourable outcomes following adrenalectomy. The next generation of RCTs may be more insightful for comparison surgical outcomes following RA, as this approach is likely to play a future role in minimally invasive adrenalectomy. **PROSPERO REGISTRATION:** CRD42022301005.

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DOI: [10.1007/s00423-023-02911-7](https://doi.org/10.1007/s00423-023-02911-7)

PMCID: PMC10163131

Minimally invasive versus open adrenalectomy for adrenocortical carcinoma: the keys surgical factors influencing the outcomes-a collective overview.

Langenbecks Arch Surg, 408(1):256.

A. Giordano, F. Feroci, M. Podda, E. Botteri, M. Ortenzi, G. Montori, M. Guerrieri, N. Vettoretto, F. Agresta and C. Bergamini. 2023.

PURPOSE: Adrenocortical carcinoma (A.C.C.) is a rare tumour, often discovered at an advanced stage and associated with a poor prognosis. Surgery is the treatment of choice. We aimed to review the different surgical approaches trying to compare their outcome. **METHODS:** This comprehensive review has been carried out according to the PRISMA statement. The literature search was performed in PubMed, Scopus, the Cochrane Library and Google Scholar. **RESULTS:** Among all studies identified, 18 were selected for the review. A total of 14,600 patients were included in the studies, of whom 4421 were treated by mini-invasive surgery (M.I.S.). Ten studies reported 531 conversions from M.I.S. to an open approach (OA) (12%). Differences were reported for operative times as well as for postoperative complications more often in favour of OA, whereas differences for hospitalization time in favour of M.I.S. Some studies showed an R0 resection rate from 77 to 89% for A.C.C. treated by OA and 67 to 85% for tumours treated by M.I.S. The overall recurrence rate ranged from 24 to 29% for A.C.C. treated by OA and from 26 to 36% for tumours treated by M.I.S. **CONCLUSIONS:** OA should still be considered the standard surgical management of A.C.C. Laparoscopic adrenalectomy has shown shorter hospital stays and faster recovery compared to open surgery. However, the laparoscopic approach resulted in the worst recurrence rate, time to recurrence and cancer-specific mortality in stages I-III ACC. The robotic approach had similar complications rate and hospital stays, but there are still scarce results about oncologic follow-up.

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DOI: [10.1007/s00423-023-02997-z](https://doi.org/10.1007/s00423-023-02997-z)

Prognostic models to predict complete resolution of hypertension after adrenalectomy in primary aldosteronism: A systematic review and meta-analysis.

Clin Endocrinol (Oxf), 99(1):17-34.

L. Marzano, A. Kazory, F. Husain-Syed and C. Ronco. 2023.

Complete resolution of hypertension (CRH) after adrenalectomy for primary aldosteronism is far from a certainty. Although several prognostic models have been proposed to predict outcome after adrenalectomy, studies have not clarified which of the available models can be used reliably in clinical practice. To identify, describe and appraise all prognostic models developed to predict CRH, and meta-analyse their predictive performances. We searched MEDLINE, Embase and Web of Science for development and validation studies of prognostic models. After selection, we extracted descriptive statistics and aggregated area under the receiver operator curve (AUC) using meta-analysis. From 25 eligible studies, we identified 12 prognostic models used for predicting CRH after total adrenalectomy in primary aldosteronism. We report the results for 3 models that had available data from at least 3 external validation studies: the primary aldosteronism surgical outcome (PASO) score (AUC: 0.81; 95% confidence interval [CI]: 0.74-0.86; 95% predictive interval [PI]: 0.04-1.00), Utsumi nomogram (AUC: 0.79; 95% CI: 0.72-0.85; 95% PI: 0.03-1.00) and the aldosteronoma resolution score (ARS) model (AUC: 0.77; 95% CI: 0.74-0.80; 95% PI: 0.59-0.86 for all studies and AUC: 0.80; 95% CI: 0.75-0.85; 95% PI: 0.57-0.93 for the studies with the same adrenal vein sampling-guided adrenalectomy rate compared to the models meta-analysed). The PASO score, Utsumi nomogram and ARS model showed comparable discrimination performance to predict CRH in primary aldosteronism. Unlike the ARS model, the number of external validation studies for the PASO score and the Utsumi nomogram was relatively low to draw definite conclusions.

PubMed-ID: [37032125](#)

DOI: [10.1111/cen.14918](#)

Prevalence of Functioning Adrenal Incidentalomas: A Systematic Review and Meta-analysis.

J Clin Endocrinol Metab, 108(7):1813-23.

E. Sconfienza, M. Tetti, V. Forestiero, F. Veglio, P. Mulatero and S. Monticone. 2023.

CONTEXT: Adrenal hyperfunction is associated with an increased risk of cardiometabolic complications in subjects with adrenal incidentaloma (AI). Reliable prevalence estimates of functioning AIs are important to direct resources allocations. OBJECTIVE: To assess the prevalence of autonomous/possible autonomous cortisol secretion (ACS), primary aldosteronism (PA), pheochromocytoma (PHEO), and Cushing syndrome (CS) in patients with AI. METHODS: We performed a comprehensive search of multiple databases (PubMed, Ovid MEDLINE, Web of Science) for potentially relevant studies without language restriction, up to February 2022. Of the 1661 publications evaluated at title and abstract levels, 161 were examined as full text and 36 were included. Study level clinical data were extracted by 3 independent reviewers. RESULTS: The overall prevalence of functioning AIs was 27.5% (95% CI 23.0, 32.5). ACS/possible ACS, with a prevalence of 11.7% (95% CI 8.6, 15.7), was the most frequent hormonal alteration, while PA occurred in 4.4% of the patients (95% CI 3.1, 6.2). Subgroup analysis showed that PA was more prevalent in patients from Asia than in patients from Europe/America; in contrast, ACS/possible ACS had a lower prevalence in Asian countries. At meta-regression analysis, the prevalence of ACS/possible ACS was influenced by the proportion of female patients, while the prevalence of PA was positively associated with the proportion of patients with hypertension and the publication year. Finally, PHEO and CS prevalence were 3.8% (95% CI 2.8, 5.0) and 3.1% (95% CI 2.3, 4.3) respectively. CONCLUSION: This meta-analysis provides extensive data on the prevalence of functioning AIs and the factors affecting heterogeneity in prevalence estimates.

PubMed-ID: [36718682](#)

DOI: [10.1210/clinem/dgad044](#)

Randomized controlled trials

- None -

Consensus Statements/Guidelines

European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors.

Eur J Endocrinol, 189(1):G1-G42.

M. Fassnacht, S. Tsagarakis, M. Terzolo, A. Tabarin, A. Sahdev, J. Newell-Price, I. Pelsma, L. Marina, K. Lorenz, I. Bancos, W. Arlt and O. M. Dekkers. 2023.

Adrenal incidentalomas are adrenal masses detected on imaging performed for reasons other than suspected adrenal

disease. In most cases, adrenal incidentalomas are nonfunctioning adrenocortical adenomas but may also require therapeutic intervention including that for adrenocortical carcinoma, pheochromocytoma, hormone-producing adenoma, or metastases. Here, we provide a revision of the first international, interdisciplinary guidelines on incidentalomas. We followed the Grading of Recommendations Assessment, Development and Evaluation system and updated systematic reviews on 4 predefined clinical questions crucial for the management of incidentalomas: (1) How to assess risk of malignancy?; (2) How to define and manage mild autonomous cortisol secretion?; (3) Who should have surgical treatment and how should it be performed?; and (4) What follow-up is indicated if the adrenal incidentaloma is not surgically removed? Selected Recommendations: (1) Each adrenal mass requires dedicated adrenal imaging. Recent advances now allow discrimination between risk categories: Homogeneous lesions with Hounsfield unit (HU) ≤ 10 on unenhanced CT are benign and do not require any additional imaging independent of size. All other patients should be discussed in a multidisciplinary expert meeting, but only lesions >4 cm that are inhomogeneous or have HU >20 have sufficiently high risk of malignancy that surgery will be the usual management of choice. (2) Every patient needs a thorough clinical and endocrine work-up to exclude hormone excess including the measurement of plasma or urinary metanephrines and a 1-mg overnight dexamethasone suppression test (applying a cutoff value of serum cortisol ≤ 50 nmol/L [≤ 1.8 microg/dL]). Recent studies have provided evidence that most patients without clinical signs of overt Cushing's syndrome but serum cortisol levels post dexamethasone >50 nmol/L (>1.8 microg/dL) harbor increased risk of morbidity and mortality. For this condition, we propose the term "mild autonomous cortisol secretion" (MACS). (3) All patients with MACS should be screened for potential cortisol-related comorbidities that are potentially attributable to cortisol (eg, hypertension and type 2 diabetes mellitus), to ensure these are appropriately treated. (4) In patients with MACS who also have relevant comorbidities surgical treatment should be considered in an individualized approach. (5) The appropriateness of surgical intervention should be guided by the likelihood of malignancy, the presence and degree of hormone excess, age, general health, and patient preference. We provide guidance on which surgical approach should be considered for adrenal masses with radiological findings suspicious of malignancy. (6) Surgery is not usually indicated in patients with an asymptomatic, nonfunctioning unilateral adrenal mass and obvious benign features on imaging studies. Furthermore, we offer recommendations for the follow-up of nonoperated patients, management of patients with bilateral incidentalomas, for patients with extra-adrenal malignancy and adrenal masses, and for young and elderly patients with adrenal incidentalomas. Finally, we suggest 10 important research questions for the future.

PubMed-ID: [37318239](#)

DOI: [10.1093/ejendo/lvad066](#)

Other Articles

Subtyping primary aldosteronism by inconclusive adrenal vein sampling.

Clin Endocrinol (Oxf), 98(6):834-5.

B. Barbar, P. Truran, J. Ramsingh, R. Bliss, C. Boot, M. Ramzan, R. Quinton, Y. H. Mamoojee and R. V. I. E. Group. 2023.

PubMed-ID: [36633166](#)

DOI: [10.1111/cen.14879](#)

Clinical, Pathophysiologic, Genetic, and Therapeutic Progress in Primary Bilateral Macronodular Adrenal Hyperplasia.

Endocr Rev, 44(4):567-628.

J. Bertherat, I. Bourdeau, L. Bouys, F. Chasseloup, P. Kamenicky and A. Lacroix. 2023.

Patients with primary bilateral macronodular adrenal hyperplasia (PBMAH) usually present bilateral benign adrenocortical macronodules at imaging and variable levels of cortisol excess. PBMAH is a rare cause of primary overt Cushing's syndrome but may represent up to one-third of bilateral adrenal incidentalomas with evidence of cortisol excess. The increased steroidogenesis in PBMAH is often regulated by various G protein-coupled receptors (GPCRs) aberrantly expressed in PBMAH tissues; some receptor ligands are ectopically produced in PBMAH tissues, creating aberrant autocrine/paracrine regulation of steroidogenesis. The bilateral nature of PBMAH and familial aggregation led to the identification of germline heterozygous inactivating mutations of the *ARMC5* gene, in 20% to 25% of the apparent sporadic cases and more frequently in familial cases; *ARMC5* mutations/pathogenic variants can be associated with meningiomas. More recently, combined germline mutations/pathogenic variants and somatic events inactivating the *KDM1A* gene were specifically identified in patients affected by glucose-dependent insulinotropic peptide (GIP)-dependent PBMAH. Functional studies demonstrated that inactivation of *KDM1A* leads to GIP-receptor (GIPR) overexpression and over- or downregulation of other GPCRs. Genetic analysis is now available for early detection of family members of index cases with PBMAH carrying identified germline pathogenic variants. Detailed biochemical, imaging, and

comorbidity assessment of the nature and severity of PBMAH is essential for its management. Treatment is reserved for patients with overt or mild cortisol/aldosterone or other steroid excesses, taking in account comorbidities. It previously relied on bilateral adrenalectomy; however, recent studies tend to favor unilateral adrenalectomy or, less frequently, medical treatment with cortisol synthesis inhibitors or specific blockers of aberrant GPCR.

PubMed-ID: [36548967](#)

DOI: [10.1210/edrev/bnac034](#)

ASO Visual Abstract: Adoption of Robotic Adrenalectomy: A Two-Institution Study of Surgeon Learning Curve.

Ann Surg Oncol, 30(7):4179.

R. A. Collins, T. S. Wang, S. Dream, C. C. Solorzano and C. M. Kiernan. 2023.

PubMed-ID: [37040051](#)

DOI: [10.1245/s10434-023-13492-6](#)

Adoption of Robotic Adrenalectomy: A Two-Institution Study of Surgeon Learning Curve.

Ann Surg Oncol, 30(7):4167-78.

R. A. Collins, T. S. Wang, S. Dream, C. C. Solorzano and C. M. Kiernan. 2023.

BACKGROUND: Robotic adrenalectomy is feasible and safe, yet concerns over increased operative times and the learning curve (LC) for proficiency have limited its adoption. This study aimed to assess the LC for robotic adrenalectomy.

METHODS: This is a two-institution retrospective review of consecutive unilateral minimally invasive adrenalectomies performed by four high-volume adrenal surgeons between 2007 and 2022. Two surgeons transitioned from laparoscopic to robotic adrenalectomy, and two surgeons adopted the approach, with proctoring, after completion of fellowship training without robotic experience. Operative time and complications were analyzed. Multivariable regression was used to identify factors associated with operative time. The number of cases required to overcome the LC was determined using the LC-cumulative-sum (LC-CUSUM) analysis. **RESULTS:** Of 457 adrenalectomies, 182 (40%) were laparoscopic and 275 (60%) robotic. The robotic approach was associated with shorter median operative time (106 vs 119 min; $p = 0.002$), fewer complications (6% vs 13%; $p = 0.018$), and fewer conversions to open adrenalectomy (1% vs 4%; $p = 0.030$), with no difference between the senior and junior surgeons. On adjusted analysis, factors associated with increased operative time were male sex ($p < 0.001$), BMI $> 30 \text{ kg/m}^2$ ($p < 0.001$), and higher gland weight ($p < 0.001$). The LC-CUSUM analysis showed proficiency after 8-29 procedures. Compared with the first 10 cases, there was a mean reduction in operative time of 14 min after 10-20 cases, 28 min after 20-30 cases, and 29 min after > 30 cases, regardless of surgeon experience.

DISCUSSION: With dedicated teams and proctoring, robotic adrenalectomy can be safely adopted at high-volume centers with a minimal LC.

PubMed-ID: [37040047](#)

DOI: [10.1245/s10434-023-13406-6](#)

Is transperitoneal laparoscopic adrenalectomy for pheochromocytoma really more challenging? A propensity score-matched analysis.

J Endocrinol Invest, 46(8):1589-96.

D. Corallino, A. Balla, L. Palmieri, I. Sperduti, M. Ortenzi, M. Guerrieri and A. M. Paganini. 2023.

PURPOSE: Minimally invasive surgery is the gold standard treatment for adrenal masses, but it may be a challenging procedure in the case of pheochromocytoma (PHEO). The aim of the present study is to report the results of transperitoneal laparoscopic adrenalectomy (TLA) in cases of PHEO in comparison to other types of adrenal lesions.

METHODS: From 1994 to 2021, 629 patients underwent adrenalectomy. Twenty-two and thirty-five patients, respectively, were excluded because they underwent bilateral and open adrenalectomy, leaving 572 patients for inclusion. Of these, 114 patients had PHEO (Group A), and 458 had other types of lesions (Group B). To adjust for potential baseline confounders, a propensity score matching (PSM) analysis was conducted. **RESULTS:** After PSM, 114 matched pairs of patients were identified from each group. Statistically significant differences were not observed when comparing the median operative time (85 and 90 min in Groups A and B, respectively, $p = 0.627$), conversion rate [6 (5.3%) in each group, $p = 1.000$], transfusion rate [4 (3.5%) and 3 (2.6%) in Groups A and B, respectively, $p = 1.000$], complication rate [7 (6.1%) and 9 (7.9%) in Groups A and B, respectively, $p = 0.796$], median postoperative hospital stay (3.9 and 3.6 days in Groups A and B, respectively, $p = 0.110$), and mortality rate [1 (0.9%) in each group, $p = 1.000$]. **CONCLUSIONS:** Based on this analysis, the results of TLA for PHEO are equivalent to those of TLA for other types of adrenal lesions, but the fundamental requirements are multidisciplinary patient management and adequate surgeon experience. Further prospective studies are required to draw definitive conclusions.

PubMed-ID: [36705839](#)

Feasibility of single-port laparoscopic partial adrenalectomy with selective adrenal venous sampling and high-resolution ultrasound for unilateral aldosterone-producing adenomas.

Surgery, 174(2):234-40.

Y. Goto, T. Kitamoto, S. Tanaka, M. Maruo, S. Sugawara, K. Chiba, K. Miyazaki, A. Inoue, K. Nakai, Y. Tsurutani, J. Saito, M. Omura, T. Nishikawa, T. Ichikawa and M. Nagata. 2023.

BACKGROUND: The surgical and endocrinological outcomes of single-port laparoscopic partial adrenalectomy for patients with aldosterone-producing adenomas are unknown. Precise diagnosis of intra-adrenal aldosterone activity and a precise surgical procedure may improve outcomes. In this study, we aimed to determine the surgical and endocrinological outcomes of single-port laparoscopic partial adrenalectomy with preoperative segmental selective adrenal venous sampling and intraoperative high-resolution laparoscopic ultrasound in patients with unilateral aldosterone-producing adenomas. We identified 53 patients with partial adrenalectomy and 29 patients with laparoscopic total adrenalectomy. Single-port surgery was performed for 37 and 19 patients, respectively. **METHODS:** A single-center, retrospective cohort study. All patients with unilateral aldosterone-producing adenomas diagnosed by selective adrenal venous sampling and treated surgically between January 2012 and February 2015 were included. Follow-up with biochemical and clinical assessments was set at 1 year after surgery for short-term outcomes and was performed every 3 months after surgery. **RESULTS:** We identified 53 patients with partial adrenalectomy and 29 patients with laparoscopic total adrenalectomy. Single-port surgery was performed for 37 and 19 patients, respectively. Single-port surgery was associated with shorter operative and laparoscopic times (odds ratio, 0.14; 95% confidence interval, 0.039-0.49; $P = .002$ and odds ratio, 0.13; 95% confidence interval, 0.032-0.57; $P = .006$, respectively). All single-port and multi-port partial adrenalectomy cases showed complete short-term (median 1 year) biochemical success, and 92.9% (26 of 28 patients) who underwent single-port partial adrenalectomy and 100% (13 of 13 patients) who underwent multi-port partial adrenalectomy showed complete long-term (median 5.5 years) biochemical success. No complications were observed with single-port adrenalectomy. **CONCLUSION:** Single-port partial adrenalectomy is feasible after selective adrenal venous sampling for unilateral aldosterone-producing adenomas, with shorter operative and laparoscopic times and a high rate of complete biochemical success.

PubMed-ID: [37188580](https://pubmed.ncbi.nlm.nih.gov/37188580/)

DOI: [10.1016/j.surg.2023.04.010](https://doi.org/10.1016/j.surg.2023.04.010)

TNM Staging and Overall Survival in Patients With Pheochromocytoma and Sympathetic Paraganglioma.

J Clin Endocrinol Metab, 108(5):1132-42.

C. Jimenez, J. Ma, A. Roman Gonzalez, J. Varghese, M. Zhang, N. Perrier, M. A. Habra, P. Graham and S. G. Waguespack. 2023.

CONTEXT: Pheochromocytomas and paragangliomas (PPGL) are rare neuroendocrine tumors. Metastases develop in 15% to 20%. The American Joint Committee on Cancer (AJCC) established inaugural guidelines for PPGL tumor-node-metastasis (TNM) staging. **OBJECTIVE:** The objective of this analysis is to investigate the associations between TNM staging and overall survival (OS). **METHODS:** We retrospectively applied the TNM staging at the time of diagnosis of the primary tumor. The primary outcome was OS. Unadjusted survival rates were estimated by the Kaplan-Meier method. Cox proportional hazards regression models were used to evaluate the associations between OS and covariates of interest. **RESULTS:** The study included 458 patients. Median OS was 18.0 (95% CI, 15.6-not reached) years. At diagnosis, 126 (27.5%) tumors were stage I, 213 (46.5%) were stage II, 47 (10.3%) were stage III, and 72 (15.7%) were stage IV. The 10-year OS probabilities were 0.844 (95% CI, 0.768-0.928) for patients with stage I tumors, 0.792 (95% CI, 0.726-0.865) for stage II, 0.595 (95% CI, 0.435-0.813) for stage III, and 0.221 (95% CI, 0.127-0.384) for stage IV. Compared with stage I, the hazard ratios (HR) for death were 1.50 (0.87-2.57) for stage II, 2.85 (1.45-5.63) for stage III, and 8.88 (5.16-15.29) for stage IV ($P < 0.001$). Compared with patients with no germline mutations, those with RET 634/918 had better OS (HR: 0.28; 95% CI, 0.12-0.69). Other germline mutations, including SDHB, did not exhibit worse OS than patients with metastasis and sporadic disease. **CONCLUSION:** OS rates correlated with the recently developed AJCC TNM staging and were not worse in hereditary disease. Stage IV disease exhibited a significantly shorter OS compared with stages I-III. Future staging systems could be adjusted to better separate stages I and II.

PubMed-ID: [36433823](https://pubmed.ncbi.nlm.nih.gov/36433823/)

DOI: [10.1210/clinem/dgac677](https://doi.org/10.1210/clinem/dgac677)

Mortality Not Increased in Patients With Nonfunctional Adrenal Adenomas: A Matched Cohort Study.

J Clin Endocrinol Metab, 108(8):e536-e41.

A. Kjellbom, O. Lindgren, M. Danielsson, H. Olsen and M. Londahl. 2023.

CONTEXT: Mild autonomous cortisol secretion (MACS) is associated with increased mortality in patients with adrenal incidentalomas, but little is known regarding the potential risk associated with nonfunctional adrenal adenomas (NFAA), which constitute the majority of adrenal incidentalomas. OBJECTIVE: Compare mortality risk in patients with NFAA, and different levels of MACS, to matched controls. METHOD: This was a retrospective matched cohort study. All patients referred to 2 endocrine centers in southern Sweden because of an adrenal incidentaloma between 2005 and 2015 were enrolled. Controls (3:1) matched for sex, age, and residency were included. Primary endpoint was all-cause mortality. Outcome data were obtained from the Cause of Death Register. Patients were grouped according to cortisol level post 1-mg dexamethasone suppression test (cortisolDST) (<50 (NFAA), 50-82, 83-137, and \geq 138 nmol/L). RESULTS: 1154 patients and 3462 matched controls were included. During a median follow-up of 6.6 years, 210 patients and 505 controls died. There were no statistically significant differences in mortality between patients with NFAA and their controls (HR 1.13 [0.87-1.46]) whereas mortality was increased compared to controls in patients with cortisolDST 83-137 (HR 1.99 [1.38-2.88]) and \geq 138 nmol/L (HR 4.09 [2.41-6.93]). Likewise, the mortality risk was increased in patients younger than 65 years with cortisolDST 50-82 nmol/L compared with controls (HR 2.33 [1.30-4.17]). CONCLUSION: NFAA does not seem to pose a clinically relevant risk for increased mortality in patients with adrenal incidentalomas while patients with MACS, and especially younger patients and those with cortisolDST \geq 83 nmol/L, have significantly increased mortality risk compared with matched controls.

PubMed-ID: [36800277](https://pubmed.ncbi.nlm.nih.gov/36800277/)

DOI: [10.1210/clinem/dgad074](https://doi.org/10.1210/clinem/dgad074)

PMCID: PMC10348456

Laparoscopic adrenalectomy for adrenal metastases of solid tumors.

Surg Endosc, 37(6):4651-7.

S. D. Quildrian, W. S. Nardi, F. Iriarte, M. Recalde, I. Califano and J. Chapela. 2023.

INTRODUCTION: In patients with history of cancer adrenal metastases can be found in up to 70% of adrenal tumors detected during follow-up. Currently, laparoscopic adrenalectomy (LA) is considered the gold standard approach for benign adrenal tumors but is still controversial in malignant disease. Depending on the patient's oncological status, adrenalectomy might be a possible treatment option. Our objective was to analyze the results of LA for adrenal metastasis from solid tumors in two referral centers. METHODS: Retrospective analysis of 17 patients with non-primary adrenal malignancy treated with LA between 2007 and 2019 was performed. Demographic and primary tumor data, type of metastasis, morbidity, disease recurrence and evolution were evaluated. Patients were compared according to type of metastases: synchronous (< 6 months) vs metachronous (\geq 6 months). RESULTS: 17 patients were included. Median metastatic adrenal tumor size was 4 cm (IQR, 3-5.4). We had one conversion to open surgery. Recurrence was found in 6 patients with one recurring in the adrenal bed. The median OS was 24 (IQR, 10.5-60.5) months and 5-year OS was 61.4% (95%CI: 36.7%-81.4%). Patients with metachronous metastases had better overall survival vs. patients with synchronous metastases (87% vs. 14%, $p = 0.0037$). CONCLUSION: LA for adrenal metastases is a procedure associated with low morbidity and acceptable oncologic outcomes. Based on our results, seems reasonable to offer this procedure to carefully selected patients, mainly those with metachronous presentation. Indication of LA must be done on a case by case evaluation in the context of a multidisciplinary tumor board.

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DOI: [10.1007/s00464-023-09961-4](https://doi.org/10.1007/s00464-023-09961-4)

Adrenal and juxta-adrenal schwannomas: A single-centre study.

Clin Endocrinol (Oxf), 99(1):52-7.

S. Rolak, P. Dogra, T. McKenzie, M. Rivera, W. F. Young and I. Bancos. 2023.

OBJECTIVE: Adrenal schwannomas and juxta-adrenal schwannomas are rare tumours. We aimed to summarise their clinical, biochemical and imaging characteristics. DESIGN: Single-centre retrospective study of eligible patients between 1995 and 2022. PATIENTS AND MEASUREMENTS: Patients with a histopathologic diagnosis of adrenal or juxta-adrenal schwannoma. RESULTS: Twenty-four patients were diagnosed with either primary adrenal schwannoma (8, 33%) or juxta-adrenal schwannoma (16, 67%). Most tumours (21, 88%) were discovered incidentally on imaging. All tumours were unilateral, with 15 (62%) on the left and 9 (38%) on the right. At diagnosis, the median tumour size was 4 cm (range, 2-13 cm). Adrenal schwannomas were smaller when compared to juxta-adrenal schwannomas (median of 3.1 cm [range, 2-9 cm] vs. 4.6 cm [range, 2.3-13.3 cm], $p = .037$). On imaging, the tumours were round or oval in shape in 16 (70%), lobulated

in 7 (30%), solid in 15 (68%), solid-cystic in 7 (32%), heterogeneous in 14 (61%) and homogeneous in 9 (39%). The median unenhanced computed tomography attenuation was 30 Hounsfield units (HU) (range, 12-38 HU). Of the 20 patients who underwent complete hormonal testing, all had nonfunctioning tumours. There was no recurrence or new tumour development in our cohort. CONCLUSIONS: Adrenal and juxta-adrenal schwannomas are nonfunctioning benign tumours that present with indeterminate radiographic features, including large tumour size and increased unenhanced CT attenuation. We did not find an imaging phenotype that was diagnostic of schwannoma. The diagnosis of this rare tumour is based on biopsy or resection.

PubMed-ID: [37143372](#)

DOI: [10.1111/cen.14927](#)

Posterior retroperitoneal versus transperitoneal laparoscopic adrenalectomy in adults: results from the EUROCRINE(R) surgical registry.

Langenbecks Arch Surg, 408(1):241.

K. Van Den Heede, S. Vatansever, T. Girgin, S. Van Slycke, O. Makay and E. Council. 2023.

PURPOSE: This study aims to compare posterior retroperitoneal laparoscopic adrenalectomy (PRLA) and laparoscopic transperitoneal adrenalectomy (LTA) in adults using pan-European data as conflicting results have been published regarding length of hospital stay, institutional volume, and morbidity. METHODS: This retrospective cohort study analyzed data from the surgical registry EUROCRINE(R). All patients undergoing PRLA and TLA for adrenal tumours and registered between 2015 and 2020 were included and compared for morbidity, length of hospital stay, and conversion to open surgery. RESULTS: A total of 2660 patients from 11 different countries and 69 different hospitals were analyzed and 1696 LTA were compared to 964 PRLA. Length of hospital stay was shorter after PRLA, with less patients (N = 434, 45.5%, vs N = 1094, 65.0%, $p < 0.001$) staying more than 2 days. In total, 96 patients (3.6%) developed a complication Clavien-Dindo grade 2 or higher. No statistical difference was found between both study groups. After propensity score matching, length of hospital stay was shorter after PRLA (> 2 days 45.2% vs 63.0%, $p < 0.001$). After multivariable logistic regression, factors associated with morbidity were age (OR 1.03), male sex (OR 1.52), and conversion to open surgery (OR 5.73). CONCLUSION: This study presents the largest retrospective observational analysis comparing LTA and PRLA. Our findings confirm the shorter length of hospital stay after PRLA. Both techniques are safe leading to comparable morbidity and conversion rates.

PubMed-ID: [37349535](#)

DOI: [10.1007/s00423-023-02975-5](#)

Adrenal Metastasectomy in the Era of Immuno- and Targeted Therapy.

Ann Surg Oncol, 30(7):4146-55.

H. Wachtel, P. Dickson, S. B. Fisher, C. M. Kiernan and C. C. Solorzano. 2023.

Adrenal metastasectomy has an increasing role in multimodality oncologic care for diverse primary cancer types. In this review, we discuss the epidemiology, evaluation, and contemporary best practices in the management of adrenal metastases from various primaries. Initial evaluation of suspected adrenal metastases should include diagnostic imaging to assess the extent of tumor involvement and determine surgical resectability, as well as biochemical evaluation for hormone secretion. Biopsy has a minimal role and should only be performed in tumors that are established to be non-hormone secreting and when the biopsy results would change clinical management. Adrenal metastasectomy is associated with survival benefit in selected patients. We suggest that adrenal metastasectomy has the greatest benefit in four clinical scenarios: (1) disease limited to the adrenal gland in which adrenalectomy renders the patient disease-free; (2) isolated progression in the adrenal gland in the setting of otherwise controlled metastatic extra-adrenal disease; (3) need for palliation of symptoms related to adrenal metastases; or (4) in the context of tissue-based clinical trials. Both minimally invasive and open adrenalectomy techniques are safe and appear to have equivalent oncologic outcomes. Minimally invasive approaches are favored when technically feasible while maintaining oncologic principles. A multidisciplinary evaluation including clinicians with expertise in the primary cancer type is essential to the successful management of adrenal metastases.

PubMed-ID: [37079202](#)

DOI: [10.1245/s10434-023-13474-8](#)

NET

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

ASO Author Reflections: Role of the Computed Tomography Maximum in Pancreatic Neuroendocrine Tumors.

Ann Surg Oncol, 30(5):2999.

H. Chen and S. Ji. 2023.

PubMed-ID: [36305988](#)

DOI: [10.1245/s10434-022-12722-7](#)

Maximum Value on Arterial Phase Computed Tomography Predicts Prognosis and Treatment Efficacy of Sunitinib for Pancreatic Neuroendocrine Tumours.

Ann Surg Oncol, 30(5):2988-98.

H. Chen, Z. Li, Y. Hu, X. Xu, Z. Ye, X. Lou, W. Zhang, H. Gao, Y. Qin, Y. Zhang, X. Chen, J. Chen, W. Tang, X. Yu and S. Ji. 2023.

PURPOSE: This study was designed to assess the computed tomography maximum (CTmax) value on pretherapeutic arterial phase computed tomography (APCT) images to predict pancreatic neuroendocrine tumours (pNETs) recurrence and clarify its role in predicting the outcome of tumour therapy. **METHODS:** This retrospective study enrolled 250 surgical patients and 24 nonsurgical patients with sunitinib-based treatment in our hospital from 2008 to 2019. CT images were assessed, the maximum value was defined as "CTmax," and recurrence-free survival (RFS) or progression-free survival (PFS) was compared between a high-CTmax group and a low-CTmax group among patients who underwent surgical resection or nonsurgical, sunitinib-based treatment according to the CTmax cutoff value. **RESULTS:** In ROC curve analysis, a CTmax of 108 Hounsfield units, as the cutoff value, achieved an AUC of 0.796 in predicting recurrence. Compared with the low-CTmax group, the high-CTmax group had a longer RFS ($p < 0.001$). Low CTmax was identified as an independent factor for RFS ($p < 0.001$) in multivariate analysis; these results were confirmed using the internal validation set. The CTmax value was significantly correlated with the microvascular density (MVD) value ($p < 0.001$) and the vascular endothelial growth factor receptor 2 (VEGFR2) score ($p < 0.001$). Furthermore, the high-CTmax group had a better PFS than the low-CTmax group among the sunitinib treatment group ($p = 0.007$). **CONCLUSIONS:** The tumour CTmax on APCT might be a potential and independent indicator for predicting recurrence in patients who have undergone surgical resection and assessing the efficacy of sunitinib for patients with advanced metastatic pNETs.

PubMed-ID: [36310316](#)

DOI: [10.1245/s10434-022-12693-9](#)

Primary tumor resection improves survival of gastrointestinal neuroendocrine carcinoma patients with nonresected liver metastases.

J Surg Oncol, 127(6):945-55.

Q. Chen, K. Li, K. E. Rhodin, S. J. Masoud, M. E. Lidsky, J. Cai, Q. Wei, S. Luo and H. Zhao. 2023.

BACKGROUND: The role of primary tumor resection (PTR) in the survival of gastrointestinal neuroendocrine carcinoma (GI-NEC) patients with liver metastases only remains poorly defined. Therefore, we investigated the impact of PTR on the

survival of GI-NEC patients with nonresected liver metastases. METHODS: GI-NEC patients with a liver-confined metastatic disease diagnosed between 2016 and 2018 were identified in the National Cancer Database. Multiple imputations by chained equations were used to account for missing data, and the inverse probability of treatment weighting (IPTW) method was used to eliminate selection bias. Overall survival (OS) was compared by adjusted Kaplan-Meier curves and log-rank test with IPTW. RESULTS: A total of 767 GI-NEC patients with nonresected liver metastases were identified. Among all patients, 177 (23.1%) received PTR and had a significantly favorable OS before (median: 43.6 months [interquartile range, IQR, 10.3-64.4] vs. 8.8 months [IQR, 2.1-23.1], $p < 0.001$ in log-rank test) and after (median: 25.7 months [IQR, 10.0-64.4] vs. 9.3 months [IQR, 2.2-26.4], $p < 0.001$ in IPTW-adjusted log-rank test) the IPTW adjustment. Additionally, this survival advantage persisted in an adjusted Cox model (IPTW adjusted hazard ratio = 0.431, 95% confidence interval: 0.332-0.560; $p < 0.001$). The improved survival persisted in subgroups stratified by primary tumor site, tumor grade, and N stage, even in the complete cohort (excluding patients with missing data). CONCLUSIONS: PTR led to improved survival for GI-NEC patients with nonresected liver metastases regardless of primary tumor site, tumor grade, and N stage. However, the decision for PTR should be made on an individualized basis following multidisciplinary evaluation.

PubMed-ID: [36807890](#)

DOI: [10.1002/jso.27213](#)

Efficacy and predictive factors of endoscopic ultrasound-guided ethanol ablation in benign solid pancreatic tumors.

Surg Endosc, 37(8):5960-8.

J. H. Choi, W. H. Paik, S. H. Lee, M. W. Lee, I. R. Cho, J. K. Ryu and Y. T. Kim. 2023.

BACKGROUND AND OBJECTIVES: Endoscopic ultrasound-guided ethanol ablation (EUS-EA) has recently been introduced for the management of solid pancreatic tumors, including pancreatic neuroendocrine tumors (PNETs) and solid pseudopapillary tumors (SPTs). The study aims to evaluate the efficacy and predictive factors for response of EUS-EA in solid pancreatic tumors. METHODS: Between October 2015 and July 2021, 72 patients who underwent EUS-EA for solid pancreatic tumors were included. The study outcomes were to evaluate the efficacy of EUS-EA with complete remission (CR) and objective response, and their predictive factors. RESULTS: During follow-up, 47 patients were diagnosed with PNETs and 25 with SPTs. Eight cases reached CR and 48 reached objective response. When compared with SPTs, PNETs showed similar duration to reach CR (median not reached; $p = 0.319$), but shorter duration to reach objective response (PNETs: median 20.6 months, 95%CI 10.26-30.88; SPTs: median 47.7 months, 95%CI 18.14-77.20; $p = 0.018$). Ethanol dosage > 0.35 ml/cm³ shortened the duration to reach CR (median not reached; $p = 0.026$) and objective response (median 42.5 months, 95%CI 25.34-59.66 vs. 19.6 months, 95%CI 10.17-29.09; $p = 0.006$). CR had no significant predictive factors, but PNETs showed significant predictive factors for objective response (HR 3.34, 95%CI 1.07-10.43; $p = 0.038$). Twenty-seven patients experienced adverse events, and there were two severe cases. CONCLUSION: EUS-EA for pancreatic solid lesions seems feasible as a local treatment for patients who refuse or are unfit for surgery. Additionally, PNETs seem to be the better candidate for EUS-EA.

PubMed-ID: [37079095](#)

DOI: [10.1007/s00464-022-09833-3](#)

PMCID: PMC10338579

ASO Visual Abstract: Survival and Symptomatic Relief After Cytoreductive Hepatectomy for Neuroendocrine Tumor Liver Metastases-Long-Term Follow-Up of Over 500 Patients.

Ann Surg Oncol, 30(8):4854-5.

H. Gudmundsdottir, E. B. Habermann, R. A. Vierkant, P. Starlinger, C. A. Thiels, S. G. Warner, R. L. Smoot, M. J. Truty, M. L. Kendrick, T. R. Halfdanarson, D. M. Nagorney and S. P. Cleary. 2023.

PubMed-ID: [37040050](#)

DOI: [10.1245/s10434-023-13424-4](#)

ASO Author Reflections: Long-Term Outcomes after Cytoreductive Hepatectomy for Neuroendocrine Tumor Liver Metastases.

Ann Surg Oncol, 30(8):4852-3.

H. Gudmundsdottir, T. R. Halfdanarson, D. M. Nagorney and S. P. Cleary. 2023.

PubMed-ID: [36940040](#)

DOI: [10.1245/s10434-023-13374-x](#)

ASO Visual Abstract: Risk Factors for Lymph Node Metastasis of Rectal Neuroendocrine Tumor and its Prognostic Impact-A Single-Center Retrospective Analysis of 195 Cases with Radical Resection.

Ann Surg Oncol, 30(7):3956.

Y. Hiyoshi, N. Daitoku, T. Mukai, T. Nagasaki, T. Yamaguchi, T. Akiyoshi, C. Yasue, A. Chino, S. Saito, M. Takamatsu and Y. Fukunaga. 2023.

PubMed-ID: [37130941](#)

DOI: [10.1245/s10434-023-13515-2](#)

Risk Factors for Lymph Node Metastasis of Rectal Neuroendocrine Tumor and Its Prognostic Impact: A Single-Center Retrospective Analysis of 195 Cases with Radical Resection.

Ann Surg Oncol, 30(7):3944-53.

Y. Hiyoshi, N. Daitoku, T. Mukai, T. Nagasaki, T. Yamaguchi, T. Akiyoshi, C. Yasue, A. Chino, S. Saito, M. Takamatsu and Y. Fukunaga. 2023.

PURPOSE: The incidence of rectal neuroendocrine tumors (NETs) has been steadily increasing. The risk factors for and prognostic impact of lymph node (LN) metastasis were analyzed in 195 patients with stage I-III rectal NET who underwent radical surgery. **METHODS:** This retrospective, single-center study analyzed risk factors for LN metastasis focusing on previously identified factors and a novel risk factor: multiple rectal NETs. The association between LN metastasis and the prognosis was also analyzed. **RESULTS:** Pathologically, the LN metastasis rate (also the rate of stage III disease) was 39%, which was higher than the clinical LN metastasis rate of 14%. Tumor size > 10 mm, presence of central depression, tumor grade G2, depth of invasion, LN swelling on preoperative imaging (cN1), venous invasion and multiple NETs were identified as risk factors for LN metastasis. As the tumor size and risk factors increased, the rate of LN metastasis increased. Among these 7 factors, venous invasion, cN1, and multiple NETs were identified as independent predictors of LN metastasis. LN metastasis of rectal NETs was associated with significantly poor disease-free and disease-specific survival. **CONCLUSIONS:** As risk factors increase, the potential for rectal NETs to metastasize to the LNs increases and LN metastasis is associated with a poor prognosis. This is the first study to report multiple NETs as a risk factor for LN metastasis. A future study examining the survival benefit of radical surgery accompanying LN dissection compared with local resection is warranted.

PubMed-ID: [36935432](#)

DOI: [10.1245/s10434-023-13348-z](#)

Development and validation of a survival prediction model and risk stratification for pancreatic neuroendocrine neoplasms.

J Endocrinol Invest, 46(5):927-37.

Z. Lu, T. Li, C. Liu, Y. Zheng and J. Song. 2023.

PURPOSE: We explored risk variables associated with cancer-specific survival (CSS) in patients with pancreatic neuroendocrine neoplasms (PNENs) and created a network dynamic nomogram model to predict patient survival time. **METHODS:** A total of 7750 patients with PNENs were included in this analysis, including 134 with functional PNENs and 7616 with nonfunctional PNENs. Clinical feature and prognosis differences between functional and nonfunctional PNENs were compared. Independent prognostic factors affecting CSS were analyzed by univariate and multifactorial Cox regression. Nomogram and web-based prognosis prediction of PNENs were developed and validated by C indices, decision curve analysis, and calibration plots. **RESULTS:** Patients with functional PNENs were younger at diagnosis than those with nonfunctional PNENs. Functional PNENs had better prognoses than nonfunctional PNENs (5-year survival rates: 78.55% and 71.10%, respectively). Univariate and multifactorial Cox regression analyses showed that tumor infiltration (T), nodal metastasis (N), metastasis (M), tumor site, differentiation grade, age, marital status, and surgical treatment were independent prognostic risk factors for CSS, which were included in the prognostic nomogram and web-based prognosis calculator. The calibration plots and decision curve analysis showed that the nomogram had excellent prediction and clinical practical ability. The C indices for CSS in the training and validation cohorts were 0.848 (95% CI 0.838-0.8578) and 0.823 (95% CI 0.807-0.839), respectively. We scored all patients according to the nomogram and divided patients into three different risk groups. The prognosis of the low-risk population was significantly better than those of the middle- and high-risk populations based on Kaplan-Meier survival curve. **CONCLUSION:** We analyzed the clinical features of PNENs and developed a convenient and web dynamic nomogram to predict CSS.

PubMed-ID: [36394822](#)

DOI: [10.1007/s40618-022-01956-7](#)

Sporadic and MEN1-related gastrinoma and Zollinger-Ellison syndrome: differences in clinical characteristics and survival outcomes.

J Endocrinol Invest, 46(5):957-65.

S. Massironi, R. E. Rossi, A. Laffusa, C. Eller-Vainicher, F. Cavalcoli, A. Zilli, C. Ciafardini, V. Sciola, P. Invernizzi and M. Peracchi. 2023.

PURPOSE: Gastrinoma with Zollinger-Ellison syndrome (ZES) may occur sporadically (Sp) or as part of the inherited syndrome of multiple endocrine neoplasia 1 (MEN-1). Data comparing Sp and MEN-1/ZES are scanty. We aimed to identify and compare their clinical features. **METHODS:** Consecutive patients with ZES were evaluated between 1992 and 2020 among a monocentric Italian patient cohort. **RESULTS:** Of 76 MEN-1 patients, 41 had gastroenteropancreatic neuroendocrine neoplasm (GEP-NEN), 18 of whom had ZES; of 320 Sp-GEP-NEN, 19 had Sp-ZES. MEN-1/ZES patients were younger ($p = 0.035$) and the primary MEN-1/ZES gastrinoma was smaller than Sp-ZES ($p = 0.030$). Liver metastases occurred in both groups, but only Sp-ZES developed extrahepatic metastases. 13 Sp-ZES and 8 MEN-1/ZES underwent surgery. 8 Sp-ZES and 7 MEN-1/ZES received somatostatin analogs (SSAs). Median overall survival (OS) was higher in MEN-1/ZES than in Sp-ZES (310 vs 168 months, $p = 0.034$). At univariate-logistic regression, age at diagnosis ($p = 0.01$, OR = 1.1), G3 grading ($p = 0.003$, OR = 21.3), Sp-ZES ($p = 0.02$, OR = 0.3) and presence of extrahepatic metastases ($p = 0.001$, OR = 7.2) showed a significant association with OS. At multivariate-COX-analysis, none of the variables resulted significantly related to OS. At univariate-logistic regression, age ($p = 0.04$, OR = 1.0), size ($p = 0.039$, OR = 1.0), G3 grade ($p = 0.008$, OR = 14.6) and extrahepatic metastases ($p = 0.005$, OR = 4.6) were independently associated with progression-free survival (PFS). In multivariate-COX-analysis, only extrahepatic metastases ($p = 0.05$, OR = 3.4) showed a significant association with PFS. Among SSAs-treated patients, MEN-1/ZES showed better PFS ($p = 0.0227$). After surgery, the median PFS was 126 and 96 months in MEN-1 and Sp, respectively. **CONCLUSION:** MEN-1/ZES patients generally show better OS and PFS than Sp-ZES as well as better SSAs response.

PubMed-ID: [36436191](https://pubmed.ncbi.nlm.nih.gov/36436191/)

DOI: [10.1007/s40618-022-01961-w](https://doi.org/10.1007/s40618-022-01961-w)

PMCID: PMC10105668

ASO Author Reflections: Preoperative Malignant Risk Assessment for Small (≤ 20 mm) Nonfunctioning Pancreatic Neuroendocrine Tumors.

Ann Surg Oncol, 30(6):3501-2.

Y. Nanno and H. Toyama. 2023.

PubMed-ID: [36765011](https://pubmed.ncbi.nlm.nih.gov/36765011/)

DOI: [10.1245/s10434-023-13201-3](https://doi.org/10.1245/s10434-023-13201-3)

ASO Visual Abstract: Reappraisal of Malignant Risk Assessment for Small (a per thousand currency20 mm) Non-functioning Pancreatic Neuroendocrine Tumors.

Ann Surg Oncol, 30(6):3503-4.

Y. Nanno, H. Toyama, I. Matsumoto, J. Uemura, S. Asari, T. Goto, D. Lee, T. Murakami, S. Komatsu, H. Yanagimoto, M. Kido, T. Ajiki, K. Okano, Y. Takeyama and T. Fukumoto. 2023.

PubMed-ID: [36929141](https://pubmed.ncbi.nlm.nih.gov/36929141/)

DOI: [10.1245/s10434-023-13322-9](https://doi.org/10.1245/s10434-023-13322-9)

Reappraisal of Malignant Risk Assessment for Small (≤ 20 mm) Non-functioning Pancreatic Neuroendocrine Tumors.

Ann Surg Oncol, 30(6):3493-500.

Y. Nanno, H. Toyama, I. Matsumoto, J. Uemura, S. Asari, T. Goto, D. Lee, T. Murakami, S. Komatsu, H. Yanagimoto, M. Kido, T. Ajiki, K. Okano, Y. Takeyama and T. Fukumoto. 2023.

BACKGROUND: Optimal management of non-functioning pancreatic neuroendocrine tumors (PanNETs) ≤ 20 mm is controversial. The biological heterogeneity of these tumors poses challenges when deciding between resection and observation. **METHODS:** In this multicenter, retrospective cohort study, we analyzed all patients ($n = 78$) who underwent resection of non-functioning PanNETs ≤ 20 mm at three tertiary medical centers from 2004 to 2020 to assess the utility of preoperatively available radiological features and serological biomarkers of non-functioning PanNETs in choosing an optimal surgical indication. The radiological features included non-hyper-attenuation pattern on enhancement computed tomography (CT; hetero/hypo-attenuation) and main pancreatic duct (MPD) involvement, and serological biomarkers included elevation of serum elastase 1 and plasma chromogranin A (CgA) levels. **RESULTS:** Of all small non-functioning PanNETs, 5/78 (6%) had lymph node metastasis, 11/76 (14%) were WHO grade II, and 9/66 (14%) had microvascular invasion; 20/78 (26%) had at least one of these high-risk pathological factors. In the preoperative assessment,

hetero/hypo-attenuation and MPD involvement were observed in 25/69 (36%) and 8/76 (11%), respectively. Elevated serum elastase 1 and plasma CgA levels were observed in 1/33 (3%) and 0/11 (0%) patients, respectively. On multivariate logistic regression analysis, hetero/hypo-attenuation (odds ratio [OR] 6.1, 95% confidence interval [CI] 1.7-22.2) and MPD involvement (OR 16.8, 95% CI 1.6-174.3) were significantly associated with the high-risk pathological factors. The combination of the two radiological worrisome features correctly predicted non-functioning PanNETs with high-risk pathological factors, with about 75% sensitivity, 79% specificity, and 78% accuracy. CONCLUSIONS: This combination of radiological worrisome features can accurately predict non-functioning PanNETs that may require resection.

PubMed-ID: [36795254](#)

DOI: [10.1245/s10434-023-13193-0](#)

ASO Visual Abstract: Prognostic Significance and Predictors of Nodal Recurrence After Surgery for Nonfunctioning Pancreatic Neuroendocrine Tumors.

Ann Surg Oncol, 30(6):3478.

S. Partelli, V. Andreasi, M. Peralta Ferreira, D. Palumbo, F. Muffatti, A. Battistella, F. Fermi, P. Mapelli, D. Tamburrino, N. Pecorelli, S. Crippa and M. Falconi. 2023.

PubMed-ID: [36859705](#)

DOI: [10.1245/s10434-023-13283-z](#)

Lymph Node Metastasis, Radical Surgery, and Prognosis in Well-Differentiated Neuroendocrine Tumors of the Rectum.

Ann Surg Oncol, 30(7):3885-6.

N. Raj. 2023.

PubMed-ID: [37040048](#)

DOI: [10.1245/s10434-023-13421-7](#)

Prognostic differences in grading and metastatic lymph node pattern in patients with small bowel neuroendocrine tumors.

Langenbecks Arch Surg, 408(1):237.

L. Reinhard, M. T. Mogl, F. Benz, A. Dukaczewska, F. Butz, E. M. Dobrindt, F. Tacke, J. Pratschke, P. E. Goretzki and H. Jann. 2023.

PURPOSE: Neuroendocrine tumors of the small intestine (si-NET) describe a heterogenous group of neoplasms. Based on the Ki67 proliferation index si-NET are divided into G1 (Ki67 < 2%), G2 (Ki67 3-20%) and rarely G3 (Ki67 > 20%) tumors. However, few studies evaluate the impact of tumor grading on prognosis in si-NET. Moreover, si-NET can form distinct lymphatic spread patterns to the mesenteric root, aortocaval lymph nodes, and distant organs. This study aims to identify prognostic factors within the lymphatic spread patterns and grading. METHODS: Demographic, pathological, and surgical data of 208 (90 male, 118 female) individuals with si-NETs treated at Charite University Medicine Berlin between 2010 and 2020 were analyzed retrospectively. RESULTS: A total of 113 (54.5%) specimens were defined as G1 and 93 (44.7%) as G2 tumors. Interestingly, splitting the G2 group in two subgroups: G2 low (Ki67 3-9%) and G2 high (Ki67 10-20%), displayed significant differences in overall survival (OS) (p = 0.008) and progression free survival (PFS) (p = 0.004) between these subgroups. Remission after surgery was less often achieved in patients with higher Ki67 index (> 10%). Lymph node metastases (N +) were present in 174 (83.6%) patients. Patients with isolated locoregional disease showed better PFS and OS in comparison to patients with additional aortocaval and distant lymph node metastases. CONCLUSION: Lymphatic spread pattern influences patient outcome. In G2 tumors, low and high grading shows heterogenous outcome in OS and PFS. Differentiation within this group might impact follow-up, adjuvant treatment, and surgical strategy.

PubMed-ID: [37332044](#)

DOI: [10.1007/s00423-023-02956-8](#)

PMCID: PMC10277262

Changes in diagnosis and operative treatment of insulinoma over two decades.

Langenbecks Arch Surg, 408(1):255.

D. Wiese, F. G. Humburg, P. H. Kann, A. Rinke, M. Luster, A. Mahnken and D. K. Bartsch. 2023.

PURPOSE: Most insulinomas are small solitary, benign neoplasms. Imaging and surgical techniques improved over the last 20 years. Thus, the aim of the present study was to analyze changes in diagnosis and surgery of insulinoma patients in a referral center over two decades. METHODS: Operated patients with a histologically proven insulinoma were retrieved from a prospective database. Clinico-pathological characteristics and outcomes were retrospectively analyzed with regard to the time periods 2000-2010 (group 1) and 2011-2020 (group 2). RESULTS: Sixty-one of 202 operated patients with pNEN

had an insulinoma, 37 (61%) in group 1 and 24 (39%) in group 2. Of those 61 insulinomas, 49 (80%) were sporadic benign, 8 (13%) benign MEN1-associated insulinomas, and 4 (7%) sporadic malignant insulinomas. In 35 of 37 (95%) patients of group 1 and all patients of group 2, the insulinoma was preoperatively identified by imaging. The most sensitive imaging modality was endoscopic ultrasound (EUS) with correctly diagnosed and localized insulinomas in 89% of patients in group 1 and 100% in group 2. In group 1, significantly less patients were operated via minimally invasive approach compared to group 2 (19% (7/37) vs. 50% (12/24), $p = 0.022$). Enucleation was the most frequently performed operation (31 of 61, 51%), followed by distal resection (15 of 61, 25%) without significant differences between groups 1 and 2. The rate of relevant postoperative complications was not different between groups 1 and 2 (24% vs. 21%, $p = 0.99$). Two patients with benign insulinoma (1 out of each group) experienced disease recurrence and underwent a second resection. After a median follow-up of 134 (1-249) months, however, all 57 (100%) patients with benign insulinoma and 3 out of 4 patients with malignant insulinoma had no evidence of disease. CONCLUSION: Insulinoma can be preoperatively localized in almost all patients, allowing for a minimally invasive, parenchyma-sparing resection in selected patients. The long-term cure rate is excellent.

PubMed-ID: [37386194](#)

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General

Meta-Analyses

- None -

Randomized controlled trials

- None -

Consensus Statements/Guidelines

- None -

Other Articles

Optimization of Opioid Discharge Prescriptions Following Thyroid and Parathyroid Surgery.

Otolaryngol Head Neck Surg, 169(1):176-84.

E. Rizk, F. Yuan, F. Zheng, E. Fink, N. Kaur, A. T. Tran, T. Iso, N. G. Mohyuddin, A. A. Thekdi, G. L. Jackson, M. A. Wanat, J. D. Thornton and J. T. Swan. 2023.

OBJECTIVE: To evaluate the impact of a quality improvement bundle on opioid discharge prescribing following thyroidectomy and parathyroidectomy. **METHODS:** This before-and-after study included patients undergoing thyroidectomy or parathyroidectomy at an academic medical center. The quality improvement bundle included a patient education flyer, electronic health record order sets with multimodal analgesia regimens, and provider education. The preimplementation cohort included patients treated from January 2018 to December 2019. The postimplementation cohort included patients treated from June 2021 to August 2021. The primary outcome was the proportion of patients who received new opioid discharge prescriptions. **RESULTS:** A total of 160 patients were included in the preimplementation cohort, and the first 80 patients treated after bundle implementation were included in the postimplementation cohort. Patients receiving new opioid discharge prescriptions decreased from 80% (128/160) in the preimplementation cohort to 35% (28/80) in the postimplementation cohort with an unadjusted absolute reduction of 45% (95% CI, 33%-57%; $P < .001$; number needed to treat = 3) and an adjusted odds ratio (OR) of 0.08 (95% CI, 0.04-0.19; $P < .001$). The bundle was associated with reductions in opioid discharge prescriptions that exceeded 112.5 oral morphine milligram equivalents (33% pre- vs 10% postimplementation; adjusted OR, 0.20; $P = .001$) or 5 days of therapy (17% pre- vs 6% postimplementation; adjusted OR, 0.34; $P = .049$). **DISCUSSION:** Implementation of a pain management quality improvement bundle reduced opioid discharge prescribing following thyroidectomy and parathyroidectomy. **IMPLICATIONS FOR PRACTICE:** Unnecessary opioid prescriptions generate unused opioids in patients' homes that can lead to opioid misuse. We believe that this bundle reduced the risk for opioid misuse in our community. **REGISTRATION:** The study was registered at ClinicalTrials.gov (NCT04955444) before implementation.

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