1. J Clin Endocrinol Metab. 2019 Apr 24. pii: jc.2019-00851. doi: 10.1210/jc.2019-00851. [Epub ahead of print]
Response to Letter to the Editor: [Time to Separate Persistent from Recurrent Differentiated Thyroid Cancer: Different Conditions with Different outcomes].
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DOI: 10.1210/jc.2019-00851
PMID: 31127825

2. J Clin Endocrinol Metab. 2019 Apr 24. pii: jc.2019-00634. doi: 10.1210/jc.2019-00634. [Epub ahead of print]
"Letter to the Editor: [Time to Separate Persistent from Recurrent Differentiated Thyroid Cancer: Different Conditions with Different outcomes]".
Burmeister LA, Drake T.
DOI: 10.1210/jc.2019-00634
PMID: 31127817

3. J Clin Endocrinol Metab. 2019 May 22. pii: jc.2018-02809. doi: 10.1210/jc.2018-02809. [Epub ahead of print]
Stage II Differentiated Thyroid Cancer Is a High-risk Disease in Patients <45/55 Years Old.
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PURPOSE: The mortality risk of stage II differentiated thyroid cancer (DTC) on
the American Joint Committee on Cancer (AJCC) staging system remains to be further investigated.
METHODS: Retrospective study of DTC in the USA Surveillance, Epidemiology, and End Results for disease-specific mortality risk in various AJCC stages, with

patient age stratification of stage II disease.
RESULTS: On AJCC 6.0, compared with stage I, hazard ratios (HRs) of mortality for stages II in patients <45 yo, II in patients ≥45 yo, III, IVA, IVB, and IVC were

46.95, 4.95, 9.82, 57.37, 222.10, and 468.68, respectively, showing a robustly higher mortality risk in stage II disease in patients <45 yo than older patients (P<0.001), comparable with stage IVA (P=0.482). Similar results were obtained on

AJCC 7.0. On AJCC 8.0, compared with stage I, HRs of mortality for stages II in patients <55 yo, II in patients ≥55 yo, III, IVA, and IVB were 75.16, 11.23, 69.45, 134.94, and 235.70, respectively, showing a robustly higher risk in stage
II disease in patients <55 yo than older patients (P<0.001), comparable with stage III (P=0.57). Kaplan-Meier survival curves displayed a sharp decline with stage II disease in patients <45/55 yo compared with older patients. CONCLUSIONS: The mortality risk of stage II DTC is sharply differentiated at patient age 45/55 years, being robustly high in younger patients and comparable with stage III/IVA; this emphasizes the importance of taking age in consideration when managing stage II DTC and not treating it as a uniformly low-risk disease. DOI: 10.1210/jc.2018-02809 PMID: 31116377

4. World J Surg. 2019 May 16. doi: 10.1007/s00268-019-05028-5. [Epub ahead of print] Prognostic Impact of the Turin Criteria in Poorly Differentiated Thyroid
Carcinoma.
Akaishi J(1), Kondo T(2), Sugino K(3), Ogimi Y(3), Masaki C(3), Hames KY(3),

Yabuta T(3), Tomoda C(3), Suzuki A(3), Matsuzu K(3), Uruno T(3), Ohkuwa K(3), Kitagawa W(3), Nagahama M(3), Katoh R(4), Ito K(3).
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BACKGROUND: The Turin criteria including solid, trabecular, and/or insular architecture, lack of typical nuclear features of papillary carcinoma, and mitoses, necrosis, or convoluted nuclei were adopted in the recent 4th edition of the World Health Organization classification published in 2017.

MATERIALS AND METHODS: Between 2006 and 2017, 11,001 cases underwent initial surgery for primary malignant thyroid tumor derived from follicular cells. A
total of 75 (0.7%) cases were diagnosed with PDTC according to the 2004 WHO classification. Based on the Turin criteria, 30 (40%) cases were re-classified as PDTC-Turin (+) and 45 (60%) cases were PDTC-Turin (-). Clinicopathological

features and prognosis were compared between PDTC-Turin (+) and PDTC-Turin (-). RESULTS: Seventy-five patients (48 females and 27 males) had a median age at the time of surgery of 57 years. Preoperative diagnosis was benign in 16 (21%), follicular tumor in 40 (53%), and malignant in 19 (25%). The 5-year

cause-specific survival (CSS) and disease-free survival (DFS) rates were 97% and 44% for PDTC-Turin (+) and 100% and 88% for PDTC-Turin (-). On univariate analysis, CSS and DFS rates were significantly worse in the PDTC-Turin (+) than in the PDTC-Turin (-) ($p = 0.0096$, and $p = 0.0016$). Multivariate analysis showed that Turin criteria status, Ki-67 labeling index ≥ 10%, and age 55 ≥ years were the independent prognostic factors for recurrence.

CONCLUSIONS: The prevalence of PDTC diagnosed with the Turin criteria was low, but it showed more aggressive behavior. The 2017 WHO classification reflects the prognosis more accurately than the 2004 WHO classification.

DOI: 10.1007/s00268-019-05028-5 PMID: 31098668

5. Nat Rev Endocrinol. 2019 Jun;15(6):319-321. doi: 10.1038/s41574-019-0204-8. Sonographic diagnosis of thyroid cancer with support of AI.
Verburg F(1), Reiners C(2).
Author information:

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DOI: 10.1038/s41574-019-0204-8

PMID: 31024088

6. Br J Surg. 2019 Apr 23. doi: 10.1002/bjs.11145. [Epub ahead of print] Predicting recurrence of papillary thyroid cancer using the eighth edition of the AJCC/UICC staging system.
Chereau N(1), Oyekunle TO(2), Zambeli-Ljepović A(2), Kazaure HS(3), Roman SA(4), Menegaux F(1), Sosa JA(4).
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BACKGROUND: The AJCC/UICC classification is widely used for predicting survival in papillary thyroid cancer (PTC), but has not been evaluated as a

predictor of recurrence. The hypothesis of this study was that the eighth edition of the AJCC system can be used in this novel way.

METHODS: All patients in the study underwent surgery for PTC at a high-volume endocrine surgery centre in France between 1985 and 2015. The seventh and eighth editions of the AJCC/UICC staging system for PTC were employed to predict recurrence and disease-specific survival using the Kaplan-Meier and log rank

tests.
RESULTS: Among 4124 patients (79·7 per cent female), median age was 50 (i.q.r. 38-60) years; 3906 patients (94·7 per cent) underwent total thyroidectomy, with lymph node dissection in 2495 (60·5 per cent). The eighth edition of the AJCC/UICC staging system placed 91·8, 7·1, 0·4 and 0·7 per cent of patients in stages I-IV respectively. After reclassifying patients from the seventh to the eighth AJCC/UICC edition, the disease was downstaged in 23·8 per cent. Over a median follow-up of 7 years, 260 patients (6·4 per cent) developed recurrent disease, including 5·2 per cent of patients with stage I, 19·6 per cent with
stage II, 59 per cent with stage III and 50 per cent with stage IV disease, according to the eighth edition. The eighth edition was a better predictor of recurrence than the seventh edition.
CONCLUSION: The eighth edition of the AJCC/UICC staging system appears to be a novel tool for predicting PTC recurrence, which is a meaningful outcome for this

indolent disease. The eighth edition can be used to risk-stratify patients, keeping in mind that other molecular and pathological predictive factors must be integrated into the assessment of recurrence risk.

DOI: 10.1002/bjs.11145
PMID: 31012500

7. J Clin Endocrinol Metab. 2019 Jun 1;104(6):2150. doi: 10.1210/jc.2019-00730. CORRIGENDUM FOR "Hemodynamic Markers and Subclinical Atherosclerosis in Postmenopausal Women With Primary Hyperparathyroidism".
[No authors listed]

DOI: 10.1210/jc.2019-00730 PMID: 30933272

8. Nat Rev Endocrinol. 2019 May;15(5):254-255. doi: 10.1038/s41574-019-0193-7. Key pathways revealed in rare thyroid cancer.
Starling S(1).
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(1)Nature Reviews Endocrinology, . nrendo@nature.com. DOI: 10.1038/s41574-019-0193-7
PMID: 30867550

9. J Clin Endocrinol Metab. 2019 May 1;104(5):1677. doi: 10.1210/jc.2019-00546. CORRIGENDUM FOR "Pilot Dose Comparison of Apatinib in Chinese Patients With Progressive Radioiodine-Refractory Differentiated Thyroid Cancer".
[No authors listed]

DOI: 10.1210/jc.2019-00546 PMID: 30860587

10. World J Surg. 2019 Jun;43(6):1525-1531. doi: 10.1007/s00268-019-04944-w. Minimally Invasive Parathyroidectomy without Intraoperative PTH Performed after Positive Ultrasonography as the only Diagnostic Method in Patients with Primary Hyperparathyroidism.

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BACKGROUND: A positive and concordant result of at least two diagnostic modalities is generally recommended prior to focused parathyroidectomy. The aim of this study was to analyze the results of surgery and the accurateness of preoperative ultrasonography (US) as single localization modality in patients who underwent parathyroidectomy without the adjunct of intraoperative Parathormone (PTH) measurement.

METHODS: The cases with a preoperative US as the only localization technique, who underwent parathyroidectomy between 10/1999 and 12/2017, were selected from a prospectively maintained database. Therefore, a total number of 242 patients with
a mean age of 58.6 ± 13.7 years were included in the present study. US was performed by referral endocrinologist or by the surgeon during office visits.
RESULTS: The overall "cure rate" was 99.2% (240 out of 242 patients). In 228/242 patients (94.2%), a drop of perioperative PTH levels consistent with the

definition of cure was observed on the day of surgery. In four of the remaining 14 patients, healing was confirmed by PTH level dropping into the normal range on the first postoperative day. Eight patients were cured after a reoperation was performed at our department. Postoperative complications included one case of permanent recurrent laryngeal nerve palsy (0.4%).
CONCLUSIONS: If performed by an experienced endocrinologist and/or endocrine surgeon, a positive US could be the only preoperative localization study in
patients with pHPT. Moreover, the add-value of intraoperative PTH is limited. Major advantages of US are a very high accuracy, the ease of performance (accessibility) and its cost-effectiveness compared with Sesta-MIBI

scintigraphy. DOI: 10.1007/s00268-019-04944-w
PMID: 30847526

11. J Clin Endocrinol Metab. 2019 Jul 1;104(7):2712-2718. doi: 10.1210/jc.2018-02471. Leukocyte Telomere Length and Risk of Papillary Thyroid Carcinoma.
Li J(1)(2), An C(3), Zheng H(4), Lei T(1)(2), Zhang N(2), Zheng Y(2), Yang M(2).
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CONTEXT: Telomere length may contribute to predisposition to papillary thyroid cancer (PTC).
OBJECTIVE: To test this hypothesis, we examined the association between leukocyte telomere length and PTC risk.

DESIGN/SETTING: Case-control study in a Chinese Han population.
PARTICIPANTS/INTERVENTION: A total of 1200 PTC cases and 1201 age- and sex-matched healthy controls were included in the study. ORs and 95% CIs were calculated by logistic regression.
RESULTS: Short relative telomere length (RTL) was significantly associated with elevated risk of PTC (OR = 1.61, 95% CI = 1.35 to 1.92; P = 1.30 × 10-7). Interestingly, when individuals were categorized into four groups on the basis of quartile distribution of relative telomere length (RTL) in controls, we observed
a reverse U-shaped association between telomere length and PTC risk. Compared with those in the first (the longest) quartile as the reference group, ORs (95%
CIs) were 5.61 (4.04 to 7.78) (P = 6.10 × 10-25), 9.33 (6.78 to 12.83) (P = 6.99

× 10-43), and 1.23 (0.83 to 1.81) (P = 0.300) for individuals in the second, third, and fourth (the shortest) quartiles, respectively. This reverse U-shaped relationship was more apparent in younger individuals.
CONCLUSIONS: Our findings suggest that RTL is significantly associated with susceptibility to PTC. There is an obvious reverse U-shaped association between telomere length and PTC risk. Telomere length may be a potential

pronouncing biomarker to identify individuals with a high risk of developing PTC.

DOI: 10.1210/jc.2018-02471
PMID: 30817819

12. World J Surg. 2019 May;43(5):1249-1255. doi: 10.1007/s00268-019-04906-2. Primary Squamous Cell Carcinoma in the Thyroid Gland: A Population-Based Analysis Using the SEER Database.
Yang S(1)(2)(3), Li C(4), Shi X(1)(2), Ma B(1)(2)(3), Xu W(1)(2)(3), Jiang H(1)(2)(3), Liu W(1)(2), Ji Q(1)(2)(3), Wang Y(5)(6)(7).
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OBJECTS: To evaluate prognostic factors and treatment outcomes of primary squamous cell carcinoma in thyroid (PSCCTh) over the past decades using a large national database.
METHODS: All patients diagnosed with PSCCTh between 1973 and 2015 were identified with the Surveillance, Epidemiology, and End Results Program (SEER) 18-registry database. Relevant clinical data were collected, and prognostic factors of overall survival (OS) and disease-specific survival (DSS) were analyzed.
RESULTS: This cohort study included 242 patients, accounting for 0.12% of all primary thyroid carcinomas from 1973 to 2015 nationwide. Of the patients with PSCCTh, 75% were older than 60 years at diagnosis. Patient age older than 60 years (HR 2.242, 95% CI 1.367-3.676, P = 0.001) and a tumor size larger than or equal to 50 mm (HR 1.479, 95% CI 1.011-2.165, P = 0.044) were independent negative prognostic factors. The univariate analysis suggested that the morphological subtype (OS, P = 0.033; DSS, P = 0.048), clinical treatment modality (OS, P < 0.0001; DSS, P < 0.0001), and T stage (OS, P = 0.004; DSS, P = 0.001) were important predictive factors for OS and DSS. In contrast, gender, race, year of diagnosis, geographic location, N stage, and M stage were not prognostic factors.
CONCLUSIONS: PSCCTh is a rare malignancy with an aggressive nature and poor

prognosis. Survival is predicted by the treatment modality, patient age, T stage, tumor size, and morphological subtypes. This study showed that early diagnosis and complete surgical resection plus adjuvant radiation therapy were associated with a better outcome.

DOI: 10.1007/s00268-019-04906-2 PMID: 30719559

13. World J Surg. 2019 May;43(5):1256-1263. doi: 10.1007/s00268-019-04924-0. High-Dose RAI Therapy Justified by Pathological N1a Disease Revealed by Prophylactic Central Neck Dissection for cN0 Papillary Thyroid Cancer Patients:
Is it Superior to Low-Dose RAI Therapy?

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OBJECTIVE: One of the presumed advantages of prophylactic central neck dissection (pCND) is offering staging basis for more aggressive radioactive iodine (RAI) therapy, which postulates the necessity of high dose for treatment efficacy. The present study aims to compare the effectiveness between low-dose and high-dose RAI in a select cohort of cN0 papillary thyroid cancer (PTC) patients with pathological N1a (pN1a) disease revealed by pCND in terms of ablation rate and response to therapy. The frequency of short-term adverse effects between the two groups was also compared.

PATIENTS AND METHODS: From January 2014 to April 2016, cN0 PTC patients with pN1a disease revealed by pCND in our hospital were retrospectively reviewed. Patients
with other indications for high-dose RAI, such as the presence of extrathyroidal extension, vascular invasion or suspicions of distant metastasis, were excluded.

For the included patients, high dose (3700 MBq) was administered between January 2014 and August 2015 and low dose (1110 MBq) between August 2015 and April 2016. Ablation assessment was performed 6 months after RAI therapy. Response evaluation after RAI therapy was performed after 46.3 ± 9.5 months for high-dose group and 29.1 ± 2.6 months for low-dose group. All patients were also evaluated for short-term adverse effects 24 and 72 hours after RAI administration.
RESULTS: A total of 84 patients were enrolled. Among them, 42 were in the

high-dose group and the other 42 in the low-dose group. There was no significant difference in ablation rate (P = 0.7707) and response to RAI therapy (P = 0.6454) between the two groups. Twenty-four hours after RAI administration, neck pain and swelling (33.3% VS. 11.9%; P = 0.0372) and gastrointestinal discomfort (45.2% vs. 21.4%; P = 0.0373) were significantly more frequent in the high-dose group. CONCLUSION: High-dose RAI therapy, with higher frequency of short-term adverse effects, appears to be not superior to low-dose RAI therapy for cN0 PTC patients

with pN1a disease revealed by pCND to achieve better response to therapy. Further randomized studies with larger series of patients and longer follow-up duration, especially with the low-dose group, are needed to validate our results.
DOI: 10.1007/s00268-019-04924-0

PMID: 30684002

14. World J Surg. 2019 May;43(5):1243-1248. doi: 10.1007/s00268-019-04920-4. Does Primary Hyperparathyroidism Have an Association with Thyroid Papillary Cancer? A Retrospective Cohort Study.
Çetin K(1), Sıkar HE(2), Temizkan Ş(3), Ofluoğlu CB(2), Özderya A(4), Aydın K(4), Gül AE(5), Küçük HF(2).

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BACKGROUND: To investigate the relationship between primary hyperparathyroidism (pHPT) and papillary thyroid cancer (PTC).
METHODS: The perioperative findings of 275 patients with pHPT who underwent surgery between January 2014 and December 2017 were retrospectively reviewed. Thirty-one patients were diagnosed with pHPT and PTC concurrently. Pathology results and demographic findings of these patients were compared with 186

patients who underwent thyroidectomy and diagnosed with PTC at the same time interval.
RESULTS: The co-occurrence of pHPT and PTC was 11.3% (31/275). The median ages of the pHPT, pHPT + PTC, and PTC groups were 55, 57, and 50 years old, respectively (p < 0.001). The diameter of tumor was smaller in the pHPT + PTC group [median

7 mm (range 0.5-25 mm) vs. 15 mm (range 1-100 mm)], with higher rates of microcarcinomas ($p < 0.001$), than the patients in the PTC group. Examination of tumor morphology showed higher rates of tumor capsule invasion and multicentricity in the pHPT + PTC group than those in the isolated PTC group ($p = 0.02$, $p = 0.04$, respectively).

CONCLUSION: The pHPT + PTC group had significantly smaller tumor diameter than the PTC group. This result may support the idea that pHPT leads to overdiagnosis of PTC. However, observation of high rates of tumor capsule invasion and multicentricity in the pHPT + PTC group may suggest an associative etiology with more aggressive PTC.

DOI: 10.1007/s00268-019-04920-4 PMID: 30680499

15. World J Surg. 2019 May;43(5):1232-1242. doi: 10.1007/s00268-019-04910-6.

18F-Fluorocholine PET/CT and Parathyroid 4D Computed Tomography for Primary Hyperparathyroidism: The Challenge of Reoperative Patients.

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BACKGROUND: To evaluate FCH-PET/CT and parathyroid 4D-CT so as to guide surgery in patients with primary hyperparathyroidism (pHPT) and prior neck surgery. METHODS: Medical records of all patients referred for a FCH-PET/CT in our institution were systematically reviewed. Only patients with pHPT, a history of

neck surgery (for pHPT or another reason) and an indication of reoperation were included. All patients had parathyroid ultrasound (US) and Tc-99m-sestaMIBI scintigraphy, and furthermore, some patients had 4D-CT. Gold standard was defined by pathological findings and/or US-guided fine-needle aspiration with PTH level measurement in the washing liquid.

RESULTS: Twenty-nine patients were included in this retrospective study. FCH-PET/CT identified 34 abnormal foci including 19 ectopic localizations. 4D-CT, performed in 20 patients, detected 11 abnormal glands at first reading and 6 more under FCH-PET/CT guidance. US and Tc-99m-sestaMIBI found concordant foci in 8/29 patients. Gold standard was obtained for 32 abnormal FCH-PET/CT foci in 27 patients. On a per-lesion analysis, sensitivity, specificity, positive and
negative predictive values were, respectively, 96%, 13%, 77% and 50% for FCH-PET/CT, 75%, 40%, 80% and 33% for 4D-CT. On a per-patient analysis, sensitivity was 85% for FCH-PET/CT and 63% for 4D-CT. FCH-PET/CT results made it possible to successfully remove an abnormal gland in 21 patients, including 12
with a negative or discordant US/Tc-99m-sestaMIBI scintigraphy result, with a global cure rate of 73%.
CONCLUSION: FCH-PET/CT is a promising tool in the challenging population of reoperative patients with pHPT. Parathyroid 4D-CT appears as a confirmatory imaging modality.

DOI: 10.1007/s00268-019-04910-6 PMID: 30659347

16. J Clin Endocrinol Metab. 2019 May 1;104(5):1655-1657. doi: 10.1210/jc.2018-02437. Still Perfecting Radioiodine in Thyroid Cancer, After All These Years.
Wirth LJ(1).
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PMID: 30462299

17. J Clin Endocrinol Metab. 2019 May 1;104(5):1417-1428. doi: 10.1210/jc.2018-01478. Vemurafenib Redifferentiation of BRAF Mutant, RAI-Refractory Thyroid Cancers.
Dunn LA(1)(2), Sherman EJ(1)(2), Baxi SS(1)(2), Tchekmedyian V(1), Grewal RK(3),
Larson SM(3), Pentlow KS(4), Haque S(3), Tuttle RM(1), Sabra MM(1), Fish S(1),

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CONTEXT: BRAFV600E mutant thyroid cancers are often refractory to radioiodine (RAI).
OBJECTIVES: To investigate the utility and molecular underpinnings of enhancing lesional iodide uptake with the BRAF inhibitor vemurafenib in patients with RAI-refractory (RAIR).

DESIGN: This was a pilot trial that enrolled from June 2014 to January 2016.
SETTING: Academic cancer center.
PATIENTS: Patients with RAIR, BRAF mutant thyroid cancer.
INTERVENTION: Patients underwent thyrotropin-stimulated iodine-124 (124I) positron emission tomography scans before and after ~4 weeks of vemurafenib. Those with increased RAI concentration exceeding a predefined lesional dosimetry threshold (124I responders) were treated with iodine-131 (131I). Response was evaluated with imaging and serum thyroglobulin. Three patients underwent research biopsies to evaluate the impact of vemurafenib on mitogen-activated protein

kinase (MAPK) signaling and thyroid differentiation.
MAIN OUTCOME MEASURE: The proportion of patients in whom vemurafenib increased RAI incorporation to warrant 131I.

RESULTS: Twelve BRAF mutant patients were enrolled; 10 were evaluable. Four patients were 124I responders on vemurafenib and treated with 131I, resulting in tumor regressions at 6 months. Analysis of research tumor biopsies demonstrated that vemurafenib inhibition of the MAPK pathway was associated with increased thyroid gene expression and RAI uptake. The mean pretreatment serum thyroglobulin value was higher among 124I responders than among nonresponders (30.6 vs 1.0 ng/mL; P = 0.0048).

CONCLUSIONS: Vemurafenib restores RAI uptake and efficacy in a subset of BRAF mutant RAIR patients, probably by upregulating thyroid-specific gene expression via MAPK pathway inhibition. Higher baseline thyroglobulin values among responders suggest that tumor differentiation status may be a predictor of vemurafenib benefit.

DOI: 10.1210/jc.2018-01478
PMCID: PMC6435099 [Available on 2019-09-25] PMID: 30256977

18. Ann Surg. 2019 May;269(5):966-971. doi: 10.1097/SLA.0000000000002710. Risk Factors for Recurrence After Treatment of N1b Papillary Thyroid Carcinoma. Lee SH(1), Roh JL(1), Gong G(2), Cho KJ(2), Choi SH(1), Nam SY(1), Kim SY(1). Author information:

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OBJECTIVES: To examine risk factors for posttreatment recurrence in papillary thyroid carcinoma (PTC) patients with initial presentation of lateral neck
metastasis (N1b).
SUMMARY OF BACKGROUND DATA: N1b PTC recurs after definitive treatment. METHODS: Study subjects were 437 consecutive PTC patients who underwent total thyroidectomy and therapeutic neck dissection of central and lateral compartments and postoperative radioactive iodine ablation therapy. The patients' demographics and pathological factors, including factors related to tumors and lymph nodes (LNs), and postoperative thyroglobulin levels were reviewed. Univariate and multivariate Cox proportional hazards regression analyses were used to identify factors associated with recurrence-free survival (RFS).

RESULTS: During a median follow-up of 83 months (range, 32-135 months), recurrence occurred in 81 (18.1%) patients. Univariate analyses showed that male sex, tumor size, macroscopic extrathyroidal extension, perineural invasion, extranodal extension, LN involvement, LN ratio, MACIS score, and postoperative serum levels of thyroglobulin were significantly associated with RFS ($P < 0.05$). Multivariate analyses revealed that LN ratio (> 0.25) in the lateral compartment (adjusted hazard ratio = 2.099, 95% confidence interval = 1.278-3.448; P =
0.003), and postoperative serum levels of stimulated (>5.0 ng/mL; 3.172, 1.661-6.056, $P < 0.001$) and unstimulated (>0.1 ng/mL; 3.200, 1.569-6.526, $P = 0.001$) thyroglobulin were independent predictors of any-site RFS. Clinical and tumor factors were not independent predictors of RFS outcomes ($P > 0.1$). CONCLUSIONS: Posttreatment recurrence is predicted by the LN ratio in the lateral compartment and postoperative serum levels of thyroglobulin in patients with metastatic PTC in the lateral neck. DOI: 10.1097/SLA.0000000000002710 PMID: 29462007

19. Exp Clin Endocrinol Diabetes. 2019 May 15. doi: 10.1055/a-0885-1568. [Epub ahead of print] Early Basal Cortisol Level as a Predictor of Hypothalamic-Pituitary-Adrenal (HPA)
Axis Function After Pituitary Tumor Surgery.

Polovina TS(1), Kraljevic I(#)(1), Solak M(#)(1), Balasko A(#)(1), Haxhiu A(#)(1), Haxhiu A(#)(1), Dusek T(#)(1)(2), Poljicanin T(#)(3), Kastelan D(#)(1)(2).
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Center Zagreb, Coatia. (2)School of Medicine University of Zagreb, Coatia.
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(#)Contributed equally

PURPOSE: The purpose of this study was to evaluate the clinical relevance of the
early postoperative basal cortisol level in assessing the postoperative hypothalamic-pituitary-adrenal (HPA) axis function after pituitary tumor surgery. METHODS: We performed a prospective observational study that enrolled 83 patients operated for pituitary adenoma or other sellar lesions at the University Hospital Center Zagreb between December 2013 and April 2017 (44 nonfunctioning pituitary adenomas, 28 somatotropinomas, 5 craniopharyngiomas, 2 prolactinomas resistant to medical therapy and 4 other lesions - Rathke's cleft cyst, arachnoid cyst, chondroma and gangliocytoma). Exclusion criteria were Cushing's disease, chronic therapy with glucocorticoids prior to surgery and preoperative adrenal insufficiency. Early postoperative basal cortisol levels (measured on the second postoperative day) and the Synacthen stimulation test (performed 3 months after the surgery with the peak cortisol level of>500 nmol/L considered as a normal response) were analyzed to assess HPA axis function during follow-up.

RESULTS: ROC analysis showed a cut-off of the basal cortisol level of ≥300 nmol/L measured on the second postoperative day to predict normal postoperative HPA axis function with the sensitivity of 92.31%, specificity of 87.14% and positive
predictive value of 57.14%.

CONCLUSION: The basal cortisol level on the second postoperative day is a valuable tool to predict integrity of the HPA axis after pituitary tumor surgery. Our data suggest that the cortisol level of ≥300 nmol/L accurately predicts adrenal sufficiency and that in these patients glucocorticoid therapy can be withdrawn.

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PMID: 31091548
Conflict of interest statement: The authors declare that they have no conflict of interest.

19. J Visc Surg. 2019 May 11. pii: S1878-7886(19)30054-2. doi: 10.1016/j.jviscsurg.2019.04.008. [Epub ahead of print]
Is it permissible to undertake surgery for adrenal metastases of esophageal adenocarcinomas?
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DOI: 10.1016/j.jviscsurg.2019.04.008

PMID: 31088734

20. BMC Surg. 2019 Apr 24;18(Suppl 1):123. doi: 10.1186/s12893-018-0457-5.
The impact of the ultrasonic, bipolar and integrated energy devices in the adrenal gland surgery: literature review and our experience.
Patrone R(1), Gambardella C(2), Romano RM(2), Gugliemo C(2), Offi C(2), Andretta C(2), Vitiello A(3), Tartaglia E(4), Flagiello L(2), Conzo A(2), Mauriello C(2), Conzo G(2).
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BACKGROUND: The gold standard approach for surgical treatment of benign and malignant adrenal lesion is considered the laparoscopic one, due to a lot of advantages compared to open approach. The rapid propagation of this surgical technique is due to the diffusion of haemostatic devices in laparoscopic adrenal surgery. The principal aim of this study is to analyze the outcome of LA using each energy modality, evaluating the eventual superiority of an instrument over the others.

METHODS: A retrospective study, involving 75 consecutive patients submitted to LA by transperitoneal lateral approach from January 2013 to June 2017, was performed. Age less than 70 years old, adrenal adenomas less than 8 cm in diameter, incidentalomas < 6 cm, myelolipomas < 13 cm, adrenal metastases < 7 cm and ASA score ≤ III were the main surgical inclusion criteria. All involved

patients were divided into three group, one for each energy device: group 1 - Harmonic Scalpel, group 2 - Ligasure vessel sealing system and group 3 - Thunderbeat. In each group only one device was applied for dissection and haemostasis during the whole operation. Each group consisted of 25 patients, well matched for histology, tumor size and site, gender and age. The following parameters were collected: age, gender, size of the tumor, side of the affected

gland, pathology, operating time, intraoperative blood losses, hospitalization time, complication and conversion rate.

RESULTS: There was no significant statistical difference between groups regarding the relationship between male/female, right site/left site, the mean age, hospitalization time and the tumor size ($p > 0.05$). Significant statistical difference are detectable in operation time and intraoperative blood losses. Thunderbeat, compared respectively with Ligasure and Harmonic Scalpel, is the fastest device ($p < 0,001$). The second faster device resulted Harmonic Scalpel, which meanly reduced the operation time compared to Ligasure ($p = 0.048$). intraoperative blood losses are reduced using Thunderbeat ($p < 0,001$) and HS ($p = 0.006$) compared to Ligasure, but between Thunderbeat and Harmonic Scalpel there isn't significant statistical difference ($p = 0.178$).

CONCLUSIONS: Analyzing the results, laparoscopic adrenalectomy carried out using Thunderbeat appeared to show a statistically significant decrease in operation time and intraoperative blood losses compared with laparoscopic adrenalectomy performed using Harmonic Scalpel and Ligasure, while hospitalization time was superimposable in all groups. According to our data, a responsible use of

advanced energy devices can improve surgical outcomes guarantying a cost savings and patient's satisfaction.
DOI: 10.1186/s12893-018-0457-5
PMID: 31074403

21. BMC Surg. 2019 Apr 24;18(Suppl 1):128. doi: 10.1186/s12893-018-0456-6. Laparoscopic adrenalectomy: preoperative data, surgical technique and clinical outcomes.
Di Buono G(1), Buscemi S(2), Lo Monte AI(2), Geraci G(2), Sorce V(2), Citarrella R(3), Gulotta E(2), Palumbo VD(2), Fazzotta S(2), Gulotta L(2), Albano D(4), Galia M(4), Romano G(2), Agrusa A(2).

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BACKGROUND: laparoscopic adrenalectomy has become the standard treatment for adrenal lesions. The better clinical outcoms of laparoscopic technique are valid
for treatment of small benign masses (< 5-6 cm), instead there are still open questions in literature regarding the correct management of larger lesions

(> 6 cm) or in case of potentially malignant adrenal tumors. The aim of this study is to evaluate the outcomes of laparoscopic adrenalectomy in a referral surgical department for endocrine surgery.
METHODS: at the University Hospital Policlinico "P. Giaccone" of Palermo between January 2010 and December 2017 we performed a total of 81 laparoscopic adrenalectomy. We created a retrospective database with analysis of patients data, morphologic and hormonal characteristics of adrenal lesions, surgical procedures and postoperative results with histological diagnosis and complications.

RESULTS: Mean size of adrenal neoplasm was 7,5 cm (range 1.5 to 18 cm). The mean

operative time was 145 min (range 75-240). In statistical analysis lenght of surgery was correlated to the lesion diameter ($p < 0.05$) but not with pre-operative features or histological results. 5 intraoperative complications occurred. Among these patients 4 presented bleeding and 1 a diaphagmatic lesion. No conversion to open surgery was necessary and no intraoperative blood transfusion were required. Mean estimated blood loss was 95 ml (range 50-350). There was no capsular disruption during adrenal dissection. Mean length of hospital stay was 3.7 days (range 3-6 days).

CONCLUSIONS: Laparoscopic adrenalectomy is a safe procedure with low rate of morbidity. An accurate preoperative radiological examination is fundamental to obtain a stringent patients selection. The lesion diameter is related to longer operative time and appeares as the main predictive parameter of intraoperative complications but these results are not statistically significant. On the other side secreting adrenal tumors require more attention in operative management without increased rate of postoperative complications.
DOI: 10.1186/s12893-018-0456-6
PMID: 31074390

22. Endocrine. 2019 May 9. doi: 10.1007/s12020-019-01948-3. [Epub ahead of print] Non-surgically treated case of nonfunctioning ruptured adrenal adenoma in a patient on hemodialysis.
Lee KA(1), Jin HY(2).

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OBJECTIVES: Herein, we report a case of rupture of nonfunctional adrenal adenoma treated by nonsurgical supportive management due to high risk for operation. METHOD AND CASE: A patient with end stage renal disease (ESRD) who was on hemodialysis visited our emergency room and complained of a sudden abdominal pain after a fall. A retroperitoneal hemorrhage with hematoma formation around the adrenal adenoma, which was caused by rupture of the adrenal adenoma, was detected by abdominal computed tomography (CT).

RESULTS: Supportive management was performed, with serial CT follow-up instead of surgical adrenalectomy treatment because of high operative risk, due to hemodialysis. After 1 week, the patient's vital signs stabilized and the patient
did not further complain about abdominal symptoms. However, supportive embolization was performed and the size of hematoma was more decreased. CONCLUSION: We report a case of a patient on hemodialysis who experienced a rupture of a nonfunctioning adrenal adenoma, which was caused by low-energy trauma. The patient's conditions improved with nonsurgical supportive management including embolization.

DOI: 10.1007/s12020-019-01948-3 PMID: 31073864

23. Ann Surg Treat Res. 2019 May;96(5):223-229. doi: 10.4174/astr.2019.96.5.223. Epub 2019 Apr 24.
Surgical outcomes of laparoscopic adrenalectomy for primary hyperaldosteronism:
20 years of experience in a single institution.

Kim K(1), Kim JK(1), Lee CR(1), Kang SW(1), Lee J(1), Jeong JJ(1), Nam KH(1), Chung WY(1).Author information: (1)Department of Surgery, Yonsei University College of Medicine, Seoul, Korea.

Purpose: Recently, posterior retroperitoneoscopic adrenalectomy (PRA) has been reported to have some advantages over laparoscopic transperitoneal adrenalectomy (LTA). The objectives of this study were to report our experience over 12 years
with laparoscopic adrenalectomy for primary hyperaldosteronism (PHA) and to examine surgical outcomes of PRA compared with LTA in patients with PHA. Methods: The medical records of 527 patients who underwent minimally invasive adrenalectomy, including LTA or PRA, from January 2006 until May 2017 were reviewed at Severance Hospital (Seoul, Korea). Clinicopathologic characteristics

and surgical outcomes of 146 patients with PHA who underwent LTA (19 patients) or PRA (127 patients) were analyzed retrospectively by complete chart review.
Results: The overall rates of biochemical and clinical cure were 91.1% and 93.1%, respectively. The mean operation time of the PRA group was significantly shorter than that of the LTA group (72.3 ± 24.1 minutes vs. 115.7 ± 69.7 minutes, P =

0.015). The length of hospital stay in the PRA group was significantly shorter than in the LTA group (3.5 ± 1.3 days vs. 4.2 ± 1.6 days, P = 0.029), and the first meal after surgery came earlier in the PRA group (0.3 ± 0.5 days vs. 0.6 ± 0.5 days, P = 0.049). The number of pain-killers used was also significantly smaller in the PRA group (2.3 ± 2.1 vs. 4.3 ± 2.3, P < 0.001).

Conclusion: PRA offers an alternative or likely superior method for treatment of small adrenal diseases such as PHA, with improved surgical outcomes.
DOI: 10.4174/astr.2019.96.5.223
PMCID: PMC6483932

PMID: 31073512

24. J Surg Oncol. 2019 May;119(6):801-806. doi: 10.1002/jso.25364. Epub 2019 Jan 30. Retrospective analysis of variant venous anatomy in 303 laparoscopic
adrenalectomies and its clinical implications.
Sun F(1), Zhuo R(1), Ma W(1), He H(1), Ye L(2)(3), Xu D(1), Wang W(2)(3), Ning G(2)(3).
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(3)Laboratory for Endocrine & Metabolic Diseases of Institute of Health Science, Shanghai Jiao Tong University School of Medicine and Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China.

BACKGROUND AND OBJECTIVES: To clarify the correlation of variant venous anatomy with adrenal tumor phenotype and surgical outcomes.
PATIENTS AND METHODS: This retrospective study included 303 consecutive minimally invasive adrenalectomies from 301 patients. All adrenal veins were identified. We compared the preoperative, intraoperative, and postoperative data between patients with and without variant adrenal venous anatomy. We also explored the factors associated with venous variants.
RESULTS: We found variant venous anatomy in 62 of 303 adrenalectomies (20.5%). Compared with patients with normal anatomy, those with variant anatomy were associated with larger tumor size, larger adrenal veins, more adrenal medullary tumors, longer operation time, more estimated intraoperative blood loss, longer length of hospitalization, and more transfusion. Computed tomography (CT) images may improve the identification of venous anatomy. Tumor size and diagnosis of pheochromocytoma were independently related to variant venous anatomy, whereas sex, tumor size, and venous variant influenced hemorrhage. For pheochromocytoma with variant venous anatomy operated on by a single surgeon, robot-assisted laparoscopic adrenalectomy was associated with shorter postoperative hospitalization.

CONCLUSIONS: Adrenal vein variants are associated with worse outcomes in adrenal tumors and an optimized surgery strategy should be applied to this group of patients.
 DOI: 10.1002/jso.25364
PMID: 30697735 [Indexed for MEDLINE]

25. Eur Urol. 2019 May;75(5):811-816. doi: 10.1016/j.eururo.2018.07.030. Epub 2018 Aug 1.
Robot-assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes.

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BACKGROUND: In the era of minimally invasive surgery, partial adrenalectomy has certainly been underused. We aimed to report surgical technique and perioperative, pathologic, and early functional outcomes of a two-center robot-assisted partial adrenalectomy (RAPA) series.

OBJECTIVE: To detail surgical technique of RAPA for unilateral aldosterone-producing adenoma (UAPA), and to report perioperative and 1-yr functional outcomes.
DESIGN, SETTING, AND PARTICIPANTS: Data of 10 consecutive patients who underwent RAPA for UAPA at two centers from June 2014 to April 2017 were prospectively collected and reported.
SURGICAL PROCEDURE: RAPA was performed using a standardized technique with the da Vinci Si in a three-arm configuration.
MEASUREMENTS: Baseline and perioperative data were reported. One-year functional outcomes were assessed according to primary aldosteronism surgery outcome guidelines. A descriptive statistical analysis was performed.
RESULTS AND LIMITATIONS: All cases were completed robotically. Median nodule size was 18mm (interquartile range [IQR] 16-20). Intraoperative blood loss was
negligible. A single (10%) postoperative Clavien grade 2 complication occurred.
Median hospital stay was 3 d (IQR 2-3). Patients became normotensive immediately after surgery (median pre- and postoperative blood pressure: 150/90 and
120/70mmHg, respectively). At both 3-mo and 1-yr functional evaluation, all patients achieved biochemical success (aldosterone level, plasmatic renin activity, and aldosterone-renin ratio within normal range). Complete clinical success was achieved in nine patients, but one required low-dose amlodipine at

6-mo evaluation. At a median follow-up of 30.5 mo (IQR 19-42), neither symptoms
nor imaging recurrence was observed.
CONCLUSIONS: We demonstrated feasibility and safety of RAPA for UAPA; this technique had very low risk of complications and excellent functional results.
Increased availability of robotic platform and increasing robotic skills among urologists make RAPA a treatment option with potential for widespread use in urologic community.
PATIENT SUMMARY: Robot-assisted partial adrenalectomy is a safe, feasible, and minimally invasive surgical approach. Promising perioperative and functional
outcomes suggest an increasing adoption of this technique in the near future.

DOI: 10.1016/j.eururo.2018.07.030
PMID: 30077398

26. NICE Guidelines for the treatment of primary hyperparathyroidism
https://www.nice.org.uk/guidance/ng132

27. Enhancing Parathyroid Gland Visualization Using a Near Infrared Fluorescence-Based Overlay Imaging System.
McWade MA[1], Thomas G[1], Nguyen JQ[1], Sanders ME[2], Solórzano CC[3], Mahadevan-Jansen A[4].
Author information. **J Am Coll Surg. 2019 May;228(5):730-743. doi: 10.1016/j.jamcollsurg.2019.01.017. Epub 2019 Feb 13.**

BACKGROUND:
Misidentifying parathyroid glands (PGs) during thyroidectomies or parathyroidectomies could significantly increase postoperative morbidity. Imaging systems based on near infrared autofluorescence (NIRAF) detection can localize PGs with high accuracy. These devices, however, depict NIRAF images on remote display monitors, where images lack spatial context and comparability with actual surgical field of view. In this study, we designed an overlay tissue imaging system (OTIS) that detects tissue NIRAF and back-projects the collected signal as a visible image directly onto the surgical field of view instead of a display monitor, and tested its ability for enhancing parathyroid visualization.

STUDY DESIGN:
The OTIS was first calibrated with a fluorescent ink grid and initially tested with parathyroid, thyroid, and lymph node tissues ex vivo. For in vivo

measurements, the surgeon's opinion on tissue of interest was first ascertained. After the surgeon looked away, the OTIS back-projected visible green light directly onto the tissue of interest, only if the device detected relatively high NIRAF as observed in PGs. System accuracy was determined by correlating NIRAF projection with surgeon's visual confirmation for in situ PGs or histopathology report for excised PGs.

RESULTS:

The OTIS yielded 100% accuracy when tested ex vivo with parathyroid, thyroid, and lymph node specimens. Subsequently, the device was evaluated in 30 patients who underwent thyroidectomy and/or parathyroidectomy. Ninety-seven percent of exposed tissue of interest was visualized correctly as PGs by the OTIS, without requiring display monitors or contrast agents.

CONCLUSIONS:

Although OTIS holds novel potential for enhancing label-free parathyroid visualization directly within the surgical field of view, additional device optimization is required for eventual clinical use.

28. Randomized clinical trial of intraoperative parathyroid gland angiography with indocyanine green fluorescence predicting parathyroid function after thyroid surgery.

Vidal Fortuny J[1], Sadowski SM[1], Belfontali V[1], Guigard S[1], Poncet A[2], Ris F[3], Karenovics W[1], Triponez F[1].

Author information.

Br J Surg. 2018 Mar;105(4):350-357. doi: 10.1002/bjs.10783. Epub 2018 Feb 6.

Abstract

BACKGROUND:

Hypoparathyroidism, the most common complication after thyroid surgery, leads to hypocalcaemia and significant medical problems. An RCT was undertaken to determine whether intraoperative parathyroid gland angiography with indocyanine green (ICG) could predict postoperative hypoparathyroidism, and obviate the need for systematic blood tests and oral calcium supplementation.

METHODS:

Between September 2014 and February 2016, patients who had at least one well perfused parathyroid gland on ICG angiography were randomized to receive standard follow-up (measurement of calcium

and parathyroid hormone (PTH) on postoperative day (POD) 1 and systematic supplementation with calcium and vitamin D; control group) or no supplementation and no blood test on POD 1 (intervention group). In all patients, calcium and PTH levels were measured 10-15 days after thyroidectomy. The primary endpoint was hypocalcaemia on POD 10-15.

RESULTS:

A total of 196 patients underwent ICG angiography during thyroid surgery, of whom 146 had at least one well perfused parathyroid gland on ICG angiography and were randomized. None of these patients presented with hypoparathyroidism, including those who did not receive calcium supplementation. The intervention group was statistically non-inferior to the control group (exact 95 per cent c.i. of the difference in proportion of patients with hypocalcaemia -0·053 to 0·053; P = 0·012). Eleven of the 50 excluded patients, in whom no well perfused parathyroid gland could be identified by angiography, presented with hypoparathyroidism on POD 1, and six on POD 10-15, which was significantly different from the findings in randomized patients (P = 0·007).

CONCLUSION:

ICG angiography reliably predicts the vascularization of the parathyroid glands and obviates the need for postoperative measurement of calcium and PTH, and supplementation with calcium in patients with at least one well perfused parathyroid gland. Registration number: NCT02249780 (http://www.clinicaltrials.gov).

29. Autofluorescence in Parathyroidectomy: Signal Intensity Correlates with Serum Calcium and Parathyroid Hormone but Routine Clinical Use is Not Justified.

DiMarco A[1,2], Chotalia R[1], Bloxham R[1], McIntyre C[1,2], Tolley N[1,2], Palazzo FF[3,4].

World J Surg. 2019 Jun;43(6):1532-1537. doi: 10.1007/s00268-019-04929-9.

Author information

Abstract

BACKGROUND:

The inability to identify the pathological gland at surgery results in failure to cure hyperparathyroidism in 2-5%. The poorly understood characteristic of parathyroid tissue to manifest autofluorescence (AF) under near-infrared (NIR) light has been promoted as an intraoperative adjunct

in parathyroid surgery. This study sought to explore potential clinical correlates for AF and assess the clinical utility of AF in parathyroid surgery.

METHODS:
Consecutive patients undergoing parathyroid surgery for primary and renal disease were included. NIR imaging was used intraoperatively and the degree of AF of parathyroid glands graded by the operating surgeon. Variables assessed for correlation with AF were: pre-operative serum calcium and PTH, SestaMIBI positivity, gland weight and histological composition.

RESULTS:
Ninety-six patients underwent parathyroidectomy over an 8-month period: 49 bilateral explorations, 41 unilateral and 6 focussed lateral approaches: 284 potentially 'visualisable' glands in total. Two hundred and fifty-seven glands (90.5%) were visualised with NIR. Correlation was found between the degree of fluorescence and pre-operative serum calcium and PTH, but not between gland weight and SestaMIBI positivity. In those with renal hyperparathyroidism, a predominance of oxyphil cells correlated with increased AF.

CONCLUSION:
Autofluorescence intensity correlates with serum calcium, PTH and gland composition. Further refinements would be required for this information to be of value in a clinical setting. Improvements allowing NIR to visualise the additional 9.5% of parathyroids and overcome the variation in signal intensity due to depth of access are required for the routine adoption of this technology. At present, its routine use in a clinical setting cannot be justified.