1. **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.
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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.

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PMID: 31012500

2. **J Clin Endocrinol Metab. 2019 Apr 3. pii: jc.2018-02686. doi: 10.1210/jc.2018-02686. [Epub ahead of print]**
Transcriptome analyses identify a metabolic gene signature indicative of dedifferentiation of papillary thyroid cancer.
Ma B(1)(2), Jiang H(1)(2), Wen D(1)(2), Hu J(1)(2), Han L(1)(2), Liu W(1)(2), Xu W(1)(2), Shi X(1)(2), Wei W(1)(2), Liao T(1)(2), Wang Y(1)(2), Lu Z(1)(2), Wang Y(1)(2), Ji Q(1)(2).

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CONTEXT: Metabolic reprogramming is a common feature of tumorigenesis. It remains unknown concerning expression pattern of metabolism-associated genes in dedifferentiated thyroid cancer (DDTC).
OBJECTIVE: This study aimed to identify a useful signature to indicate dedifferentiation of papillary thyroid cancer (PTC).
DESIGN AND SETTING: We utilized one discovery and two validation cohorts to screen out aberrant metabolic genes in DDTC, and further used The Cancer Genome Atlas (TCGA) cohort to search for independent risk factors for the low-differentiated phenotype of PTC as a signature of dedifferentiation. The prediction of the signature for DDTC was validated in the TCGA cohort and the combined Gene Expression Omnibus (GEO) cohort. We also analyzed the correlations of the signature risk score with clinicopathological features of PTC. Gene set enrichment analyses were performed in the TCGA cohort.
RESULTS: Significant enrichment of metabolic pathways correlated with differentiation status of PTC. A signature of metabolic genes including LPCAT2, ACOT7, HSD17B8, PDE8B and ST3GAL1 was discovered and validated across three cohorts. The signature was not only predictive of DDTC but also significantly associated with BRAFV600E mutation ($p<0.001$), T3/T4 stage ($p<0.001$), extrathyroidal extension ($p<0.001$), lymph node metastasis ($p<0.001$) and III/IV stage ($p<0.001$) in PTC. Downregulations of LPCAT2 expression ($p=0.009$) and ST3GAL1 expression ($p=0.005$) increased risks of decreased disease-free survival for patients. Furthermore, the signature was implicated in a number of oncogenic biological pathways.
CONCLUSIONS: Our findings suggest metabolic deregulations mediate dedifferentiation of PTC, and the metabolic gene signature can be used as a biomarker for DDTC.

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PMID: 30942873

3. **J Clin Endocrinol Metab. 2019 Mar 27. pii: jc.2018-02483. doi: 10.1210/jc.2018-02483. [Epub ahead of print]**
Predictors of nephrolithiasis, osteoporosis and mortality in primary hyperparathyroidism.
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CONTEXT: Primary Hyperparathyroidism (PHPT) has a prevalence of 0.86% and is

associated with increased risk of nephrolithiasis and osteoporosis. PHPT may also be associated with an increased risk of cardiovascular disease and mortality.
OBJECTIVE: To identify risk factors for nephrolithiasis, osteoporosis and mortality in PHPT.
DESIGN: Retrospective cohort study.
SETTING: University teaching hospital.
PATIENTS: PHPT presenting between 2006 - 2014 (n = 611).
MAIN OUTCOME MEASURES: Assessment of nephrolithiasis, osteoporosis and mortality.
RESULTS: 13.9% of PHPT patients had nephrolithiasis. Most had already documented stone disease and only 4.7% of asymptomatic patients screened for renal stones had calculi identified, not very dissimilar to the rate in the non-PHPT population. Younger age (P < 0.001) and male gender (P = 0.003) were the only independent predictors of nephrolithiasis. 48.4% of patients with DXA data had osteoporosis (223/461). Older age (P < 0.001), lower BMI (P = 0.002) and lower creatinine (P = 0.006) were independently associated with a diagnosis of osteoporosis. Higher PTH was independently associated with lower Z-score at the hip (P = 0.009), but otherwise calcium and PTH were not associated with lower Z-score. Mortality in PHPT was associated with older age (P < 0.008), social deprivation (P = 0.028) and adjusted calcium (P = 0.009) but not independently with PTH at diagnosis.
CONCLUSIONS: Screening for nephrolithiasis has a low yield, particularly in lower risk patients. Osteoporosis is only minimally associated with biochemical indices of PHPT. Mortality is associated with higher calcium (and possibly vitamin D deficiency) but not PTH.

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PMID: 30916764

4. **Endocrinology. 2019 Mar 27. pii: en.2019-00017. doi: 10.1210/en.2019-00017. [Epub ahead of print]**

Attenuated Dentin Matrix Protein 1 Enhances Fibroblast Growth Factor 23 in Calvaria in Primary Hyperparathyroidism Model.

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Fibroblast growth factor 23 (FGF23) secretion is facilitated by parathyroid hormone (PTH), particularly in hyperparathyroidism. PTH also attenuates dentin matrix protein 1 (DMP1), which is produced by osteocytes to contribute to bone mineralization and suppress FGF23 expression. Nevertheless, it remains unknown whether attenuated DMP1 affects FGF23 expression in hyperparathyroidism. We examined their expression in bone tissue using a mouse model of primary hyperparathyroidism (PHPT). PHPT mice increased serum FGF23 levels along with a high level of serum PTH. Fgf23 expression increased and Dmp1 decreased significantly in the calvariae of PHPT mice as compared with WT mice, and primary osteoblasts treated with PTH. In UMR106 mature osteoblasts, PTH increased Fgf23 expression and decreased Dmp1 expression and stimulation of PKA signaling by forskolin also increased Fgf23 expression and decreased Dmp1 expression in a

dose-dependent manner, whereas inhibition of PKA signaling with 10-5 M H89 reversed the changes in Fgf23 and Dmp1 expression when cells were stimulated with PTH. Silencing Dmp1 along with PTH treatment led to an additive increase in Fgf23 expression, accompanied by additive phosphorylation of the cAMP-response element-binding protein, CREB. These results indicate that persistent and high levels of PTH lead to the continuous activation of PKA signaling in osteoblasts/osteocytes, resulting in an increase in FGF23 and a decrease in DMP1 in bone. Moreover, suppression of DMP1 enhanced FGF23 expression in PHPT, besides having a direct effect on PTH. These mechanisms may describe one of the pathogenesis behind the increase in FGF23 transcription in bone tissue in patients with PHPT.

DOI: 10.1210/en.2019-00017
PMID: 30916761

5. **Lancet Diabetes Endocrinol. 2019 Apr;7(4):252. doi: 10.1016/S2213-8587(19)30070-1.**
Thyroid cancer recurrence in the HiLo trial.
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DOI: 10.1016/S2213-8587(19)30070-1
PMID: 30902264

6. **Lancet Diabetes Endocrinol. 2019 Apr;7(4):252-253. doi: 10.1016/S2213-8587(19)30088-9.**
Thyroid cancer recurrence in the HiLo trial - Authors' reply.
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DOI: 10.1016/S2213-8587(19)30088-9
PMID: 30902263

7. **J Clin Endocrinol Metab. 2019 Mar 18. pii: jc.2018-01167. doi: 10.1210/jc.2018-01167. [Epub ahead of print]**
Immune Profiling of Thyroid Carcinomas Suggests the Existence of Two Major Phenotypes: an ATC-like and a PDTC-like.
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OBJECTIVES: The understanding of the mechanisms underlying thyroid cancer immune escape can lead to the identification of new molecular targets and/or efficacy biomarkers. For this purpose, we performed immune expression profiling in thyroid cancers to obtain a comprehensive view on immune mechanisms activated during cancer progression.
METHODS: The study was conducted retrospectively in 25 papillary thyroid carcinomas (PTC), 14 poorly differentiated thyroid carcinomas (PDTC), 13 anaplastic thyroid carcinomas (ATC) and 7 normal thyroid tissue samples (NT). Gene expression profiling was obtained on RNA samples using the Nanostring platform and its nCounter PanCancer Immune Profiling Panel.
RESULTS: Gene expression comparison of ATC, PTC and PDTC vs NT showed high number of regulated genes in cancer samples. In detail, immune-related gene sets were significantly up-regulated (ATC > PTC >> PDTC). Most ATC and about half of PTC showed a microenvironment infiltrated by macrophages and T-cells with CD8+ effector phenotype, part of which appeared to be functionally exhausted. Conversely, most PDTC, as NT samples, as the remaining part of PTC, displayed a poor or absent infiltration by immune cells. Interestingly, an up-regulation of inhibitory immune checkpoint mediators, including PDL1, PDL2, PD1, LAG-3, TIM-3, PVR and TIGIT, could be detected in ATC and PTC.
CONCLUSIONS: These data indicated the existence of two major immune phenotypes in thyroid carcinoma: an ATC-like one, including hot and altered-immunosuppressed tumors and a PDTC-like one, including altered-excluded and cold tumors. Confirmation of the findings in locally advanced or metastatic cancer tissues is expected to have important immunotherapeutic implications.

DOI: 10.1210/jc.2018-01167
PMID: 30882858

8. **J Clin Endocrinol Metab. 2019 Mar 15. pii: jc.2019-00177. doi: 10.1210/jc.2019-00177. [Epub ahead of print]**
Risk Stratification in Differentiated Thyroid Cancer: From Detection to Final Follow-up.
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CONTEXT: Modern management of differentiated thyroid cancer requires individualized care plans which tailor the intensity of therapy and follow-up to the estimated risks of recurrence and disease-specific mortality.

EVIDENCE ACQUISITION: This summary is based on the authors' knowledge and extensive clinical experience supplemented by review of published review articles, thyroid cancer management guidelines, published staging systems, and original articles identified through a PubMed search which included terms such as risk stratification, staging, clinical outcomes, and differentiated thyroid cancer.
EVIDENCE SYNTHESIS: In the past, risk stratification in differentiated thyroid cancer usually referred to a static estimate of disease-specific mortality that was based on a small set of clinicopathological features available within a few weeks of completing initial therapy (thyroidectomy with or without radioactive iodine). Today, risk stratification is a dynamic, active process used to predict the appropriateness for minimalistic initial therapy, disease-specific mortality, risk of recurrence, and the most likely response to initial therapy. Rather than being a static prediction available only after initial therapy, modern risk stratification is a dynamic, iterative process that begins as soon as a suspicious nodule is detected and continues through final follow-up.
CONCLUSIONS: Dynamic risk assessment should be used to guide all aspects of thyroid cancer management, beginning before a definitive diagnosis is made and continuing through the final follow-up visit.

DOI: 10.1210/jc.2019-00177
PMID: 30874735

9. **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).
Author information:
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DOI: 10.1038/s41574-019-0193-7
PMID: 30867550

10. **J Clin Endocrinol Metab. 2019 Mar 12. pii: jc.2018-02456. doi: 10.1210/jc.2018-02456. [Epub ahead of print]**
Effect of Parathyroidectomy on cardiovascular risk factors in primary hyperparathyroidism: A randomised clinical trial.
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CONTEXT: It remains unclear whether risk of cardiovascular diseases is increased in patients with mild (<1.45 mmol/l) to moderate (≥1.45-1.60 mmol/l) primary hyperparathyroidism (PHPT).
OBJECTIVE: We aimed to determine the short-term effect of parathyroidectomy (PTX) on arterial stiffness, cholesterol levels, and blood pressure (BP).
DESIGN: This study was a clinical trial randomly allocating patients to either PTX- or a control-group (no surgery). Follow-up was performed three months after

surgery in the PTX- and three months after baseline in the control-group.
SETTING: University Hospital Patients or Other Participants: We recruited 79 patients with PHPT among whom 69 participants completed the study.
MAIN OUTCOMES: Office- and ambulatory 24hour BP, pulse wave velocity (PWV), augmentation index (AIx), fasting plasma cholesterol levels.
RESULTS: At baseline, participants had a median level of ionized calcium of 1.41 mmol/l (range: 1.33-1.60 mmol/l) and PTH of 10.4 pmol/l (4.5-30.4 pmol/l). Median age was 64 years (range 18-81 yrs.) and 72% were females. Following PTX, plasma total cholesterol levels decreased significant compared with the controls (p=0.04). Changes in PWV, AIx, and ambulatory 24hour BP did not differ between groups, except for an increase in ambulatory diastolic BP following PTX. However, in patients with baseline levels of ionized calcium ≥1.45 mmol/l, PWV decreased significantly in response to PTX- compared with the control-group (p=0.03).
CONCLUSION: PTX may decrease risk of cardiovascular diseases in PHPT by lowering total cholesterol levels, although ambulatory diastolic BP increases in response to surgery. Patients with moderate-to-severe hypercalcemia may benefit from PTX by a decrease in PWV.

DOI: 10.1210/jc.2018-02456
PMID: 30860588

11. **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

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.
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PMID: 30659347

16. **World J Surg. 2019 Apr;43(4):1038-1046. doi: 10.1007/s00268-018-04877-w.**
Transoral Robotic Thyroidectomy for Papillary Thyroid Carcinoma: Perioperative Outcomes of 100 Consecutive Patients.
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BACKGROUND: Endoscopic transoral thyroidectomy is a recently introduced technique of remote access thyroidectomy. We previously reported the feasibility of the robotic approach (TORT). Nevertheless, experience to date is limited, with scant data on outcomes in patients with papillary thyroid carcinoma (PTC).
METHODS: This was a retrospective analysis of prospectively collected data. Patients with PTC, who underwent TORT at a single center between March 2016 and February 2017, were analyzed.
RESULTS: There were a total of 100 patients (85 women, 15 men) with a mean age of 40.7 ± 9.8 years, and a mean tumor size of 0.8 ± 0.5 cm. Nine patients underwent

a total thyroidectomy, and 91 underwent a lobectomy. The operative time for a total thyroidectomy and lobectomy was 270.0 ± 9.3 and 210.8 ± 32.9 min, respectively. Ipsilateral prophylactic central neck compartment dissection was performed routinely with retrieval of 5.0 ± 3.6 lymph nodes. Perioperative morbidity was present in nine patients including transient recurrent laryngeal nerve palsy (n = 1), postoperative bleeding requiring surgical intervention (n = 1), zygomatic bruising (n = 2), chin flap perforation (n = 1), oral commissure tearing (n = 2), and chin dimpling (n = 2). There was no conversion to endoscopic or conventional open thyroid surgery.
CONCLUSION: In this study, TORT could be safely performed in a large series of patients with PTC without serious complications. In selected patients, TORT by experienced surgeons could be considered an alternative approach for remote access thyroidectomy.
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PMID: 30539261

17. **World J Surg. 2019 Apr;43(4):1029-1037. doi: 10.1007/s00268-018-04879-8.**
Percutaneous Microwave Ablation of Metastatic Lymph Nodes from Papillary Thyroid Carcinoma: Preliminary Results.
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BACKGROUND: Our purpose is to assess the effectiveness and safety of ultrasound-guided percutaneous microwave ablation (MWA) for lymph node metastases (LNMs) from papillary thyroid carcinomas (PTC).
METHODS: In total, 14 patients with recurrent PTC were enrolled in this retrospective study. The vascularity within the ablation zone was evaluated by contrast-enhanced ultrasonography (CEUS) after MWA. Patients were followed up with measurement of the size and volume of tumor, serum thyroglobulin, and clinical evaluation at 7 days, 1, 3, 6 months, and every 6 months thereafter.
RESULTS: Twenty-one LNMs were confirmed by biopsy and successfully treated by MWA in a single session. No incomplete ablation was detected by CEUS after treatment. The average largest diameter and volume of the tumors were reduced from 10.1 ± 4.7 mm (range, 3.1-20.0 mm) and 291.9 ± 255.6 mm3 (range, 11.6-766.6 mm3) to 0.9 ± 1.6 mm (range, 0-4.1 mm; $p < 0.05$) and 4.0 ± 9.0 mm3 (range, 0-31.6 mm3; $p < 0.05$) at the final follow-up. Neither progression of treated tumors nor newly suspicious LNMs could be detected after treatment. The overall complication rate was 7.1% (1/14).
CONCLUSIONS: Ultrasound-guided MWA can effectively control LNMs from PTC, but it is less safe for tumors in the central compartment. MWA may become an alternative therapy in selected PTC patients, who were ineligible or refused to undergo repeated neck explorations.
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PMID: 30536023

18. **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.
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DOI: 10.1210/jc.2018-02437
PMID: 30462299

19. **J Clin Endocrinol Metab. 2019 Apr 1;104(4):1020-1028. doi: 10.1210/jc.2018-01589.**
Recombinant Thyrotropin vs Levothyroxine Withdrawal in 131I Therapy of N1 Thyroid Cancer: A Large Matched Cohort Study (ThyrNod).
Leenhardt L(1), Leboulleux S(2), Bournaud C(3), Zerdoud S(4), Schvartz C(5), Ciappuccini R(6), Kelly A(7), Morel O(8), Dygai-Cochet I(9), Rusu D(10), Chougnet CN(11), Lion G(12), Eberlé-Pouzeratte MC(13), Catargi B(4), Kabir-Ahmadi M(14), Le Peillet Feuillet E(15), Taïeb D(16).
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CONTEXT: Recombinant human thyrotropin (rhTSH) has been shown to be an effective stimulation method for radioactive iodine (RAI) therapy in differentiated thyroid cancer, including in those with nodal metastases (N1 DTC).
OBJECTIVES: To demonstrate the noninferiority of rhTSH vs thyroid hormone withdrawal (THW) in preparation to RAI regarding disease status at the first evaluation in the real-life setting in patients with N1 DTC.
DESIGN: This was a French multicenter retrospective study. Groups were matched according to age (<45/≥45 years), number of N1 nodes (≤5/>5 lymph nodes), and stage (pT1-T2/pT3).
RESULTS: The cohort consisted of 404 patients pT1-T3/N1/M0 DTC treated with rhTSH (n = 205) or THW (n = 199). Pathological characteristics and initially administrated RAI activities (3.27 ± 1.00 GBq) were similar between the two groups. At first evaluation (6 to 18 months post-RAI), disease-free status was defined by thyroglobulin levels below threshold and a normal ultrasound. Disease-free rate was not inferior in the rhTSH group (75.1%) compared with the

THW group (71.9%). The observed difference between the success rates was 3.3% (-6.6 to 13.0); rhTSH was therefore considered noninferior to THW because the upper limit of this interval was <15%. At the last evaluation (29.7 ± 20.7 months for rhTSH; 36.7 ± 23.8 months for THW), 83.5% (rhTSH) and 81.5% (THW) of patients achieved a complete response. This result was not influenced by any of the known prognostic factors.
CONCLUSIONS: A preparation for initial RAI treatment with rhTSH was noninferior to that with THW in our series of pT1-T3/N1/M0-DTC on disease-free status outcomes at the first evaluation and after 3 years.

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20. **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.
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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.

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21. **Ann Surg. 2019 May;269(5):966-971. doi: 10.1097/SLA.0000000000002710.**
Risk Factors for Recurrence After Treatment of N1b Papillary Thyroid Carcinoma.
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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.
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