

**1. World J Surg. 2019 Nov 11. doi: 10.1007/s00268-019-05269-4. doi: 10.1007/s00268-019-05269-4. [Epub ahead of print]**

*Stepwise Approach for Parathyroid Localisation in Primary Hyperparathyroidism.*  
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**INTRODUCTION:** Primary hyperparathyroidism (PHPT) is a relatively common condition in surgical practice. Availability of localisation studies has shifted the treatment from bilateral neck exploration to selective parathyroidectomy. Several imaging modalities, each with varying sensitivities, are available to detect abnormal parathyroid glands. Ultrasound is almost universally accepted as the first line radiological investigation however its sensitivity is particularly heterogeneous and operator-dependent.

**MATERIAL AND METHODS:** We studied 250 consecutive patients with PHPT who underwent parathyroidectomy in our hospital over a period of 33 months. Pre-operative neck ultrasound, 99mTc-sestamibi and single-photon emission computed tomography (SPECT CT) were performed in 249, 237 and 198 patients respectively. Unilateral and bilateral neck exploration was performed in 190 and 60 patients, respectively. Sensitivity, positive predictive value (PPV) and accuracy were calculated comparing the results with surgical and pathology findings.

**RESULTS:** Mean pre and postoperative PTH and adjusted calcium were,  $11 \pm 10.6$  pmol/L,  $1.9 \pm 3.6$ ,  $2.81 \pm 0.2$  and  $2.45 \pm 0.2$  mmol/L. There were 71 (29.95%) discordant results between US, compared to sestamibi and SPECT CT. An average of 1.9 parathyroid glands were removed with a mean weight of 0.92 g. Overall success rate based on postoperative PTH levels was 94.8%. Overall sensitivity, PPV and accuracy for US were 80.80%, 92.35%, and 75.73% respectively; for sestamibi were 71.82%, 94.61%, 69.00% and for SPECT CT were; 70.21%, 97.78%, 69.11% respectively.

**CONCLUSION:** Ultrasound performed by an experienced specialist sonographer is highly sensitive in localising abnormal parathyroid glands. It can be used as a main and sole investigation in the majority of patients. Sestamibi, SPECT CT and other investigations should be performed in a step-wise manner and reserved for patients with negative US, failed primary procedure and recurrences.

DOI: 10.1007/s00268-019-05269-4

PMID: 31712842

**2. World J Surg. 2019 Nov 4. doi: 10.1007/s00268-019-05260-z. doi: 10.1007/s00268-019-05260-z. [Epub ahead of print]**

*Usefulness of a 3D-Printed Thyroid Cancer Phantom for Clinician to Patient Communication.*

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**BACKGROUND:** Thyroid glands and surrounding structures are very complex, and this complexity can pose a challenge for clinicians when explaining and communicating to the patient the details of a proposed surgery for thyroid cancer. A three-dimensional (3D) thyroid cancer model could help and improve this communication.

**METHODS:** A 3D-printed phantom of a thyroid gland and its presenting cancer was produced from segmented head and neck contrast-enhanced computed tomography (CT) data from a patient with thyroid cancer. The phantom reflects the complex anatomy of the arteries, veins, nerves, and other surrounding organs, and the printing materials and techniques were adjusted to represent the texture and color of the actual structures. Using this phantom, patients and clinicians completed surveys on the usefulness of this 3D-printed thyroid cancer phantom.

**PARTICIPANTS:** patients (n = 33) and clinicians (n = 10).

**RESULTS:** In the patient survey, the patients communicated that the quality of understanding of their thyroid disease status was enhanced when clinicians explained using the phantom. The clinicians communicated that the 3D phantom was advantageous for explaining complex thyroid surgery procedures to patients, and that the 3D phantom was helpful in educating patients with relatively poor anatomical knowledge.

**CONCLUSIONS:** Using 3D printing technology, we produced a CT-based 3D thyroid cancer phantom, and patient and clinician surveys on its utility indicated that it successfully helped educate patients, providing them with an improved understanding of the disease.

DOI: 10.1007/s00268-019-05260-z

PMID: 31686159

**3. World J Surg. 2019 Nov 4. doi: 10.1007/s00268-019-05231-4. doi: 10.1007/s00268-019-05231-4. [Epub ahead of print]**

*Risks of Hypoparathyroidism After Total Thyroidectomy in Children: A 21-Year Experience in a High-Volume Cancer Center.*

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**BACKGROUND:** Hypoparathyroidism occurs relatively frequently after thyroid surgery in children. However, few studies have reported risk factors. We aimed to identify risk factors for hypoparathyroidism that occurred after total thyroidectomy for proven or suspected malignancy in children.

**METHODS:** Children (aged  $\leq 18$  years) who underwent total thyroidectomy for neoplasm or RET germline mutation at our institution between 1997 and 2018 were included. We retrospectively reviewed demographics, surgical indications, perioperative and follow-up laboratory results, pathologic results, and duration of calcium/calcitriol supplementation. Risk factors for hypoparathyroidism were identified by multivariate analysis.

**RESULTS:** Of 184 consecutive patients, 111 had undergone surgery for neoplasm; these diseases were primarily malignancies (106, 95.5%), predominantly papillary carcinoma (103, 92.8%). The remaining 73 patients had undergone early thyroidectomy for RET germline mutation. Among all patients, 67 (36.4%) had hypoparathyroidism: 61 transient and 6 permanent. In a multivariate analysis, central neck dissection (odds ratio 4.3, 95% confidence interval 2.0-9.1) and gross extrathyroidal extension (odds ratio 4.9, 95% confidence interval 2.0-12.1) predicted overall hypoparathyroidism; however, no significant factors were associated with permanent hypoparathyroidism. Most patients with permanent hypoparathyroidism (5 of 6) had undergone therapeutic central neck dissection. When central neck dissection was performed, younger children had a higher risk of overall hypoparathyroidism.

**CONCLUSIONS:** In pediatric total thyroidectomies, central neck dissection and gross extrathyroidal extension were major predictors for overall hypoparathyroidism. Surgeons performing thyroidectomy in such patients should be aware of the relatively high risk, preserve parathyroid tissue to the extent possible, and be conscientious regarding postoperative calcium monitoring and replacement.

DOI: 10.1007/s00268-019-05231-4

PMID: 31686157

**4. J Clin Endocrinol Metab. 2019 Oct 28. pii: dgz129. doi: 10.1210/clinem/dgz129. [Epub ahead of print]**

*Clinically silent thyroid cancers: drop those needles and scalpels!*

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DOI: 10.1210/clinem/dgz129

PMID: 31665325

**5. J Clin Endocrinol Metab. 2019 Oct 28. pii: dgz130. doi: 10.1210/clinem/dgz130.**

**[Epub ahead of print]**

*Letter to the Editor: "An Analysis of the American Joint Committee on Cancer 8th Edition T Staging System for Papillary Thyroid Carcinoma".*

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DOI: 10.1210/clinem/dgz130

PMID: 31665320

**6. J Clin Endocrinol Metab. 2019 Oct 28. pii: dgz137. doi: 10.1210/clinem/dgz137.**

**[Epub ahead of print]**

*Evaluation of the 2015 ATA Guidelines in Patients with Distant Metastatic Differentiated Thyroid Cancer.*

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**CONTEXT:** Current ATA Guidelines for differentiated thyroid cancer (DTC) stratify patients to decide on additional radioiodine (RAI) therapy after surgery, and to predict recurring/persisting disease. However, studies evaluating the detection of distant metastases and how these Guidelines perform in patients with distant metastases are scarce.

**OBJECTIVE:** To evaluate the 2015 ATA Guidelines in DTC patients with respect to 1) the detection of distant metastases, and 2) the accuracy of its Risk Stratification System in patients with distant metastases.

**PATIENTS AND MAIN OUTCOME MEASURES:** We retrospectively included 83 DTC patients who were diagnosed with distant metastases around initial therapy, and a control population of 472 patients (312 Low, 160 Intermediate Risk) who did not have a certain indication for RAI therapy. We used the control group to assess the percentage of distant metastases that would have been missed if no RAI therapy was given.

**RESULTS:** Two hundred-forty-six patients had no routine indication for RAI therapy of which four (1.6%) had distant metastases. Further, of the 83 patients

with distant metastases, 14 patients (17%) had excellent response, while 55 (67%) had structural disease after a median follow-up of 62 months. None of the 14 patients that achieved an excellent response had a recurrence.

**CONCLUSIONS:** In patients without a routine indication for RAI therapy according to the 2015 ATA Guidelines, distant metastases would initially have been missed in 1.6% of the patients. Further, in patients with distant metastases upon diagnosis, the 2015 ATA Guidelines are an excellent predictor of both persistent disease and recurrence.

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DOI: 10.1210/clinem/dgz137

PMID: 31665318

**7. World J Surg. 2019 Oct 28. doi: 10.1007/s00268-019-05249-8. doi:**

**10.1007/s00268-019-05249-8. [Epub ahead of print]**

*Cardiovascular Incidence in 6900 Patients with Differentiated Thyroid Cancer: a Swedish Nationwide Study.*

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**INTRODUCTION:** To minimize recurrence risk in differentiated thyroid cancer (DTC), TSH is usually lifelong suppressed with levothyroxine. A common consequence of this treatment is subclinical hyperthyroidism which can induce cardiovascular disease (CV). This study's aim was to compare CV incidence in DTC patients with the general population in Sweden.

**MATERIALS AND METHODS:** All Swedish patients diagnosed with DTC in 1987-2013 were included in the cohort study. Lifelong TSH suppression treatment was assumed to be administered to patients in compliance with prevalent national guidelines.

Patients were followed from 1 year after DTC diagnosis until December 31, 2014, death, or migration. The event of interest was hospitalization due to any of the following diseases: atrial fibrillation (AF), cerebrovascular disease, cerebral infarction, ischemic heart disease, ischemic heart attack, and heart failure. Standardized incidence ratios (SIRs) were calculated to compare CV incidence between DTC patients and the general population.

**RESULTS:** The cohort consisted of 6900 patients with DTC. Hospitalization was increased among DTC patients for AF (SIR 1.66, CI 95% 1.41-1.94), and women faced increased hospitalization for cerebrovascular disease (SIR 1.20 CI 95% 1.04-1.38). Regarding the remaining CV diseases, no consistent difference in SIR

between the groups was observed.

**CONCLUSION:** Compared to the general population, DTC patients have a higher incidence in AF, and female face a slightly higher incidence in cerebrovascular disease. However, there was no difference in hospitalization for other studied CV diseases between DTC patients and the general population.

DOI: 10.1007/s00268-019-05249-8

PMID: 31659412

**8. J Clin Endocrinol Metab. 2019 Oct 23. pii: dgz078. doi: 10.1210/clinem/dgz078.**

**[Epub ahead of print]**

*Divergent metastatic patterns between subtypes of thyroid carcinoma results from the nationwide Dutch pathology registry.*

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**BACKGROUND:** Metastatic disease is the main cause of cancer related mortality in thyroid carcinoma (TC) patients. Clinical studies have suggested differences in metastatic patterns between the different subtypes of TC. This study systematically evaluates the metastatic patterns of different subtypes in TC patients.

**METHODS:** A nationwide review of pathological records of all 650 patients diagnosed with a primary malignancy in the thyroid who underwent an autopsy between 1991 and 2010 was performed. Patients were selected from the Dutch pathology registry (PALGA).

**RESULTS:** Metastatic disease was present in 228 (35.1%) patients and was found in 38.7%, 17.3%, 75.4% and 47.8% of patients with follicular, papillary, anaplastic and medullary type of TC, respectively ( $P < 0.0001$ ). The majority of patients had more than one metastasis. The most common site of metastatic disease was the lung for papillary (79.7%), follicular (72.9%) and anaplastic (92.1%) carcinoma, but not for medullary carcinoma (56.3%),  $P < 0.0001$ . Medullary carcinoma patients most frequently had metastases to the liver (81.3%). The combination of metastases also differed between subtypes.

**CONCLUSION:** There are major differences in metastatic patterns between different subtypes of TC. The patterns and frequencies identified in this autopsy study may reflect the underlying biology of metastatic thyroid cancer and have potential to influence future monitoring and treatment strategies depending on clinical correlations.

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DOI: 10.1210/clinem/dgz078

PMID: 31641763

9. **Nat Rev Endocrinol. 2019 Oct 15. doi: 10.1038/s41574-019-0263-x. doi: 10.1038/s41574-019-0263-x. [Epub ahead of print]**

*Geographic influences in the global rise of thyroid cancer.*

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The incidence of thyroid cancer is on the rise, and this disease is projected to become the fourth leading type of cancer across the globe. From 1990 to 2013, the global age-standardized incidence rate of thyroid cancer increased by 20%. This global rise in incidence has been attributed to several factors, including increased detection of early tumours, the elevated prevalence of modifiable individual risk factors (for example, obesity) and increased exposure to environmental risk factors (for example, iodine levels). In this Review, we explore proven and novel hypotheses for how modifiable risk factors and environmental exposures might be driving the worldwide increase in the incidence of thyroid cancer. Although overscreening and the increased diagnosis of possibly clinically insignificant disease might have a role in certain parts of the world, other areas could be experiencing a true increase in incidence due to elevated exposure risks. In the current era of personalized medicine, national and international registry data should be applied to identify populations who are at increased risk for the development of thyroid cancer.

DOI: 10.1038/s41574-019-0263-x

PMID: 31616074

10. **World J Surg. 2019 Oct 11. doi: 10.1007/s00268-019-05222-5. doi: 10.1007/s00268-019-05222-5. [Epub ahead of print]**

*Biochemical Profile Affects IPTH Kinetics and Cure Rate in Primary Hyperparathyroidism.*

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DOI: 10.1007/s00268-019-05222-5

PMID: 31605178

11. **World J Surg. 2019 Oct 11. doi: 10.1007/s00268-019-05230-5. doi: 10.1007/s00268-019-05230-5. [Epub ahead of print]**

*Surgical Management of Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma. Experience in 25 Patients.*

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**PURPOSE:** To delineate the clinicopathologic features and biologic behavior of the diffuse sclerosing variant of papillary thyroid carcinoma (DSV-PTC) and to report its outcome.

**METHODS:** The clinical records of 25 patients who had surgery for DSV-PTC from 2004 to 2017 were retrospectively analyzed. Comparisons were made to similar studies in the literature reporting  $\geq 8$  cases and a cohort of classical PTC.

**RESULTS:** There were 20 females and 5 males with an average age of 23 years (range 10-39 years). Bilateral disease occurred in 80% of cases. The mean size of the dominant mass was  $4.2 \pm 1.92$  cm. In 92% of cases, therapeutic neck dissection was performed. Male sex significantly correlated with a higher yield of positive lymphadenopathy ( $p = 0.045$ ). 62% of patients had recurrent disease. Recurrence significantly correlated with male sex, the number of metastatic lymph nodes (cutoff: 22 lymph nodes), and multifocality ( $p = 0.044$ ,  $p < 0.008$ ,  $p < 0.003$ , respectively). However, it did not correlate with the age at presentation. No disease-specific mortality occurred after an average follow-up of 77 months (range 12-168 months). The two comparisons made demonstrated a statistically significant greater tendency of the current series of DSV-PTC toward more aggressive clinicopathologic features and biologic behavior. No differences in overall survival were observed.

**CONCLUSION:** The DSV-PTC should be considered a high-risk PTC that mandates an aggressive therapeutic strategy with the intent of optimizing disease-free survival.

DOI: 10.1007/s00268-019-05230-5

PMID: 31605177

**12. World J Surg. 2019 Oct 11. doi: 10.1007/s00268-019-05232-3. doi: 10.1007/s00268-019-05232-3. [Epub ahead of print]**

*Prognostic Value of Extranodal Tumor Extension in Papillary Thyroid Carcinoma: Proposal for Upstaging of Cases with Extranodal Tumor Extension.*

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**BACKGROUND:** Recently, we have created a revised version of the eighth edition of the tumor-node-metastasis classification for papillary thyroid carcinomas (PTCs) by subdividing the T4a (T4a1 [moderate] and T4a2 [significant]) and N (N1 [ $N \leq 3$  cm] and N2 [ $N > 3$  cm]) classifications. This re-staging better stratified patient outcomes. In this study, we investigated the prognostic significance of extranodal tumor extension (LNEx) in PTC.

**METHODS:** Five thousand six hundred and eighty-three patients with PTC surgically treated in Kuma Hospital were enrolled. We evaluated LNEx based on intraoperative findings.

**RESULTS:** One hundred and twenty-seven patients (2%) displayed LNEx. In contrast to what we observed for extrathyroid extension, the prognostic value of LNEx did not change based on the organ that had been invaded, and we therefore analyzed LNEx patients as a single group. In patients aged 55 or older, LNEx independently affected patients' prognoses, as did T4a2 and N2. The cancer-specific survival (CSS) of patients in Stage I but having LNEx demonstrated the similar prognosis to patients in Stage II. Further, in the subset analysis for Stage II patients aged 55 or older, LNEx had a significant prognostic value for CSS in both the univariate and multivariate analyses, as did N2. The CSS of Stage II patients aged 55 or older with LNEx did not differ from that of Stage III patients.

**CONCLUSIONS:** It is appropriate that, similar to T4a2 or N2 patients, LNEx-positive patients younger than 55 years in Stage I and those aged 55 or older in Stage II are re-staged to II and III, respectively.

DOI: 10.1007/s00268-019-05232-3

PMID: 31605175

**13. Ann Surg. 2019 Oct 9. doi: 10.1097/SLA.0000000000003632. doi: 10.1097/SLA.0000000000003632. [Epub ahead of print]**

*Does Aggressive Variant Histology Without Invasive Features Predict Overall Survival in Papillary Thyroid Cancer?: A National Cancer Database Analysis.*

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**OBJECTIVE:** We aimed to clarify whether aggressive histology of papillary thyroid cancer (PTC) impacts overall survival (OS).

**SUMMARY BACKGROUND DATA:** Aggressive variants of PTC (AVPTC) are associated with invasive features. However, their behavior in the absence of these features is not well characterized.

**METHODS:** Patients treated from 2004 to 2015 for classic PTC (cPTC) or AVPTCs were identified from the National Cancer Database. Patients were further stratified based on presence of at least 1 invasive feature-extrathyroidal extension, multifocality, lymphovascular invasion, nodal or distant metastasis. Demographics, treatments, and OS were compared.

**RESULTS:** A total of 170,778 patients were included-162,827 cPTC and 7951 AVPTC. Invasive features were more prevalent in AVPTC lesions compared to cPTC (70.7% vs 59.7%,  $P < 0.001$ ). AVPTC included tall cell/columnar cell (89.5%) and diffuse sclerosing (10.5%) variants. Patients with invasive features had worse OS irrespective of histology. Furthermore, when controlling for demographics, tumor size, and treatment variables in patients with noninvasive lesions, AVPTC histology alone was not associated with worse OS compared to cPTC ( $P = 0.209$ ). In contrast, among patients who had at least 1 invasive feature, AVPTC histology was independently predictive of worse OS ( $P < 0.05$ ) {TCV/Columnar hazard ratio [HR] 1.2; [95% confidence interval (CI) 1.1-1.3] and diffuse sclerosing HR 1.3;

95% CI 1.0-1.7}]. All invasive features, except multifocality, were independently associated with worse OS, with metastasis being the most predictive [HR 2.9 (95% CI 2.6-3.2) P < 0.001].

CONCLUSIONS: In the absence of invasive features, AVPTC histology has similar OS compared to cPTC. In contrast, diffuse sclerosing and tall cell/columnar variants are associated with worse OS when invasive features are present.

DOI: 10.1097/SLA.0000000000003632

PMID: 31599802

**14. Br J Surg. 2019 Oct 9. doi: 10.1002/bjs.11319. doi: 10.1002/bjs.11319. [Epub ahead of print]**

*Short-term medical treatment of hypercalcaemia in primary hyperparathyroidism predicts symptomatic response after parathyroidectomy.*

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**BACKGROUND:** Primary hyperparathyroidism is often associated with non-disease-specific symptoms. The aim of this study was to evaluate whether normalization of hypercalcaemia with short-term medical treatment can be used to predict the effects of parathyroidectomy and guide in surgical decision-making.

**METHODS:** This observational study included patients who received calcimimetic treatment for 4 weeks before parathyroidectomy (30-60 mg daily). A panel of tests was used to assess various aspects of quality of life (European Organisation and Treatment of Cancer QLQ-C30 core questionnaire, Hospital Anxiety and Depression Scale and Positive State of Mind questionnaire), cognitive function (Montreal Cognitive Assessment) and muscle strength (timed-stands test). The tests were carried out at baseline, after 4 weeks of calcimimetic treatment, and at 6 weeks and 6 months after parathyroidectomy. The predictive values of changes during calcimimetic treatment were determined for each test.

**RESULTS:** The study included 110 patients of median age 62 years (91 women). Calcimimetic treatment resulted in normalization of calcium levels and improvements in quality-of-life parameters. The time spent on the timed-stands test was significantly shortened. Eleven of 38 participants with a baseline Montreal Cognitive Assessment score below 26, indicating mild cognitive impairment, reached scores of at least 26 during treatment with calcimimetic. Improvements during treatment with calcimimetic correlated well with postoperative outcomes (positive predictive values 74-96 per cent).

**CONCLUSION:** The method described in this study may be used to aid surgical decision-making for patients with primary hyperparathyroidism and

non-disease-specific symptoms by predicting the effects of normalization of hypercalcaemia.

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DOI: 10.1002/bjs.11319

PMID: 31595982

**15. Lancet Diabetes Endocrinol. 2019 Oct 4. pii: S2213-8587(19)30324-9. doi: 10.1016/S2213-8587(19)30324-9. [Epub ahead of print]**

*Screening for differentiated thyroid cancer in selected populations.*

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The main purpose of cancer screening programmes should not be to detect all cancers, but to discover potentially fatal or clinically relevant cancers. The US Preventive Services Task Force recommends against screening for thyroid cancer in the general, asymptomatic adult population, as such screening would result in harms that outweigh any potential benefits. This recommendation does not apply to patients with symptoms or to individuals at increased risk of thyroid cancer because of a history of exposure to ionising radiation (in childhood, as radioactive fallout, or in medical treatment as low-dose radiotherapy for benign conditions or high-dose radiation for malignancy), inherited genetic syndromes associated with thyroid cancer (eg, familial adenomatous polyposis), or one or more first-degree relatives with a history of thyroid cancer. We discuss the evidence for and against screening individuals who are at high risk, and consider the different screening tools available.

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DOI: 10.1016/S2213-8587(19)30324-9

PMID: 31591051

**16. J Clin Endocrinol Metab. 2019 Oct 7. pii: dgz060. doi: 10.1210/clinem/dgz060. [Epub ahead of print]**

*Analysis of bone impairment by 3D DXA hip measures in patients with primary hyperparathyroidism: a pilot study.*

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CONTEXT: primary hyperparathyroidism (PHPT) has been related to bone loss. Dual-energy X-ray absorptiometry (DXA) cannot distinguish between trabecular and cortical bone compartments but the recently developed 3D-DXA software might overcome this issue.

OBJECTIVE: to examine the differences in DXA-derived areal bone mineral density (aBMD) and 3D-DXA parameters at the hip site between patients with PHPT and a healthy control group.

DESIGN: cross-sectional pilot study.

SETTING: hospital.

PATIENTS: 80 adults (59.5 ± 9.1 yrs), 40 with PHPT and 40 healthy age- and sex-matched healthy controls.

MEASURES: aBMD (g/cm<sup>2</sup>) of the femoral neck, trochanter, shaft and total hip was assessed using DXA. Cortical surface (sBMD, mg/cm<sup>2</sup>), cortical volumetric BMD (vBMD, mg/cm<sup>3</sup>), trabecular vBMD (mg/cm<sup>3</sup>), integral vBMD (mg/cm<sup>3</sup>) and cortical thickness (mm) was assessed using 3D-DXA software.

RESULTS: mean-adjusted values showed lower aBMD (7.5% to 12.2%, effect size: 0.51-1.01) in the PHPT group compared to the control group (all p<0.05). 3D-DXA revealed bone impairment (3.7% to 8.5%, effect size: 0.47-0.65) in patients with PHPT, mainly in cortical parameters (all p<0.05). However, differences in trabecular vBMD were not statistically significant (p=0.055). The 3D mapping showed lower cortical sBMD, cortical vBMD and cortical thickness at the trochanter and diaphysis in the PHPT group (p<0.05) compared to the control group. In both groups, the presence of osteopenia or osteoporosis is related to lower cortical bone.

CONCLUSIONS: aBMD and cortical 3D parameters are impaired in patients with PHPT versus healthy controls. The vBMD of the trabecular compartment seems to be affected though to a lower extent.

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DOI: 10.1210/clinem/dgz060

PMID: 31588503

17. **World J Surg. 2019 Oct 3. doi: 10.1007/s00268-019-05218-1. doi: 10.1007/s00268-019-05218-1. [Epub ahead of print]**

*Sentinel Lymph Node Biopsy in Thyroid Cancer.*

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**BACKGROUND:** Prophylactic central neck dissection in patients with papillary thyroid carcinoma is controversial. Sentinel node biopsy might be an adjunct to optimize surgical treatment for these patients. Earlier studies reported inconsistent detection rates and diagnostic value of this technique, and the role of sentinel lymph node biopsy in thyroid cancer needs to be established. **PATIENTS AND METHODS:** During a single-center prospective interventional study between 2010 and 2017, sentinel lymph node biopsy using 99mTc-nanocolloidal albumin tracer was performed on patients undergoing thyroid surgery for suspected thyroid cancer by fine needle aspiration cytology. All eligible patients without clinical lymph node involvement were invited to participate. Central neck dissection was performed on all patients after the detection of sentinel lymph nodes.

**RESULTS:** Ninety-six patients participated in the study. The detection rates of the sentinel node were 67% and 45% by scintigraphy and intraoperative gamma probe, respectively. The detection rate was not associated with Bethesda score, malignancy, or presence of lymph node metastases. Sensitivity, negative predictive value, and accuracy were 80%, 97%, and 98%, respectively, for the sentinel node to represent the status of lymph node metastasis in the central neck compartment. The false negative rate was 20%.

**CONCLUSION:** Sentinel lymph node biopsy had a low detection rate and only moderate sensitivity in patients with suspected thyroid carcinoma and is not a useful adjunct to surgery in the context of current treatment concepts.

DOI: [10.1007/s00268-019-05218-1](https://doi.org/10.1007/s00268-019-05218-1)

PMID: 31583456

**18. World J Surg. 2019 Oct 1. doi: 10.1007/s00268-019-05176-8. doi: 10.1007/s00268-019-05176-8. [Epub ahead of print]**

*Understanding Thyroidectomy Cost Variations Among National Cancer Institute-Designated Cancer Centers.*

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**BACKGROUND:** The cost of thyroidectomy varies across the USA, while the causes of

this variation are poorly understood. We examined the cost of inpatient thyroidectomy among National Cancer Institute-designated cancer centers nationwide to determine why it differs.

**METHODS:** A retrospective study of inpatient thyroidectomies was performed using the Vizient Clinical Data Base. Fifty-two of 70 eligible hospitals were grouped into five geographic regions (Mid-Atlantic and New England, East Central, South Atlantic, West Central, and Mountain and Pacific). We identified drivers of cost variation in the five geographic regions and used risk adjustment model to evaluate the rationality of cost from each hospital.

**RESULTS:** Male sex, more extended hospital stays, and occurrence of complications were consistently associated with increased costs in all regions. Also, the cost was significantly lower in the Mid-Atlantic and New England region. The higher than expected costs did not correlate well with the case mix index among hospitals ( $p = 0.289$ ), but the lower than expected costs were more common in high-volume hospitals. The average length of stay was the shortest in high-volume hospitals, which might account for the lower cost in the Mid-Atlantic and New England region; however, the overages of costs still varied widely among hospitals in all regions even if the length of stay was adjusted.

**CONCLUSIONS:** Cost variation may result from both patient-related factors and volume-related practice pattern differences among hospitals. A more standard of care and charge transparency is still needed for patients seeking affordable care at cancer centers.

DOI: 10.1007/s00268-019-05176-8

PMID: 31576441

**19. World J Surg. 2019 Sep 30. doi: 10.1007/s00268-019-05207-4. doi: 10.1007/s00268-019-05207-4. [Epub ahead of print]**

*Effects of Social Disparities on Management and Surgical Outcomes for Patients with Secondary Hyperparathyroidism.*

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**INTRODUCTION:** Nearly 80% of chronic renal failure patients have secondary hyperparathyroidism. Cinacalcet is used to lower parathyroid hormone; however, it is expensive and has side effects. When secondary hyperparathyroidism is resistant to medication or medications are inaccessible, parathyroidectomy is performed. Race and socioeconomic status influence access to care and surgical outcomes. We sought to evaluate the effect of race and socioeconomic status on parathyroidectomy rate as well as surgical outcomes of patients with secondary hyperparathyroidism.

**METHODS:** We undertook cross-sectional analysis of adults diagnosed with secondary hyperparathyroidism in the USA between 2012 and 2014, using the National Inpatient Sample. Univariate and multivariate analyses were used to determine associations between social disparities, likelihood to undergo parathyroidectomy, and surgical outcomes.

**RESULTS:** Between 2012 and 2014, a national estimate of 724,170 hospitalizations were identified where patients had a diagnosis of secondary hyperparathyroidism. Operative rate was 0.67%. By socioeconomic status, differences in rates of surgery in the poorest compared to the richest were not significant (0.74% vs. 0.55%, OR 1.08,  $p = 0.5$ ). African-American patients had higher rates of parathyroidectomy compared to Caucasians (1 vs. 0.74%, OR 1.49,  $p < 0.001$ ). African-American patients also had a trend toward more complications and greater length of stay.

**CONCLUSIONS:** According to a large administrative dataset, parathyroidectomy for secondary hyperparathyroidism is seldom used in the USA. African-American patients have higher rates of surgical management. Surgical outcomes may be affected by race. Clinicians treating secondary hyperparathyroidism should be aware of existing disparities within their health system.

DOI: 10.1007/s00268-019-05207-4

PMID: 31570954

**20. World J Surg. 2019 Sep 12. doi: 10.1007/s00268-019-05161-1. doi: 10.1007/s00268-019-05161-1. [Epub ahead of print]**

*Needle Tract Implantation Following Fine-Needle Aspiration of Thyroid Cancer.*

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**BACKGROUND:** Needle tract implantation (NTI) can occur after thyroid fine-needle aspiration cytology (FNAC). To date, no studies enrolling a large number of patients and studying the cumulative incidence (CI) of NTI have been published. This study analyzed the clinicopathological features of NTI and calculated the CI.

**METHODS:** A total of 11,745 patients who underwent first FNAC, resection for thyroid carcinomas and related lymph node metastases, and postoperative ultrasonography in Kuma Hospital between 2006 and 2017 were evaluated. NTI was defined as macroscopically visible and/or sonographically detected recurrent tumors at the sites of the previous aspiration. Lymphovascular invasion and/or nodal metastasis were excluded.

**RESULTS:** We found 22 NTI-THY (originated from aspiration of thyroid tumors) and 8 NTI-LN (originating from lymph nodes) cases with CI of 0.15% and 0.37%, and 0.37% and 0.58% at 5 and 10 years after FNAC, respectively. A large percentage (53%) of cases are presented as more aggressive histologic subtypes than their original tumors. Of these NTI patients, 4 (12.1%) died of disease and 10 (33.3%)

developed distant metastases but remained alive with stable disease, three (9.1%) developed local recurrences, and the remaining 15 (10%) were free of recurrence.

**CONCLUSIONS:** We demonstrated for the first time the CI and detailed clinicopathological features of thyroid NTI associated with possible histological transformation. Despite the low CI, the risk of death and distant metastases increase manifold in NTI patients than that in patients without recurrence. Therefore, NTI could be an important prognostic variable and impact patient survival.

DOI: 10.1007/s00268-019-05161-1

PMID: 31515571

**21. World J Surg. 2019 Sep 11. doi: 10.1007/s00268-019-05157-x. doi: 10.1007/s00268-019-05157-x. [Epub ahead of print]**

*Biochemical Profile Affects IOPTH Kinetics and Cure Rate in Primary Hyperparathyroidism.*

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**BACKGROUND:** Recently, normocalcemic (NC) and normohormonal (NH) variants of primary hyperparathyroidism (pHPT) have been described, with distinct biochemical profiles from the typical high serum calcium and parathyroid hormone (PTH) levels. Here, we investigate whether biochemical profile affects cure rate, as well as the kinetics of intraoperative PTH (IOPTH).

**METHODS:** This is a single-center, retrospective study of pHPT patients undergoing parathyroidectomy. Patients were grouped based on preoperative calcium and PTH levels into typical, NC (normal calcium, elevated PTH, no evidence of secondary hyperparathyroidism), and NH (elevated calcium, unsuppressed PTH) biochemical profiles. All patients had IOPTH monitoring and  $\geq 6$ -month post-op serum studies to confirm surgical cure. Patient variables were analyzed with Kruskal-Wallis test and Chi-square analysis. IOPTH kinetic curves were analyzed using a linear mixed model.

**RESULTS:** From June 2006 to October 2014, 646 patients met inclusion criteria. Biochemical profile was typical in 460 patients (71%), NC in 101 (16%), and NH in 85 (13%). IOPTH levels were higher at all time points in typical patients,  $p < 0.001$ . Surgical cure rates were significantly lower for NC patients (90.1%) than for typical (98.5%) or NH patients (97.7%),  $p < 0.001$ , although a stricter criteria for cure was used in this group (normal calcium AND normal PTH). In a multivariable linear mixed model, NC patients had a significantly slower rate of IOPTH decline ( $p < 0.001$  at 10 min).

**CONCLUSIONS:** Here, we better characterize the atypical variants of pHPT. Using a stricter definition of cure in the NC variant, these patients have a lower surgical cure rate than typical or NH variants in pHPT. The IOPTH curve is affected by biochemical profile, with both NC and NH patients having lower absolute values and NC patients having a slower decline.

DOI: 10.1007/s00268-019-05157-x  
PMID: 31511943

**22. World J Surg. 2019 Sep 9. doi: 10.1007/s00268-019-05153-1. doi: 10.1007/s00268-019-05153-1. [Epub ahead of print]**

*Anti-Thyroid Antibodies and TSH as Potential Markers of Thyroid Carcinoma and Aggressive Behavior in Patients with Indeterminate Fine-Needle Aspiration Cytology.*

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**BACKGROUND:** Indeterminate fine-needle aspiration cytology (FNAC) imposes challenges in the management of thyroid nodules. This study aimed to examine whether preoperative anti-thyroid antibodies (Abs) and TSH are indicators of thyroid malignancy and aggressive behavior in patients with indeterminate FNAC. **METHODS:** This was a retrospective study of thyroidectomy patients from 2008 to 2016. We analyzed Abs and TSH levels, FNAC, and histopathology. Serum antibody levels were categorized as 'Undetectable', 'In-range' if detectable but within normal range, and 'Elevated' if above upper limit of normal. 'Detectable' levels referred to 'In-range' and 'Elevated' combined.

**RESULTS:** There were 531 patients included. Of 402 patients with preoperative FNAC, 104 (25.9%) had indeterminate cytology (Bethesda III-V). Of these, 39 (37.5%) were malignant and 65 (62.5%) benign on histopathology. In the setting of indeterminate FNAC, an increased risk of malignancy was associated with 'Elevated' thyroglobulin antibodies (TgAb) (OR 7.25, 95% CI 1.13-77.15,  $P = 0.01$ ) and 'Elevated' thyroid peroxidase antibodies (TPOAb) (OR 6.79, 95% CI 1.23-45.88,  $P = 0.008$ ). Similarly, while still 'In-range',  $TSH \geq 1$  mIU/L was associated with an increased risk of malignancy (OR 3.23, 95% CI 1.14-9.33,  $P = 0.01$ ). In all patients with malignancy, the mean tumor size was 8 mm larger in those with  $TSH \geq 1$  mIU/L ( $P = 0.03$ ); furthermore, in PTC patients, 'Detectable' TgAb conferred a 4 × risk of lymph node metastasis (95% CI 1.03-13.77,  $P = 0.02$ ).

**CONCLUSION:** In this cohort, in indeterminate FNAC patients, Abs and TSH were associated with an increased risk of malignancy. Additionally, TgAb and TSH were potential markers of aggressive biology. As such, they may be diagnostic and prognostic adjuncts.

DOI: 10.1007/s00268-019-05153-1  
PMID: 31502005

23. *World J Surg.* 2019 Sep 6. doi: 10.1007/s00268-019-05156-y. doi: 10.1007/s00268-019-05156-y. [Epub ahead of print]

*Long-Term Outcomes of Parathyroidectomy in Hyperparathyroidism-Jaw Tumor Syndrome: Analysis of Five Families with CDC73 Mutations.*

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**BACKGROUND:** Hyperparathyroidism-jaw tumor syndrome (HPT-JT) is a rare disease caused by CDC73 germline mutations, with familial primary hyperparathyroidism (pHPT), ossifying jaw tumors, genito-urinary neoplasms. The present study was aimed at determining the long-term postoperative outcome of parathyroidectomy in HPT-JT.

**METHODS:** A retrospective analysis of a single-center series of 20 patients from five unrelated HPT-JT families undergoing parathyroid surgery was performed.

**RESULTS:** Pathology confirmed a single-gland involvement in 95% of cases at onset. Parathyroid carcinoma occurred in three patients undergoing en-bloc parathyroidectomy and thyroid lobectomy; parathyroid benign lesions in 17 patients undergoing subtotal parathyroidectomy for evident multiglandular involvement (n = 1) or selective parathyroidectomy for single-gland involvement (n = 16), during bilateral (n = 13) or targeted unilateral neck exploration (n = 7). At a median overall follow-up of 16 years (range 2.5-42), patients with parathyroid carcinoma had a persistent/recurrent disease in 66.6%; patients with benign lesions had recurrent pHPT in 23.5% after a prolonged disease-free period; recurrent benign pHPT occurred slightly more often in cases of discordant preoperative localization (60% vs 9%; p = 0.06).

**CONCLUSION:** pHPT in HPT-JT is generally characterized by a benign and single-gland involvement, with a relatively increased risk of malignancy (15%). Parathyroid carcinoma needs extensive surgery because of high risk of permanent/recurrent disease (66.6%). In benign involvement, targeted unilateral exploration with selective parathyroidectomy may be effective in cases of concordant single-gland localization at preoperative localization imaging techniques. Bilateral neck exploration with subtotal parathyroidectomy might be preferred in cases of negative or discordant preoperative localization, because of the increased risk of multiglandular involvement and long-term recurrences (23.5%).

DOI: 10.1007/s00268-019-05156-y  
PMID: 31493194

**24. World J Surg. 2019 Aug 19. doi: 10.1007/s00268-019-05120-w. doi: 10.1007/s00268-019-05120-w. [Epub ahead of print]**

*Subclassification of Tumor Extension and Nodal Metastasis in Papillary Thyroid Cancer to Improve Prognostic Accuracy of the Eighth Edition of the Tumor-Node-Metastasis Classification.*

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**BACKGROUND:** The eighth edition of the tumor-node-metastasis classification system (TNM-8th) reflects the prognosis of papillary thyroid cancer (PTC) better than the seventh edition. This study investigated methods to further improve the prognostic accuracy of the TNM-8th.

**METHODS:** We enrolled 5683 patients who underwent surgery for PTC at the Kuma Hospital. We subdivided tumor extension (T4a) into T4a1 and T4a2 based on intraoperative gross findings and N1 according to size (< 3 cm and ≥ 3 cm) based on preoperative imaging findings.

**RESULTS:** The corresponding 20-year cancer-specific survival (CSS) rates of 4846, 403, 406, and 28 patients with TNM-8th stages I, II, III, and IVB, respectively, were 99.3%, 93.4%, 82.6%, and 11.3%. Owing to a CSS similar to that of stage II patients, N2 or T4a2 patients <55 years were upstaged to revised stage (re-stage) II. The CSS of stage III patients with T4a1 was significantly better ( $p < 0.0001$ ) than that of those with T4a2, and the CSS of T4a1 patients was similar to that of stage II patients. Therefore, T4a1 patients ≥ 55 years were downstaged to re-stage II. Owing to a CSS similar to that of T4a2 stage III patients, N2 stage II patients were upstaged to re-stage III. The 20-year CSS was poorer in re-stage III (69.5%) than in stage III patients and similar in re-stage II patients (91.8%) and stage II patients.

**CONCLUSION:** Subdivision of clinical tumor extension and node metastasis further improves the TNM-8th for PTC and identifies poor risk patients more accurately.

DOI: 10.1007/s00268-019-05120-w

PMID: 31428837

**25. Br J Surg. 2019 Oct;106(11):1495-1503. doi: 10.1002/bjs.11297. Epub 2019 Aug 19.**

*Outcomes of surgery for benign and malignant adrenal disease from the British Association of Endocrine and Thyroid Surgeons' national registry.*

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Lansdown M, Lennard TMJ, Lim B, Maddox P, Mihai R, Nicholson M, Palazzo F, Parrott N, Parvanta L, Rew D, Sadler G, Schulte KM, Sharma A, Shore S, Sinha P, Skene A, Smellie J, Smith D, Sutcliffe R, Thomas M, Thomas P, Thomas WEG, Titus A, Tomlinson M, Truran P, Ubhi C, Uppal H, Waghorn A, Walls G, Williams S, Zammitt C.

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**BACKGROUND:** This study investigated the indications, procedures and outcomes for adrenal surgery from the UK Registry of Endocrine and Thyroid Surgery database from 2005 to 2017, and compared outcomes between benign and malignant disease. **METHODS:** Data on adrenalectomies were extracted from a national surgeon-reported registry. Preoperative diagnosis, surgical technique, length of hospital stay, morbidity and in-hospital mortality were examined.

**RESULTS:** Some 3994 adrenalectomies were registered among patients with a median age of 54 (i.q.r. 43-65) years (55.9 per cent female). Surgery was performed for benign disease in 81.5 per cent. Tumour size was significantly greater in malignant disease: 60 (i.q.r. 34-100) versus 40 (24-55) mm ( $P < 0.001$ ). A minimally invasive approach was employed in 90.2 per cent of operations for benign disease and 48.2 per cent for cancer ( $P < 0.001$ ). The conversion rate was 3.5-fold higher in malignant disease (17.3 versus 4.7 per cent;  $P < 0.001$ ). The length of hospital stay was 3 (i.q.r. 2-5) days for benign disease and 5 (3-8) days for malignant disease ( $P < 0.050$ ). In multivariable analysis, risk factors for morbidity were malignant disease (odds ratio (OR) 1.69, 1.22 to 2.36;  $P = 0.002$ ), tumour size larger than 60 mm (OR 1.43, 1.04 to 1.98;  $P = 0.028$ ) and conversion to open surgery (OR 3.48, 2.16 to 5.61;  $P < 0.001$ ). The in-hospital mortality rate was below 0.5 per cent overall, but significantly higher in the setting of malignant disease (1.2 versus 0.2 per cent;  $P < 0.001$ ). Malignant disease (OR 4.88, 1.17 to 20.34;  $P = 0.029$ ) and tumour size (OR 7.47, 1.52 to 39.61;  $P = 0.014$ ) were independently associated with mortality in multivariable analysis.

**CONCLUSION:** Adrenalectomy is a safe procedure but the higher incidence of open surgery for malignant disease appears to influence postoperative outcomes.

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DOI: 10.1002/bjs.11297

PMID: 31424578

26. *World J Surg.* 2019 Aug 9. doi: 10.1007/s00268-019-05098-5. doi:

10.1007/s00268-019-05098-5. [Epub ahead of print]

*Prognostic Characteristics of Primary Squamous Cell Carcinoma of the Thyroid: A National Cancer Database Analysis.*

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**BACKGROUND:** Primary squamous cell carcinoma of the thyroid (ThySCC) is a rare cancer, primarily described only in case reports. We aimed to characterize the prognosis of ThySCC and compare its oncologic behavior to other thyroid malignancies.

**METHODS:** The National Cancer Database was queried to identify patients with ThySCC, papillary, tall cell variant, poorly differentiated (PDTC), and anaplastic (ATC) subtypes of thyroid cancer treated from 2004 to 2015. Demographics, tumor characteristics, and treatments were compared by tumor type and assessed to identify independent predictors of overall survival (OS).

**RESULTS:** Of 123,684 patients included, 314 had ThySCC. ThySCC patients had a 5-year OS of 17.7%, more closely resembling ATC (8.3%) than PDTC or PTC. ThySCC and ATC patients had similar demographics, except ThySCC patients who were younger (68.0 vs. 70.2 years,  $p < 0.01$ ). ThySCC tumors were smaller (mean  $53.5 \pm 45.7$  vs.  $69.5 \pm 75.2$  mm) with less frequent extrathyroidal extension (ETE) (64.0% vs. 73.8%), lymphovascular invasion (8.3% vs. 12.3%), and positive margins (22.0% vs. 28.3%) compared to ATCs ( $p < 0.05$ ). ETE [HR 3.1 (95% CI 1.5-6.4),  $p < 0.05$ ] and lymph node metastases [HR 2.2 (95% CI 1.2-4.0)  $p < 0.05$ ] were independently associated with worse OS for ThySCC patients. Both ThySCC and ATC patients had similar surgical success rates, with R1 resection possible in 37.3% versus 35.0% of patients, respectively ( $p < 0.05$ ). However, in contrast to ATC patients, adjuvant therapy was not associated with improved OS for ThySCC patients after complete resection.

**CONCLUSIONS:** ThySCC has a poor prognosis, similar to ATC, but with fewer aggressive features and no apparent survival benefit with adjuvant therapy after complete macroscopic surgical resection.

DOI: 10.1007/s00268-019-05098-5

PMID: 31399796

**27. World J Surg. 2019 Aug 9. doi: 10.1007/s00268-019-05113-9. doi: 10.1007/s00268-019-05113-9. [Epub ahead of print]**

*Utility of Activated Carbon Nanoparticle (CNP) During total Thyroidectomy for Clinically Nodal Positive Papillary Thyroid Carcinoma (PTC).*

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**BACKGROUND:** Activated carbon nanoparticle (CNP) is a novel tracer that may facilitate nodal dissection in clinically nodal positive (cN1) papillary thyroid carcinoma (PTC). The present study compared the nodal yield and surgical outcomes between surgery with CNP and without CNP.

**METHODS:** Patients who underwent total thyroidectomy with therapeutic nodal dissection for cN1 PTC were given the option of intraoperative CNP injection. Among those who received CNP, 0.2 mL CNP suspension was injected in both thyroid lobes before dissection. Study endpoints included number of total and metastatic

lymph nodes, inadvertently removed parathyroid glands (PGs), postoperative parathyroid hormone, calcium, and post-6-month thyroglobulin (Tg). Biochemical complete response (BCR) was defined as Tg  $\leq$  1 ng/mL and/or stimulated Tg  $\leq$  2 ng/mL.

**RESULTS:** One-hundred and twenty patients (58.3%) received CNP, while 86 (41.7%) had surgery without CNP. Demographics, tumor characteristics, and operative time were comparable between the two groups. However, total mean number of normal and metastatic lymph nodes retrieved were significantly greater in CNP group (10.0 vs. 8.1,  $p = 0.032$  and 4.5 vs. 2.7,  $p = 0.002$ , respectively). Rate of inadvertently removed PG was significantly less in CNP group (13.3% vs. 23.3%,  $p = 0.042$ ). Postoperative Tg level and BCR were significantly lower in CNP group (9.9 ng/mL vs. 14.7 ng/mL,  $p = 0.297$  and 82.4% vs. 72.9%,  $p = 0.002$ , respectively). However, large-sized ( $\geq 3$  cm) PTCs had a significantly lower nodal staining rate than smaller-sized PTCs (10.3% vs. 69.4%,  $p < 0.001$ ).

**CONCLUSIONS:** CNP injection can facilitate therapeutic central nodal dissection by increasing the nodal yield rates and reducing inadvertent PG removal. To enhance its utility, a greater volume of CNP might be necessary in larger-sized ( $> 3$  cm) PTCs.

DOI: 10.1007/s00268-019-05113-9

PMID: 31399795

**28. World J Surg. 2019 Nov;43(11):2842-2849. doi: 10.1007/s00268-019-05094-9.**

*Recurrent Papillary Thyroid Carcinoma to the Cervical Lymph Nodes: Outcomes of Compartment-Oriented Lymph Node Resection.*

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**INTRODUCTION:** Recurrence of papillary thyroid carcinoma after initial treatment is challenging. Surgical reintervention is recommended, but cure after surgery is uncertain and surgical morbidity may be high. This study evaluates the effect of compartment-oriented lymph node dissection (LND) on clinical and biochemical cure rate as well as the related complications.

**PATIENTS AND METHODS:** All patients who underwent LND for recurrent papillary thyroid carcinoma between 2000 and 2015 were included. Demography, the extent of the initial surgery, usage of  $^{131}\text{I}$ , the pattern of recurrence, diagnosis, details of the surgical reintervention, histological findings, surgical morbidity, and clinical and biochemical outcomes were analyzed.

**RESULTS:** There were 11 (12.7%) males and 75 (87.2%) females with a mean age of  $42.8 \pm 14.6$  years. Seventy-seven patients had undergone total thyroidectomy and in 67 (77.9%) some type of LN resection. In 76 (88.3%),  $^{131}\text{I}$  was administered after the initial surgery. We localized suspicious lymph nodes by US in all

patients, and metastases were documented before surgery by FNA in 63. Seven (8.13%) patients underwent central LND, 63 (73.2%) lateral LND and 16 (18.6%) both, central and lateral LND. Major complications occurred in 6 patients (6.9%). Sixty-two (72.0%) patients received 131I after surgery. A second surgical re-exploration was performed in 30 (34.8%) patients, and 7 patients required 3 or more additional LND. In a mean follow-up of  $59.4 \pm 39$  months, 51 (59.3%) patients are clinically, radiologically and biochemically free of disease.

**CONCLUSIONS:** In this series, compartment-oriented lymph node resection of recurrent papillary thyroid carcinoma leads to a final clinical and biochemical disease-free status of 59.3% with 6.9% of major complications.

DOI: 10.1007/s00268-019-05094-9

PMID: 31372725