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1. Sunitinib achieved fast and sustained control of VIPoma symptoms.
The RET oncogene in papillary thyroid carcinoma.

Prescott JD¹, Zeiger MA.

Abstract
Papillary thyroid carcinoma (PTC) is the most common form of thyroid cancer, accounting for greater than 80% of cases. Surgical resection, with or without postoperative radioiodine therapy, remains the standard of care for patients with PTC, and the prognosis is generally excellent with appropriate treatment. Despite this, significant numbers of patients will not respond to maximal surgical and medical therapy and ultimately will die from the disease. This mortality reflects an incomplete understanding of the oncogenic mechanisms that initiate, drive, and promote PTC. Nonetheless, significant insights into the pathologic subcellular events underlying PTC have been discovered over the last 2 decades, and this remains an area of significant research interest. Chromosomal rearrangements resulting in the expression of fusion proteins that involve the rearranged during transfection (RET) proto-oncogene were the first oncogenic events to be identified in PTC. Members of this fusion protein family (the RET/PTC family) appear to play an oncogenic role in approximately 20% of PTCs. Herein, the authors review the current understanding of the clinicopathologic role of RET/PTC fusion proteins in PTC development and progression and the molecular mechanisms by which RET/PTCs exert their oncogenic effects on the thyroid epithelium. Cancer 2015. © 2015 American Cancer Society.

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KEYWORDS:
oncogene; papillary thyroid cancer; pediatric thyroid cancer; radiation; rearranged during transfection

PMID: 25731779  Makale sayfası

Rare metastases of well-differentiated thyroid cancers: a systematic review.

Madani A¹, Jozaghi Y, Tabah R, How J, Mitmaker E.

Abstract
BACKGROUND:
A minority of metastatic well-differentiated thyroid cancer (WDTC) patients present with end-organ disease other than in the lung, bone or lymph nodes. These metastases tend to be overlooked because of their low incidence, and this results in delayed diagnosis. The purpose of this study was to perform a systematic review of the clinical and histologic features of unusual WDTC metastases.

METHODS:
A systematic literature search of bibliographic databases, reference lists of articles, and conference proceedings was performed up to 2013. Studies were included if they reported on adult patients with WDTC and pathology-proven metastases to end-organs other than lung, bone, or lymph nodes. A total of 238 studies were included in a qualitative analysis. Data is expressed as N (%) and median [interquartile range].

RESULTS:
A total of 492 patients (median age, 62 years [50-70 years]) were identified in 197 case reports and 42 case series. There were 22 different end-organ metastatic sites documented with either papillary [255 (57 %)], follicular [172 (39 %)], or Hürtthle-cell [18 (4 %)] histology. A total of 181 (41 %) patients presented with solitary metastasis and 54 (93 %) with elevated serum thyroglobulin. Positron emission tomography and whole-body radioactive iodine scans revealed hypermetabolic foci in 28 (97 %) and 50 (81 %) cases, respectively. Disease-free interval following the initial diagnosis of the primary thyroid cancer was highly variable, ranging from synchronous presentation [66 (33 %)] to metachronous disease after 516 months [mean 86 months (SD 90)].

CONCLUSIONS:
WDTC can manifest with highly variable and unusual clinical features. Rare sites of metastases should be considered in the absence of the more common extra-cervical disease recurrence locations.

PMID: 25192681

Analysis of age and disease status as predictors of thyroid cancer-specific mortality using the Surveillance, Epidemiology, and End Results database.

Orosco RK1, Hussain T, Brumund KT, Oh DK, Chang DC, Bouvet M.

Abstract
BACKGROUND:
Age at diagnosis is incorporated into all relevant staging systems for differentiated thyroid carcinoma (DTC). There is growing evidence that a specific age cutoff may not be ideal for accurate risk stratification. We sought to evaluate the interplay between age and oncologic variables in patients with DTC using the largest cohort to date.

METHODS:
The Surveillance, Epidemiology, and End RESULTS (SEER) database was queried to identify patients with DTC as their only malignancy for the period 1973 to 2009. Multivariate analyses using a range of age cutoffs and age subgroupings were utilized in order to search for an optimal age that would provide the most significant risk stratification between young and old patients. The primary outcome was disease-specific survival (DSS) and covariates included: age, race, sex, tumor/nodal/metastasis (TNM) stage, decade of diagnosis, and radioactive iodine therapy.

RESULTS:
A total of 85,740 patients were identified. Seventy-six percent of patients were American Joint Committee on Cancer (AJCC) stage I, 8% were stage II, 7% were stage III, and 8% were stage IV. Age over 45 years (hazard ratio [HR] 19.2, p<0.001) and metastatic disease (HR 13.1, p<0.001) were the strongest predictors of DSS. Other factors that significantly predicted DSS included: not receiving radioactive iodine (RAI; HR 1.3, p=0.002), T3 (HR 2.6, p<0.001), and T4 disease (HR 3.3, p<0.001), and nodal spread (HR 2.6 to 3.3, p<0.001). Female sex showed a significant protective effect (HR 0.7, p=0.001). Adjusting the age-group
cutoff from 25 to 55 years showed consistently high HRs for advanced age, without a distinct change at any point. Comparing HRs for T, N, and M stage between young and old patient subgroups showed that advanced disease increased the risk for DSS regardless of age, and was oftentimes a worse prognosticator in young patient groups.

CONCLUSIONS:
The contribution of age at diagnosis to a patient's DSS is considerable, but there is no age cutoff that affords any unique risk-stratification in patients with DTC.

PMID: 25369076


What to do with incidental thyroid nodules identified on imaging studies? Review of current evidence and recommendations.

Hoang JK¹, Grady AT, Nguyen XV.
Author information
Abstract
PURPOSE OF REVIEW:
To discuss the problem of incidental thyroid nodules (ITN) detected on imaging; summarize the literature for workup methods; and provide recommendations based on current evidence.

RECENT FINDINGS:
ITN are a common problem, seen in 40-50% of ultrasound and 16% of computed tomography (CT) and MRI studies that include the thyroid. The personal and financial costs of workup frequently outweigh the benefits when considering that the majority of ITN are benign; 25-41% of patients undergo surgery after biopsy, of which more than half ultimately result in a benign diagnosis, and small thyroid cancers have an indolent course. Workup should consider reduction in unnecessary workup in addition to cancer diagnosis. The Society of Radiologists in Ultrasound recommendations have been proposed for ITN detected on ultrasound and found to reduce workup by 30%. For ITN detected on CT, MRI, or PET/CT, a three-tiered system categorization method reduces workup of ITN by 35-46%.

SUMMARY:
The ideal approach to selecting ITN detected on imaging for workup would not be to diagnose all cancers, but to diagnose cancers that have reached clinical significance, while avoiding unnecessary tests and surgery in patients with benign nodules, especially those who have limited life expectancy. The three-tiered system and the Society of Radiologists in Ultrasound recommendations are supported by existing studies and focus on reducing unnecessary biopsy.

PMID: 25310642

5. Int J Mol Sci. 2015 Mar 17;16(3):6153-6182. IF: 2.34

New Therapies for Dedifferentiated Papillary Thyroid Cancer.

Fallahi P¹, Mazzi V², Vita R³, Ferrari SM⁴, Materazzi G⁵, Galleri D⁶, Benvenga S⁷, Miccoli P⁸, Antonelli A⁹.
Author information
Abstract
The number of thyroid cancers is increasing. Standard treatment usually includes primary surgery, thyroid-stimulating hormone suppressive therapy, and ablation of the thyroid remnant with radioactive iodine (RAI). Despite the generally good prognosis of thyroid carcinoma, about 5% of patients will develop metastatic disease, which fails to respond to RAI, exhibiting a more aggressive behavior. The lack of specific, effective
and well-tolerated drugs, the scarcity of data about the association of multi-targeting drugs, and the limited role of radiiodine for dedifferentiated thyroid cancer, call for further efforts in the field of new drugs development. Rearranged during transfection (RET)/papillary thyroid carcinoma gene rearrangements, BRAF (B-RAF proto-oncogene, serine/threonine kinase) gene mutations, RAS (rat sarcoma) mutations, and vascular endothelial growth factor receptor 2 angiogenesis pathways are some of the known pathways playing a crucial role in the development of thyroid cancer. Targeted novel compounds have been demonstrated to induce clinical responses and stabilization of disease. Sorafenib has been approved for differentiated thyroid cancer refractory to RAI.
WFUMB Guidelines and Recommendations for Clinical Use of Ultrasound Elastography: Part 2; Breast.


Author information

Abstract

The breast section of these Guidelines and Recommendations for Elastography produced under the auspices of the World Federation of Ultrasound in Medicine and Biology (WFUMB) assesses the clinically used applications of all forms of elastography used in breast imaging. The literature on various breast elastography techniques is reviewed, and recommendations are made on evidence-based results. Practical advice is given on how to perform and interpret breast elastography for optimal results, with emphasis placed on avoiding pitfalls. Artifacts are reviewed, and the clinical utility of some artifacts is discussed. Both strain and shear wave techniques have been shown to be highly accurate in characterizing breast lesions as benign or malignant. The relationship between the various techniques is discussed, and recommended interpretation based on a BI-RADS-like malignancy probability scale is provided. This document is intended to be used as a reference and to guide clinical users in a practical way.

KEYWORDS:
Breast; Breast Cancer; Shear wave; artifacts; elastography; guidelines; strain

PMID: 25795620


Association of thyroid carcinoma with pregnancy: A meta-analysis.

Zhou YQ¹, Zhou Z¹, Qian ME¹, Gong T¹, Wang JD¹.

Author information

Abstract

A number of scholars reported that reproductive factors play a significant role in thyroid cancer and the correlation between the two may affect the diagnosis and treatment of thyroid carcinoma during pregnancy. To determine whether pregnancy reproductive factors affect thyroid carcinoma, we conducted a meta-analysis of studies that investigated the association between pregnancy factors and thyroid carcinoma. PubMed, OVID and the Cochrane Library were searched from their inception to April 1st, 2013. The searched publications mainly investigated reproductive factors and the morbidity or prognosis of female thyroid carcinoma. The studies were filtered by predetermined standards and the quality of the included studies was evaluated by the Newcastle-Ottawa scale inventory. Two researchers independently extracted information on first author, year of publication, study design (case-control or prospective cohort), compared populations, inclusion and exclusion criteria and total sample size. Other researchers assessed the studies for publication bias and performed statistical analyses. Discrepancies were resolved by consensus. A total of 21 studies were selected for the meta-analysis, including 406,329 cases in total. Compared to the control group, the risk of thyroid carcinoma in women with a history of pregnancy was not significantly discrepant, [odds ratio (OR)=1.00, 95% confidence interval (CI): 0.91-1.11]. However, the risk of thyroid carcinoma in women with a history of ≥ 3 pregnancies was significantly increased (OR=1.39, 95% CI: 1.21-1.59). Furthermore, an interval of ≤ 5 years since the last pregnancy was closely associated with thyroid carcinoma (OR=1.53, 95% CI: 1.29-1.81). The patients developed thyroid carcinoma during
pregnancy did not exhibit an increased risk of lymphatic metastasis (OR=0.94, 95% CI: 0.53-1.67); the risk of distant metastasis also did not increase significantly (OR=1.03, 95% CI: 0.86-1.24). Therefore, multiple pregnancies and a ≤ 5-year interval between pregnancies were identified as high-risk factors for thyroid carcinoma, whereas thyroid carcinoma during pregnancy was not associated with a significant risk of lymphatic and distant metastasis.

**KEYWORDS:**
meta-analysis; pregnancy; reproduction; thyroid neoplasm

PMID: 25798264
Recurrence of papillary thyroid cancer after optimized surgery.

Grant CS1

Abstract

Recurrence of papillary thyroid cancer (PTC) after optimized surgery requires a full understanding of the disease, especially as it has changed in the last 15 years, what comprises optimized surgery, and the different types and implications of disease relapse that can be encountered. PTC has evolved to tumors that are much smaller than previously seen, largely due to various high quality imaging studies obtained for different reasons, but serendipitously identifying thyroid nodules that prove to be papillary thyroid microcarcinomas (PTMC). With rare exception, these cancers are cured by conservative surgery without additional therapy, and seldom result in recurrent disease. PTC is highly curable in 85% of cases because of its rather innocent biologic behavior. Therefore, the shift in emphasis from disease survival to recurrence is appropriate. As a result of three technologic advances-high-resolution ultrasound (US), recombinant TSH, and highly sensitive thyroglobulin (Tg)-disease relapse can be discovered when it is subclinical. Endocrinologists who largely control administration of radioactive iodine have used it to ablate barely detectable or even biochemically apparent disease, hoping to reduce recurrence and perhaps improve survival. Surgeons, in response to this new intense postoperative surveillance that has uncovered very small volume disease, have responded by utilizing US preoperatively to image this disease, and incorporated varying degrees of lymphadenectomy into their initial treatment algorithm. Bilateral thyroid resection—either total or near-total thyroidectomy—remains the standard for PTC >1 cm, although recent data has re-emphasized the value of unilateral lobectomy in treating even some PTC measuring 1-4 cm. Therapeutic lymphadenectomy has universal approval, but when lymph nodes in the central neck are not worrisome to the surgeon's intraoperative assessment, although that judgment in incorrect up to 50%, whether they should be excised has reached a central point of controversy. Disease relapse can occur individually or in combination of three different forms: lymph node metastasis (LNM), true soft tissue local recurrence, and distant disease. The latter two are worrisome for potentially life-threatening consequences whereas nodal metastases are often persistent from the initial operation, and mostly comprise a biologic nuisance rather than virulent disease. A moderate surgical approach of bilateral thyroid resection, with usual central neck nodal clearance, and lateral internal jugular lymphadenectomy for node-positive disease can be performed safely, and with about a 5% recurrence rate.

KEYWORDS:
Papillary thyroid cancer (PTC); lymph nodes; recurrence; surgery

PMID: 25713780
Prospective Evaluation of Zoledronic Acid in the Treatment of Bone Metastases from Differentiated Thyroid Carcinoma.

Orita Y, Sugitani I, Takao S, Toda K, Manabe J, Miyata S.

Abstract
PURPOSE:
The objectives of this study were to prospectively delineate the efficacy and safety of zoledronic acid for treating bone metastases (BM) from differentiated thyroid carcinoma (DTC), and to evaluate the relationships between levels of bone metabolic markers and occurrence of skeletal-related events (SREs).

METHODS:
This was a prospective, single-arm, single-center study. Nineteen patients with BM from DTC were assigned to receive zoledronic acid therapy every 4-5 weeks. Imaging studies for sites of BM were conducted every 6 months, and levels of bone metabolic markers, including serum bone-specific alkaline phosphatase (BAP) and urinary N-telopeptide of type I collagen (NTx), were assessed every 3 months. To evaluate the efficacy of zoledronic acid use, data of SREs were compared with those of 16 historical controls.

RESULTS:
SREs developed in eight patients (42%), but metastatic spinal cord compression (MSCC) appeared in only one patient. Pain scores were ameliorated in five patients, but aggravated in six patients. Ten patients had stable disease, six showed progressive disease, and none showed partial or complete response during the observation period. Decreases in levels of bone metabolic markers were observed in ten patients for BAP and 15 for NTx. However, no significant correlations were identified between changes in bone metabolic marker levels and development of SREs.

CONCLUSIONS:
Zoledronic acid may offer a mainstay of multidisciplinary treatment for patients with BM for the purpose of reducing SREs. Levels of serum BAP and urinary NTx do not appear reliable as indicators of amelioration of BM symptoms.

PMID: 25762482

Ipsilateral Central Neck Dissection Plus Frozen Section Examination Versus Prophylactic Bilateral Central Neck Dissection in cN0 Papillary Thyroid Carcinoma.

Raffaelli M, De Crea C, Sessa L, Fadda G, Bellantone C, Lombardi CP.

Abstract
BACKGROUND:
Ipsilateral central compartment node dissection (IpsiCCD) can reduce the morbidity of prophylactic bilateral central compartment node dissection (BilCCD) in papillary thyroid carcinoma (PTC) but it carries the risk of contralateral metastases being overlooked. Frozen section examination (FSE) of removed ipsilateral nodes has been proposed to intraoperatively assess nodal status. We compared IpsiCCD plus FSE and BilCCD in clinically unifocal and node negative PTC.

METHODS:
One hundred patients were prospectively assigned to undergo total thyroidectomy (TT) plus BilCCD or TT plus IpsiCCD. In the IpsiCCD group, removed lymph nodes were sent for FSE. If FSE was positive for metastases, a BilCCD was accomplished.

RESULTS:
The two groups included 50 patients each. Overall, occult lymph node metastases were found in 41 patients-20 in the IpsiCCD group and 21 in the BilCCD group. FSE correctly identified occult node metastases in 13 of 20 pN1a patients in the IpsiCCD group (overall accuracy 86%). Seven node metastases were not detected at FSE-five were micrometastases (≤2 mm). Six of 13 patients in the IpsiCCD group who underwent BilCCD and 6 of 21 BilCCD pN1a patients had bilateral metastases. More patients in the BilCCD group showed transient hypocalcemia (27/50 vs. 18/50, respectively) [p = NS]. No patient experienced recurrent disease.

CONCLUSIONS:
FSE of ipsilateral nodes is accurate in determining nodal status, allowing the extension of the central neck clearance to be reliably modulated. Routine IpsiCCD plus FSE of the ipsilateral nodes could be a valid alternative to prophylactic BilCCD since it allows accurate staging and may reduce morbidity.

PMID: 25652046

3. Thyroid. 2015 Mar 12. [Epub ahead of print] IF: 3.84

Serum thyroglobulin measured with a second-generation assay in patients undergoing total thyroidectomy without radioiodine remnant ablation: A prospective study.
Rosario PW1, Mourão GF, Siman TL, Calsolari MR.

Author information
Abstract
BACKGROUND:
Follow-up consisting of the measurement of nonstimulated serum thyroglobulin (Tg) combined with neck ultrasonography (US) is recommended for patients with papillary thyroid carcinoma (PTC) without indication for radioiodine ablation. There is no recommendation of TSH suppression during this follow-up. New-generation Tg assays have been increasingly used, but few studies involve patients submitted only to thyroidectomy and they have several limitations. The objective of this prospective study was to define expected concentrations of nonstimulated Tg measured with a second-generation assay after total thyroidectomy in the absence of tumor.

METHODS:
Serum Tg was measured using a second-generation assay in 69 patients without tumor and serum TSH between 0.5-2 mIU/l, 3, 6, 12 and 24 months after total thyroidectomy. All patients had undetectable anti-Tg antibodies (TgAb).

RESULTS:
Serum Tg was undetectable in 44.4%, 57%, 62.5% and 62.1% of the patients 3, 6, 12 and 24 months after thyroidectomy, respectively, and was ≤ 0.5 ng/ml in 60.3%, 80%, 90.6% and 90.9%. All patients had a Tg ≤ 2 ng/ml 6 months after thyroidectomy and 97% had a Tg ≤ 1 ng/ml 24 months after surgery. There was no
case of Tg conversion from undetectable to detectable and none of the patients presented an increase in Tg.

CONCLUSIONS:
An important decline in serum Tg occurred between 3 and 6 months after total thyroidectomy. One year after surgery, Tg was undetectable in approximately 60% of the patients and ≤ 2 ng/ml in all of them.

PMID: 25763842

4. Thyroid. 2015 Mar 26. [Epub ahead of print] IF: 3.84
Using diffusion-weighted MRI to predict aggressive histological features in papillary thyroid carcinoma: a novel tool for pre-operative risk stratification in thyroid cancer.
Lu Y', Moreira AL, Hatzoglou V, Stambuk HE, Gonen M, Mazaheri Y, Deasy JO, Shaha AR Md, Tuttle RM Md, Shukla-Dave A,
Author information
Abstract
BACKGROUND:
Initial management recommendations of papillary thyroid carcinoma (PTC) are very dependent on pre-operative studies designed to evaluate the presence of PTC with aggressive features. The purpose of this study was to evaluate whether diffusion-weighted magnetic resonance imaging (DW-MRI) before surgery can be used as a tool to stratify tumor aggressiveness in patients with PTC.

METHODS:
In this prospective study, 28 patients with PTC underwent DW-MRI studies on a 3T MR scanner prior to thyroidectomy. Due to image quality, 21 patients were finally suitable for further analysis. Apparent diffusion coefficients (ADCs) of normal thyroid tissues and PTCs for 21 patients were calculated. Tumor aggressiveness was defined by surgical histopathology. The Mann-Whitney U test was used to compare the difference in ADCs among groups of normal thyroid tissues and PTCs with and without features of tumor aggressiveness. Receiver operating characteristic (ROC) analysis was performed to assess the discriminative specificity, sensitivity and accuracy of and determine the cut-off value for the ADC in stratifying PTCs with tumor aggressiveness.

RESULTS:
There was no significant difference in ADC values between normal thyroid tissues and PTCs. However, ADC values of PTCs with extrathyroidal extension (ETE; 1.53±0.25 ×10⁻³ mm²/s) were significantly lower than corresponding values from PTCs without ETE (2.37±0.67 ×10⁻³ mm²/s; p<0.005). ADC values identified 3 papillary carcinoma patients with extrathyroidal extension that would have otherwise been candidates for observation based on ultrasound evaluations. The cut-off value of ADC to discriminate PTCs with and without ETE was determined at 1.85 ×10⁻³ mm²/s with a sensitivity of 85%, specificity of 85% and ROC curve area of 0.85.

CONCLUSION:
ADC value derived from DW-MRI before surgery has the potential to stratify ETE in patients with PTCs.

PMID: 25809949
Post-operative stimulated thyroglobulin and neck ultrasound as personalized criteria for risk stratification and radioactive iodine selection in low- and intermediate-risk papillary thyroid cancer.

Orlov S¹, Salari F, Kashat L, Freeman JL, Vescan A, Witterick IJ, Walfish PG.

Abstract
The purpose of this study was to demonstrate the utility of a personalized risk stratification and radioactive iodine (RAI) selection protocol (PRSP) using post-operative stimulated thyroglobulin (Stim-Tg) and neck ultrasound in low- and intermediate-risk papillary thyroid carcinoma (PTC) patients. Patients with PTC tumors ≥1 cm were prospectively followed after total thyroidectomy and selective therapeutic central compartment neck dissection. Low/intermediate risk was defined as PTC confined to the thyroid or central (level VI) lymph nodes. Stim-Tg and neck ultrasound were performed approximately 3 months after surgery and used to guide RAI selection. Patients with Stim-Tg < 1 µg/L did not receive RAI, while those with Stim-Tg >5 µg/L routinely did. Those with Stim-Tg 1-5 µg/L received RAI on the basis of several clinical risk factors. Patients were followed for >6 years with serial neck ultrasound and basal/stimulated thyroglobulin. Among the 129 patients, 84 (65 %) had undetectable Stim-Tg after initial surgery, 40 (31 %) had Stim-Tg of 1-5 µg/L, and 5 (4 %) had Stim-Tg >5 µg/L. RAI was administered to 8 (20 %) patients with Stim-Tg 1-5 µg/L and 5 (100 %) with Stim-Tg >5 µg/L. Using this approach, RAI therapy was avoided in 17/20 (85 %) patients with tumors >4 cm, in 72/81 (89 %) patients older than 45 years, and in 6/9 (67 %) patients with central lymph node involvement. To date, 116 (90 %) patients in this cohort have not received RAI therapy with no evidence of residual/recurrent disease, whereas among the 13 patients who received RAI, 1 (8 %) had pathologic residual/recurrence disease. Using the proposed PRSP, RAI can be avoided in the majority of low/intermediate-risk PTC patients. Moreover, traditional risk factors considered to favor RAI treatment were not always concordant with the PRSP and may lead to overtreatment.

PMID: 25792004
original thyroid bed on a rhTSH stimulated 150 MBq 131I whole body scan (WBS) 9 months after remnant ablation, or no visible uptake in the original thyroid bed on a post therapeutic WBS when a second high dose was necessary.

RESULTS:
After interim analysis of the first 8 patients, the failure rate was estimated to be 69% (90% confidence interval (CI) 20-86%) and the inclusion of new patients had to be stopped. Final analysis resulted in an ablation success in 11 out of 17 patients (65%, 95% CI 38-86%).

CONCLUSION:
According to this study, the efficacy of rhTSH in the preparation of 131I ablation therapy is inferior, when using a strict definition of ablation success. The current lack of agreement as to the definition of successful remnant ablation, makes comparison between different ablation strategies difficult. Our results point to the need for an international consensus on the definition of ablation success, not only in routine patient's care but also for scientific reasons.

TRIAL REGISTRATION:
Dutch Trial Registration NTR2395.

PMID: 25793762
Circulating Thyrotropin Receptor Messenger RNA as a Marker of Tumor Aggressiveness in Patients with Papillary Thyroid Microcarcinoma.

Aliyev A¹, Gupta M¹, Nasr C², Hatipoglu B², Milas M¹, Siperstein A¹, Berber E¹.

Abstract

BACKGROUND:
We have previously shown that thyrotropin receptor messenger RNA (TSHR-mRNA) was detectable in the peripheral blood of patients with papillary thyroid microcarcinoma (PTmC). The aim of this study was to analyze the utility of TSHR-mRNA status as a marker of tumor aggressiveness in patients with PTmC.

METHODS:
Preoperative TSHR-mRNA values were obtained in 152 patients who underwent thyroidectomy and were found to have PTmC on final pathology. Clinical parameters were analyzed from an IRB-approved database using Chi square and t-test.

RESULTS:
Preoperatively, TSHR-mRNA was detected in the peripheral blood in 46%, which was less than that for macroscopic papillary thyroid carcinoma (80%), but higher than for benign thyroid disease (18%) (p<0.001). The focus of cancer was larger in TSHR-mRNA positive compared to negative group (0.41 vs. 0.30 cm, respectively, p=0.015). The prevalence of tall cell variant was higher in the TSHR-mRNA positive group. The rates of lymph node (LN) metastasis (16% vs. 10%), multifocality (46% vs. 49%) and extrathyroidal extension (10% vs. 5%) were similar between the TSHR-mRNA positive and negative groups, respectively. In patients 45 years or older, rate of LN metastasis was higher in TSHR-mRNA positive (10%) versus negative (2%) group (p=0.039). TSHR-mRNA positivity predicted a higher likelihood of radioactive iodine treatment (36% vs. 17%, p=0.009) postoperatively.

CONCLUSION:
This study shows that TSHR-mRNA, which is a marker of circulating thyroid cancer cells, is detectable in about half of the patients with PTmC. The positivity of this marker predicts a higher likelihood of LN involvement in patients with PTmC, who are 45 years or older.

KEYWORDS:
Papillary thyroid microcarcinoma; Thyrotropin receptor messenger-RNA
The Implementation of the Bethesda System for Reporting Thyroid Cytopathology Improves Malignancy Detection Despite Lower Rate of Thyroidectomy in Indeterminate Nodules.

Hirsch D¹, Robenshtok E, Bachar G, Braslavsky D, Benbassat C.

Author information

Abstract

BACKGROUND:
The Bethesda system for reporting thyroid cytopathology (TBSRTC) was developed in 2009 to standardize the terminology for interpreting fine-needle aspiration (FNA) specimens.

METHODS:
A historical prospective case series design was employed. The study group included patients with a thyroid nodule classified as TBSRTC AUS/FLUS (B3) or FN/SFN (B4) in 2011-2012 in a tertiary university-affiliated medical center. Rates of surgery and malignancy detection were compared to our pre-TBSRTC (1999-2000) study.

RESULTS:
Of 3927 nodules aspirated, 575 (14.6 %) were categorized as B3/B4. Complete data were available for 322. Thyroidectomy was performed in 123 (38.2 %) cases: 66/250 (26.4 %) B3 and 57/72 (79.2 %) B4. Differentiated thyroid cancer was found in 66 (53.7 %) patients: 30/66 (45.5 %) B3 and 36/57 (63.2 %) B4 (p = 0.075). Operated patients were younger than the non-operated (B3: 52.4 ± 16 vs. 59.7 ± 13 years, p = 0.009; B4: 51.7 ± 15 vs. 60.5 ± 14 years, p = 0.042), and operated B3 nodules were larger than the non-operated (27.2 vs. 22.2 mm, p = 0.014). Additional FNA was done in 160 patients (49.7 %): 137/250 (54.8 %) B3 and 23/72 (31.9 %) B4 (p = 0.002). The additional B3 nodules aspirations yielded a diagnosis of B2 in 84 patients (61.3 %), B3 in 48 (35 %), and B4 in 5 (3.6 %). Of the 23 repeated B4 aspirations, B2 was reported in 5 (21.7 %), B3 in 12 (52.2 %), B4 in 4 (17.4 %), and B6 in 2 (8.7 %). The number of aspirated nodules was twice that reported in 1999-2000. The rate of indeterminate nodules increased from 6 to 14.6 %, the surgery rate decreased from 52.3 to 38.2 %, and the accuracy of malignancy diagnosis increased from 25.9 to 53.7 %.

CONCLUSIONS:
The application of TBSRTC significantly improves diagnostic accuracy for indeterminate thyroid nodules, leading to higher rates of malignancy detection despite lower rates of thyroidectomies.

PMID: 25809059

Antimicrobial Prophylaxis for the Prevention of Surgical Site Infection After Thyroid and Parathyroid Surgery: A Prospective Randomized Trial.


Author information

Abstract

BACKGROUND AND OBJECTIVE:
The effectiveness of antimicrobial prophylaxis (AMP) in the prevention of surgical site infection (SSI) following thyroid and parathyroid surgery remains uncertain. The objective of this prospective randomized
controlled trial (Ito-RCT1) was to assess the effectiveness of AMP in clean neck surgery performed to treat thyroid and parathyroid disease.

METHODS:
Participants comprised patients scheduled for clean neck surgery for thyroid and parathyroid disease at Ito Hospital. Patients whose surgery included sternotomy or resection of the trachea, larynx, pharynx, or esophagus were excluded. AMP consisted of 2 g of piperacillin (PIPC) (group A, n = 541) or 1 g of cefazolin (CEZ) (group B, n = 541) administered intravenously immediately after endotracheal intubation. Patients in the control group (Group C, n = 1,082) did not receive AMP.

RESULTS:
Statistical analysis was performed to compare the AMP group (Group A + Group B) with the control group (Group C). Drug-induced acute reactions correlated to PIPC or CEZ did not occur in the AMP group. No significant differences in the postoperative incidence of liver or renal dysfunction were seen between the AMP and control groups. Postoperative incidence of urinary tract infection was significantly higher in the control group (p = 0.002). The incidence of SSI events was very low, with only 1 event (0.09 %) in the AMP group and 3 events (0.28 %) in the control group, and this difference between groups was not significant (p = 0.371).

CONCLUSIONS:
AMP is not necessary to prevent SSI after clean thyroid or parathyroid surgery.

PMID: 25566977


Intraoperative diagnosis of central compartment lymph node metastasis predicts recurrence of patients with papillary thyroid carcinoma and clinically node-negative lateral neck and may guide extent of initial surgery.

Lee CW1, Gong G, Roh JL.

Author information

Abstract

BACKGROUND:
Although lymph node (LN) metastasis (LNM) of papillary thyroid carcinoma (PTC) is common, routine prophylactic LN dissection (LND) is still controversial. The purpose of this study was to investigate risk factors for recurrence of PTC with clinically node-negative lateral neck to determine the utility of intraoperative LN biopsy.

MATERIALS AND METHODS:
This study involved 185 patients with pathologically confirmed PTC and clinically node-negative lateral neck. All patients underwent thyroidectomy with or without ipsilateral or bilateral central LND after intraoperative central LN biopsy. Routine lateral neck LND was not performed. Clinicopathologic and intraoperative findings and post-treatment recurrences were recorded. Univariate and multivariate analyses with Cox-proportional hazards model were used to identify factors associated with recurrence.

RESULTS:
During a follow-up of 50-96 months, six (3.2 %) patients had recurrences in lateral cervical LNs at a median 28 months (range 7-57 months) after surgery. Overall, 2- and 5-year RFS rates were 98.4 and 96.7 %, respectively. Univariate analyses revealed that tumor size (P = 0.005), bilaterality (P = 0.033), T4 disease (P < 0.001), and intraoperative diagnosis of central LNM (P = 0.001) were significantly predictive of recurrence. Multivariate analyses showed that T4 disease (P = 0.049) and intraoperative diagnosis of central LNM (P = 0.027) were independently predictive of recurrence.
CONCLUSIONS:
Prophylactic lateral neck LND is not advocated for PTC with clinically node-negative lateral neck. Intraoperative LN biopsy may help identify patients at risk for recurrence and those who would benefit from LND.

PMID: 25234198
Prognostic value of microscopic lymph node involvement in patients with papillary thyroid cancer.

Bardet S\(^1\), Ciappuccini R, Quak E, Rame JP, Blanchard D, de Raucourt D, Babin E, Michels JJ, Vaur D, Heutte N.

Author information

Abstract

CONTEXT:
The impact of microscopic nodal involvement on the risk of persistent/recurrent disease (PRD) remains controversial in patients with papillary thyroid carcinoma (PTC).

OBJECTIVE:
The goal of the study was to assess the risk of PRD and the 4-year outcome in PTC patients according to their initial nodal status [pNx, pN0, pN1 microscopic (cN0/pN1) or pN1 macroscopic (cN1/pN1)].

DESIGN:
We conducted a retrospective cohort study.

PATIENTS:
The study included 305 consecutive PTC patients referred for radioiodine ablation from 2006 to 2011.

MAIN OUTCOME MEASURE:
We evaluated the risk of structural PRD and the disease status at the last follow-up. At ablation, persistent disease was consistently assessed by using post-radioiodine ablation scintigraphy combining total body scan and neck and thorax single-photon computed tomography-computed tomography (SPECT-CT) acquisition.

RESULTS:
Of 305 patients, 128 (42%) were pNx, 84 (28%) pN0, 44 (14%) pN1 microscopic, and 49 (16%) pN1 macroscopic. The 4-year cumulative risk of PRD was higher in pN1 macroscopic than in pN1 microscopic patients (49% vs 24%, P = .03), and higher in pN1 microscopic than in pN0 (12%, P = .01) or pNx patients (6%, P < .001). On multivariate analysis, tumor size of 20 mm or greater [relative risk (RR) 3.4; P = .0001], extrathyroid extension (RR 2.6; P < .003), pN1 macroscopic (RR 4.5; P < .0001), and pN1 microscopic (RR 2.5; P < .02) were independent risk factors for PRD. At the last visit, the proportion of patients with no evidence of disease decreased from pNx (98%), pN0 (93%), and pN1 microscopic (89%) to pN1 macroscopic patients (70%) (P < .0001, Cochran-Armitage trend test). Extrathyroid extension (odds ratio 9.7; P < .0001) and N1 macroscopic (OR 4.9; P < .001) independently predicted persistent disease at the last visit, but N1 microscopic did not.

CONCLUSIONS:
Patients with microscopic lymph node involvement present an intermediate outcome between that observed in pN0-pNx patients and pN1 macroscopic patients. These data may justify modifications to the risk recurrence staging systems.

PMID: 25303481  Makale sayfası
False negative cytology in large thyroid nodules.
Giles WH¹, Maclellan RA, Gawande AA, Ruan DT, Alexander EK, Moore FD Jr, Cho NL.

Author information
Abstract

BACKGROUND:
Controversy exists regarding the accuracy of fine-needle aspiration (FNA) in large thyroid nodules. Recent surgical series have documented false-negative rates ranging from 0.7 to 13%. We examined the accuracy of benign FNA cytology in patients with thyroid nodules ≥3 cm who underwent surgical resection and identified features characteristic of false-negative results.

METHODS:
We retrospectively studied all thyroidectomy specimens between January 2009 and October 2011 and identified nodules ≥3 cm with corresponding benign preoperative FNA cytology. We collected clinical information regarding patient demographics, nodule size, symptoms, sonographic features, FNA results, and final surgical pathology. For comparison, we analyzed nodules <3 cm from this cohort also with benign FNA cytology.

RESULTS:
A total of 323 nodules with benign preoperative cytology were identified. Eighty-three nodules were <3 cm, 94 nodules were 3-3.9 cm, and 146 nodules were ≥4 cm in size. The false-negative rate was 11.7% for all nodules ≥3 cm and 4.8% for nodules <3 cm (p = 0.03). Subgroup analysis of nodules ≥3 cm revealed a false-negative rate of 12.8% for nodules 3-3.9 cm and 11% for nodules ≥4 cm. Age ≥55 years and asymptomatic clinical status were the only patient characteristics that reached statistical significance as risk factors. Final pathology of the false-negative specimens consisted mainly of follicular variant of papillary thyroid cancer and follicular thyroid cancer.

CONCLUSIONS:
When referred for thyroidectomy, patients with large thyroid nodules demonstrate a modest, yet significant, false-negative rate despite initial benign aspiration cytology. Therefore, thyroid nodules ≥3 cm may be considered for removal even when referred with benign preoperative cytology.

PMID: 25074665

Factors Affecting the Locoregional Recurrence of Conventional Papillary Thyroid Carcinoma After Surgery: A Retrospective Analysis of 3381 Patients.
Suh YJ¹, Kwon H, Kim SJ, Choi JY, Lee KE, Park YJ, Park DJ, Youn YK.

Abstract

BACKGROUND:
Papillary thyroid carcinoma (PTC) does recur, despite its favorable long-term outcome. The incidence of thyroid cancer in South Korea increased during the 1990s, then increased rapidly after the turn of the century. In 2011, the rate of thyroid cancer diagnoses was 15 times that observed in 1993. The present study aimed to identify factors associated with the locoregional recurrence of recently increasing conventional PTC.

METHODS:
The records of 3381 patients with conventional PTC were reviewed for this retrospective cohort study. Between January 2004 and January 2012, these patients underwent ultrasonography, computed tomography, and preoperative and total thyroidectomy with central neck dissection. Disease recurrence was defined as structural evidence of disease following the remission period.

RESULTS:
Median length of follow-up was 5.6 (range 2.1-10.1) years. Of 3381 patients, 75 (2.2 %) experienced recurrence. The univariate analysis suggested that locoregional recurrence was associated with tumor size, multifocality, extrathyroidal extension (ETE), lymph node metastasis, lymphatic invasion, vascular invasion, and positive surgical margin. However, multivariate analysis showed that only tumor size (p < 0.001), bilaterality (p < 0.001), gross ETE (p = 0.049), lymph node metastasis (p < 0.001), and vascular invasion (p = 0.013) were independently associated with locoregional recurrence.

CONCLUSIONS:
Tumor size, bilaterality, gross ETE, lymph node metastasis, and vascular invasion were associated with locoregional recurrence. Evaluation of these prognostic factors appears to help identify patients who require close monitoring.

PMID: 25743326

Surgical Management of Cricotracheal Invasion by Papillary Thyroid Carcinoma.

Moritani S¹
Author information
Abstract
BACKGROUND:
In general, patients with papillary thyroid carcinoma (PTC) have an excellent postoperative prognosis. Those with cricoid and/or tracheal PTC invasion, however, are at a higher risk of postoperative morbidity and airway insufficiency.

METHODS:
We investigated postoperative airway outcomes, locoregional recurrence, and survival rates in patients with PTC who underwent cricotracheal resection. The records of PTC patients who underwent surgery at our institution between 1981 and 2009 were reviewed retrospectively, and 110 patients with cricotracheal invasion were enrolled. Curative resection was performed in all patients, and cricotracheal function was preserved or reconstructed when possible.

RESULTS:
Of the 110 patients, 57 and 53 patients had superficial and intraluminal invasion of the larynx, respectively. After the initial surgery, the 10-year disease-specific survival rates were 90.8 and 44.4 % in patients with superficial and intraluminal invasion of the cricotracheal area, respectively. Only six patients (5.5 %) had an isolated upper aerodigestive tract recurrence. Five patients were managed with an additional window resection as salvage surgery. Consequently, only one patient (0.9 %) underwent total laryngectomy. Altogether, 31 patients (28.0 %) had a permanent stoma, 9 and 15 of which were caused by cricotracheal invasion and invasion of other aerodigestive structures, respectively.

CONCLUSIONS:
Window resection for intraluminal cricotracheal invasion by PTC produced good surgical outcomes that resulted in a low local recurrence rate and survival rates that resembled those associated with other surgical treatments. Treatment of multiple organ invasion of the aerodigestive tract was necessary to improve postoperative functional outcomes in these patients.

Size distribution of metastatic lymph nodes with extranodal extension in patients with papillary thyroid cancer: a pilot study.

Alpert EH¹, Wenig BM, Dewey EH, Su HK, Dos Reis L, Urken ML.

**Author information**

**Abstract**

**BACKGROUND:**
Extranodal extension (ENE) is a documented negative prognostic factor in patients with papillary thyroid cancer (PTC). ENE is presumed to manifest in larger lymph nodes. Yet, to date, no study has proven this. This is a pilot study that specifically examines the size distribution of positive lymph nodes manifesting ENE in patients with PTC.

**METHODS:**
An Institutional Review Board approved review examined the size of all lymph nodes demonstrating ENE in postoperative PTC patients that underwent surgery for PTC under the care of a single surgeon between 2004 and 2014. All patients in the study had regional metastatic lymph nodes with ENE. Analysis of the size distribution for all lymph nodes with ENE was performed.

**RESULTS:**
A total of 47% of lymph nodes with ENE were ≤10 mm.

**CONCLUSIONS:**
RESULTS indicate that clinically nonevident, small lymph nodes are at risk of harboring aggressive disease biology reflected in ENE. A total of 47% of all nodes fell within Randolph et al.’s classification of “small” lymph nodes, while 59% of the nodes with ENE were <1.5 cm-the threshold size that was deemed to be prognostically significant by Ito et al. It is apparent that clinically nonevident regional lymph nodes can have adverse histologic features and that the previous presumption that nodes with ENE only appear in clinically evident, macroscopic nodes is flawed.

PMID: 25422987

6. **Thyroid.** 2015 Mar 6. [Epub ahead of print] **IF: 3.84**

PROGNOSTIC VALUE OF VASCULAR INVASION IN WELL-DIFFERENTIATED PAPILLARY THYROID CARCINOMA.


**Author information**

**Abstract**

Background: Vascular invasion (VI) is an important predictor of distant metastasis and possible radioactive iodine (RAI) benefit in follicular, Hurthle cell, and poorly differentiated thyroid carcinomas, but its role in well-differentiated papillary thyroid cancer (WDTC) remains unclear. Methods: Archived pathological material of all differentiated thyroid carcinoma patients undergoing primary surgical treatment at Memorial Sloan-Kettering Cancer Center between 1986 and 2003 was reviewed by two dedicated thyroid pathologists. Only WDTCs were included in the present study. Standard statistical methods were used to assess the relationship between VI on outcomes of interest, including 10-year disease-specific survival (DSS), regional recurrence-free survival (RRFS), and distant recurrence-free survival (DRFS). Results: VI was present in 47 of 698 WDTC (6.7%). VI was significantly associated with
tumor size > 4.0 cm, extrathyroid extension, distant metastasis and RAI treatment. On univariate analysis, VI was predictive of decreased 10-year DRFS, but not DSS, or RRFS. On multivariate analysis, VI was not an independent predictor of DRFS. Univariate survival analysis of 422 RAI-naïve WDTC, showed that both size > 4cm, and VI were predictors of outcome, but only size remained independently predictive on multivariate analysis. Conclusion: The presence of VI is not an independent predictor of outcome in WDTC.

PMID: 25748079

7. Endocrine. 2015 Jan 20. [Epub ahead of print] IF: 3.52

Thyroid nodules ≤5 mm on ultrasonography: are they "leave me alone" lesions?

Moon HJ, Lee HS, Kim EK, Ko SY, Seo JY, Park WJ, Park HY, Kwak JY.

Abstract

The incidence of small thyroid malignancy has increased. However, there is no evidence-based guideline for managing thyroid nodules ≤5 mm on ultrasonography (US). We evaluated how to manage thyroid nodules ≤5 mm. Thyroid nodules ≤5 mm in size on US that had undergone surgery and US-guided fine-needle aspiration were eligible. A total of 3,117 thyroid nodules in 3,012 patients were included. The size changes of malignant and benign nodules during follow-up were evaluated. Thyroid malignancies were classified according to follow-up and surgery time within and after 12 months. Clinico-pathological characteristics were compared. Of 3,117 nodules, 1,639 nodules in 1,619 patients were benign and 1,478 in 1,427 were malignant. Only 5.8 and 1.2 % of malignant nodules and 6.8 and 4.2 % of benign nodules increased in size when a 2-mm and 3-mm change on US were referenced. Of 1,079 patients with an index malignancy ≤5 mm, extrathyroidal extension, lymph node metastasis, recurrence, and mortality were not significantly different between patients with and without follow-up and between patients with surgery within 12 months and after 12 months. None of the patients who underwent surgery had distant metastasis and none died of thyroid malignancy. In thyroid nodules ≤5 mm found on US, US-FNA could be recommended in cases of increased size during US follow-up if lateral LNM was not found because a delay in surgery did not impact cancer recurrence and mortality.

PMID: 25600483


Validation and Comparison of Nomograms in Predicting Disease-Specific Survival for Papillary ThyroidCarcinoma.

Lang BH, Wong CK.

Abstract

BACKGROUND: Nomogram could estimate individualized prognosis in papillary thyroid carcinoma (PTC). We aimed to create and validate a new nomogram and compare it with other published nomograms using a large patient cohort.

METHODS: Eight-hundred and forty-nine PTC patients with ≥7 years follow-up were randomly assigned to the development (n = 425) and validation (n = 424) groups. The former was used for developing a nomogram for disease-specific survival (DSS), while the latter was for validating the nomogram by discrimination [or area under curve (AUC)]. AUC of the newly developed nomogram was compared to other published nomograms.
RESULTS:
The 5- and 10-year risk of dying from PTC were 1.4 and 3.3 %, respectively, while dying from non-PTC-related causes were 2.3 and 5.1 %, respectively. The new nomogram was developed from age, tumor size, multifocality, nodal status and distant metastases. The discrimination was excellent (AUC (95 % CI) for 5- and 10-year DSS were 0.896 (0.683-0.971) and 0.919 (0.871-0.967), respectively). Its predictability was similar to other published nomograms (p > 0.05). Based on the new nomogram, a total score of <28 meant 99.72 % chance of surviving from PTC at 10 years while a score of ≥28 meant 9.09 % chance of dying from PTC at 10 years.

CONCLUSIONS:
Using variables from the current tumor node metastasis (TNM) staging system, a new nomogram was developed. It exhibited excellent discriminatory ability and accuracy in predicting 10-year DSS relative to other published nomograms. However, given the excellent prognosis of PTC, the new nomogram was better at ruling out than predicting PTC-related death. Further validation by an external cohort is required.

PMID: 25809064


Predictive Factors for Occult Contralateral Carcinoma in Patients with Unilateral Papillary Thyroid Microcarcinoma by Preoperative Ultrasonographic and Pathological Features.

Lee YC¹, Eun YG, Sohn YM, Rhee SY, Hong IK, Chon S, Oh SJ, Kim DY.

Author information

Abstract

BACKGROUND:
The surgical extent and indication for treatment in patients with papillary thyroid microcarcinoma (PTMC) remain a controversial issue. The aim of this study was to investigate the predictive factor for contralateral occult carcinoma in patients with unilateral PTMC by preoperative ultrasonographic and pathological features.

METHODS:
Of the total patients who underwent thyroidectomy, 455 patients with PTMC confined to one unilateral lobe as diagnosed using preoperative ultrasonography (US) were enrolled in the study. Occult contralateral carcinoma was defined as tumor foci in the contralateral lobe that was not detected preoperatively, but was detected pathologically. All patients underwent preoperative US review to investigate the US features of PTMC such as laterality, location, size, internal component, echogenicity, margin, calcification shape, multifocality, bilaterality, extrathyroidal extension, and location with respect to the trachea. Clinicopathological data were also analyzed.

RESULTS:
Of the total of 455 patients who underwent total thyroidectomy for preoperatively detected unilateral PTMC, 71 patients (15.6 %) had contralateral occult carcinoma. Clinicopathological characteristics did not significantly differ between patients with and without contralateral occult carcinoma. Multivariate analysis showed that the absence of a well-defined margin and the presence of a probably benign nodule in the contralateral lobe were independent predictive factors for contralateral occult carcinoma in patients with unilateral PTMC in preoperative US images.

CONCLUSION:
We demonstrated that an absence of a well-defined margin and the presence of a probably benign nodule in the contralateral lobe were independent predictive factors for contralateral occult carcinoma in patients with unilateral PTMC in preoperative US. The prediction of contralateral occult carcinoma in unilateral PTMC using preoperative US features could be useful for determining the optical extent of surgery.
Clinicopathologic Features and Outcomes in Patients with Diffuse Sclerosing Variant of Papillary ThyroidCarcinoma.


Abstract

BACKGROUND: Diffuse sclerosing variant (DSV) of papillary thyroid carcinoma (PTC) is a rare variant more common among younger patients.

MATERIALS AND METHODS: Excluding patients with microcarcinoma, 5848 patients with PTC underwent initial surgery between 1995 and 2011. Twenty-two patients (0.4%) were histologically diagnosed with DSV, of whom 20 (91%) were <45 years old. We compared clinicopathologic characteristics and outcomes between patients with DSV and those with classical PTC <45 years old. Univariate analysis by the Kaplan-Meier method in relation to cause-specific survival (CSS) and disease-free survival (DFS) rates was performed with regard to the following variables: sex; anti-thyroglobulin antibody (TgAb) positivity; presence of distant metastasis; pathological lymph node metastasis; extra-thyroidal invasion; and pathological variant (classical vs. DSV).

RESULTS: The 20 patients with DSV <45 years old comprised 18 females and 2 males. Frequencies of TgAb, pN1b, and local recurrence were higher in the DSV group than in the classical PTC group. Ten-year CSS and DFS rates for PTC patients <45 years old were 99.7 and 88.6% in the classical PTC group and 100 and 60.5% in the DSV group. CSS rate did not differ between groups, but DFS rate was significantly lower in the DSV group than in the classical PTC group (p < 0.0001, log-rank test). Multivariate analysis identified DSV group and pN1b as prognostic factors for recurrence in young PTC patients.

CONCLUSIONS: Most DSV patients were young and had a background of chronic thyroiditis. Outcomes for DSV were very good, but recurrence was more common than in classical PTC.

PMID: 25743484

Thyroid Nodules with Repeat Nondiagnostic Cytologic Results: The Role of Clinical and Ultrasonographic Findings.

Woo SH, Kim KH, Kim RB.

Abstract

OBJECTIVES: Ultrasound-guided fine-needle aspiration (FNA) is the most valuable procedure in the diagnosis of thyroid nodules. One possible result of FNA of thyroid nodules, however, is "nondiagnostic" cytology. In these cases, consensus guidelines suggest repeating FNA with ultrasound guidance, but the results obtained may continue to be nondiagnostic. These results cause confusion due to the fact that there exist conflicting potential treatment modalities, such as performing diagnostic surgery or recommending follow-
up. Hence, the present study aimed to establish a protocol for performing diagnostic operations for thyroid nodules with repeat nondiagnostic cytology.

**MATERIALS AND METHODS:**
This study was performed on patients who underwent ultrasound-guided FNA and molecular testing for BRAF gene mutation. Out of 1,203 patients, 84 had nondiagnostic cytology and were BRAF negative, and ultrasound-guided FNA was repeated on these patients. Out of this group, 54 patients once again had nondiagnostic cytology, and 51 of these underwent diagnostic surgery. We analyzed the characteristics and ultrasonographic findings of the group of patients with repeat nondiagnostic cytology.

**RESULTS:**
On the initial ultrasound-guided FNA, the percentage of patients with nondiagnostic cytology was 6.98%, and on repeat ultrasound-guided FNA, the percentage of patients with nondiagnostic cytology was 67.5%. The majority of these patients underwent diagnostic surgery, and 36 (70.6%) patients were diagnosed as having a malignant thyroid nodule, while 15 (29.4%) patients were diagnosed with a benign nodule. Univariate analysis showed a significant difference in the size of the nodule, hypoechogenicity, and microcalcification in the ultrasonography findings. Multivariate analysis revealed only hypoechogenicity as a factor that showed a significant difference (p value 0.017, 95% confidence interval 1.494-62.426). The diagnostic accuracy of the ultrasonography was 76.5%.

**CONCLUSIONS:**
Hypoechogenicity on ultrasonography represents an excellent parameter for the selection of those who should be referred for diagnostic operation among patients with thyroid nodules and repeat nondiagnostic cytology.

PMID: 25663015

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**Papillary Thyroid Carcinoma in Children and Adolescents: Long-Term Follow-Up and Clinical Characteristics.**


**Author information**

**Abstract**

**BACKGROUND:**
The aim of this study was to analyze the clinical features and clinical outcomes of papillary thyroid carcinoma (PTC) in the pediatric and adolescent population treated in our institution.

**METHODS:**
The subjects were 227 PTC patients 20 years of age or under treated initially between 1979 and 2012. Their mean age at diagnosis was 18-year old (range 7-20 years). Patient characteristics and outcomes in the period before 1999 and the period after 2000 were compared. Cause-specific survival (CSS) rates and disease-free survival (DFS) rates were calculated by the Kaplan-Meier method.

**RESULTS:**
Two patients died of their disease and 45 patients had recurrent disease (36 in lymph node, seven in a remnant thyroid, and 11 in the form of distant metastasis). The 10-, 20-, and 30-CSS rates were 99.3, 99.3, and 96.5 %, respectively, and the 10-, 20-, and 30-DFS were 83.6, 70.7, and 64.0 %, respectively. Gender and preoperative lymph node metastasis were identified as significant factors related to DFS in the multivariate analysis. After the year 2000, there were significantly more patients with a small primary tumor size, significantly more patients without distant metastasis at presentation and significantly more patients without extrathyroidal invasion.

**CONCLUSION:**
The number of patients with advanced cancer has been declining in recent years. Lobectomy with prophylactic unilateral central neck dissection is considered acceptable for patients without the risk factors for recurrence.

PMID: 25802237


**Computed tomography for preoperative evaluation of need for sternotomy in surgery for retrosternal goitre.**

Malvemyr P¹, Liljeberg N, Hellström M, Muth A.

**Author information**

**Abstract**

**PURPOSE:** The purposes of this study are to evaluate the usefulness of available CT classifications of retrosternal goitre (RSG) to identify patients needing sternotomy and to examine the effect of neck extension on goitre position.

**METHODS:** From the Scandinavian Quality Register for Thyroid and Parathyroid Surgery, all patients treated for RSG at Sahlgrenska (January 2005 through August 2012) were identified. Medical records and preoperative CT scans were retrospectively reviewed. Paired CT (normal position/neck extension) was done in three patients.

**RESULTS:** Of 1698 patients undergoing thyroid surgery, 158 (9.3 %) were registered as having RSG, of these 38 were excluded (no preoperative CT n = 27, no RSG at preoperative CT n = 11). Of 120 included patients (71 % females, median age 67 years, rate of malignancy 14 %), 104 were managed with a cervical approach only, 16 (13.3 %) needed sternotomy, of these 13/16 had growth below the aortic arch concavity. Predictors for sternotomy were goitre extension below the aortic arch concavity (positive/negative predictive value (PPV/NPV) 54/97 %, sensitivity/specificity 81/89 %, odds ratio (OR) 36.6, p < 0.001); main mass of RSG to the right of the midline (PPV/NPV 21/95 %, sensitivity/specificity 81/53 %, OR 4.9, p < 0.008); and main mass of RSG retrotracheal (PPV/NPV 31/92 %, sensitivity/specificity 50/83 %, OR 4.8, p < 0.005). The goitre was displaced cranially a mean 11 mm with neck extension, but the relationship to the aortic arch was unchanged.

**CONCLUSIONS:** RSG extension below the aortic arch concavity was confirmed as a significant risk factor for sternotomy, with a NPV for sternotomy of 97 % for less extensive goitres. CT in neck extension provided no additional clinically relevant information.

PMID: 25557494


**Surgery for recurrent goiter: complication rate and role of the thyroid-stimulating hormone-suppressive therapy after the first operation.**

Miccoli P¹, Frustaci G, Fosso A, Miccoli M, Materazzi G.

**Author information**
Abstract

PURPOSE:
This report examines outcomes in our series of patients who underwent surgery for recurrent goiter to assess the efficacy of thyroid-stimulating hormone (TSH)-suppressive therapy after the first less than total thyroidectomy. A further outcome was to understand whether redosurgery was burdened with a higher rate of complications.

METHODS:
We evaluated 214 patients undergoing a completion thyroidectomy for recurrent goiter who had received, as their first surgery, a bilateral subtotal thyroidectomy. After the first operation, 84 patients were given TSH-suppressive therapy with levothyroxine, 32 were treated with antithyroid drugs, and 92 did not receive any suppressive treatment but only a substitutive therapy. The 84 patients who received levothyroxine at a suppressive dosage (group A) were compared with 92 patients who did not receive levothyroxine or received it only at substitutive dosage (group B). We further compared the complication rate of a similar group of 175 patients who had undergone a primary thyroidectomy.

RESULTS:
The average age at intervention for relapse in group A patients was significantly lower than that of group B patients: 54.18 vs 60.8 years (p < 0.001). The average interval between the first intervention and the intervention for relapse was significantly shorter in group A than in group B: 24 vs 27 years (p = 0.03). After the operation, temporary hypoparathyroidism occurred in 37.7 % of patients and definitive hypoparathyroidism in 7.2 %.

CONCLUSIONS:
Our results clearly show that the interval between the two surgical interventions was significantly reduced in patients undergoing TSH-suppressive therapy with levothyroxine. The incidence of hypoparathyroidism dramatically increased.

PMID: 25432523

Sternotomy for substernal goiter: retrospective study of 52 operations.

Rolighed L¹, Rønning H, Christiansen P.

Abstract

PURPOSE:
Surgical treatment of substernal goiter occasionally involves sternotomy. Classification and handling of these operations are widely discussed. We aimed to review surgical results after thyroid operations including median sternotomy.

METHODS:
A retrospective review of all thyroid operations performed in the department from 01.01.95 to 31.12.12. In 55 of 2065 thyroid operations (2.7 %), median sternotomy was performed. All hospital journals of the patients were collected and carefully reviewed.

RESULTS:
We included 52 of 55 identified patients. Pathologic examinations discovered malignant disease in 4 patients (8 %) and multinodular goiter in 48 patients (92 %). Mean operation time was 4 h and 5 min (n = 48). Mean estimated blood loss was 464 ml (n = 48). Blood transfusion was given in nine operations (17 %). Median duration of postoperative hospitalization was 7 days (range 4-27 days). Pulmonary complications occurred in 11 patients (21 %): six with pneumonia or atelectasis, three with pneumothorax,
and two with pleural effusion. Three patients (6%) had postoperative hypocalcaemia (permanent in two patients (4%)). Three patients (6%) had transient voice changes. Permanent vocal cord paresis was not observed in this series of patients.

CONCLUSION:
Thyroid operations with sternotomy are complicated procedures accompanied with considerable pulmonary complications. In spite of a large invasive procedure, the risk of hypoparathyroidism or recurrent laryngeal nerve injury was not increased.

PMID: 25691265


**Examining the Bethesda criteria risk stratification of thyroid nodules.**

Deniwar A¹, Hambleton C², Thethi T³, Moroz K⁴, Kandil E⁵.

*Author information*

**Abstract**

**BACKGROUND:**
The Bethesda criteria are proposed for appropriate stratification of malignancy risk in thyroid nodules, but controversy exists regarding their accuracy and reliability in decision making. Additionally, previous studies have suggested higher rates of both malignancy and false negative fine needle aspiration biopsy (FNA) associated with increasing nodule size. This study aims to determine the accuracy of ultrasound (US)-guided FNA using the current Bethesda criteria in surgical practice. We also aimed to investigate the relationship between nodule size and malignancy.

**METHODS:**
A retrospective analysis of US-guided FNAs by a single surgeon during a 4.5 year period. FNA results using Bethesda criteria were compared to final surgical pathology.

**RESULTS:**
611 patients with thyroid nodules underwent US-guided FNA. FNA results in 375 subsequently excised thyroid nodules were recorded according to the Bethesda criteria: 192 (51%) benign, 65 (17%) atypia of unknown significance/follicular lesion of undetermined significance (AUS/FLUS), 42 (11%), suspicious for follicular neoplasm (SFN), 17 (5%) suspicious for malignancy (SM), 28 (8%) malignancy, and 31 (8%) non-diagnostic. Malignancy was confirmed by surgical pathology in 15%, 34%, 50%, 88%, 100%, and 39% of the above groups respectively. Sensitivity, specificity, and false-negative rate were 61%, 99%, and 15% respectively. No correlation existed between the size of nodules with indeterminate FNA results and malignancy rate (p=0.89), or size of nodules with non-diagnostic FNA and malignancy rate (p=0.50).

**CONCLUSION:**
The current Bethesda risk stratification system underestimated malignancy rates in benign, indeterminate and non-diagnostic cytopathologic categories in our experience. There was no positive linear correlation between nodule size and malignancy rate in these cytopathologic categories.

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**KEYWORDS:**
Thyroid cancer; Thyroid cytology/FNA; Thyroid nodule evaluation; Thyroid pathology; Thyroid surgery

PMID: 25796296
Bilateral recurrent laryngeal nerve injury in a specialized thyroid surgery unit: would routine intraoperative neuromonitoring alter outcomes?

Sarkis LM, Zaidi N, Norlén O, Delbridge LW, Sywak MS, Sidhu SB.

**Abstract**

**BACKGROUND:** Bilateral recurrent laryngeal nerve (RLN) palsy following total thyroidectomy is a rare complication, however, poses significant morbidity to the patient when it does occur. The purpose of this paper was to determine the incidence of bilateral RLN palsy in a specialized thyroid unit and determine whether the routine use of intraoperative nerve monitoring (IONM) would alter the outcome.

**METHODS:**

This is a retrospective review of prospectively gathered data. A total of 7406 patients underwent total thyroidectomy at the University of Sydney Endocrine Surgical Unit between January 1990 and February 2014. IONM was utilized on a selective basis and we sought to assess whether IONM would have altered outcome in those patients who developed bilateral RLN palsy.

**RESULTS:**

Of the 7406 patients who underwent total thyroidectomy, seven patients (0.09%) developed bilateral RLN palsy during the study period. There was one permanent RLN palsy (0.01%) and routine IONM may have prevented one death and altered the outcome in two of the seven patients.

**CONCLUSION:**

Bilateral RLN palsy is a rare entity occurring in one out of 1000 cases in a specialized thyroid unit. IONM may facilitate the decision to pursue delayed surgery where the signal is lost on the first surgical side and has the potential to avoid bilateral RLN palsy following total thyroidectomy.

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**KEYWORDS:** bilateral; nerve monitoring; palsy; recurrent laryngeal nerve; total thyroidectomy

PMID: 25648744

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Stressing the recurrent laryngeal nerve during thyroidectomy.

Serpell JW, Lee JC, Chiu WK, Edwards G.

**Abstract**

**BACKGROUND:** In thyroidectomy, little has been reported on the differential recurrent laryngeal nerve (RLN) palsy rates between the left and right sides. Even less is known about the potential differences causing these differential rates. This study reports the left versus right RLN palsy rates of total thyroidectomy cases in a single institution, relating them to the comparative stiffness of the left and right porcine RLNs. Computed stress modelling was also used to estimate the differential levels of tension within each RLN.
METHODS:
For the comparison of the left and right RLN palsy rates, 1926 cases of total thyroidectomy (between 2007 and 2013) from the Monash University Endocrine Surgery Unit were included. Stiffness of porcine RLNs was experimentally determined by measuring nerve extension against incremental increase in load. Additionally, the tension of intraoperatively stretched RLNs was estimated by computer modelling.

RESULTS:
The left RLN had a palsy rate of 0.9% (18/1926), which was significantly lower (P = 0.025) than the right RLN palsy rate of 1.8% (34/1926). The left porcine RLN was 22% stiffer than the right RLN (P = 0.004). The stress modelling estimated that at the apex of the artificial RLN genu during anteromedial rotation of the thyroid lobe, the right RLN experiences twice the tension experienced by the left RLN.

CONCLUSION:
The stiffer left RLN and the higher tension generated in the right RLN during thyroidectomy may jointly contribute to the higher right RLN palsy rate.

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KEYWORDS:
palsy, recurrent laryngeal nerve; stress; stretch; thyroidectomy

PMID: 25801287


IF: 1.2

Impact of tumor size on subclinical central lymph node metastasis in papillary thyroid microcarcinoma depends on age.

Kim JY1, Jung EJ, Park T, Jeong SH, Jeong CY, Ju YT, Lee YJ, Hong SC, Choi SK, Ha WS.

Author information

Abstract

BACKGROUND:
The aim of this study is to evaluate whether the associations between clinicopathologic factors of papillary thyroid microcarcinoma (PTMC), especially tumor size, and subclinical central lymph node metastasis (LNM) are dependent on patient age.

METHODS:
The medical records of 428 patients who underwent thyroid surgery for PTC measuring ≤1 cm were reviewed. All patients were clinically lymph node negative and underwent thyroidectomy with unilateral or bilateral central lymph node dissection. Univariate and multivariate analyses were performed to identify clinicopathologic factors associated with central LNM.

RESULTS:
Central LNM was identified in 96 of 428 (22.4%) patients. Mean tumor size was significantly greater in patients with than without central LNM (0.74 ± 0.22 cm vs. 0.64 ± 0.23 cm, P = 0.001). Tumor size > 0.5 cm was significantly predictive of central LNM. Subgroup analysis according to age groups showed that tumor size was an independent predictor of subclinical central LNM only in patients aged ≥45 years.

CONCLUSIONS:
Factors predictive of central LNM in patients with PTMC differed by age. PTMC size was an independent predictor of subclinical central LNM only in patients aged ≥45 years.

PMID: 25778051
Cytomorphologic features and ultrasonographic characteristics of thyroid nodules with Hurthle cells.

Tuzun D¹, Ersoy R², Yazgan AK³, Kiyak G⁴, Yalcin S⁵, Cakir B².

Abstract
This study was designed to evaluate the ultrasonographic and histopathologic features of nodules composed predominantly of Hurthle cells detected during cytological examination. Fifty-seven patients with thyroid nodules composed predominantly of Hurthle cells on fine needle aspiration cytology were retrospectively analyzed. Patients were evaluated by thyroid ultrasonography (US), and biopsy samples taken by US-guided fine needle aspiration cytology were assessed histopathologically. There were 57 patients and 57 nodules with Hurthle cells in cytological examination; 49 (86%) were classified as Bethesda 1, and 8 (14%) were classified as Bethesda 3. Histopathologically, 45 (78.9%) nodules were benign and 12 (21.1%) were malignant. Nuclear groove, transgressing blood vessel, and absence of colloid were observed with a higher frequency in malignant nodules compared to benign nodules (P < .05). There were no specific morphological features (nodule echogenity, presence of microcalcification, presence of cystic areas, absence of halo, margin irregularity, and increased blood flow) predicting malignancy in the US evaluation of nodules including Hurthle cells. Nuclear groove, transgressing blood vessel, and absence of colloid on cytomorphological evaluation are indicative of malignancy in nodules containing Hurthle cells.

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KEYWORDS:
Cytomorphology; Hurthle cell; Thyroid nodule; Ultrasonography

PMID: 25804256

Relationship between obesity, diabetes and the risk of thyroid cancer.

Oberman B¹, Khaku A¹, Camacho F², Goldenberg D³.

Abstract
PURPOSE: Analyze the relationship between obesity and type-2 diabetes mellitus (DM) and the development of differentiated thyroid cancer (DTC).

MATERIALS AND METHODS: A randomized case-controlled retrospective chart review of outpatient clinic patients at an academic medical center between January 2005 and December 2012. DTC patients were compared to two control groups: primary hyperparathyroidism (PHPT) patients with euthyroid state and Internal Medicine (IM) patients. Exposure variables included historical body-mass-index (BMI), most recent BMI within 6months and DM. Multivariate logistic regressions adjusting for gender, age, and year of BMI assessed the adjusted Odds Ratio (OR) of DTC with both BMI and DM.

RESULTS:
Comparison of means showed a statistically significant higher BMI in DTC (BMI=37.83) than PHPTH, IM, and pooled controls, BMI=30.36 p=<0.0001, BMI=28.96 p=<0.0001, BMI=29.53 p=<0.0001, respectively. When compared to PHPTH, DM was more frequent in DTC (29% vs. 16%) and prevalence trended towards significance (p=0.0829, 95% CI =0.902-5.407). BMI adjusted OR was significant when compared to PHPTH, IM and pooled controls: 1.125 (p=0.0001), 1.154 (p=<0.0001), and 1.113 (p=<0.0001), respectively. DM adjusted OR was significant when compared to PHPTH and pooled controls at 3.178 (95% 1.202,8.404, p=0.0198) and 2.237 (95% 1.033,4.844, p=0.0410), respectively.

**CONCLUSION:**
Our results show that obesity and, to a lesser degree, DM are significantly associated with DTC. BMI in particular was a strong predictive variable for DTC (C=0.82 bivariate, C=0.84 multivariate).

**F-18 FDG PET/CT imaging in the diagnostic work-up of thyroid cancer patients with high serum thyroglobulin, negative I-131 whole body scan and suppressed thyrotropin: 8-year experience.**

**OBJECTIVE:**
Fluorodeoxyglucose positron emission tomography/computed tomography imaging in the follow-up of patients with differentiated thyroid carcinoma who have high serum thyroglobulin, negative iodine-131 whole body scan and suppressed thyrotropin.

**PATIENTS AND METHODS:**
A total of 90 patients (31 male and 59 female) with differentiated thyroid carcinoma who have high serum thyroglobulin and negative iodine-131 whole body scan were included in the study between July 2006 and March 2014. All patients had undergone surgery (total thyroidectomy ± lymph node dissection) followed by iodine-131 ablation. Of the patients, 82 had papillary thyroid carcinoma and 8 follicular thyroid carcinoma. Serum thyrotropin was suppressed (< 2 μIU/ml) during the Fluor-18 fluorodeoxyglucose positron emission tomography/computed tomography imaging procedure.

**RESULTS:**
The overall sensitivity of fluor-18 fluorodeoxyglucose positron emission tomography/computed tomography imaging in the detection of metastasis of differentiated thyroid cancer was 84.8%, the specificity 79.1%, respectively. The sensitivity and specificity of fluor-18 fluorodeoxyglucose positron emission tomography/computed tomography imaging in classic type of papillary cancer was 83.3% and 54.5%, respectively. The corresponding figures for the tall cell variant was 85.7% and 87.5%, respectively. The difference between the two histological subtypes was statistically significant (p < 0.05).

**CONCLUSIONS:**
Our results suggest that fluor-18 fluorodeoxyglucose positron emission tomography/computed tomography imaging could be a valuable test for the routine follow-up of patients with differentiated thyroid carcinoma.
Differentiated thyroid cancer with liver metastases: lessons learned from managing a series of 14 patients.


Abstract
Liver metastases from differentiated thyroid carcinoma (LMDTC) are rare and usually occur in disseminated metastatic disease. The aim of this study was to review the diagnosis and management of LMDTC. Between 1995 and 2011, 14 patients with a mean age of 59.7 years (+/-10.2) were treated for LMDTC. Data were retrospectively reviewed and analyzed. Seven patients had distant metastases at diagnosis, including 2 with synchronous liver lesions. The average time of onset of LMDTC from initial diagnosis was 52.2 months (+/-49.5). All LMDTC were discovered during routine radiologic monitoring. Histologic analysis confirmed LMDTC in 5 patients. Eight patients received tyrosine kinase inhibitors, 1 patient underwent resection of their LMDTC after chemotherapy. Six patients (disseminated metastases, significant comorbidities) did not receive any specific treatment. The median survival after diagnosis of LMDTC was 17.4 months (+/-3.3): 23.6 months (+/-2.9) for patients who underwent chemotherapy versus 3.9 months (+/-0.9) for patients who did not receive any specific treatment (P < 0.001). Developing DTC liver metastasis is a very poor prognostic sign. Chemotherapy by TKIs, especially, hold promise in the cure of LMDTC for selected patients.

KEYWORDS:
Liver metastasis; Thyroid carcinoma

PMID: 25785333

The reliability of fine-needle aspiration biopsy in terms of malignancy in patients with hashimoto thyroiditis.

Kapan M1, Onder A, Girgin S, Ulger BV, Fırat U, Uslukaya O, Oguz A.

Abstract
The aim of this study was to analyze the presence of malignancy in patients with Hashimoto's thyroiditis and to investigate the reliability of preoperative fine-needle aspiration biopsy (FNAB). The retrospective study included 44 patients who were operated on for nodular goiter between December 2010 and October 2011. The patients underwent thyroidectomy following a cytologic analysis plus FNAB. Hashimoto's thyroiditis was confirmed on histopathology in all patients. FNAB results were defined as benign in 14 (31.8%), suspicion for malignancy in 17 (38.6%), malignant in 9 (20.5%), and inadequate in 4 (9.1%). Following the thyroidectomy, presence of papillary thyroid carcinoma and follicular variant of papillary thyroid carcinoma were detected in 10 patients (22.7%) and 1 (2.3%) patient, respectively. The FNAB results were interpreted in terms of malignancy, which revealed the sensitivity as 80%; specificity, 40%; false positives, 69.2%; false negatives, 14.3%; positive predictive value, 31.8%; negative predictive value, 85.7%; and diagnostic accuracy, 50%. The coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma is quite common. The FNAB results for such cases are hard to evaluate, and they are likely to increase the number of false positives.

KEYWORDS:
Fine needle aspiration biopsy; Hashimoto's thyroiditis; Papillary thyroid carcinoma

PMID: 25692426
Disseminated bone metastases from occult thyroid cancer effectively treated with debulking surgery and a single dosimetry-guided administration of radioiodine.

Borsò E¹, Boni G², Mazzarri S², Cocciaro A³, Gambacciani C³, Traino AC⁴, Manca G², Grosso M², Scatena C⁵, Ortenzi V⁵, Vannozzi R², Marzola MC⁶, Rubello D⁵, Mariani G².

Abstract

In this paper we report on a successful management of multiple bone metastases from differentiated thyroid cancer. In 2007, a 75-year-old female patient, previously referred for thyroidectomy for multinodular goiter, underwent surgical removal of a lumbar mass with histological findings of metastasis from well differentiated thyroid cancer. After surgery, serum thyroglobulin (sTg) was 204.4ng/mL. A diagnostic/dosimetric (123)I WBS was performed, following stimulation by rTSH. Serial WBSs were acquired, along with SPECT/CT and bone scan for localization of lesions. sTg raised to 3.810ng/mL, and (123)I WBS showed thyroid remnants and numerous areas with high iodine-uptake corresponding to skeletal sites, the two largest loading on the skull, with osteolytic pattern. Calculated radiation absorbed dose for skull lesions, determined by mean of MIRD methodology, was 63.5mGy/MBq. The patient underwent surgical removal of the two major skull lesions. Successively, 100mCi (131)I was administered after stimulation by rTSH, with stimulated sTg 297ng/mL. After 8 months, diagnostic WBS was negative both for remnants and metastases and rTSH-stimulated Tg was 0.6ng/mL. To date, the patient has maintained sTg values <1ng/mL during L-T4 suppressive therapy and after rTSH stimulations. In this unusual case of extensive bone cancerous involvement with high iodine avidity, a multidisciplinary approach based on surgery and dosimetry-guided radiometabolic therapy allowed to accurately assess the patient, execute a small number of treatments and achieve a complete remission of the disease in a very short time, with no additive morbidity.

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KEYWORDS:

Bone metastases; Cirugía; Dosimetry; Dosimetria; Metástasis ósea; Surgery; Thyroid; Tiroides; rTSH

PMID: 25455505
Papillary Carcinoma Occurrence in a Thyroglossal Duct Cyst with Synchronous Papillary Thyroid Carcinoma without Cervical Lymph Node Metastasis: Two-Cases Report.

Sobri FB¹, Ramli M¹, Sari UN¹, Umar M¹, Mudrick DK¹.

Abstract
Background. We present two rare cases of papillary carcinomas which appeared in thyroglossal duct cysts. These cases highlight that thyroglossal duct cyst can serve as malignancy of thyroid gland. Methods. A retrospective case report was carried out on 2 patients at Cipto Mangunkusumo Hospital. Results. A 57-year-old man presented with enlarged right anterior and midline neck mass, which preoperatively were diagnosed as thyroglossal duct cyst (TDC) and nontoxic multinodular goiter. A total thyroidectomy and Sistrunk procedure were performed. In the second case, a 35-year-old woman presented with a lump which occurred at anterior neck region without palpable mass at the thyroid. Preoperatively, it was diagnosed as TDC. Sistrunk procedure was performed, followed by total thyroidectomy a month after the first operation. Histopathology showed papillary thyroid carcinoma in both patients. Conclusion. The occurrence of carcinoma in TDC is very rare but should always be considered as an option in making diagnosis for a neck mass.

PMID: 25785223

Medullary carcinoma of the thyroid with axillary metastasis: a case report.

Ozdemir M¹, Makay O, Simsir I, Ertan Y, Icoz G, Saygili F, Akyildiz M.

Abstract
We report a case of axillary lymph node metastasis as a consequence of medullary thyroid carcinoma (MTC) in a 42-year-old man. On January 2009, the patient was referred to us for the management of right cervical lymph node enlargement. Total thyroidectomy was performed with right-sided functional neck dissection. Postoperative histopathology revealed MTC in the right lobe of the thyroid, with extrathyroidal extension and right-sided neck metastases. Multiple left cervical, mediastinal, and right axillary lymphadenopathies were detected at the third year follow-up exam. Left-sided functional neck dissection, axillary lymph node dissection, and mediastinal lymph node dissection were performed, and the pathologic outcomes revealed as the metastatic dissemination of MTC. After a disease-free term for 1 year, multiple metastatic lesions were detected in the patient.

KEYWORDS: Axillary involvement; Lymph node metastasis; Medullary thyroid cancer

PMID: 25785315
Impact of recombinant PTH on management of hypoparathyroidism: a systematic review.
Ramakrishnan Y¹, Cocks HC.

Author information

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Abstract

The treatment of postsurgical hypoparathyroidism (following thyroid or parathyroid surgery) is challenging. Presently, this condition is treated with calcium and vitamin D supplements rather than replacing the missing parathyroid hormone. Not only is it challenging to maintain normocalcaemia, but concerns of hypercalciuria and ectopic calcification have also been raised using these supplements. There is an ongoing debate whether recombinant parathyroid hormone (rPTH), which as yet is unlicensed for treating hypoPTH, may offer a more physiological solution. The objective of the study was to assess the effectiveness and safety of rPTH in maintaining normocalcaemia and normocalcuria in hypoparathyroidism. This was a systematic review performed using independently developed search strategies including Medline, Embase, CINAHL, Cochrane, Zetoc, conference proceedings and a manual search until 15 July 2014. Data extraction was undertaken by one reviewer (YR). Studies were synthesised through narrative review with tabulation of results. Of 2,141 studies identified, only eleven studies fitted the inclusion criteria. These studies suggest that rPTH is useful in normalising serum calcium levels. Excretion of urinary calcium levels is reduced with PTH 1-34 but remained unchanged in a number of studies using PTH 1-84. Recombinant PTH is well tolerated. The majority of studies included postsurgical hypoparathyroidism with marked heterogeneity. Further prospective, larger, long-term trials are necessary to evaluate the long-term efficacy and adverse profile of rPTH, including head to head comparisons between PTH 1-34 and PTH 1-84.

PMID: 25567344

The current status of intraoperative iPTH assay in surgery for primary hyperparathyroidism.
Barczyński M¹, Golkowski F¹, Nawrot I¹.

Author information

¹Department of Endocrine Surgery, Third Chair of General Surgery, 2 Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; 3 Department of General, Vascular and Transplantation Surgery, Medical University of Warsaw, Warsaw, Poland.

Abstract
Intraoperative intact parathyroid hormone (iPTH) monitoring has been accepted by many centers specializing in parathyroid surgery as a useful adjunct during surgery for primary hyperparathyroidism. This method can be utilized in three discreet modes of application: (I) to guide surgical decisions during parathyroidectomy in one of the following clinical contexts: (i) to confirm complete removal of all hyperfunctioning parathyroid tissue, which allows for termination of surgery with confidence that the hyperparathyroid state has been successfully corrected; (ii) to identify patients with additional hyperfunctioning parathyroid tissue following the incomplete removal of diseased parathyroid/s, which necessitates extended neck exploration in order to minimize the risk of operative failure; (II) to differentiate parathyroid from non-parathyroid tissue by iPTH measurement in the fine-needle aspiration washout; (III) to lateralize the side of the neck harboring hyperfunctioning parathyroid tissue by determination of jugular venous gradient in patients with negative or discordant preoperative imaging studies, in order to increase the number of patients eligible for unilateral neck exploration. There are many advantages of minimally invasive parathyroidectomy guided by intraoperative iPTH monitoring, including focused dissection in order to remove the image-indexed parathyroid adenoma with a similar or even higher operative success rate, lower prevalence of complications and shorter operative time when compared to conventional bilateral neck exploration. However, to achieve such excellent results, the surgeon needs to be aware of hormone dynamics during parathyroidectomy and carefully choose the protocol and interpretation criteria that best fit the individual practice. Understanding the nuances of intraoperative iPTH monitoring allows the surgeon for achieving intraoperative confidence in predicting operative success and preventing failure in cases of unsuspected multiglandular disease, while safely limiting neck exploration in the majority of patients with sporadic primary hyperparathyroidism. Thus, parathyroidectomy guided by intraoperative iPTH monitoring for the management of sporadic primary hyperparathyroidism is an ideal option for the treatment of this disease entity. However, the cost-benefit aspects of the standard application of this method still remain a matter of controversy.

**KEYWORDS:**

Primary hyperparathyroidism; a solitary parathyroid adenoma; intraoperative intact parathyroid hormone (iPTH) assay; multiglandular parathyroid disease

PMID: 25713778  
[Makale sayfası]
Importance of in situ preservation of parathyroid glands during total thyroidectomy.

Lorente-Poch L, Sancho JJ, Ruiz S, Sitges-Serra A.

Author information

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Abstract

BACKGROUND:

Parathyroid failure is the most common complication after total thyroidectomy but factors involved are not completely understood. Accidental parathyroidectomy and parathyroid autotransplantation resulting in fewer than four parathyroid glands remaining in situ, and intensity of medical treatment of postoperative hypocalcaemia may have relevant roles. The aim of this study was to determine the relationship between the number of parathyroid glands remaining in situ and parathyroid failure after total thyroidectomy.

METHODS:

Consecutive patients undergoing first-time total thyroidectomy were studied prospectively, recording the number of Parathyroid Glands Remaining In Situ (PGRIS = 4 - (glands autografted + glands in the specimen)) and the occurrence of postoperative hypocalcaemia, and protracted and permanent hypoparathyroidism. Demographic, disease-related, laboratory and surgical variables were recorded. Patients were classified according to the PGRIS number into group 1-2 (one or two PGRIS), group 3 (three PGRIS) and group 4 (all four glands remaining in situ), and were followed for at least 1 year.

RESULTS:

A total of 657 patients were included, 43 in PGRIS group 1-2, 186 in group 3 and 428 in group 4. The prevalence of hypocalcaemia, and of protracted and permanent hypoparathyroidism was inversely related to the PGRIS score (group 1-2: 74, 44 and 16 per cent respectively; group 3: 51·1, 24·7 and 6·5 per cent; group 4: 35·3, 13·1 and 2·6 per cent; P < 0·001). Intact parathyroid hormone concentrations at 24 h and 1 month were inversely correlated with PGRIS score (P < 0·001). Logistic regression identified PGRIS score as the most powerful variable influencing acute and chronic parathyroid failure. In addition, a normal-high serum calcium concentration 1 month after thyroidectomy influenced positively the recovery rate from protracted hypoparathyroidism in all PGRIS categories.

CONCLUSION:

In situ parathyroid preservation is critical in preventing permanent hypoparathyroidism after total thyroidectomy. Active medical treatment of postoperative hypocalcaemia has a positive synergistic effect.
Dynamic Parathyroid Computed Tomography (4DCT) Facilitates Reoperative Parathyroidectomy and Enables Cure of Missed Hyperplasia.

Cham S¹, Sepahdari AR, Hall KE, Yeh MW, Harari A.

Author information

¹Section of Endocrine Surgery, Department of Surgery, UCLA David Geffen School of Medicine, Los Angeles, CA, USA.

Abstract

BACKGROUND:

Four-dimensional computed tomography (4DCT) is an emerging imaging modality in the evaluation of primary hyperparathyroidism (PHPT). We assessed the role of 4DCT in patients presenting for reoperative parathyroidectomy.

METHODS:

A prospective database of patients with persistent or recurrent PHPT undergoing reoperative parathyroidectomy during the years 2006-2014 was analyzed. Patients treated before versus after the advent of 4DCT were compared for operative eligibility, operative success, operative time, and concordance of imaging results with surgical findings.

RESULTS:

Ninety patients were included in the study (61 before 4DCT, 29 after 4DCT). The post-4DCT group had a higher rate of surgical concordance with imaging results (63 vs. 90 %, p < 0.01) and shorter operative time (114 vs. 76 min, p < 0.05). The operative success rate was not different (87 vs. 86 %). A similar pattern was observed in the subset of sestamibi-negative patients, with post-4DCT patients having a higher rate of surgical concordance (12 vs. 83 %, p < 0.0001) and shorter operative time (181 vs. 89 min, p < 0.05). Among patients ultimately found to have parathyroid hyperplasia, 4DCT correctly identified multiple enlarged glands in 80 % (4 of 5) and correctly lateralized one or more glands in 100 % (5 of 5) of cases, facilitating successful subtotal parathyroidectomy in the reoperative setting.

CONCLUSIONS:

4DCT enables successful and efficient reoperative parathyroidectomy. These benefits extend to difficult cases, including sestamibi-negative patients and those with missed hyperplasia.

PMID: 25691276
Hypocalcaemia after total thyroidectomy: could intact parathyroid hormone be a predictive factor for transient postoperative hypocalcemia?

Puzziello A¹, Gervasi R², Orlando G², Innaro N², Vitale M³, Sacco R².

Abstract

BACKGROUND:

Hypocalcemia, the most common complication of thyroidectomy, is a transient condition in up to 27% of patients and a permanent condition approximately 1% of patients. The aim of this prospective study was to evaluate reliability of postoperative intact parathyroid hormone (iPTH) assessment for predicting clinically relevant postthyroidectomy hypocalcemia for a safe early discharge of patients with no overtreatment.

METHODS:

Seventy-five consecutive patients (age 51 ± 13 years [mean ± SD]) undergoing total or completion thyroidectomy with no concomitant parathyroid diseases or renal failure were included in the present study. Serum iPTH level was determined before and 2 hours after thyroidectomy. Serum calcium concentration was determined 1 day before and 2 days postoperatively.

RESULTS:

The occurrence of postoperative hypocalcemia was correlated both with the absolute and relative iPTH decrease, determined as a ratio of the preoperative value (P < .0001). There was a greater difference in relative decrease in iPTH between patients remaining normocalcemic and those with hypocalcemia present on the second postoperative day. Hypocalcemic patients on the second postoperative day had a 62% relative decrease in iPTH 2 hours after thyroidectomy.

CONCLUSION:

The relative decrease in serum iPTH was greater in patients with hypocalcemia arising on the second postoperative day rather than in patients who remained normocalcemic. The relative decrease in iPTH determined 2 hours after total thyroidectomy together with the serum calcium concentration 24 hours after thyroidectomy proved to be useful predictors of sustained hypocalcemia and might change the clinical management of patients after thyroid surgery to support a longer hospitalization in these selected patients.

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PMID: 25616948
Intraoperative scintigraphy using a large field-of-view portable gamma camera for primary hyperparathyroidism: initial experience.

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Abstract

BACKGROUND:

We investigated a novel technique, intraoperative (99 m)Tc-Sestamibi (MIBI) imaging (neck and excised specimen (ES)), using a large field-of-view portable gamma camera (LFOVGC), for expediting confirmation of MIBI-avid parathyroid adenoma removal.

METHODS:

Twenty patients with MIBI-avid parathyroid adenomas were preoperatively administered MIBI and intraoperatively imaged prior to incision (neck) and immediately following resection (neck and/or ES). Preoperative and intraoperative serum parathyroid hormone monitoring (IOPTH) and pathology (path) were also performed.

RESULTS:

MIBI neck activity was absent and specimen activity was present in 13/20 with imaging after initial ES removal. In the remaining 7/20 cases, residual neck activity and/or absent ES activity prompted excision of additional tissue, ultimately leading to complete hyperfunctioning tissue excision. Postexcision LFOVGC ES imaging confirmed parathyroid adenoma resection 100% when postresection imaging qualitatively had activity (ES) and/or no activity (neck). The mean ± SEM time saving using intraoperative LFOVGC data to confirm resection versus first IOPTH or path result would have been 22.0 ± 2 minutes (specimen imaging) and 26.0 ± 3 minutes (neck imaging).

CONCLUSION:

Utilization of a novel real-time intraoperative LFOVGC imaging approach can provide confirmation of MIBI-avid parathyroid adenoma removal appreciably faster than IOPTH and/or path and may provide a valuable adjunct to parathyroid surgery.

PMID: 25629056
Preoperative 11C-Methionine PET/CT Enables Focussed Parathyroidectomy in MIBI-SPECT Negative Parathyroid Adenoma.

Lenschow C\(^1\), Gassmann P, Wenning C, Senninger N, Colombo-Benkmann M.

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Abstract

BACKGROUND:

Precise preoperative localization is essential for focussed parathyroidectomy. The imaging standard consists of cervical ultrasonography (cUS) and \(^{99}\)Tc-MIBI-SPECT (MIBI-SPECT). \(^{11}\)C-methionine positron emission tomography/computed tomography (Met-PET/CT) is a promising method for localizing parathyroid adenomas. The objective of our study was to elucidate whether additional Met-PET/CT increases the rate of focussed parathyroidectomy.

METHODS:

Fourteen patients with primary hyperparathyroidism (HPT) and three patients with tertiary HPT underwent cUS and MIBI-SPECT. Met-PET/CT was carried out in patients with negative MIBI results. Subsequent surgical strategy was adapted according to imaging results.

RESULTS:

cUS localized a single parathyroid adenoma in 10/17 patients (59\%), while MIBI-SPECT/CT identified 11/17 single adenomas (65\%). In the remaining six patients, Met-PET/CT identified five single adenomas. This step-up approach correctly identified single adenomas in 16/17 patients (94\%).

CONCLUSION:

Met-PET/CT raises the rate of correctly localized single parathyroid adenomas in patients with negative cUS and MIBI-SPECT/CT and increases the number of focussed surgical approaches.

PMID: 25665676
Justified follow-up: a final intraoperative parathyroid hormone (ioPTH) Over 40 pg/mL is associated with an increased risk of persistence and recurrence in primary hyperparathyroidism.

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Author information

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Abstract

INTRODUCTION:

After parathyroidectomy for sporadic primary hyperparathyroidism (PHPT), overall rates of persistence/recurrence are extremely low. A marker of increased risk for persistence/recurrence is needed. We hypothesized that final intraoperative parathyroid hormone (FioPTH) ≥40 pg/mL is indicative of increased risk for disease persistence/recurrence, and can be used to selectively determine the degree of follow-up.

METHOD:

A retrospective review of PHPT patients undergoing parathyroidectomy with ioPTH monitoring was performed. An ioPTH decline of 50 % was the only criteria for operation termination. Patients were grouped based on FioPTH of <40, 40-59, and >60 pg/mL.

RESULTS:

Between 2001 and 2012, 1,371 patients were included. Mean age was 61 ± 0.4 years, and 78 % were female. Overall persistence rate was 1.4 %, with a 2.9 % recurrence rate. Overall, 976 (71 %) patients had FioPTH < 40, 228 (16.6 %) had FioPTH 40-59, and 167 (12.2 %) had FioPTH ≥60. Mean follow-up was 21 ± 0.6 months. Patients with FioPTH <40 were younger, with lower preoperative serum calcium, PTH, and creatinine (all p ≤ 0.001). Patients with FioPTH <40 had the lowest persistence rate (0.2 %) versus patients with FioPTH 40-59 (3.5 %) or FioPTH ≥60 (5.4 %; p < 0.001). Recurrence rate was also lowest in patients with FioPTH <40 (1.3 vs. 5.9 vs. 8.2 %, respectively; p < 0.001). Disease-free status was greatest in patients with FioPTH <40 at 2 years (98.5 vs. 96.8 vs. 90.5 %, respectively) and 5 years (95.7 vs. 72.3 vs. 74.8 %, respectively; p < 0.01).

CONCLUSIONS:
Patients with FioPTH < 40 pg/mL had lower rates of persistence and recurrence, than patients with FioPTH 40-59, or ≥60. Differences became more apparent after 2 years of follow-up. Patients with FioPTH ≥40 pg/mL warrant close and prolonged follow-up.

PMID: 25192677


**Predictors of Multigland Disease in Primary Hyperparathyroidism: A Scoring System with 4D-CT Imaging and Biochemical Markers.**

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**Abstract**

**BACKGROUND AND PURPOSE:**

Multigland disease represents a challenging group of patients with primary hyperparathyroidism. Additional lesions may be missed on imaging because they are not considered or are too small to be seen. The aim of this study was to identify 4D-CT imaging and biochemical predictors of multigland disease.

**MATERIALS AND METHODS:**

This was a retrospective study of 155 patients who underwent 4D-CT and successful surgery with a biochemical cure that compared patients with multigland and single-gland disease. Variables studied included the size of the largest lesion on 4D-CT, the number of lesions prospectively identified on 4D-CT, serum calcium levels, serum parathyroid hormone levels, and the Wisconsin Index (the product of serum calcium and parathyroid hormone levels). Imaging findings and the Wisconsin Index were used to calculate a composite multigland disease scoring system. We evaluated the predictive value of individual variables and the scoring system for multigland disease.

**RESULTS:**

Thirty-six patients with multigland disease were compared with 119 patients with single-gland disease. Patients with multigland disease had significantly lower Wisconsin Index scores, smaller lesion size, and a higher likelihood of having either multiple or zero lesions identified on 4D-CT (P ≤ .01). Size cutoff of <7 mm had 85% specificity for multigland disease, but including other variables in the composite multigland disease score improved the specificity. Scores of ≥4, ≥5, and 6 had specificities of 81%, 93%, and 98%, respectively.

**CONCLUSIONS:**

The composite multigland disease scoring system based on 4D-CT imaging findings and biochemical data can identify patients with a high likelihood of multigland disease. Communicating the suspicion for
multigland disease in the radiology report could influence surgical decision-making, particularly when considering re-exploration in a previously operated neck or initial limited neck exploration.

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PMID: 25556203


The utility of 4-dimensional computed tomography for preoperative localization of primary hyperparathyroidism in patients not localized by sestamibi or ultrasonography.

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**Abstract**

**BACKGROUND:**

To determine the sensitivity and clinical application of 4-dimensional computed tomography (4D CT) for the localization of patients with primary hyperparathyroidism when ultrasonography (US) and sestamibi scans (STS) are negative.

**METHODS:**

We compiled a database of 872 patients with primary hyperparathyroidism who underwent parathyroid operation by a single surgeon from January 2003 to September 2013. Seventy-three patients who failed to have positive localization by US or STS were identified. Thirty-six underwent operation without a preoperative 4D CT, and 37 underwent operation after 4D CT.

**RESULTS:**

In patients not localized by US or STS, 4D CT was 89% sensitive in localizing an abnormal parathyroid gland when reviewed blindly by a radiologist specializing in endocrine localization studies, yielding a positive likelihood ratio of 0.89 and positive predictive value of 74%. Sensitivity, positive likelihood ratio, and positive predictive value for correct gland lateralization were 93%, 0.93, and 80%. The average size of parathyroid glands removed after preoperative localization by 4D CT was 404 mg and 0.57 cm(3) (SD = 280, 0.64), compared with 259 mg and 0.39 cm(3) (SD = 166, 0.21) in patients not localized by 4D CT. A focused, unilateral exploration was performed in 38% of patients with preoperative localization by 4D CT compared with 19% of patients without 4D CT (χ(2) = 3.0, P = .041).

**CONCLUSION:**
4D CT provided a positive localization in a clinically substantial number of patients not able to be localized by US or STS, which enabled an increased rate of successful, focused, unilateral operations compared with patients who did not undergo a 4D CT.

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PMID: 25660183  Makale sayfası


The Weight of the Resected Gland Predicts Rate of Success After Image-Guided Focused Parathyroidectomy.

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Abstract

BACKGROUND:

A recent study of focused minimally invasive parathyroidectomy (FPTX) in sporadic primary hyperparathyroidism (pHPT) using intraoperative parathyroid hormone (ioPTH) measurements shows that inadequate ioPTH drop and multiglandular disease are more commonly found when a first gland <200 mg is resected. Our aim was to study if a resected gland that weighed <200 mg was associated with an increased persistence rate after FPTX.

METHODS:

This is a cohort study of FPTX for pHPT performed in the period 1998-2013. FPTX was performed in patients with pHPT where Sestamibi and Ultrasound imaging localized single-gland disease, only one gland was excised and the weight recorded. IoPTH was not used routinely. Two groups were composed according to the weight of the resected gland: Group A <200 mg and Group B ≥200 mg. Persistent or recurrent disease was defined if it occurred within, or after 6 months. The primary outcome measure was the rate of persisting pHPT.

RESULTS:

A total of 3,511 parathyroidectomies were performed, and a total 1,745 FPTX (1,347 female) met inclusion criteria. There were 245 and 1,500 patients in groups A and B, respectively. The rate of persistent pHPT was higher in Group A, 6.1 versus 2.0 % (p < 0.001). Findings at re-operative surgery showed that the ipsilateral gland was diseased in 47 % (7/15) of persistent cases in group A.

CONCLUSION:

The risk of persistent disease after MIP was higher if the resected gland weighed ≤200 mg, and this corroborates the findings of a recent study. A heightened awareness of the possibility of multigland disease should be raised, and ioPTH monitoring, identification of the ipsilateral gland or bilateral exploration may be advisable in such cases.

PMID: 25677011
The utility of neck ultrasound and sestamibi scans in patients with secondary and tertiary hyperparathyroidism.

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Abstract

INTRODUCTION:

Secondary hyperparathyroidism (SHPT) and tertiary hyperparathyroidism (THPT) are disease entities in patients with chronic kidney disease that are caused by parathyroid hyperplasia. The role of preoperative localization studies in patients undergoing parathyroidectomy for these conditions remains poorly defined.

AIM:

To evaluate the utility of surgeon-performed neck ultrasound (US) as well as sestamibi scans in the localization of parathyroid glands in patients with SHPT/THPT.

MATERIALS AND METHODS:

A retrospective analysis of patients with SHPT/THPT who underwent parathyroidectomy at a single institution. Results of preoperative localization studies were compared to intraoperative findings.

RESULTS:

One hundred and three patients underwent parathyroidectomy for SHPT/THPT. All patients underwent surgeon-performed neck US, while 92 (89%) underwent sestamibi scans. US failed to localize any of the parathyroids in 4 patients (3.8%), while sestamibi was negative in 11 (12%). Forty-seven ectopic glands were identified in 38 patients in whom sestamibi was performed. In five patients (13%), ectopic glands were identified by both modalities, by US only in 6 (16%), by sestamibi only in 8 (21%), and by neither study in 19 patients (50%). US showed new thyroid nodules in 19 patients (18.4 %), leading to lobectomy or thyroidectomy at the time of parathyroidectomy in 16 patients (15.5%). Pathology showed malignancy in 7 patients (6.8%).

CONCLUSION:

US and MIBI offer little benefit in localizing ectopic glands and rarely change the conduct of a standard four-gland exploration. Although there was a benefit of US in the assessment of thyroid nodules, in only 8.7% of patients was sestamibi of benefit in identifying ectopic glands.

PMID: 25409841
Is intraoperative parathyroid hormone testing in patients with renal insufficiency undergoing parathyroidectomy for primary hyperparathyroidism accurate?

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Abstract

BACKGROUND:

Our aim was to determine whether chronic renal insufficiency (CRI) impacted intraoperative parathyroid hormone (ioPTH) monitoring during parathyroidectomy. We hypothesized that ioPTH monitoring in patients with CRI would show slower decline, but would still accurately predict cure.

METHODS:

A retrospective review was conducted of patients with primary hyperparathyroidism who underwent curative single adenoma parathyroidectomy. The percentage of patients reaching 50% decline of ioPTH was compared between groups stratified by renal function.

RESULTS:

Between 2000 and 2013, 950 patients met inclusion criteria. At 5 minutes, 66% of patients with CRI met curative criteria versus 77% of normal renal function patients (P = .001). At 10 minutes, 89% vs 92% met criteria (P = .073), and by 15 minutes, the gap narrowed to 95% vs 97% (P = .142), respectively.

CONCLUSIONS:

Despite CRI patients with primary hyperparathyroidism having slower ioPTH decline after curative parathyroidectomy, 95% met ioPTH criteria by 15 minutes. Standard ioPTH criteria can be used with CRI patients.

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KEYWORDS:

Chronic renal insufficiency; Intraoperative PTH monitoring; Minimally invasive parathyroidectomy; Primary hyperparathyroidism

PMID: 25556028
Necessity of therapy for post-thyroidectomy hypocalcaemia: a multicentre experience.


Author information

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Abstract

PURPOSE:

Hypoparathyroidism is one of the most common and most feared complications of total thyroidectomy (TT). The aim of this study is to detect possible markers that may facilitate early tracing of hypocalcaemia-prone patients in order to reduce clinical cost by optimizing patient discharge and to avoid unnecessary treatment.

METHODS:

Over an 18-month period, 995 patients, 23% male and 77% female, aged 52.9 ± 13.4 years, underwent TT in ten Lombardy hospitals. The following parameters were analyzed: calcaemia before and 12-24 and 48 h after surgery, pre- and post-operative parathyroid hormone (PTH) at 24 h and pre-operative 25OH vitamin D.

RESULTS:

Mortality was nil and morbidity was 22.4%. Mean 24-h calcaemia and PTH were 2.17 ± 0.15 mmol/l and 31.81 ± 20.35 pg/ml, respectively; mean 24-h PTH decay was 36.7 ± 34.12 %. Four hundred seventy-three (47.5%) patients were hypocalcaemic at discharge; 142 of whom had transient hypoparathyroidism that became permanent in 27. Patients developing hypocalcaemia had significantly higher values of PTH and calcium decay. At multiple logistic regression, only 24-h calcium decay, PTH drop and the presence of symptoms and parathyroid auto-grafting were significantly related to hypoparathyroidism. The association of these factors had a 99.2 % negative predictive value (NPV) for the development of hypoparathyroidism. A 70 % PTH drop had a 93.75 NPV for transient hypoparathyroidism. A 12 % calcaemia decay had a 95.7 NPV for hypoparathyroidism.

CONCLUSIONS:

Hypocalcaemic asymptomatic patients with less than 70 % PTH and 12 % calcaemia decay may be safely discharged without treatment. Symptomatic patients and those with parathyroid grafting should receive calcium and vitamin D.

PMID: 25749741
Diagnostic value and clinical impact of complementary CT scan prior to surgery for non-localized primary hyperparathyroidism.

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Abstract

INTRODUCTION:

Successful localization is mandatory for focused parathyroidectomy. If ultrasound and sestamibi scan are negative, bilateral neck exploration is necessary. We examined the contribution of complementary computed tomography (CT) scan to identify the affected parathyroid gland.

METHODS:

Between November 1999 and April 2014, 25 patients (20 females and 5 males; mean age 67 ± 11 years) with negative or dubious standard imaging (ultrasound and sestamibi scan) underwent CT scan prior to parathyroidectomy and were included in this study. Fifteen patients had had previous neck surgery for parathyroidectomy (n = 11) or thyroidectomy (n = 4). Thin-slice CT (n = 9) or four-dimensional (4D) CT imaging (n = 16) was used. Cure was defined as >50 % post-excision fall of intraoperatively measured parathyroid hormone or fall into the normal range, confirmed by normocalcaemia at least 6 months after surgery.

RESULTS:

Preoperative CT scan provided correct localization in 13 out of 25 patients (52 %) and was false positive once. Parathyroidectomy was performed by a focused approach in 11 of these 13 patients as well as in 1 patient guided by intraoperatively measured parathyroid hormone (ioPTH). Thirteen patients required bilateral neck exploration. The cure rate was 96 % (24/25 patients). One patient has persistent primary hyperparathyroidism (pHPT) and one a recurrent disease. Six patients presented a multiglandular disease.

CONCLUSION:

A CT scan identifies about half of abnormal parathyroid glands missed by conventional imaging and allows focused surgery in selected cases.

PMID: 25702138
Management of thyroid nodules incidentally discovered on MIBI scanning for primary hyperparathyroidism.


Author information

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Abstract

INTRODUCTION:

Parathyroid sestamibi scan is routinely performed before parathyroid surgery. A large number of thyroid cancers take up 99mTc-sestamibi (MIBI). Since 2001, thyroid nodules discovered on sestamibi, nodules >2 cm, and/or with suspicious criteria were resected. The aim of this study was to evaluate the results of this policy.

METHODS:

All patients operated on for hyperparathyroidism, with a MIBI and cervical ultrasonography (US) with a thyroid resection for nodule, were retrospectively included.

RESULTS:

From 2001 to 2013, 685 patients were operated on for hyperparathyroidism. Some 137 (85 % females) had both preoperative MIBI and cervical US and a thyroid resection. The mean age was 63.2 ± 12.8 years. Sixty-three patients had a total thyroidectomy and 74 a lobectomy. Thirty-six patients had a thyroid cancer. The median size of cancers was 6.5 mm (0.3-22 mm), and 23 (16.7 %) patients had microcarcinoma. Among the 137 patients, 44 (32 %) had a MIBI+ nodule including 22 cancers. Sixty-one percent of malignant nodules were MIBI+ (22/36). The median size of MIBI+ cancers was 15 mm (9-22 mm) versus 2 mm (0.3-17 mm) for MIBI- cancers (p = 0.03). Twenty-two percent of benign nodules were MIBI+ (22/101). Finally, the sensitivity, specificity, positive predictive value, and negative predictive value of MIBI were 61, 78, 50, and 85 %, respectively.

CONCLUSION:

Thyroid nodules incidentally discovered on MIBI in hyperparathyroidism patients should be resected.

PMID: 25694271
Computed tomography for preoperative evaluation of need for sternotomy in surgery for retrosternal goitre.

Malvemyr P¹, Liljeberg N, Hellström M, Muth A.

Abstract

PURPOSE:
The purposes of this study are to evaluate the usefulness of available CT classifications of retrosternal goitre (RSG) to identify patients needing sternotomy and to examine the effect of neck extension on goitre position.

METHODS:
From the Scandinavian Quality Register for Thyroid and Parathyroid Surgery, all patients treated for RSG at Sahlgrenska (January 2005 through August 2012) were identified. Medical records and preoperative CT scans were retrospectively reviewed. Paired CT (normal position/neck extension) was done in three patients.

RESULTS:
Of 1698 patients undergoing thyroid surgery, 158 (9.3 %) were registered as having RSG, of these 38 were excluded (no preoperative CT n = 27, no RSG at preoperative CT n = 11). Of 120 included patients (71 % females, median age 67 years, rate of malignancy 14 %), 104 were managed with a cervical approach only, 16 (13.3 %) needed sternotomy, of these 13/16 had growth below the aortic arch concavity. Predictors for sternotomy were goitre extension below the aortic arch concavity (positive/negative predictive value (PPV/NPV) 54/97 %, sensitivity/specificity 81/89 %, odds ratio (OR) 36.6, p < 0.001); main mass of RSG to the right of the midline (PPV/NPV 21/95 %, sensitivity/specificity 81/53 %, OR 4.9, p < 0.008); and main mass of RSG retrotracheal (PPV/NPV 31/92 %, sensitivity/specificity 50/83 %, OR 4.8, p < 0.005). The goitre was displaced cranially a mean 11 mm with neck extension, but the relationship to the aortic arch was unchanged.

CONCLUSIONS:
RSG extension below the aortic arch concavity was confirmed as a significant risk factor for sternotomy, with a NPV for sternotomy of 97 % for less extensive goitres. CT in neck extension provided no additional clinically relevant information.

PMID: 25557494
Preoperative localization of hyperfunctioning parathyroid glands with 4D-CT.

Lundstroem AK¹, Trolle W, Soerensen CH, Myschetzky PS.

Abstract

Primary hyperparathyroidism (pHPT) is almost exclusively the result of a solitary parathyroid adenoma. In most cases, the affected gland can be surgically removed, but precise preoperative imaging is essential for adenoma localization prior to surgical intervention. In this study, we evaluated the diagnostic value of four-dimensional computed tomography (4D-CT) as a preoperative imaging tool in relation to the localization of pathologic parathyroid glands in patients with pHPT and negative sestamibi scans. This study included 43 consecutive patients with pHPT referred for parathyroidectomy at the Department of Head and Neck Surgery of Copenhagen University Hospital Rigshospitalet in 2011 and 2012. All patients had a 4D-CT performed prior to parathyroidectomy. CT localization of the suspected adenoma was correlated to the actual surgical findings and subsequent histological diagnosis was also available as references for the accuracy of this imaging tool. Hyperfunctioning parathyroid glands were found in 40 patients. 4D-CT identified 32 solitary hyperfunctioning parathyroid glands located on the correct side of the neck (PPV 76%) and 21 located within the correct quadrant (PPV 49%). Unilateral resection was performed in 72% of patients due to the localization findings of preoperative imaging. 4D-CT can, therefore, be considered an effective method for the preoperative localization of parathyroid adenomas and is an important tool in surgical intervention for patients referred to parathyroidectomy.

PMID: 25773486

Co-existent thyroid disease in patients treated for primary hyperparathyroidism: implications for clinical management.

Ryan S¹, Courtney D, Timon C.

Abstract

Treatment for primary hyperparathyroidism necessitates complete excision of involved parathyroid tissue. Simultaneous thyroidectomy may also be required in order to optimise operative access and/or where suspicion of synchronous abnormal thyroid pathology exists. We sought to determine how often simultaneous removal of thyroid tissue was required during parathyroidectomy and the nature of any associated pathology. Radiology reports were also reviewed to determine how often confirmed thyroid pathology from histological specimens, benign or malignant, had been identified pre-operatively. A retrospective chart review of 135 parathyroidectomy procedures performed between 2003 and 2013 was
performed. Of 135 parathyroidectomy procedures, 39 patients (29%) underwent simultaneous partial thyroidectomy of which 36 (27% of total parathyroidectomies) had dual pathology confirmed. Specifically, malignant lesions were identified in 14% (n = 5), Graves’ disease 3% (n = 1), thyroiditis 17% (n = 6), multinodular goitre 50% (n = 18), unilateral nodule 6% (n = 2), hyperplasia 8% (n = 3) and intra-thyroid adenoma 3% (n = 1). Reference to these thyroid lesions was made in only 47% of preoperative radiology reports. In conclusion, synchronous thyroid surgery was required in 29% of all parathyroidectomy procedures performed for treatment of primary hyperparathyroidism with malignant thyroid lesions incidentally detected in 14% of cases. Less than half of all confirmed concomitant thyroid pathology had been referred to or recognised on pre-operative radiology studies. These findings highlight the importance of considering the potential need to perform thyroid surgery during parathyroidectomy and obtaining appropriate informed consent.

PMID: 24633247


Accuracy of early-phase versus dual-phase single-photon emission computed tomography/computed tomography (SPECT/CT) in the localization of Parathyroid disease.

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Abstract

OBJECTIVES/HYPOTHESIS:

Preoperative localization for parathyroid disease has improved in recent years with the advent of dual-phase 99mTc-sestamibi single-photon emission computed tomography/computed tomography (SPECT/CT) imaging. However, dual-phase imaging is associated with increased cost, time, and radiation dose. The aim of this study was to investigate the need for late-phase imaging when using SPECT/CT for the preoperative localization of parathyroid disease.

STUDY DESIGN:

Retrospective chart analysis.

METHODS:

A retrospective review of 75 patients who underwent preoperative imaging localization and subsequent surgical resection for parathyroid disease at a tertiary referral center was performed. Of these, 50 patients met study criteria including preoperative SPECT/CT imaging and specific reporting of early- and late-phase focal radiotracer uptake. Localization accuracy was verified with definitive surgical findings confirmed by histological analysis and evidence of biochemical cure.

RESULTS:

Accurate localization of adenoma(s) was seen in 78.0% of patients using dual-phase SPECT/CT. Early-phase imaging alone localized 76.0%, whereas late-phase imaging alone localized 74.0%. Sensitivity and
specificity for dual-phase imaging was 84.8% and 89.6%, respectively. In comparison, early-phase localization alone was found to have a sensitivity/specificity of 84.4%/89.4%; sensitivity/specificity of late-phase scanning alone was found to be 80.4%/89.1%. Dual-phase SPECT/CT scanning did not provide a statistically significant improvement in adenoma localization when compared to early-phase scanning alone.

CONCLUSIONS:

Although further investigation is needed, the results of this study suggest that early-phase SPECT/CT scanning alone may obviate the need for dual-phase SPECT/CT scanning in the initial preoperative localization workup of parathyroid disease.

LEVEL OF EVIDENCE:


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KEYWORDS:

Parathyroid; minimally invasive parathyroidectomy; parathyroid preoperative localization; parathyroid single-photon emission computed tomography/computed tomography

PMID: 25645695       Makale sayfası
A novel non-surgical, minimally invasive technique for parathyroid autotransplantation: a case report.
Aysan E, Kilic U, Gok O, Altug B, Ercan C, Idiz UO, Kesgin C, Muslumanoglu M.

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Abstract

We present a case report of intramuscular autotransplantation of the parathyroid cell suspension acquired after total parathyroidectomy. A 15-yr-old female patient who had been undergoing hemodialysis due to chronic renal failure for eight yr was diagnosed with secondary hyperthyroidism and subsequently underwent total parathyroidectomy. The parathyroid cells were acquired from the resected tissues, processed through isolation and cultivation phases, and counted using a cell counter. A total of two million cells were injected into the left deltoid muscle using a 22-gauge needle. After surgery, five and 10 million cells were injected in the fifth and 12 week, respectively. The desired serum levels of parathyroid hormones and calcium were not achieved after the first two transplantations. In addition, there was no regression in the patient's symptoms. However, at four wk after the third transplantation, serum parathyroid hormone level did not decrease to <3 pg/mL, the patient was asymptomatic, and the oral treatment was stopped. Our findings indicate that this new technique is applicable because it is minimally invasive, and it can be easily repeated.

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KEYWORDS:

autotransplantation; invasive; minimally; non-surgical; parathyroid

PMID: 25495657  Makale sayfası
Life-threatening intrathyroidal parathyroid adenoma.

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Abstract

Acute primary hyperparathyroidism and parathyroid crisis are characterized by life-threatening hypercalcemia, a rare disorder. A 69-year-old female patient presented at our hospital's neurology clinic with weakness, nausea, vomiting, depression, and hypercalcemia. Treatment of hypercalcemia resulted in no improvement in neurological symptoms, indicating resistance to treatment. Thyroid ultrasonography and parathyroid scintigraphy revealed hypoechoic nodules in the right lobe, pieces of nodules in the left lobe, and high serum calcium and parathyroid hormone levels. After provision of intensive medical treatment including hydration, diuresis, and bisphosphonate infusion resulted in only minimal decrease in the calcium level, urgent surgical treatment was performed. Frozen biopsy of the right intrathyroidal giant parathyroid adenoma in the right lobe confirmed initial diagnosis of primary hyperparathyroidism. Based on the biopsy findings, right parathyroidectomy and right total and left subtotal thyroidectomy were performed. Histopathologic examination revealed a parathyroid adenoma localized inside large thyroid nodules. Review of the findings resulted in diagnosis of intrathyroidal parathyroid adenoma. Symptoms of hypercalcemia improved rapidly during the postoperative period.

KEYWORDS:

Acute primary hyperparathyroidism; hypercalcemia; hyperplasia; intrathyroidal parathyroid adenoma; parathyroid crisis; parathyroidectomy

PMID: 25785164
Systematic review of surgical treatment of subclinical Cushing's syndrome.

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Abstract

BACKGROUND:

Subclinical Cushing's syndrome (SCS) is a condition of biochemical cortisol excess without the classical clinical features of overt hypercortisolism; it may be associated with some consequences of metabolic syndrome. The most appropriate treatment remains controversial. This study aimed to assess the outcomes of adrenalectomy for SCS.

METHODS:

A systematic review was performed. MEDLINE, Embase and Cochrane Databases (1980-2013) were searched for studies reporting the outcomes of unilateral adrenalectomy with respect to hypertension, diabetes, dyslipidaemia, obesity and osteoporosis in patients with SCS. Studies with a questionable diagnosis of SCS, bilateral adrenal involvement and insufficient data were excluded.

RESULTS:

Of the 105 papers screened, seven were selected; there were six retrospective studies and one randomized clinical trial, including 230 patients. Data analysis was limited by heterogeneity in definition of SCS and endpoints. Hypercortisolism was cured in all operated patients. Laparoscopy was the preferred approach, with a morbidity rate of 0.8 per cent. A beneficial effect of surgery on blood pressure, glucometabolic control and obesity was evident in all studies, with cure or improvement in 72, 46 and 39 per cent of patients respectively, compared with conservative management. The results for lipid metabolism were equivocal, because of a decrease in triglyceridaemia but discordant effects on cholesterol metabolism among the different studies. No beneficial effects on osteoporosis were found.

CONCLUSION:

Laparoscopic adrenalectomy seems to be beneficial in reversing several metabolic effects of hypercortisolism, with a low morbidity rate. However, the heterogeneity and low quality of the available studies preclude definitive recommendations.
Diagnosis, treatment and outcome of adrenocortical cancer.

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Abstract

BACKGROUND:

Adrenocortical cancer (ACC) is a rare disease with a dismal prognosis. The majority of patients are diagnosed with advanced disease and raise difficult management challenges.

METHODS:

All references identified in PubMed, published between 2004 and 2014, using the keywords 'adrenocortical cancer' or 'adrenal surgery' or both, were uploaded into a database. The database was interrogated using keywords specific for each field studied.

RESULTS:

In all, 2049 publications were identified. There is ongoing debate about the feasibility and oncological outcomes of laparoscopic adrenalectomy for small ACCs, and data derived from institutional case series have failed to provide an evidence level above expert opinion. The use of mitotane (1-(2-chlorophenyl)-1-(4-chlorophenyl)-2,2-dichloroethane) in combination with chemotherapy in the treatment of metastatic disease has been assessed in an international randomized trial (FIRM-ACT trial) involving patients with ACC. Based on this trial, mitotane plus etoposide, doxorubicin and cisplatin is now the established first-line cytotoxic therapy owing to a higher response rate and longer median progression-free survival than achieved with streptozocin-mitotane. For patients with tumours smaller than 5 cm and with no signs of lymph node or distant metastases, survival is favourable with a median exceeding 10 years. However, the overall 5-year survival rate for all patients with ACC is only 30 per cent.

CONCLUSION:

Open and potentially laparoscopic adrenalectomy for selected patients is the main treatment for non-metastatic ACC, but the overall 5-year survival rate remains low.

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PMID: 25689291  Makale sayfası
What is the appropriate role of minimally invasive vs. open surgery for small adrenocortical cancers?

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Abstract

PURPOSE OF REVIEW:

The role of endoscopic adrenalectomy for adrenocortical carcinoma is the most controversial and debated points in adrenal surgery. We reviewed the most recent literature on this topic.

RECENT FINDINGS:

From the amount of available data (even if not conclusive), the following could be extrapolated: first, for patients with apparently localized disease the adrenal gland should be removed en bloc with the entire retroperitoneal fat pad, which also includes some periadrenal lymph nodes, but no extended resection is necessary in absence of involvement of adjacent structures; second, in experienced centers, oncologic outcome for endoscopic adrenalectomy is not inferior to open adrenalectomy when strict selection criteria and the principles of oncologic surgery are respected. When performed by nonexperienced surgeons, endoscopic adrenalectomy may be associated with a higher rate of positive margin and local recurrence; third, patients observed at specialized referral centers receive a more accurate preoperative workup that allows a better operative planning and a more comprehensive postoperative treatment.

SUMMARY:

Although waiting for further more exhaustive studies, we think that for suspected adrenocortical carcinoma, smaller than 8-10 cm and without pre or intraoperative evidence of local invasion, endoscopic adrenalectomy in a referral center seems to be an acceptable option.
OBJECTIVE:
To explain differences over time between operative approach and surgeon type for adrenal surgery in the USA.

PATIENTS AND METHODS:
A retrospective cohort analysis was performed on all patients undergoing adrenalectomy between 2002 and 2011 using the Nationwide Inpatient Sample. Patients undergoing concurrent nephrectomy were excluded. Surgeon specialty was only available for 2003-2009. Descriptive analyses and multivariable logistic regression models were used to assess variables associated with minimally invasive surgery (MIS) and urologist-performed procedures.

RESULTS:
In all, 58,948 adrenalectomies were identified. A MIS approach was used in 20% of these operations. There was a 4% increase in MIS throughout the study period (P < 0.001). Cases performed at teaching hospitals were more likely to be MIS (odds ratio [OR] 1.47, P < 0.001). We were able to identify surgical specialty in 23,746 cases, of which 60% were performed by urologists. Cases performed in the Midwest compared with Northeast were at increased adjusted odds of being performed by urologists (OR 1.38, P = 0.11). Despite most cases being performed by urologists, adrenalectomy by urologists showed a 15% annual decrease over the analysed period (P < 0.001).

CONCLUSIONS:
The use of a MIS technique to perform adrenalectomy is increasing at a slower rate compared with most other surgical extirpative procedures. Further investigation to explain the decreased performance of adrenalectomy by urologists is warranted.

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KEYWORDS:
adrenalectomy; economics; laparoscopy; national trend; open surgery; robotics

PMID: 24974910    Makale sayfası


Patterns of Use and Short-Term Outcomes of Minimally Invasive Surgery for Malignant Pheochromocytoma: A Population-Level Study.
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Abstract

BACKGROUND:
Malignant pheochromocytoma is rare, and there is a scarcity of data on the use of minimally invasive surgery (MIS) for treatment. The aims of this study were to analyze patterns of use of MIS for malignant pheochromocytoma in the U.S. and compare short-term outcomes to those of open adrenalectomy.

METHODS:

Patients with malignant pheochromocytoma undergoing MIS, including laparoscopy, robotic assisted, laparoscopy converted to open, or open adrenalectomy, were culled from the National Cancer Database, from 1998 to 2011. Data were examined using simple summary statistics, X² and student's t tests, Mann-Whitney test, and logistic regression.

RESULTS:

A total of 36 MIS and 67 open adrenalectomies were identified in 2010-2011. No significant differences were observed between the two treatment groups in demographic characteristics or comorbidities. Preoperative diagnosis of malignancy was made in 52.8 % of MIS and 48.5 % of open patients (p = NS). MIS and open adrenalectomies did not differ with respect to lymph node metastases, vascular invasion, extra-adrenal-extension, and distant metastases (all p = NS). MIS tended to more often be used to perform partial adrenalectomy (38.9 vs. 20.4 % open, p = 0.061); surgical margins, 30-day readmission and mortality rates were similar to open adrenalectomy (all p = NS). Tumors removed via MIS were smaller (48.7 vs. 73.3 mm open, p = 0.003) and associated with a shorter length of stay.

CONCLUSIONS:

A significant proportion of patients with malignant pheochromocytomas underwent MIS, with short-term outcomes which are comparable to those of open surgery. Further studies focused on long-term survival and recurrence are needed to assess the role of MIS in the management of these rare tumors.

PMID: 25821949


Recurrence and functional outcomes of partial adrenalectomy: A systematic review and meta-analysis.

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Abstract

BACKGROUND:

Partial adrenalectomy is typically performed for the treatment of hereditary and sporadic bilateral tumours, to reduce the risk of adrenal failure, particularly in younger patients. Partial adrenalectomy proposes a postoperative steroid-free course nevertheless, is associated with the risk of local recurrence. In this study we evaluate the recurrence and functional outcomes of partial adrenalectomy.
METHODS:

A systematic search was conducted using MEDLINE, PubMed, EMBASE, Current Contents Connect, Cochrane library, Google Scholar, Science Direct, and Web of Science. The search identified 60 relevant articles reporting on patients who underwent partial adrenalectomy. Data was extracted from each study and used to calculate a pooled event rate and 95% confidence interval (95% CI).

RESULTS:

The overall recurrence rate was 8% (95% CI: 0.05-0.12) and the 85% (95% CI: 0.78-0.9) of the patients were steroid free. The recurrence rates were the least in the retroperitoneoscopic group 1% (95% CI: 0-0.04) and Conn's syndrome group 2% (95% CI: 0.01-0.05) and highest in open group 15% (95% CI: 0.07-0.28) and Pheochromocytoma group 10% (95% CI: 0.07-0.16). Steroid independence rates were best in the Conn's syndrome group 97% (95% CI: 0.85-0.99) and laparoscopic group 88% (95% CI: 0.75-0.95).

CONCLUSIONS:

Partial adrenalectomy can obviate the need for steroid replacement in the majority of patients and local recurrence rates appear to be infrequent. For patients with hereditary and bilateral adrenal tumours, partial adrenalectomy should be recommended as a primary surgical approach whenever possible.

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KEYWORDS:

Adrenalectomy; Meta-analysis; Outcomes; Surgery; Systematic review

PMID: 25681039

Approach to the surgical management of primary aldosteronism.

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Abstract

Primary aldosteronism (PA) is the most common cause of endocrine hypertension; it has been reported in more than 11% of referred hypertensive patients. PA may be caused by unilateral adrenal involvement [aldosterone producing adenoma (APA) or unilateral adrenal hyperplasia (UAH)], and bilateral disease (idiopathic adrenal hyperplasia). Only patients with unilateral adrenal hypersecretion may be cured by unilateral adrenalectomy, while patients with bilateral and non-surgically correctable PA are usually treated by mineralocorticoid receptor antagonists; thus the distinction between unilateral and bilateral aldosterone hypersecretion is crucial. Most experts agree that the referral diagnostic test for lateralization of aldosterone hypersecretion should be adrenal venous sampling (AVS) because the interpretation of other imaging techniques [computed tomography (CT), magnetic resonance imaging (MRI) and scintigraphy] may lead to inappropriate treatment. Adrenalectomy represents the elective treatment in unilateral PA variants. Laparoscopic surgery, using transperitoneal or retroperitoneal approaches, is the preferred
strategy. Otherwise, the indications to laparoscopic unilateral total or partial adrenalectomy in patients with unilateral PA remain controversial. Adrenalectomy is highly successful in curing the PA, with correction of hypokalemia in virtually all patients, cure of hypertension in about 30-60% of cases, and a marked improvement of blood pressure values in the remaining patients. Interestingly, in several papers the outcomes of surgery focus only on blood pressure changes and the normalization of serum potassium levels is often used as a surrogate of PA recovery. However, the goal of surgery is the normalization of aldosterone, because chronically elevated levels of this hormone can lead to cardiovascular complications, independently from blood pressure levels. Thus, we strongly advocate the need of considering the postoperative normalization of aldosterone-renin ratio (ARR) as the main endpoint for determining outcomes of PA.

KEYWORDS:

Adrenalectomy; hypertension; hypokalemia; laparoscopy; primary aldosteronism (PA)

PMID: 25713782
Does contralateral suppression at adrenal venous sampling predict outcome following unilateral adrenalectomy for primary aldosteronism? A retrospective study.

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Abstract

Context: In primary aldosteronism (PA), adrenal vein sampling (AVS) distinguishes unilateral and bilateral disease by comparison of aldosterone/cortisol (A/F) ratios. There is controversy about criteria for interpretation however, and in particular it is unclear if contralateral suppression (CS - defined as: A/F (adrenal) ≤ A/F (peripheral) on the unaffected side) is important. We therefore performed a retrospective study to determine if CS in surgically treated unilateral PA was associated with blood pressure (BP) and biochemical outcomes. Setting and Design: Patients who underwent unilateral adrenalectomy for PA after successful AVS were included if the lateralisation index (LI - A/F dominant : A/F non-dominant) was ≥2. Cases were reviewed at 6-24 months follow up for outcomes with respect to the presence and degree of CS. Results: 66 of 80 patients had CS. Baseline characteristics were similar. At post-operative follow up, those with CS had lower systolic BP (SBP; 128mmHg vs. 144mmHg p=0.001), a greater proportion with cure or improvement of hypertension (96% vs. 64%, p=0.0034), a greater proportion with biochemical cure of PA on fludrocortisone suppression testing (43/49 [88%] vs. 4/9 [44%], p=0.002) and were on a lower median number of antihypertensive medications (0 vs. 1.5 p=0.0032). In a multivariate model, the degree of CS and pre-operative SBP were both significantly correlated with post-operative SBP, but LI, gender and age were not. Conclusion: In this study the presence of CS correlated with good BP and biochemical outcomes from surgery. This suggests that CS should be a factor in deciding whether to offer surgery for treatment of PA.

PMID: 25636049

Clinicopathologic characteristics of incidentally identified pheochromocytoma.

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Abstract

BACKGROUND:

Pheochromocytomas are rare neuroendocrine tumors. With the widespread use of cross-sectional imaging, increasing numbers are identified incidentally, but their clinicopathologic traits have been incompletely characterized.

METHODS:

We performed a retrospective cohort study of patients who underwent initial adrenalectomy for pheochromocytoma (1997-2014). Patients were classified as identified by guided investigation (GIP) if imaging was performed for symptoms or surveillance and as incidentally identified pheochromocytomas (IIP) if imaging was performed for other indications. Student's t test, Chi square test, or rank-sum tests were used as appropriate.

RESULTS:

Of 126 patients, 47 % were IIP (n = 59). IIP patients had more nonspecific symptoms, including abdominal or back pain (39.0 vs. 6.0 %, p < 0.001), but lower rates of classic symptoms, such as hypertension (54.2 vs. 77.6 %, p = 0.005), palpitations or arrhythmias (18.9 vs. 50.0 %, p = 0.001), flushing or diaphoresis (25.4 vs. 46.3 %, p = 0.015), and headache (20.3 vs. 44.8 %, p = 0.004). IIP was associated with lower median 24-hour urine metanephrine (2102 vs. 7299 μg, p = 0.020), normetanephrine (2253 vs. 4383 μg, p = 0.005), and epinephrine (23 vs. 116 μg, p = 0.004) levels. Histopathology demonstrated no difference between IIP and GIP in malignant traits, including extraadrenal extension (8.6 vs. 12.3 %, p = 0.568), capsular invasion (26.9 vs. 20.3 %, p = 0.133), lymphovascular invasion (25.0 vs. 24.6 %, p = 0.264), and necrosis (32.4 vs. 20.0 %, p = 0.224). Rates of malignancy were equivalent (5.1 vs. 6.0 %, p = 0.862) between IIP and GIP cohorts.

CONCLUSIONS:

Half of patients presenting for surgical resection of pheochromocytoma were identified incidentally. These patients had equivalent rates of malignancy and pathologic traits associated with malignant potential and require definitive evaluation and early surgical referral.

PMID: 25047479


Factors associated with higher risk of complications after adrenal surgery.

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Abstract
BACKGROUND:

Surgeon experience has been demonstrated to result in better outcomes after a variety of advanced operations. Less information is available regarding adrenal surgery. We compared the outcomes after adrenalectomy for a variety of indications and determined the effect of surgeon’s case volume.

METHODS:

Cross-sectional analysis was performed using ICD-9 procedure codes included in the Nationwide Inpatient Sample from 2003 to 2009 to identify all adult patients who underwent unilateral or bilateral adrenalectomy for benign or malignant conditions. Logistic regression was used to test for interaction between surgeon case volume (low = 1, intermediate = 2-5, and high = >5 adrenalectomies per year), diagnosis, type of operation performed, and risk of complications.

RESULTS:

A total of 7,829 adrenalectomies were included. Risk of complications after bilateral adrenalectomy was 23.4 % compared to 15.0 % for unilateral adrenalectomy (odds ratio 2.165, 95 % confidence interval 1.335, 3.512). Malignancy was associated with higher risk of complication (23.1 %) than benign disease (13.2 %) (odds ratio 1.685, 95 % confidence interval 1.371, 2.072). Complication rates for low- and intermediate-volume surgeons were 18.8 and 14.6 %, respectively, and both were significantly higher than complications by high-volume surgeons (11.6 %, p < 0.05). Length of stay and charges were both significantly less for high-volume surgeons compared to lower-volume groups (p < 0.05).

CONCLUSIONS:

Low surgeon case volumes and adrenal surgery for malignant or bilateral disease are associated with increased risk of postoperative complications. Length of stay and charges were significantly less when high-volume surgeons perform adrenal surgery.

PMID: 24793341


The current status and management of blunt adrenal gland trauma.

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Abstract

BACKGROUND:

Blunt adrenal gland trauma (BAGT) is a potentially devastating event if unrecognized during the treatment course of patients with trauma. Because of its rarity, no current algorithm or consensus exists for BAGT. In the present study, we demonstrated the feasibility and safety of transcatheter angiographic embolization (TAE) in BAGT and analyzed the clinical presentation and outcome of BAGT.
METHODS:

We conducted a prospective collection and retrospective review at a level I trauma center in Taiwan. This study included all of the patients that sustained BAGT from May 2004 to May 2013. We retrieved and analyzed the patient demographic data, clinical presentation, BAGT grade, injury severity score, management, hospital stay, and mortality.

RESULTS:

The cohort consisted of 77 patients: 59 men and 18 women. The mean age was 34.3 ± 15.5 years. The right side was the predominant site of injury (59/77; 76.6%). Six patients underwent operation; 18 patients underwent angiography, including four TAEs, and the remaining patients underwent conservative management. The mortality rate was 9.1% (7/77), and a high injury severity score was an independent factor to predict mortality.

CONCLUSION:

In conclusion, BAGT is a rare injury with a benign prognosis. Most patients can be treated conservatively. Furthermore, this study demonstrates that both TAE and operation can be used to achieve hemostasis. The mortality of BAGT was related to severe associated injuries. BAGT is an indicator of severe multiple trauma; however, it does not increase mortality or prolong hospital stay.

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PMID: 25616947  Makale sayfasi


Surgical resection of metastases to the adrenal gland: a single center experience.

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Abstract

BACKGROUND:

Only limited data exist on the treatment and outcome of adrenal metastases that derive from different primary tumor entities. Due to the lack of evidence, it is difficult to determine the indication for surgical resection.

METHODS:

We assessed the outcome of 45 patients (28 men, 17 women) with adrenal metastases who underwent surgery (1990-2014). The median age at the time of adrenal surgery was 62 years (range 44-77 years). We were able to evaluate follow-up data of 41 patients.
RESULTS:

Primary tumor types were liver n = 12 (hepatocellular carcinoma n = 9, cholangiocellular carcinoma n = 2, sarcoma n = 1), upper GI tract n = 5 (esophagus n = 2, stomach n = 3), lung n = 9, kidney n = 6, neuroendocrine tumors n = 3, colon n = 2, ovarian n = 2, melanoma n = 2, others n = 4. The overall median survival time was 14 months (95% CI 8.375-19.625). The survival rates at 1, 2, 5, and 10 years were 60, 31, 21, and 11%, respectively. There were statistically significant differences in the survival time according to the resection status (R0 vs. R1/R2) (p < 0.001) and the type of the primary tumor (p = 0.009), while the metachronous or synchronous occurrence of adrenal metastases did not affect the prognosis.

CONCLUSIONS:

Resection of adrenal metastases can improve the survival if patients are carefully selected, the tumor is completely resected, and the intervention is integrated into a multidisciplinary oncologic treatment strategy.

PMID: 25726026


Outcome of surgical treatment of primary aldosteronism.

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Author information

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Abstract

PURPOSE:

The aim of this retrospective study was to analyze the early and long-term outcomes of the surgical treatment of primary aldosteronism (PA), the most common surgically correctable cause of endocrine hypertension.

METHODS:

Serum Potassium levels, blood pressure values, and aldosterone/renin ratio (ARR) were assessed in 128 patients undergoing unilateral adrenalectomy for PA, before and after surgery. The role of lateralizing techniques and the relationship between outcome and histopathology findings were also evaluated.

RESULTS:

Biochemical cure of PA (ARR and kalemia normalization) was achieved in 95% of patients, at early follow-up. Single aldosterone-producing adenoma, multinodular hyperplasia, and diffuse hyperplasia were found in 46, 45, and 9% of the patients, respectively. No relationship between histopathology and persistence or recurrence of PA was found. The use of further lateralizing techniques in addition to computed tomography or magnetic resonance was the main predictor of PA cure (p = 0.02); adrenal venous sampling (AVS) was more accurate than scintigraphy in PA lateralization (p < 0.05). After surgery, hypertension was cured in 55% and improved in 36% of patients. Female gender, a lower number of antihypertensive drugs, and a shorter duration of hypertension were the main predictors of hypertension cure. At long-term, recurrent PA occurred in 3.7% of cases.
CONCLUSIONS:

Early diagnosis and correct lateralization of hyperaldosteronism by means of AVS are keys to achieve surgical cure of PA and PA-related hypertension. PA may be also caused by unilateral hyperplasia, which may be cured by unilateral adrenalectomy. Recurrences of PA are rare, although a prolonged follow-up is required.

PMID: 25567077


Value of 18-F-FDG PET/CT and CT in the Diagnosis of Indeterminate Adrenal Masses.

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Abstract

The purpose of this paper was to study the value of 18-F-FDG PET/CT and reassess the value of CT for the characterization of indeterminate adrenal masses. 66 patients with 67 indeterminate adrenal masses were included in our study. CT/MRI images and 18F-FDG PET/CT data were evaluated blindly for tumor morphology, enhancement features, apparent diffusion coefficient values, maximum standardized uptake values, and adrenal-to-liver maxSUV ratio. The study population comprised pathologically confirmed 16 adenomas, 19 metastases, and 32 adrenocortical carcinomas. Macroscopic fat was observed in 62.5% of the atypical adenomas at CT but not in malignant masses. On 18F-FDG PET/CT, SUVmax and adrenal-to-liver maxSUV ratio were significantly lower in adenomas than in malignant tumors. An SUVmax value of less than 3.7 or an adrenal-to-liver maxSUV ratio of less than 1.29 is highly predictive of benignity.

PMID: 25722719
Long-term outcomes of laparoscopic adrenalectomy for adrenal masses.

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Author information

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Abstract

BACKGROUND:

Laparoscopic adrenalectomy is the gold standard procedure for most adrenal masses. However, long-term data regarding this procedure are limited. We report our institution's experience with laparoscopic adrenalectomy, determine if this procedure results in durable weight loss and resolves hypertension, diabetes mellitus, or hyperlipidemia, and identify predictors of pathology in nonfunctioning tumors.

MATERIALS AND METHODS:

We retrospectively reviewed laparoscopic adrenalectomies performed for adrenal masses between May 2000 and September 2010 by nine surgeons at a single institution. Data gathered included demographics, body mass index (BMI), preoperative and postoperative imaging and biochemical testing results, length of stay, complications, pathology, medications, and resolution of hypertension, diabetes, or hyperlipidemia.

RESULTS:

We removed 96 adrenal glands in 95 patients. Their average age was 55.6 years. The average length of stay was 1.8 days. Average BMI was 32.9 kg/m(2) preoperatively and 31.9 kg/m(2) postoperatively (P=.46). We experienced no conversions to open procedure and no perioperative mortality. Minor complications occurred at a rate of 1.2%. Indications for adrenalectomy were nonfunctioning tumor (n=35), pheochromocytoma (n=18), aldosteronoma (n=17), subclinical Cushing's syndrome (n=15), Cushing's syndrome (n=9), and sex hormone-secreting tumor (n=1). Hypertension improved or resolved in 63% of patients with Cushing's syndrome, 56% with aldosteronoma, and 47% with pheochromocytoma. When adrenalectomy was performed for nonfunctioning tumors, neoplasia was identified in 22.9% of patients. The most predictive factors for neoplasia were previous history of cancer and abnormal appearance on computed tomography, magnetic resonance imaging, or positron emission tomography scan.

CONCLUSIONS:

Laparoscopic adrenalectomy is a safe procedure with a low complication rate and short hospital stay. Hypertension improves in the majority of patients with Cushing's syndrome and aldosteronoma and just under the majority of those with pheochromocytoma. In our study, abnormal radiologic appearance was a better predictor of neoplasia than size.

PMID: 25654541  Makale sayfası
Should the diagnostic and therapeutic protocols for adrenal incidentalomas be changed?

[Article in English, Spanish]
Mateo-Gavira I¹, Vilchez-López FJ², Larrán-Escándón L², Ojeda-Schuldt MB², Tinoco CL², Aguilar-Diosdado M².

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Abstract

BACKGROUND:

The prevalence of adrenal incidentalomas is increasing with the aging of the population and the use of high resolution imaging technics. Current protocols propose a comprehensive monitoring of their functional and morphological state, but with no conclusive clinical evidence that endorses it.

METHOD:

Retrospective study of 96 patients diagnosed with adrenal incidentaloma between 2008 and 2012. We evaluated clinical, functional and imaging at baseline and during follow-up.

RESULTS:

Initially, 9 cases were surgically removed: 4 due to hyperfunction (2 Cushing syndromes and 2 pheochromocytomas) and 5 due to size larger than 4cm. During follow-up one case of pheochromocytoma was diagnosed and another grew more than 1cm, needing surgery. In 98.86% of nonfunctional and benign lesions, there was no functional and/or morphological changes in the final evaluation.

CONCLUSIONS:

The results of our study challenge the validity of current diagnostic-therapeutic protocols of incidentalomas, which should be reassessed in prospective studies taking into account efficiency characteristics.

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KEYWORDS:

Adrenal incidentaloma; Adrenalectomy; Adrenalectomía; Cushing syndrome; Feocromocitoma; Incidentaloma suprarrenal; Pheochromocytoma; Síndrome de Cushing

PMID: 25064523
Robot-assisted radical adrenalectomy with clamping of the vena cava for excision of a metastatic adrenal vein thrombus: a case report.

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Author information

1 Department of Urology, OLV Vattikuti Robotic Surgery Institute, Aalst, Belgium.

Abstract

BACKGROUND:

Renal or adrenal neoplastic vein thrombi are relative contra-indications for laparoscopic treatment. To the best of our knowledge, we present the first robot-assisted radical adrenalectomy (RARA) with the presence of a thrombus in the adrenal vein.

METHODS:

A 54 year-old male with a history of laparoscopic left radical nephrectomy for clear cell carcinoma was referred to our department with a diagnosed right adrenal tumour extending into the adrenal vein. A RARA was planned through a trans-peritoneal approach, and an en bloc resection of the adrenal and its vein with clamping of the vena cava was performed.

RESULTS:

Console time was 94 min and the estimated blood loss was 44 ml. The pathology report confirmed clear cell carcinoma with negative surgical margins. Convalescence was uneventful.

CONCLUSION:

RARA with thrombectomy and vascular reconstruction can be safe, effective and feasible in experienced hands, using robotic bulldogs. Copyright © 2015 John Wiley & Sons, Ltd.

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KEYWORDS:

adrenalectomy; robot; vein thrombus

PMID: 25727563  Makale sayfası
Cystic lymphangioma of the adrenal gland: report of a case and review of the literature.

Joliat GR¹, Melloul E, Djafarrian R, Schmidt S, Fontanella S, Yan P, Demartines N, Halkic N.

Author information

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Abstract

BACKGROUND:

Cystic lymphangioma is a rare tumor of the lymphatic vessels that occurs more frequently in women. Location of this pathology can be diverse but most commonly occurs in the neck or axilla. Cystic lymphangioma originating from the adrenal tissue represents a very rare entity.

CASE PRESENTATION:

We report here the case of a 38-year-old woman who was diagnosed with a cystic retroperitoneal mass. After further investigations, the patient was suspected to have a left adrenal cystic lymphangioma. She underwent successful open left adrenalectomy as curative treatment, and the diagnosis of cystic lymphangioma of the left adrenal gland was confirmed at histology. The postoperative course was uneventful.

CONCLUSION:

This case report and review of the literature bring new insights into the diagnostic difficulty and management of cystic lymphangioma of the adrenal gland.

PMID: 5778062
Abstract

INTRODUCTION:

Adrenal cortical carcinoma (ACC) is a very rare type of tumor that generally has a poor prognosis. Little has been reported on repeated liver resections with recurrent metastasis still confined to the liver. In this report, we describe a case of functioning ACC in a 65-year-old woman with 2 liver metastases of the ACC (at 1.5 and 4 years) after the right adrenalectomy.

PRESENTATION OF CASE:

A 65-year-old woman was referred to our hospital based on a suspicion of hyperaldosteronism. Abdominal computed tomography revealed a lesion at the right adrenal gland; therefore, we performed right adrenalectomy and subsequently diagnosed the lesion as ACC. However, follow-up computed tomography at 1.5 and 4 years after the right adrenalectomy revealed liver metastasis of ACC; liver resection was performed for both metastases.

DISCUSSION:

Complete surgical resection is the established approach for the treatment of ACC. The prognosis of ACC is usually dismal, and recurrence rates of up to 85% have been reported. However, the appropriate treatment for recurrent ACC is not well established, and the effectiveness of other modalities, such as chemotherapy and radiotherapy, is not proven. Therefore, surgical resection may currently be the most appropriate treatment modality, as the patient achieved a disease-free interval of 2.5 years after the first liver resection.

CONCLUSION:

In selected patients with recurrent or metastatic ACC, resection is likely to be associated with prolonged survival. However, a full cure is generally not achievable, and a multidisciplinary approach is likely needed to achieve long-term disease-free status and survival.

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KEYWORDS:

Adrenal cortical carcinoma; Liver metastasis; Resection

PMID: 25765741

Makale sayfası


**Aldosterone deficiency after unilateral adrenalectomy for Conn's syndrome: a case report and literature review.**

Yorke E¹, Stafford S², Holmes D³, Sheth S³, Melck A⁴.

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INTRODUCTION:

Approximately 35% of cases of Conn's syndrome (primary aldosteronism) result from a solitary functioning adrenal adenoma, and these patients are best managed by adrenalectomy. Postoperative hypoaldosteronism after unilateral adrenalectomy is uncommon.

CASE PRESENTATION:

We present a case and literature review of hypoaldosteronism after unilateral adrenalectomy for Conn's syndrome, which demonstrates the insidious and sometimes delayed presentation.

DISCUSSION:

In this clinical case we summarize the previously published cases of post-adrenalectomy hypoaldosteronism based on a PUBMED and EBSCOhost search of all peer-reviewed publications (original articles and reviews) on this topic. A few cases of aldosterone insufficiency post-adrenalectomy for Conn's syndrome were identified. The etiological factors for prolonged selective suppression of aldosterone secretion after unilateral adrenalectomy remain unclear.

CONCLUSION:

It is important to be aware of the risk of postoperative hypoaldosteronism in this patient population. Close postoperative follow-up is necessary and strongly recommended, especially in patients with certain risk factors. Patients may need mineralocorticoid supplementation during this period.

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KEYWORDS:

Adrenalectomy; Aldosterone; Conn's; Hypertension; Hypokalemia

PMID: 25604311

**Updating the Surgical Management of Peritoneal Carcinomatosis in Patients with Neuroendocrine Tumors.**

de Mestier L, Lardièrè-Deguelte S, Brix H, O’Toole D, Ruszniewski P, Cadiot G, Kianmanesh R.

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**Abstract**

Well-differentiated digestive neuroendocrine tumors (NET) are a heterogeneous group of neoplasms usually associated with slow growth but a high rate of metastases, including peritoneal carcinomatosis (PC). Herein, we aimed to comprehensively review the current knowledge of PC in terms of implications for the management and prognosis of patients with NET, including the latest studies and expert statements. NET-derived PC concerns about 17% of NET patients and up to 30% of those with small intestine primary NET. It has an independent pejorative prognostic impact. The extent of PC in NET patients and its severity can be expressed by analogy to other malignancies. However, it must be placed in the context of NET disorders, which usually vary from other PC-related malignancies. Recently, a gravity PC score was proposed by a consensus European Neuroendocrine Tumor Society (ENETS) expert group, but it requires validation. In addition, the form of peritoneal involvement (nodular or fusiform/infiltrative) might influence its prognosis and management. Aggressive surgical management seems justified for subsets of NET-related PC but requires careful selection of the candidates most likely to benefit. Cytoreductive surgery prolongs survival, especially when the peritoneal lesions are completely resected. Too little is known about the benefit of hyperthermic intraperitoneal chemotherapy for NET-derived PC, but if it confers an advantage, it would have to be counterbalanced by its high morbidity. © 2015 S. Karger AG, Basel.

PMID: 25592061


**First Surgery for Pancreatic Neuroendocrine Tumors in a Patient with MEN-1: Enucleation vs. Disease-Modifying Surgery.**

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**Abstract**
Pancreatic neuroendocrine tumors (PNETs) are the second most common manifestation of MEN1, affecting up to 80% of patients. The secretion of peptide hormones by PNETs cause clinical syndromes requiring therapeutic intervention. Malignant progression of PNETs is a leading cause of mortality in MEN1 patients. The goal of surgery, when required, is to alleviate a biochemical syndrome or to treat established tumor(s) to reduce the risk of local progression or metastases against the background of preservation of pancreatic function. Determining the need and optimum timing for an operative intervention is complex and requires an approach individualised for each patient. When a clinically significant biochemical syndrome is confirmed the time course to surgery is clear. In patients with a potentially malignant PNET the decision as to when to intervene is more challenging. In all cases surgical treatment carries the potential for harm, of more than usual concern because many of the patients are young. In this article we explain an approach to the surgical treatment of MEN1patients with biochemical or radiological evidence of PNETs where other manifestations of the syndrome are either treated or controlled and the patient lacks co-morbidity that would preclude pancreatic surgery. In each scenario we present, a normal serum gastrin will be assumed as the surgical approach to this usually duodenal manifestation of MEN1 is significantly different to the management of other PNETs. This article is protected by copyright. All rights reserved.

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PMID: 25807996  

Makale sayfası

3.  

Clinical features of pancreatic neuroendocrine tumors.  

Grozinsky-Glasberg S¹, Mazeh H, Gross DJ.  

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Abstract  

Pancreatic neuroendocrine tumors (PNETs), also known as islet cell tumors, are rare neoplasms that arise in the endocrine tissues of the pancreas. Most of pancreatic NETs (50-75%) are nonfunctioning (not associated with a hormonal clinical syndrome); however, in up to one third they can secrete a variety of peptide hormones, including insulin, gastrin, glucagon, vasoactive intestinal peptide, somatostatin etc., resulting in rare but unique clinical syndromes. In this article, the clinical features of the different types of PNETs will be reviewed. Other aspects of the management of these tumors (surgery, treatment of advanced disease, tumor localization) are not dealt with here, as they are covered by other papers in this volume.


KEYWORDS:  

Functioning; Metastatic; Pancreatic neuroendocrine tumors

PMID: 25689919  

Makale sayfası
Determinants of surgical resection for pancreatic neuroendocrine tumors.

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Abstract

Pancreatic neuroendocrine tumors (pNETs) include functioning and non-functional tumors. Functioning tumors consist of tumors that produce a variety of hormones and their clinical effects. Therefore, determinants of resection of pNETs should be discussed for each group of tumors. Less than 10% of insulinomas are malignant, therefore more than 90% of the cases can be cured by surgical resection. Lymphadenectomy is generally not necessary in insulinoma operation. If preoperative localization of the insulinoma is completed, enucleation from the pancreatic body or tail, and distal pancreatectomy can be performed safely by laparoscopy. When preoperative localization of a sporadic insulinoma is not confirmed, surgical exploration is needed. Intraoperative localization of a tumor, intraoperative insulin sampling and frozen section are required. The crucial purpose of surgical resection is to control inappropriate insulin secretion by removing all insulinomas. Gastrinomas are usually located in the duodenum or pancreas, which secrete gastrin and cause Zollinger-Ellison syndrome (ZES). Duodenal gastrinomas are usually small, therefore they are not seen on preoperative imaging studies or endoscopic ultrasound, and can be found only at surgery if a duodenotomy is performed. In addition, lymph node metastasis is found in 40-60% of cases. Therefore, the experienced surgeons should direct operation for gastrinomas. Surgical exploration with duodenotomy should be performed at a laparotomy. Other functioning pNETs can occur in the pancreas or in other locations. Curative resection is always recommended whenever possible after optimal symptomatic control of the clinical syndrome by medical treatment. Indications for surgery depend on clinical symptom control, tumor size, location, extent, malignancy and presence of metastasis. A lot of non-functioning pNETs are found incidentally according to the quality improvement of imaging techniques. Localized, small, malignant non-functioning pNETs should be operated on aggressively, while in possibly benign tumors smaller than 2 cm the surgical risk-benefit ratio should be carefully weighted. Surgical liver resection is generally proposed in curative intent to all patients with operable metastases from G1 or G2 pNET. The benefits of surgical resection of liver metastases have been demonstrated in terms of overall survival and quality of life. Complete resection is associated with better long-term survival.


KEYWORDS:

Distal pancreatectomy; Gastrinoma; Insulinoma; Non-functioning tumor; Pancreaticoduodenectomy

PMID: 25773163  Makale sayfası
Advances in the management of unresectable or metastatic pancreatic neuroendocrine tumors: chemotherapy, targeted therapy, hormonal treatment, and future directions.

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**Abstract**

Pancreatic neuroendocrine tumors (pNETs) are rare and heterogenous tumors and surgery to remove the primary tumor is the mainstay of treatment for resectable disease. However, curative surgery is often not feasible, because half of patients with pNET have metastases at the time of diagnosis. Palliative debulking surgery and liver-directed therapies are appropriate options for these patients. Streptozocin-based regimens are standard, although temozolamide-based treatments are rapidly gaining wide clinical application. Somatostatin analogs are mainly indicated in hormonally active tumors to ameliorate symptoms. In addition, anti-tumoral activity has been proven in well-differentiated NETs. Recently, there has been tremendous progress in the molecular biology of pNETs; thereby, the efficacy of sunitinib and everolimus in the treatment of patients with metastatic pNETs has been proven by large placebo-controlled phase III trials. Currently, there are no definitively proven predictive biomarkers to evaluate response to medical therapies in patients with pNET. Therefore, further studies are needed to individualize and optimize their management. This article reviews systemic chemotherapy, targeted therapies, and anti-secretory treatments for the management of patients with unresectable or metastatic pNETs, summarized in the light of recent advances.

PMID: 25824731

**NONFUNCTIONAL PANCREATIC NEUROENDOCRINE TUMORS: ADVANCES IN DIAGNOSIS, MANAGEMENT AND CONTROVERSIES.**

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**Author information**

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**Abstract**

Objective: In this article, we aimed to review the literature on the clinics and management of nonfunctional pancreatic neuroendocrine tumors (NPNET). Summary of Background Data: Pancreatic neuroendocrine tumors (PNET) are rare tumors with a <1/100,000 incidence and constitute approximately 2-10% of all pancreatic tumors. Nonfunctional PNETs are difficult to detect at early stages since they have no symptoms. Nonfunctional PNETs are difficult to detect at early stages since they have no symptoms. Except those detected accidentally during different diagnoses, the majority of PNETs are detected in the advanced stages, with symptoms related to tumor size or liver metastasis. Methods: We reviewed the studies published in the English medical literature through PubMed and summarized the clinical features
and current approaches to the treatment and follow-up of the NPNET. Results: The common imaging techniques used for the detection of tumor localization, size, locoregional and metastatic involvement are contrasted computed tomography, magnetic resonance imaging, endoscopic ultrasonography and somatostatin receptor scintigraphy. Surgical resection is the only curative treatment. However, in advanced locoregional disease and liver metastasis, interventional ablative therapies such as palliative reductive surgery, selective hepatic arterial embolization, radiofrequency ablation; and systemic therapies such as peptide receptor radionuclide therapy, chemotherapy, somatostatin analogous therapy, interferon, VEGF inhibitor and mTOR inhibitor may be used as symptom relieving or may improve progression-free survival and total survival. Conclusions: Current knowledge on NPNET shows that the treatment should be personalized considering the prognostic features and life expectancy of the patient.

KEYWORDS:
Surgical resection; diagnosis criteria; nonfunctional pancreatic neuroendocrine tumor; treatment options

PMID: 25590518


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Abstract

Pancreatic neuroendocrine tumors (PNETs) are frequent and can be non-functional (NF) in patients with multiple endocrine neoplasia type 1 (MEN1). Their identification is of clinical importance because malignant PNETs are reported to be the most common cause of death in patients with MEN1. Once the diagnosis of MEN1 is established in an individual based on clinical manifestations and/or genetic testing results, an active surveillance program is instituted for early detection and treatment of MEN1-associated disease. Ultrasonography, endoscopic ultrasonography (EUS), CT, MRI, selective arterial angiography and somatostatin receptor scintigraphy are all used for localization of tumors. Managing PNETs can be challenging and includes diagnosis, surveillance, adequate staging, and interdisciplinary, multimodal treatments to optimize patient outcome. Treatment includes surgical resection for loco-regional disease, as well as liver directed and targeted chemotherapies for advanced progressive disease. To date, the recommendation for surgical resection in NF-PNETs is based on tumor size, as a higher rate of metastases was found in patients with larger tumors. This review summarizes key concepts in managing PNETs in patients with MEN1.

KEYWORDS:
Pancreatic neuroendocrine tumors (PNETs); multiple endocrine neoplasia type 1 (MEN1); surgical management

PMID: 25713781
Cystic pancreatic neuroendocrine tumors: outcomes of preoperative endosonography-guided fine needle aspiration, and recurrence during long-term follow-up.

Ridtitid W¹, Halawi H¹, DeWitt JM¹, Sherman S¹, LeBlanc J¹, McHenry L¹, Coté GA¹, Al-Haddad MA².

Abstract

Background and study aims: The role of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in the diagnosis and management of cystic pancreatic neuroendocrine tumors (PNETs) is unclear. We aimed to compare clinical/endosonographic characteristics of cystic with solid PNETs, determine diagnostic accuracy of preoperative EUS-FNA, and evaluate recurrence rates after resection. Patients and methods: All patients with cystic or solid PNET confirmed by EUS-FNA between 2000 and 2014 were identified. A matched case-control study compared 50 consecutive patients with cystic PNETs with 50 consecutive patients with solid PNETs, matched by gender and age at diagnosis of index cystic PNET. We compared clinical/endosonographic characteristics, assessed diagnostic accuracy of preoperative EUS-FNA for identifying malignancy, and analyzed tumor-free survival of patients with cystic and solid PNETs. Results: Cystic PNETs tended to be larger than solid PNETs (mean 26.8 vs. 20.1 mm, P=0.05), more frequently nonfunctional (96% vs. 80%, P=0.03), and less frequently associated with multiple endocrine neoplasia type 1 (10% vs. 28%, P=0.04). With surgical pathology as reference standard, EUS-FNA accuracies for malignancy of cystic and solid PNETs were 89.3% and 90%, respectively; cystic PNETs were less associated with metastatic adenopathy (22% vs. 42%, P=0.03) and liver metastasis (0% vs. 26%, P<0.001). Cystic fluid analysis (n=13), showed benign cystic PNETs had low carcinoembryonic antigen (CEA), Ki-67 ≤2%, and no loss of heterozygosity. Patients with cystic and solid PNETs had similar recurrence risk up to 5 years after complete resection. Conclusions: Cystic PNETs have distinct clinical and EUS characteristics, but were associated with less aggressive biological behavior compared with solid PNETs. EUS-FNA is accurate for determining malignant potential on preoperative evaluation. Despite complete resection, recurrence is observed up to 5 years following surgery.
Exploring the rising incidence of neuroendocrine tumors: a population-based analysis of epidemiology, metastatic presentation, and outcomes.

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Author information

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Abstract

BACKGROUND:

An increased incidence of neuroendocrine tumors (NETs) has been reported worldwide, but the reasons underlying this rise have not been identified. By assessing patterns of metastatic presentation, this study sought to examine the epidemiologic characteristics of NETs and the contribution of early-stage detection to the rising incidence.

METHODS:

A population-based retrospective cohort study was conducted with prospectively maintained databases linked at the Institute for Clinical Evaluative Sciences. Adult patients with a NET diagnosis from 1994 to 2009 in Ontario, Canada were included. The main outcomes included the overall and site-specific incidence, proportion of metastatic disease, overall survival (OS), and recurrence-free survival (RFS).

RESULTS:

Five thousand six hundred nineteen NET cases were identified. The incidence of NETs increased from 2.48 to 5.86 per 100,000 per year. Metastases were found in 20.8% at presentation and in another 38% after the initial diagnosis. The proportion of metastases at presentation decreased from 1994 to 2009 (from 29% to 13%). Therefore, although the incidence of all NETs increased, the overall incidence of metastases did not change (0.63-0.69 per 100,000 per year). The 10-year OS rate was 46.5%, and the RFS rate was 64.6%. In addition to the primary tumor site, independent predictors of worse OS included an advanced age (P < .0001), male sex (P < .0001), a low socioeconomic status (P < .0001), and rural living (P = 0.049).

CONCLUSIONS:

The incidence of NETs has markedly increased over the course of 15 years. This is the first study to provide evidence suggesting that the increase in the incidence of NETs may be due to increased detection. In addition to tumor characteristics, low income and rural residency portend worse survival for patients with NETs.

KEYWORDS:
carcinoid; detection; epidemiology; incidence; neuroendocrine

PMID: 25312765
TNM Staging of Pancreatic Neuroendocrine Tumors: An Observational Analysis and Comparison by Both AJCC and ENETS Systems From 1 Single Institution.


Author information

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Abstract

We aimed to analyze the clinical characteristics and compare the surgical outcome of pancreatic neuroendocrine tumors (p-NETs) using the 2 tumor-node-metastasis (TNM) systems by both the American Joint Committee on Cancer (AJCC) Staging Manual (seventh edition) and the European Neuroendocrine Tumor Society (ENETS). Moreover, we sought to validate the prognostic value of the new AJCC criterion. Data of 145 consecutive patients who were all surgically treated and histologically diagnosed as p-NETs from January 2002 to June 2013 in our single institution were retrospectively collected and analyzed. The 5-year overall survival (OS) rates for AJCC classifications of stages I, II, III, and IV were 79.5%, 63.1%, 15.0%, and NA, respectively, (P < 0.005). As for the ENETS system, the OS rates at 5 years for stages I, II, III, and IV were 75.5%, 72.7%, 29.0%, and NA, respectively, (P < 0.005). Both criteria present no statistically notable difference between stage I and stage II (P > 0.05) but between stage I and stages III and IV (P < 0.05). Difference between stage III and IV by ENETS was significant (P = 0.031), whereas that by the AJCC was not (P = 0.144). What’s more, the AJCC Staging Manual (seventh edition) was statistically significant in both uni- and multivariate analyses by Cox regression (P < 0.005 and P = 0.025, respectively). Our study indicated that the ENETS TNM staging system might be superior to the AJCC Staging Manual (seventh edition) for the clinical practice of p-NETs. Together with tumor grade and radical resection, the new AJCC system was also validated to be an independent predictor for p-NETs.

PMID: 25816036

Surgical resection improves the outcome of the patients with neuroendocrine tumor liver metastases: large data from Asia.


Author information

- 1From the Department of Liver Surgery (SD, ZW, XS, XL, YZ, HX, YX, TC, HZ, SZ, JH, YM); and Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and PUMC, 1# Shuai-Fu-Yuan, Wang-Fu-Jing, Beijing, China (WW, QC).

Abstract

How to properly manage neuroendocrine liver metastasis (NELM) remains debatable, and only limited clinical data have been published from Asian population. The objective of this study is to identify possible prognostic factors affecting overall survival time and to provide a guideline for future clinical practice. A
A retrospective study was performed on 1286 patients who had neuroendocrine tumors in our specialized center, and data from 130 patients who had NELM were summarized. Demographic and clinicopathologic data, tumor grade, treatment method, and prognosis were statistically analyzed. Most of the NELMs originated from pancreas (65.4%). Important prognostic factors that included tumor location and size were identified with multivariate analysis. Patients with either primary tumor resection or liver metastasis resection showed a 5-year survival of 35.7% or 33.3%, respectively, whereas resection of both resulted in a 50% 5-year survival. More importantly, resection was performed on 7 patients with grade 3 (G3) tumors, and resulted in 1-year, 3-year, and 5-year survival of 100%, 42.8%, and 28.6%, respectively, whereas the other 9 G3 patients without resection died within 3 years. P = 0.49 comparing the resected group with nonresected group in G3 patients. Besides, the overall 5-year survival rates for resected and nonresected patients were 40.5% and 5.4%, respectively. Multiple prognostic factors influenced the overall outcome of NELM including patient age, tumor location, and size, etc. Aggressive surgical approaches could be considered for maximum survival time disregarding the pathological grade of the tumor. Study with larger sample size should be considered to reevaluate the recommendation of the WHO guidelines for G3 neuroendocrine tumors.

PMID: 25590842


Octreoscan Versus FDG-PET for Neuroendocrine Tumor Staging: A Biological Approach.


Author information

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Abstract

BACKGROUND:

Clinicians may order Octreoscan or positron emission tomography (PET) scan for staging patients with neuroendocrine tumors (NETs). [¹¹]In-Octreoscan (Octreoscan) identifies tumors by radiolabeled targeting of somatostatin receptors, while 18F-fluorodeoxyglucose-positron emission tomography (¹⁸FDG-PET) measures differential tissue glucose transport. We assessed the sensitivity of both nuclear imaging modalities with pathologic correlation to define the best initial choice for NET staging after standard cross-sectional imaging.

METHODS:

We identified all patients diagnosed with NETs of gastrointestinal or pancreatic origin who underwent nuclear imaging staging by Octreoscan and/or PET from 2000 to 2013. Imaging results were correlated with tumor differentiation and grade of pathology specimens.

RESULTS:

Imaging and pathology results were identified for 153 patients. Of these, 131 underwent Octreoscan, 43 underwent PET, and 21 patients had both performed. Overall sensitivity of Octreoscan and PET for NET detection was similar (77 vs. 72 %; p = not significant). For well-differentiated NETs, Octreoscan (n = 124)
demonstrated sensitivity of 80 vs. 60 % (p = 0.28) for PET (n = 30). For poorly-differentiated NETs, Octreoscan (n = 7) proved significantly less sensitive than PET (n = 13) (57 vs. 100 %; p = 0.02). The sensitivity of Octreoscan versus PET varied similarly when analyzed by WHO tumor grade: Grade 1 (79 vs. 52 %; p = 0.16), Grade 2 (85 vs. 86 %; p = not significant), and Grade 3 (57 vs. 100 %; p = 0.02).

CONCLUSIONS:

Tumor differentiation can be used to guide selection of nuclear imaging modalities for staging gastrointestinal and pancreatic NETs. Octreoscan appears more sensitive than 18FDG-PET for well-differentiated NETs, whereas 18FDG-PET demonstrates superior sensitivity for poorly-differentiated NETs.

PMID: 25786743


Surgical management of advanced pancreatic neuroendocrine tumors: short-term and long-term results from an international multi-institutional study.

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Abstract

BACKGROUND:

The role of extended resections in the management of advanced pancreatic neuroendocrine tumors (PNETs) is not well defined.

METHODS:

Between 1995 and 2012, 134 patients with PNET underwent isolated (isoPNET group: 91 patients) or extended pancreatic resection (synchronous liver metastases and/or adjacent organs) (advPNET group: 43 patients).

RESULTS:

The associated resections included 27 hepatectomies, 9 vascular resections, 12 colectomies, 10 gastrectomies, 4 nephrectomies, 4 adrenalectomies, and 3 duodenojejunal resections. R0 was achieved in 41 patients (95%) in the advPNET. The rates of T3-T4 (73 vs 16%; p < .0001) and N+ (35 vs 13%; p = .007) were higher in the advPNET group. Mortality (5 vs 2%) and major morbidity (21 vs 19%) rates were similar between the 2 groups. The 5-year overall survival (OS) of the series was 87% in the isoPNET group and 66% in the advPNET group (p = .006). Only patients with both locally advanced disease and liver metastases showed worse survival (p = .0003). The advPNET group developed recurrence earlier [disease-free survival (DFS) at 5 years: 26 vs 81%; p < .001]. In univariate analysis, negative prognostic factors of survival were: poor degree of differentiation (p < .001), liver metastasis (p = .011), NEC carcinoma (p < .001), and resection of adjacent organs (p = .013). The multivariate analysis did not highlight any factor that influenced OS. In multivariate analysis independent DFS factors were a poor degree of differentiation (p = .03) and the European Neuroendocrine Tumor Society stage (p = .01).
CONCLUSIONS:
An aggressive surgical approach for locally advanced or metastatic tumors is safe and offers long-term survival.

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Clinical management of patients with gastric neuroendocrine neoplasms associated with chronic atrophic gastritis: a retrospective, multicentre study.

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Abstract
To provide data regarding clinical presentation, pathological features, management, and response to different treatments of patients with type I gastric neuroendocrine tumors in stages 0-2A. The study design consist of an Italian multicentre, retrospective analysis of patients with type I gastric neuroendocrine tumors managed with different therapeutic approaches: surgery, endoscopic surveillance, endoscopic resection, or somatostatin analog therapy. Among the 97 patients included, 3 underwent surgery, 45 (46.4 %) radical endoscopic resection of the neoplastic lesions, 13 (13.4 %) follow-up with upper endoscopy, and 36 (37.1 %) somatostatin analog therapy. At the end of the follow-up, all patients were alive and there was no evidence of metastatic disease. Somatostatin analog therapy resulted in a complete response in 76.0 % of the patients and stable disease in 24.0 %. A prolonged period of therapy, the use of a full dose of somatostatin analogs and higher gastrin levels at diagnosis were related to a complete response to the therapy. The recurrence rate was 26.3 % in patients treated with somatostatin analog therapy and 26.2 % in patients treated with endoscopic resection, without a statistically significant difference in terms of disease-free survival. Regarding recurrence of the disease, no statistical difference was found according to type of therapy, number of neoplastic lesions, and 2010 WHO classification. The only risk factor for tumor recurrence was a short period of medical treatment. In conclusion, our study suggested that endoscopic surveillance, endoscopic resection and somatostatin analog therapy represent valid options in the management of patients with type I gastric neuroendocrine tumors in stages 0-2A.

PMID: 25814125


Surgical resection provides an overall survival benefit for patients with small pancreatic neuroendocrine tumors.
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Abstract

BACKGROUND:

The optimal management of small (≤2 cm) pancreatic neuroendocrine tumors (PNETs) remains controversial. We evaluated these tumors in the National Cancer Data Base (NCDB) to determine if resection provides a survival advantage over observation.

METHODS:

The NCDB was queried to identify patients with nonmetastatic PNETs ≤2 cm treated between 1998 and 2006. Kaplan-Meier survival estimates, stratified by grade and treatment type, evaluated the difference in 5-year overall survival (OS) between patients who underwent resection and observation. Multivariable Cox regression was used to determine the importance of resection in OS.

RESULTS:

Three hundred eighty patients met inclusion criteria. Eighty-one percent underwent resection; 19% were observed. Five-year OS was 82.2% for patients who underwent surgery and 34.3% for those who were observed (p < 0.0001). When controlling for age, comorbidities, income, facility type, tumor size and location, grade, margin status, nodal status, surgical management, and nonsurgical therapy in the Cox model, observation [hazard ratio (HR) 2.80], poorly differentiated histology (HR 3.79), lymph node positivity (HR 2.01), and nonsurgical therapies (HR 2.23) were independently associated with an increase in risk of mortality (p < 0.01).

CONCLUSION:

Patients with localized PNETs ≤2 cm had an overall survival advantage with resection compared to observation, independent of age, comorbidities, tumor grade, and treatment with nonsurgical therapies.

PMID: 25155459

Surgical therapy of neuroendocrine neoplasm with hepatic metastasis: patient selection and prognosis.


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PATIENTS AND METHODS:

In a retrospective single-center study (1990 to 2014), 204 patients with hepatic metastasis of NEN were included. Ninety-four were subjected to various forms of liver resection. According to the overall survival, the influence of several prognostic factors like the Ki-67 index, stage of disease, and resection status was evaluated.

RESULTS:

The primary tumor was located in the small intestine (n = 73), pancreas (n = 58), colon (n = 26), esophagus or stomach (n = 9) and in 38 patients the primary site was unknown. The Ki-67 index was associated with significant different overall survival. Patients with an R0 resection (n = 38) of their hepatic metastasis had a very good 10-year survival of 90.4 %. Patients in whom an R1 (n = 23) or R2 (n = 33) resection of their hepatic metastasis could be achieved had a 10-year survival of 53.4 and 51.4 %, respectively. The majority of the patients (53.9 %) could not be resected and had a poor 10-year survival rate of 19.4 %. Partial or complete control of endocrine-related symptoms was achieved in all patients with functioning tumors following surgery. The overall 5- and 10-year survival rates were 77.9 and 65.2 %, respectively.

CONCLUSION:

Surgical resection of hepatic NEN metastases can reduce symptoms and improve the survival in selected patients with a Ki-67 index less than 20 %. The expected outcome has to be compared to the outcome of alternative treatment strategies. An R0 situation should be the aim of hepatic surgery, but also patients with R1 or R2 resection show a good survival benefit.

PMID: 25682055
Sunitinib achieved fast and sustained control of VIPoma symptoms.

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Abstract

VIPomas are rare-functioning neuroendocrine tumors (NETs). Overproduction of vasointestinal peptide (VIP) leads to the Verner-Morrison syndrome, whose management is challenging when refractory to somatostatin analogs. Two patients with progressive metastatic pancreatic NETs and refractory VIPoma symptoms were treated with sunitinib. This led to fast and sustained total relief of VIPoma symptoms, enabling earlier discharge from hospital and improvement in their quality of life. In both cases, sunitinib discontinuation led to the quick recurrence of watery diarrhea, which resolved within a few days after reintroducing sunitinib. The anti-secretory effect of sunitinib on VIPoma syndrome was probably not related to any anti-tumor effect. These observations agree with the rare reported cases of anti-secretory effects with targeted therapies. The sunitinib-driven inhibition of multiple-tyrosine kinase receptors might act on secretory pathways and describe sunitinib's ability to improve VIPoma symptoms. Sunitinib could be a therapeutic option to control refractory VIPoma symptoms in patients with NETs.

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