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Molecular Pathology of Hereditary and Sporadic Medullary Thyroid Carcinomas.

Chernock RD¹, Hagemann IS².

Abstract

OBJECTIVES:
Medullary thyroid carcinoma (MTC) is a relatively uncommon type of thyroid malignancy, with unique histologic features and molecular pathology. It is important to recognize, because its management, which is in part driven by the genetic basis of this disease, is different from follicular-derived thyroid tumors. The aim of this article is to briefly review the histopathologic features of MTC and then explore its molecular pathology, including the role of molecular diagnostic testing and the use of targeted therapy for advanced disease.

METHODS:
A review of published literature was performed.

RESULTS:
A subset of MTC cases is hereditary and due to germline mutations in the RET tyrosine kinase receptor gene. Somatic mutations in either RET or RAS are also present in most sporadic tumors.

CONCLUSIONS:
Molecular genetic testing is routinely performed to identify hereditary cases. In addition, understanding the molecular basis of both hereditary and sporadic MTC has led to the development of targeted therapy with tyrosine kinase inhibitors. Although additional data are needed, tumor mutation status may affect response to targeted therapy. Therefore, it is possible that genetic testing of tumor tissue to predict treatment response, as is currently done for other cancer types, may come into practice in the future.

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KEYWORDS:
Familial medullary thyroid carcinoma; Medullary thyroid carcinoma; Multiple endocrine neoplasia; RAS; RET; Tyrosine kinase

PMID: 25972318

Total thyroidectomy versus lobectomy as initial operation for small unilateral papillary thyroid carcinoma: A meta-analysis.

Macedo FI¹, Mittal VK².

Abstract
INTRODUCTION:
Consensus guidelines have recommended total thyroidectomy for papillary thyroid carcinoma (PTC) > 1 cm. However, the optimal surgical approach for small and unilateral (≤1 cm) PTC remains controversial.

METHODS:
A meta-analysis was performed using MEDLINE and EMBASE databases to identify all studies investigating at thyroid surgery options, total thyroidectomy (TT) versus thyroid lobectomy (TL), for PTC ≤ 1 cm. The primary endpoints were locoregional recurrence and mortality rates.

RESULTS:
The initial literature search identified 305 publications (1980-2014). Six studies met the inclusion criteria comprising 2939 patients (2002-2013). Among these patients, 2134 (72.6%) underwent TT and 805 (27.4%) underwent TL. Mean follow-up was 10.9 ± 3.4 years (range, 1 month to 54 years). Overall, the recurrence rate was 5.4%: 4.4% in the TT group and 8.3% in the TL group (p < 0.001; RR 0.50, 95% CI 0.37-0.67). The mortality rates were 0.3% (8 cases) versus 1.1% (9 cases) in TT and TL groups, respectively (p = 0.14; RR 0.43, 95% CI 0.17-1.09).

CONCLUSION:
TT was associated with lower recurrence rates, possibly due to a more complete nodal dissection of the central neck compartment at the time of initial surgery. Based on these data, it is unclear to establish a definitive correlation between the extent of thyroid resection and long-term survival rates due to the small number of mortality events. However, there is a trend toward lower mortality rates in the TT group. Other factors need to be taken into consideration while planning thyroid resection for small PTC, such as multifocality, locoregional involvement, mode of presentation and age at diagnosis. Refinement of current guidelines for the optimal surgical management of PTC <1 cm may be warranted.

KEYWORDS:
Lobectomy; Mortality; Papillary thyroid cancer; Recurrence; Total thyroidectomy

PMID: 25956302 Makale sayfası


Li Y1, Jian WH2, Guo ZM3, Li QL1, Lin SJ4, Huang HY5.

Author information
Abstract
OBJECTIVE:
To investigate the ability of carbon nanoparticles (CNs) to identify lymph nodes and protect parathyroid glands during thyroid cancersurgery.

DATA SOURCES:
English and Chinese literature in PubMed, ClinicalTrials.gov, EMBASE, the Cochrane Database of Systematic Reviews, the China Biology Medicine Database, the China Master's and Doctoral Theses Full-Text Database, the China National Knowledge Infrastructure, the WANGFANG database, and the Cqvip database (from January 2009 to July 2014).

REVIEW METHODS:
Studies were included if they were randomized controlled trials or nonrandomized controlled trials for thyroidectomy and central neck dissections that compared the use of CNs with methylene blue or a blank
control in patients undergoing initial thyroid cancer surgery. The primary outcomes were the number of retrieved central lymph nodes and the accidental parathyroid removal rate.

RESULTS:
This meta-analysis identified 11 randomized controlled trials and 4 nonrandomized controlled trials comprising 1055 patients. Compared with the outcomes of the blank controls, the use of CNs resulted in an average of 2.71 more lymph nodes removed per patient (weighted mean difference = 2.71, 95% confidence interval [CI] = 1.68-3.74, P < .001), a 23% lower rate of accidental parathyroid removal (odds ratio = 0.23, 95% CI = 0.10-0.54, P = .0008), and similarly reduced rates of transient hypoparathyroidism and hypocalcemia. Compared with methylene blue, the use of CNs resulted in an average of 1.50 more lymph nodes removed per patient (weighted mean difference = 1.50, 95% CI = 0.11-2.89, P = .03) and a 5% reduction in the rate of accidental parathyroid removal (odds ratio = 0.05, 95% CI = 0.01-0.29, P = .0007).

CONCLUSION:
CNs partially improve the extent and accuracy of neck dissection and preserve the normal anatomic structure and physiologic function of the parathyroid glands during thyroid cancer surgery.


KEYWORDS:
carbon nanoparticles; lymph node; methylene blue; parathyroid; thyroid cancer

PMID: 25897006


Qualitative elastography can replace thyroid nodule fine-needle aspiration in patients with soft thyroid nodules. A systematic review and meta-analysis.

Nell S1, Kist JW1, Debray TP2, de Keizer B3, van Oostenbrugge TJ1, Borel Rinkes IH1, Valk GD4, Vriens MR5.

Author information
Abstract
CONTEXT:
Only a minority of thyroid nodules is malignant; nevertheless, many invasive diagnostic procedures are performed to distinguish between benign and malignant nodules. Qualitative ultrasound elastography is a non-invasive technique to evaluate thyroid nodules.

OBJECTIVE:
To investigate the diagnostic value of qualitative elastography in distinguishing benign from malignant thyroid nodules in patients referred for fine-needle aspiration (FNA).

DATA SOURCES:
A systematic literature search (PubMed, Embase and Cochrane Library) was performed.

STUDY SELECTION:
Included studies reported thyroid nodule elastography color scores and the related cytologic or histologic findings in patients with a thyroid nodule referred for FNA.

DATA EXTRACTION:
Two independent reviewers extracted study data and assessed study quality. Pooled sensitivities and specificities of different populations were calculated using a bivariate Bayesian framework.

DATA SYNTHESIS:
Twenty studies including thyroid nodules were analyzed. Pooled results of elastography indicate a summary sensitivity of 85% (95% confidence interval [CI], 79-90%) and specificity of 80% (95% CI, 73-86%). The respective pooled negative predictive and positive predictive values were 97% (95% CI, 94-98%) and 40% (95% CI, 34-48%). The pretest probability of a benign nodule was 82%. Only 3.7% of the false-negative nodules was a follicular thyroid carcinoma. A pooled negative predictive value of 99% (95% CI, 97-100%) was found when only complete soft nodules (Asteria elastography 1) were classified as benign, which included 14% of the studied population.

CONCLUSIONS:
Elastography has a fair specificity and sensitivity for diagnostic accuracy. Its major strength entails the detection of benignity, especially when only completely soft nodules are qualified as benign. The outcomes of our analysis show that FNA could safely be omitted in patients referred for analysis of their thyroid nodule when elastography shows it to be completely soft (Asteria elastography 1). This could prevent unnecessary invasive diagnostic procedures in a substantial portion of patients.

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KEYWORDS:
Elastography; Fine-needle aspiration; Malignancy; Meta-analysis; Review; Thyroid nodule; Ultrasound

PMID: 25638577 Makale sayfası


Targeted therapy: a new hope for thyroid carcinomas.
Perri F¹, Pezzullo L², Chiofalo MG², Lastoria S³, Di Gennaro F², Scarpati GD⁴, Caponigro F⁵.

Author information

Abstract
Thyroid carcinomas are rare and heterogeneous diseases representing less than 1% of all malignancies. The majority of thyroid carcinomas are differentiated entities (papillary and follicular carcinomas) and are characterized by good prognosis and good response to surgery and radioiodine therapy. Nevertheless, about 10% of differentiated carcinomas recur and become resistant to all therapies. Anaplastic and medullary cancers are rare subtypes of thyroid cancer not suitable for radioiodine therapy. A small percentage of differentiated and all the anaplastic and medullary thyroid carcinomas often recur after primary treatments and are no longer suitable for other therapies. In the last years, several advances have been made in the field of molecular biology and tumorigenesis mechanisms of thyroid carcinomas. Starting from these issues, the targeted therapy may be employed as a new option. The MAP-Kinase pathway has been found often dysregulated in thyroid carcinomas and several upstream signals have been recognized as responsible for this feature. RET/PTC mutations are often discovered both in papillary and in medullary carcinomas, while B-RAF mutation is typical of papillary and anaplastic histologies. Also mTOR disruptions and VEGFR pathway disruption are common features in all advanced thyroid cancers. Some angiogenesis inhibitors and a number of RET/PTC pathway blocking agents are yet present in the clinical armamentarium. Vandetanib, cabozatinib and sorafenib have reached clinical use. A number of other biological compounds have been tested in phase II and III trials. Understanding the biology of thyroid cancers may help us to design a well shaped targeted therapy.

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KEYWORDS:
Anaplastic; Follicular; Medullary; Papillary; Pathway; Radioiodine therapy; Targeted therapy; Thyroid carcinoma
Thyroid incidentalomas on PET imaging--evaluation of management and clinical outcomes.

Elzein S¹, Ahmed A², Lorenz E³, Balasubramanian SP².

Abstract

OBJECTIVES: 1. To determine the incidence of 'thyroid incidentaloma' in patients undergoing PET/CT in Sheffield. 2. To assess the distribution of cancer type, stage and short term outcomes of incidentally detected thyroid cancer in this cohort.

METHODOLOGY: Patients with an unexpected thyroid radio-isotope uptake on reports of whole body nuclear imaging performed in Sheffield Teaching Hospitals NHS Foundation Trust for 'non-thyroid' indications from April 2008 to March 2011 were identified. Patients who have undergone PET imaging were then selected. The management, clinical and pathology details and short term 'thyroid-related' outcomes of patients with thyroid incidentaloma on PET scans were analysed.

RESULTS: 1730 PET nuclear imaging studies were performed in this period. Thyroid incidentalomas were detected in 65 (3.8%) of these scans. Two thyroid cancers were detected in this cohort, both demonstrated focal uptake on the PET scan. Histology showed papillary thyroid cancer (TNM classification; pT1N1Mx and pT1bNxMx).

CONCLUSION: The risk of cancer in PET detected thyroid incidentaloma in this series (3%) is low compared to published literature (5-50%). Potential reasons are discussed. The low rate of thyroid cancer in our incidentaloma cohort will influence decision making regarding management of these lesions. Only two thyroid cancers were detected in our cohort, limiting the narrative on type, stage of PET detected thyroid cancer and outcomes. Further observational research is required to study the natural history of these lesions in settings where there is a clear protocol for imaging, biopsy and treatment.

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KEYWORDS: Incidentaloma; Nuclear imaging; PET CT; Thyroid

Rapidly enlarging neck masses of the thyroid with Horner's syndrome: a concise clinical review.

Donaldson JF¹, Rodriguez-Gomez IA², Parameswaran R³.

Abstract

BACKGROUND:
Horner's syndrome (HS) presenting with a neck mass is a rare but challenging clinical scenario which may be caused by malignant thyroid disease.

METHODS:
A concise review of the literature (PubMed database; 1990-2013) on the clinical management of neck masses with HS. An example case is also discussed.

RESULTS:
1.3% of HS is caused by thyroid pathology. Thyroid pathology is the commonest cause of a neck mass associated with HS: the majority are caused by benign pathology; with carcinoma and lymphoma accounting for the remainder. Anaplastic thyroid carcinoma (ATC), thyroid lymphoma (TL) and thyroid sarcoma (TS) typically present with rapidly enlarging anterior neck masses in the elderly and are difficult to distinguish clinically. Although fine needle aspirate cytology (FNAC) is the diagnostic tool of choice for thyroid masses, core or incisional biopsy may be necessary when FNAC is inconclusive.

CONCLUSION:
Differentiation between ATC, TL and TS is imperative as their treatment and prognoses differ greatly. Where feasible a combination of surgical debulking, radiotherapy and chemotherapy is the treatment of choice in ATC. Advanced cases benefit from 2 monthly endoscopic surveillance ± tracheostomy, stenting or Nd-YAG laser therapy. Aggressive oncological resection alone is recommended in TS. Treatment regimes in thyroid lymphoma (typically chemotherapy ± radiotherapy) differ for histological sub-types. 5-year failure-free survival is 90% in TL compared with a mean survival of 6-8 months in ATC and 10 months in TS.

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KEYWORDS:
Anaplastic thyroid carcinoma; Hodgkin's lymphoma; Horner's syndrome; Recurrent laryngeal nerve palsy; Sarcoma; Thyroid neoplasm

PMID: 25073932

Should small papillary thyroid cancer be observed? A population-based study.

Nilubol N1, Kebebew E.
Author information
Abstract
BACKGROUND:
Some centers have advocated selecting patients with small papillary thyroid cancer (PTC) to undergo active surveillance without surgical treatment. The objectives of the current study were to analyze thyroid cancer (TC)-related mortality in a population-based cohort and to determine the impact of small PTCs (defined as tumors ≤ 2 cm in greatest dimension) on TC-related mortality.

METHODS:
Data on patients with TC of follicular cell origin from the National Cancer Institute's Surveillance, Epidemiology, and End Results 17 Registries database (1988-2007) were used to analyze the characteristics of PTCs ≤ 2 cm in patients who died from TC-related causes. The effects of clinical features on disease-specific survival were analyzed.

RESULTS:
Over the 20-year study period, the rate of TC-related mortality was 2.8% (n = 1753 of 61,523 patients). Of the patients who died from TC-related causes, 38% had PTC, 10% had follicular TC, and 31.3% had anaplastic TC. PTCs ≤ 2 cm accounted for 12.3% of TC-related mortalities. Compared with patients who did not experience TC-related mortality from PTCs ≤ 2 cm, there were significantly higher rates of men (30% vs 17%; P < .01), patients aged ≥ 45 years (92% vs 52%; P < .01), tumors measuring >1 cm (59% vs 46%; P < .01), extrathyroid extension (41% vs 11%; P < .01), lymph node metastases (77% vs 28%; P < .01), and distant metastases (31% vs 1%; P < .01) among the patients who died from PTCs ≤ 2 cm. Independent risk factors for death from PTCs ≤ 2 cm included age ≥ 45 years, lymph node and distant metastases, extrathyroid extension, and undergoing less than thyroid lobectomy.

CONCLUSIONS:
Because 12.3% of patients who experienced TC-related deaths had PTCs ≤ 2 cm despite undergoing thyroidectomy, the current results indicate that nonoperative management for patients who have PTCs ≤ 2 cm should be used with caution. Patients aged ≥ 45 years with PTCs ≤ 2 cm should undergo thyroidectomy.

Published 2014. This article is a U.S. Government work and is in the public domain in the USA.

KEYWORDS:
Surveillance, Epidemiology, and End Results Program; cancer-specific survival; mortality; prognostic factor; thyroid cancer

PMID: 25425528


Identifying the most appropriate age threshold for TNM stage grouping of well-differentiated thyroid cancer.

Hendrickson-Rebizant J¹, Sigvaldason H¹, Nason RW¹, Pathak KA².

Author information

Abstract

OBJECTIVE:
Age is integrated in most risk stratification systems for well-differentiated thyroid cancer (WDTC). The most appropriate age threshold for stage grouping of WDTC is debatable. The objective of this study was to evaluate the best age threshold for stage grouping by comparing multivariable models designed to evaluate the independent impact of various prognostic factors, including age based stage grouping, on the disease specific survival (DSS) of our population-based cohort.

METHODS:
Data from population-based thyroid cancer cohort of 2125 consecutive WDTC, diagnosed during 1970-2010, with a median follow-up of 11.5 years, was used to calculate DSS using the Kaplan Meier method. Multivariable analysis with Cox proportional hazard model was used to assess independent impact of different prognostic factors on DSS. The Akaike information criterion (AIC), a measure of statistical model fit, was used to identify the most appropriate age threshold model. Delta AIC, Akaike weight, and evidence ratios were calculated to compare the relative strength of different models.

RESULTS:
The mean age of the patients was 47.3 years. DSS of the cohort was 95.6% and 92.8% at 10 and 20 years respectively. A threshold of 55 years, with the lowest AIC, was identified as the best model. Akaike weight indicated an 85% chance that this age threshold is the best among the compared models, and is 16.8 times more likely to be the best model as compared to a threshold of 45 years.
CONCLUSION:
The age threshold of 55 years was found to be the best for TNM stage grouping.

KEYWORDS:
Outcome; Prognosis; Risk stratification; Staging; Survival; Thyroid carcinoma

PMID: 25986855  Makale sayfası


Management of recurrent and persistent metastatic lymph nodes in well-differentiated thyroid cancer: a multifactorial decision-making guide for the thyroid cancer care collaborative.


Author information

Abstract

BACKGROUND:
Well-differentiated thyroid cancer (WDTC) recurs in up to 30% of patients. Guidelines from the American Thyroid Association (ATA) and the National Comprehensive Cancer Network (NCCN) provide valuable parameters for the management of recurrent disease, but fail to guide the clinician as to the multitude of factors that should be taken into account. The Thyroid Cancer Care Collaborative (TCCC) is a web-based repository of a patient's clinical information. Ten clinical decision-making modules (CDMMs) process this information and display individualized treatment recommendations.

METHODS:
We conducted a review of the literature and analysis of the management of patients with recurrent/persistent WDTC.

RESULTS:
Surgery remains the most common treatment in recurrent/persistent WDTC and can be performed with limited morbidity in experienced hands. However, careful observation may be the recommended course in select patients. Reoperation yields biochemical remission rates between 21% and 66%. There is a reported 1.2% incidence of permanent unexpected nerve paralysis and a 3.5% incidence of permanent hypoparathyroidism. External beam radiotherapy and percutaneous ethanol ablation have been reported as therapeutic alternatives. Radioactive iodine as a primary therapy has been reported previously for metastatic lymph nodes, but is currently advocated by the ATA as an adjuvant to surgery.

CONCLUSION:
The management of recurrent lymph nodes is a multifactorial decision and is best determined by a multidisciplinary team. The CDMMs allow for easy adoption of contemporary knowledge, making this information accessible to both patient and clinician.

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KEYWORDS:
clinical decision-making modules (CDMMs); persistent thyroid cancer; recurrent thyroid cancer; reoperation; thyroid cancer care collaborative (TCCC)

PMID: 24436291  Makale sayfası
Presence and Number of Lymph Node Metastases Are Associated With Compromised Survival for Patients Younger Than Age 45 Years With Papillary Thyroid Cancer.

Adam MA¹, Pura J¹, Goffredo P¹, Dinan MA¹, Reed SD¹, Scheri RP¹, Hyslop T¹, Roman SA¹, Sosa JA².

Abstract

PURPOSE:
Cervical lymph node metastases are recognized as a prognostic indicator only in patients age 45 years or older with papillary thyroid cancer (PTC); patients younger than age 45 years are perceived to have low-risk disease. The current American Joint Committee on Cancer staging for PTC in patients younger than age 45 years does not include cervical lymph node metastases. Our objective was to test the hypothesis that the presence and number of cervical lymph node metastases have an adverse impact on overall survival (OS) in patients younger than age 45 years with PTC.

PATIENTS AND METHODS:
Adult patients younger than age 45 years undergoing surgery for stage I PTC (no distant metastases) were identified from the National Cancer Data Base (NCDB; 1998-2006) and from SEER 1988-2006 data. Multivariable models were used to examine the association of OS with the presence of lymph node metastases and number of metastatic nodes.

RESULTS:
In all, 47,902 patients in NCDB (11,740 with and 36,162 without nodal metastases) and 21,855 in the SEER database (5,188 with and 16,667 without nodal metastases) were included. After adjustment, OS was compromised for patients with nodal metastases compared with patients who did not have them (NCDB: hazard ratio (HR), 1.32; 95% CI, 1.04 to 1.67; P = .021; SEER: HR, 1.29; 95% CI, 1.08 to 1.56; P = .006). After adjustment, increasing number of metastatic lymph nodes was associated with decreasing OS up to six metastatic nodes (HR, 1.12; 95% CI, 1.01 to 1.25; P = .03), after which more positive nodes conferred no additional mortality risk (HR, 0.99; 95% CI, 0.99 to 1.05; P = .75).

CONCLUSION:
Our results suggest that cervical lymph node metastases are associated with compromised survival in young patients, warranting consideration of revised American Joint Committee on Cancer staging. A change point of six or fewer metastatic lymph nodes seems to carry prognostic significance, thus advocating for rigorous preoperative screening for nodal metastases.

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PMID: 26077238

American Thyroid Association Statement on Surgical Application of Molecular Profiling for Thyroid Nodules: current impact on perioperative decision-making.

Ferris RL¹, Baloch ZW², Bernet V³, Chen A⁴, Fahey T 3rd⁵, Ganly I⁶, Hodak S⁷, Kebebew E⁸, Patel KN⁹, Shaha AR Md¹¹, Steward D¹², Tufano RP¹³, Wiseman S¹⁴,¹⁵, Carty SE¹⁶,¹⁷.

Abstract

BACKGROUND:
Recent advances in research on thyroid carcinogenesis have yielded applications of diagnostic molecular biomarkers and profiling panels in the management of thyroid nodules. The specific utility of these novel, clinically available molecular tests is becoming widely appreciated, especially in perioperative decision-making by the surgeon regarding the need for surgery and the extent of initial resection.

**METHODS:**
A task force was convened by the Surgical Affairs Committee of the American Thyroid Association and was charged with writing this article.

**RESULTS/CONCLUSIONS:**
This review covers the clinical scenarios by cytologic category for which the thyroid surgeon may find molecular profiling results useful, particularly for cases with indeterminate fine needle aspiration (FNA) cytology. Distinct strengths of each ancillary test are highlighted to convey the current status of this evolving field, which has already demonstrated potential to streamline decision making and reduce unnecessary surgery, with the accompanying benefits. However, the performance of any diagnostic test, i.e. its positive predictive value (PPV) and negative predictive value (NPV), are exquisitely influenced by the prevalence of cancer in that cytologic category, which is known to vary widely at different medical centers. Thus, it is crucial for the clinician to know the prevalence of malignancy within each indeterminate cytologic category, at one’s own institution. Without this information, the performance of the diagnostic tests discussed below may vary substantially.

PMID: 26058403
Detection of BRAF mutations on direct smears of thyroid fine-needle aspirates through cell transfer technique.

Shi Q¹, Ibrahim A¹, Herbert K¹, Carvin M¹, Randolph M¹, Post KM¹, Curless K¹, Chen S¹, Cramer HM², Cheng L³, Wu HH².

Abstract

OBJECTIVES: To determine the utility of the cell transfer technique (CTT) for BRAF molecular testing on thyroid fine-needle aspiration (FNA) specimens.

METHODS: Polymerase chain reaction (PCR)-based BRAF molecular testing was performed on tissues obtained through CTT from both air-dried and ethanol-fixed direct smears of thyroid FNA specimens and then compared with the corresponding thyroidectomy formalin-fixed, paraffin-embedded (FFPE) tissues on 30 cases.

RESULTS: BRAF testing was successfully performed on 29 of 30 air-dried CTT, 27 of 30 ethanol-fixed CTT, and 27 of 30 FFPE tissues. The results exhibited 11, 13, and 13 BRAF mutations and 18, 14, and 14 wild types for the air-dried CTT, the ethanol-fixed CTT, and the FFPE tissues, respectively. The concordance rate was 96% between air-dried and ethanol-fixed CTT tissues, 88% between air-dried CTT and FFPE tissues, and 92% between ethanol-fixed CTT and FFPE tissues.

CONCLUSIONS: PCR-based BRAF mutational testing can be reliably performed on the direct smears of the thyroid FNA specimens through the application of CTT.

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KEYWORDS: BRAF mutation; Cell transfer; Cytology; Molecular; Thyroid

PMID: 25780001 Makale sayfası

Multiple thyroid nodules in the lung: metastasis or ectopia?

Cheng H¹, Yang L², Xiong J³, Peng J⁴, Ruan Q⁵.

Abstract

BACKGROUND: Intrapulmonary thyroid tissue with no malignant history of the thyroid gland is extremely rare. Usually, it is interpreted as ectopic thyroid tissue. Here we describe a case of bilateral pulmonary thyroid nodules with a history of multinodular thyroid goiter.
HISTORY:
A 37-year-old female had recurrent multinodular thyroid goiter and showed bilateral pulmonary nodules on CT scan. Video-assisted thoracic surgery (VATS) was performed for the largest nodule biopsy. Pathological and molecular examinations were done after biopsy, and both were shown the characters of benign thyroid tissues. To eliminate the possibility of thyroid carcinoma metastases, total thyroidectomy with modified radical neck dissection was performed, and there were no malignant pathological findings. After surgery, this patient accepted adjuvant radiometabolic treatment for ablation of the remaining intrapulmonary nodules. Her thyroglobulin level decreased to an undetectable level, and she has currently survived for 24 months after surgery.

CLINICAL SIGNIFICANCE:
In this case, pulmonary ectopic thyroid and metastasizing thyroid carcinoma should both be considered, but the metastatic pattern and benign pathological characters were inconsistent with any of the corresponding diagnosis. Ultimately, this patient accepted postoperative treatment of thyroid carcinoma metastasis.

CONCLUSIONS:
This is a rare thyroid disease with malignant behavior but no pathological evidence. Careful diagnosis and postoperative follow-up should be carried out whenever such nodules are encountered in clinical practice.

VIRTUAL SLIDES:
The virtual slide(s) for this article can be found here:

PMID: 26047938 Makale sayfasi

Impact of Positional Changes in Neural Monitoring Endotracheal Tube on Amplitude and Latency of Electromyographic Response in Monitored Thyroid Surgery - Results from the Porcine Experiment.


Abstract

BACKGROUND:
The aim of this study is to evaluate electromyography (EMG) amplitude and latency changes during tube dislocation in monitored thyroid surgery, which might be observed without recurrent laryngeal nerve injury.

METHODS:
Duroc-Landrace-piglets were intubated with the TriVantage EMG Tube. We measured EMG changes during both upward and downward tube dislocation (10-20 mm) and rotation (45-90°) with continuous neuromonitoring.

RESULTS:
The EMG amplitude varied significantly with induced endotracheal tube rotation and depth changes. However, the EMG latency was relatively unaffected by such tube dislocation, just except transient artifactual latency change observed in the situation of extreme amplitude variation.

CONCLUSION:
Amplitude changes without latency changes may be due to changes in tube position alone during surgery, but could still reflect a neurophysiologic event: amplitude changes during neuropraxic injury merit additional investigation. Thus, the combined event-concordant amplitude decrease and latency increase- serves as
appropriate adverse EMG event correlating with impending neural injury. This article is protected by
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KEYWORDS:
amplitude; electromyography; latency; recurrent laryngeal nerve; thyroid

PMID: 26040955 Makale sayfası


Locoregional control of recurrent papillary thyroid carcinoma by ultrasound-guided percutaneous microwave ablation: A prospective study.

Yue W1, Chen L, Wang S, Yu S.

Author information

Abstract

PURPOSE:
The aim of this study was to evaluate the safety and efficiency of ultrasound-guided percutaneous microwave (MW) ablation for the control of locally recurrent papillary thyroid carcinoma (LR-PTC) in patients for whom surgery is not viable.

MATERIALS AND METHODS:
The inclusion criteria for MW ablation were three or fewer LR-PTCs and no recurrence beyond the neck, with ineligibility or refusal to undergo surgery. MW ablation was carried out using a 16-gauge MW antenna under local anaesthesia. Patients were then followed at 1, 3, 6 and 12 months after treatment and every 6 months thereafter. Technical success usually meant volume reduction more than 50%.

RESULTS:
Between October 2010 to March 2013 a total of 17 patients (14 women, 3 men; average age 54.1 years) with 23 LR-PTCs, were treated with MW ablation in our department. All the LR-PTCs were technical successes with the number of treatment sessions for one tumour ranging from 1 to 4 (mean, 2.3 ± 0.9). The mean volume reduction ratio of the LR-PTCs was 1 ± 86%, 47 ± 12%, 70 ± 33%, 91 ± 14% at the 1, 3, 6 and 18 months follow-up visit respectively (all p < 0.05). All treated nodules decreased in size: 30.4% nodules (7/23) had completely disappeared, 52.2% nodules (12/23) remained as small scar-like lesions. One patient experienced transient dysphonia immediately after MW ablation. No other severe and permanent complications occurred.

CONCLUSION:
Although with some limitations, our preliminary results are encouraging and show MW ablation may be an alternative treatment option for the control of LR-PTCs in selected patients for whom surgery is not viable.

KEYWORDS:
Lymph node; microwave ablation; papillary thyroid carcinoma; recurrent thyroid carcinoma; ultrasound

PMID: 25792224 Makale sayfası
Prophylactic central compartment lymph node dissection in papillary thyroid carcinoma: clinical implications derived from the first prospective randomized controlled single institution study.


Author information

Abstract

BACKGROUND:
The benefits of prophylactic central compartment lymph node dissection (pCCND) in papillary thyroid cancer (PTC) are still under investigation. This treatment seems to reduce PTC recurrence/mortality rates but has a higher risk of surgical complications. The lack of prospective randomized trials does not allow definitive recommendations. The aim of this prospective randomized controlled study was to evaluate the clinical advantages and disadvantages of pCCND.

PATIENTS:
A total of 181 patients with PTC without evidence of preoperative/intraoperative lymph node metastases (cN0) were randomly assigned to either Group A (n = 88) and treated with total thyroidectomy (TTx) or Group B (n = 93) and treated with TTx + pCCND.

RESULTS:
After 5 years of followup, no difference was observed in the outcome of the two groups. However, a higher percentage of Group A were treated with a higher number of (131)I courses (P = .002), whereas a higher prevalence of permanent hypoparathyroidism was observed in Group B (P = .02). No preoperative predictors of central compartment lymph node metastases (N1a) were identified. Only three patients were upstaged, and the therapeutic strategy changed in only one case.

CONCLUSIONS:
cN0 patients with PTC treated either with TTx or TTx + pCCND showed a similar outcome. One advantage of TTx + pCCND was a reduced necessity to repeat (131)I treatments, but the disadvantage was a higher prevalence of permanent hypoparathyroidism. Almost 50% of patients with PTC had micrometastatic lymph nodes in the central compartment, but none of the presurgical features analyzed, including BRAF mutation, was able to predict their presence; moreover, to be aware of their presence does not seem to have any effect on the outcome.

Comment in

- Surgery. Papillary thyroid cancer--how aggressive should surgery be? [Nat Rev Endocrinol. 2015]

PMID: 25590215 Makale sayfası

Should asymptomatic retrosternal goitre be left untreated? A prospective single-centre study.

Landerholm K1, Järhult J2.

Author information

Abstract
BACKGROUND AND AIMS:
Retrosternal goiter may cause symptoms of airway obstruction and dysphagia, but often it is asymptomatic and is increasingly detected incidentally with imaging investigations. Consensus has been reached that sternotomy is not necessary in most cases, as a collar incision normally suffices. Yet, surgery for retrosternal goiter is associated with more complications than cervical goiter. There is controversy over whether patients with asymptomatic retrosternal goiter should be operated. Proponents argue that retrosternal goiter may be a risk for thyroid cancer and may progress to later cause symptoms, although clear evidence is missing.

PATIENTS AND METHODS:
Between 1984 and 2012, 132 patients underwent surgery for benign retrosternal goiter. Preoperatively, the benign nature was clinically apparent and confirmed by fine needle cytology in most cases.

RESULTS:
Sternotomy was required in only 4 of the 132 operations. Three patients died in the postoperative period. The risk of morbidity and mortality was 16.7% in 60 patients with compression symptoms and 13.9% in 72 patients without compression symptoms (P = 0.808). Histology revealed no case of unsuspected cancer.

CONCLUSION:
Surgery for retrosternal goiters involves a higher risk for complications than do cervical goiters, and the risk does not differ between patients with and without symptoms. This, and the fact that no patient in this study had unsuspected cancer, calls into question the rationale for surgery in patients with asymptomatic retrosternal goiter without suspected cancer.

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KEYWORDS:
Retrosternal goiter; complications to surgery; intrathoracic goiter; nodular goiter; recurrent laryngeal nerve injury; substernal goiter; surgical treatment

PMID: 24759378 Makale sayfası

7. Thyroid. 2015 Jun 17. [Epub ahead of print] IF: 3.84

Is Preoperative Vitamin D Deficiency a Risk Factor for Postoperative Symptomatic Hypocalcemia in Thyroid Cancer Patients Undergoing Total Thyroidectomy Plus Central Compartment Neck Dissection?

Kim WW1, Chung SH2, Ban EJ1, Lee CR1, Kang SW1, Jeong JJ1, Nam KH1, Chung WY1, Park CS1.

Author information
Abstract

BACKGROUND:
Although some studies have reported that preoperative vitamin D deficiency (VDD) is a risk factor for hypocalcemia after total thyroidectomy (TT) in patients with nontoxic multinodular goiter or Graves’ disease, the association between VDD and postoperative hypocalcemia in thyroid cancer patients undergoing TT plus central compartment neck dissection (CCND) remains unclear. This study evaluated whether preoperative VDD was associated with postoperative symptomatic hypocalcemia.

MATERIALS AND METHODS:
Data were collected prospectively between September 2012 and May 2013. A total of 267 consecutive thyroid cancer patients who underwent TT with CCND were analyzed. Patients were divided into two groups-VDD or non-VDD-by preoperative vitamin D level of <10 or ≥10 ng/mL. Symptomatic hypocalcemia was defined as serum calcium <8.2 mg/dL and symptoms or signs of hypocalcemia. The
rates of postoperative symptomatic hypocalcemia and clinicopathological features were compared between the two patient groups.

RESULTS:
The rate of postoperative symptomatic hypocalcemia was higher in the VDD group than in the non-VDD group (43.8% vs. 30.4%, p=0.043). By logistic regression analysis, predictive factors for postoperative symptomatic hypocalcemia included a preoperative vitamin D level of <10 ng/mL (p=0.007; odds ratio=3.00). In patients who had postoperative intact parathyroid hormone (iPTH) levels <15 pg/mL, symptomatic hypocalcemia was more common in the VDD group than in the non-VDD group (77.5% vs. 53.2%, p=0.008). The findings show that a preoperative vitamin D threshold level of >20 ng/mL reduced the risk of symptomatic hypocalcemia by 72% when compared with patients with VDD (p=0.003).

CONCLUSION:
VDD is significantly associated with postoperative symptomatic hypocalcemia in thyroid cancer patients undergoing TT plus CCND. VDD was predictive for symptomatic hypocalcemia when patients had postoperative serum iPTH levels <15 pg/mL. Thus, preoperative supplementation with oral vitamin D should be considered to minimize postoperative symptomatic hypocalcemia.

PMID: 26061175

Using diffusion-weighted MRI to predict aggressive histological features in papillary thyroid carcinoma: a novel tool for preoperative risk stratification in thyroid cancer.

Lu Y1, Moreira AL2, Hatzoglou V3, Stambuk HE, Gonen M4, Mazaheri Y1,2, Deasy JO, Shaha AR5, Tuttle RM, Shukla-Dave A1,3.

Abstract

BACKGROUND:
Initial management recommendations of papillary thyroid carcinoma (PTC) are very dependent on preoperative 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 three Tesla 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 cutoff 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) mm(2)/s) were significantly lower than corresponding values from PTCs without ETE (2.37±0.67×10(-3) mm(2)/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 cutoff value of ADC to discriminate PTCs with and without ETE was determined at 1.85×10(-3) mm(2)/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  Makale sayfası

9. Thyroid. 2015 Apr 13. [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 PW', 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 is recommended for patients with papillary thyroid carcinoma without indication for radioiodine ablation. There is no recommendation of thyrotropin 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 thyrotropin between 0.5 and 2 mIU/L, 3, 6, 12, and 24 months after total thyroidectomy. All patients had undetectable anti-Tg antibodies.

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% of patients. 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 was ≤2 ng/mL in all of them.

PMID: 25763842
Use of radioiodine after thyroid lobectomy in patients with differentiated thyroid cancer: does it change outcomes?

Kiernan CM¹, Parikh AA¹, Parks LL², Solórzano CC³.

Abstract

BACKGROUND:
Radioiodine (RAI) lobe ablation in lieu of completion thyroidectomy is not recommended. This study describes RAI use patterns and outcomes in patients with well-differentiated thyroid cancer (DTC) after thyroid lobectomy (TL).

STUDY DESIGN:
A total of 170,330 patients diagnosed with DTC between 1998 and 2011 were identified using the National Cancer Database. Demographic, tumor, and treatment variables were analyzed using both univariate and multivariate regression.

RESULTS:
A total of 32,119 patients (20%) underwent TL as the definitive procedure. Mean age at diagnosis was 48 years, median tumor size was 1 cm, 4% had extrathyroidal extension, 4% had positive lymph nodes, and <1% distant metastases. Radioiodine was administered to 24% of patients in the TL cohort and represented 10% of the overall RAI use. In multivariate analysis, RAI use was associated with age younger than 45 years (odds ratio [OR] = 1.51), community facilities (OR = 1.26), ≥ 1 cm tumors (OR = 5.67), stage II (OR = 1.54) or III (OR = 2.05), positive lymph nodes (OR = 1.78), and extrathyroidal extension (OR = 1.36). On both univariate and multivariate analysis, RAI after TL was associated with improved survival at both 5 and 10 years follow-up (97% vs 95% and 91% vs 89%, respectively; hazard ratio = 0.53; 95% CI, 0.38-0.72; p < 0.001) CONCLUSIONS: Nearly one quarter of TL patients received RAI. The strongest predictors of RAI use were larger cancers and advanced stage. Use of RAI in these patients was associated with improved overall survival. Future studies and guidelines will need to more clearly address this practice and educate providers about the appropriate use of RAI in TL patients.

Comment in

- Discussion. [J Am Coll Surg. 2015]

PMID: 25667136 Makale sayfasi

Thyroid cancer in patients with toxic nodular goiter—is the incidence increasing?

Choong KC¹, McHenry CR².

Abstract

BACKGROUND: There has been a dramatic increase in the incidence of thyroid cancer, but it is unclear if this has occurred in patients with toxic nodular goiter (TNG).

METHODS: TNG was defined as one or more thyroid nodules in combination with a low serum TSH level. Patients who underwent thyroidectomy for TNG were identified from a prospectively maintained database. The rates of incidental thyroid cancer were compared over the intervals 1990 to 1999, 2000 to 2009, and 2010 to 2014.

RESULTS: There was no significant difference in cancer rate between the 3 time periods. Overall, 7 (4.7%) of the 148 patients had thyroid cancer; similarly, 1 (3.2%) of the 31 patients from 1990 to 1999, 3 (4.2%) of 72 patients from 2000 to 2009, and 3 (6.7%) of the 45 patients from 2010 to 2014 (P > .05) had thyroid cancer.

CONCLUSIONS: No significant increase in the rate of carcinoma was observed in patients with TNG. As a result, the risk benefit analysis should not change when considering therapeutic options for TNG.

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KEYWORDS: Thyroid cancer; Thyroidectomy; Toxic nodular goiter

PMID: 25896315


Survival in anaplastic thyroid cancer in relation to pre-existing goiter: a population-based study.

Steggink LC¹, van Dijk BA², Links TP³, Plukker JT⁴.

Abstract

BACKGROUND: We investigated whether pre-existent goiter and well-differentiated thyroid cancer (WDTC) are associated with survival in anaplastic thyroid carcinoma (ATC).

METHODS: We analyzed medical records from 94 ATC patients, drawn from the Netherlands Cancer Registry, diagnosed in 17 hospitals between 1989 and 2009.

RESULTS:
The 29 patients (31%) with pre-existing goiter, including 8 with WDTC, were younger than those without (median, 69 vs 76 years; P = .02). One-year overall survival was 9% (95% confidence interval [CI], 3% to 14%) with no difference between pre-existing goiter or not (overall survival, 14%; 95% CI, 1% to 26% vs overall survival, 6%; 95% CI, 0% to 13%). Higher age was associated with a worse survival (hazard rate, 1.03; 95% CI, 1.01 to 1.06), whereas the hazard to die was lower after surgery and/or radiotherapy (hazard rate, .37; 95% CI, .21 to .67 and hazard rate, .22; 95% CI, .12 to .41, respectively).

CONCLUSIONS:
ATC patients with pre-existing goiter were younger, yet survival was not significantly different between those with or without pre-existing goiter or WDTC.

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KEYWORDS:
Anaplastic thyroid carcinoma; Goiter; Survival

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 microcalsification, 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
A risk model to determine surgical treatment in patients with thyroid nodules with indeterminate cytology.

Macias CA¹, Arumugam D, Arlow RL, Eng OS, Javidian P, Davidov T, Trooskin SZ.

Abstract

BACKGROUND: Thyroid nodules are present in 19-67% of the population and have a 5-10% risk of malignancy. Fine needle aspiration biopsies are indeterminate in 20-30% of patients, often necessitating thyroid surgery for diagnosis. We hypothesized that developing a risk model incorporating factors associated with malignancy could help predict the risk of malignancy in patients with indeterminate thyroid nodules.

METHODS: We identified 151 patients with a cytologic diagnosis of follicular neoplasm (Bethesda IV) who progressed to surgery. We retrospectively analyzed demographic, clinical, sonographic, and cytological variables in relation to thyroid carcinoma.

RESULTS: Of 151 patients, 51 (33.8%) had a final diagnosis of thyroid carcinoma. Papillary carcinoma was diagnosed in 34 patients (66.7%), follicular carcinoma in 15 (29.4%), and Hürthle cell carcinoma in 2 (3.9%). On univariate analysis, younger age, male gender, tobacco use, larger nodule size, and calcifications on ultrasound, nuclear atypia on cytology, and suspicious frozen section were associated with the presence of malignancy. When determining odds ratios, four factors were most predictive of malignancy: nodule calcification [odds ratio (OR) 6.37, 95% confidence interval (CI) 1.62-25.1, p < 0.01] and nodule size (OR 1.75, 95% CI 1.19-2.57, p < 0.01) on ultrasound, nuclear atypia on cytology (OR 4.91, 95% CI 1.90-12.66, p < 0.01), and tobacco use (OR 4.59, 95% CI 1.30-16.27, p < 0.02). A multivariable model based on these four factors resulted in a c-statistic of 0.82.

CONCLUSIONS: A multivariable model based on calcification, nodule size, nuclear atypia, and tobacco use may predict the risk of thyroid cancer requiring a total thyroidectomy in patients with thyroid nodules of indeterminate cytology.

PMID: 25388058

Undetectable Thyroglobulin Levels in Poorly Differentiated Thyroid Carcinoma Patients Free of Macroscopic Disease After Initial Treatment: Are They Useful?


Abstract

BACKGROUND: Predictive role of undetectable thyroglobulin (Tg) in patients with poorly differentiated thyroid carcinoma (PDTC) is unclear. Our goal was to report on Tg levels following total thyroidectomy and adjuvant RAI in PDTC patients and to correlate Tg levels with recurrence.

METHODS:
Forty patients with PDTC with no distant metastases at presentation (M0) and managed by total thyroidectomy and adjuvant RAI were identified from a database of 91 PDTC patients. Of these, 31 patients had Tg values recorded and formed the basis of our analysis. A nonstimulated Tg level <1 ng/ml was used as a cutoff point for undetectable Tg levels. Association of patient and tumor characteristics with Tg levels was examined by χ² test. Recurrence-free survival (RFS) stratified by postop Tg level was calculated by Kaplan-Meier method and compared by log-rank test.

RESULTS:
Twenty patients had undetectable Tg (<1 ng/ml) and 11 had detectable Tg (≥1 ng/ml; range 2-129 ng/ml) following surgery. After adjuvant RAI, 24 patients had undetectable Tg (<1 ng/ml) and 7 had detectable Tg (≥1 ng/ml; range 1-57 ng/ml). Patients with undetectable Tg were less likely to have pathologically positive margins compared to those with detectable Tg (33 vs. 72 % respectively; p = 0.03). Patients with undetectable Tg levels had better 5-year regional control and distant control than patients with detectable Tg level (5-year regional recurrence-free survival 96 vs. 69 %; p = 0.03; 5-year distant recurrence-free survival 96 vs. 46 %, p = 0.11).

CONCLUSION:
Postoperative thyroglobulin levels in subset of patients with PDTC appear to have predictive value for recurrence. Patients with undetectable Tg have a low rate of recurrence.

PMID: 25893415


IF:4.33

Fewer cancer reoperations for medullary thyroid cancer after initial surgery according to ATA guidelines.

Verbeek HH¹, Meijer JA, Zandee WT, Kramp KH, Sluiter WJ, Smit JW, Kievit J, Links TP, Plukker JT.

Author information

Abstract

BACKGROUND:
Surgery is still the only curative treatment for medullary thyroid cancer (MTC). We evaluated clinical outcome in patients with locoregional MTC with regard to adequacy of treatment following ATA guidelines and number of sessions to first intended curative surgery in different hospitals.

METHODS:
We reviewed all records of MTC patients (n = 184) treated between 1980 and 2010 in two tertiary referral centers in the Netherlands. Symptomatic MTC (palpable tumor or suspicious lymphadenopathy) patients without distant metastasis were included (n = 86). Patients were compared with regard to adequacy of surgery according to ATA recommendations, tumor characteristics, number of local cancer reoperations, biochemical cure, clinical disease-free survival (DFS), overall survival (OS), and complications.

RESULTS:
Adherence to ATA guidelines resulted in fewer cancer-related reoperations (0.24 vs. 0.60; P = 0.027) and more biochemical cure (40.9 vs. 20 %; P = 0.038). Surgery according to ATA-guidelines on patients treated in referral centers was significantly more often adequate (59.2 vs. 26.7 %; P = 0.026). Tumor size and LN+ were the most important predictors for clinical recurrence [relative risk (RR) 4.1 (size > 40 mm) 4.1 (LN+) and death (RR 4.2 (size > 40 mm) 8.1 (LN+)].

CONCLUSIONS:
ATA-compliant surgery resulted in fewer local reoperations and more biochemical cure. Patients in referral centers more often underwent adequate surgery according to ATA-guidelines. Size and LN+ were the most important predictors for DFS and OS.

PMID: 25316487


Navigating the management of follicular variant papillary thyroid carcinoma subtypes: a classic PTC comparison.

Finnerty BM1, Kleiman DA, Scognamiglio T, Aronova A, Beninato T, Fahey TJ 3rd, Zarnegar R.

Author information

Abstract

BACKGROUND:
There are three subtypes of follicular variant papillary thyroid carcinoma (fvPTC): completely encapsulated, well circumscribed, and infiltrative. While infiltrative tumors are more aggressive than completely encapsulated, controversy exists regarding management of fvPTC subtypes. We compared the clinicopathologic features of fvPTC subtypes to those of classic PTC (cPTC) to help guide fvPTC management, using cPTC as a reference.

METHODS:
A retrospective review was performed on 316 patients with PTC treated at a single institution from 2004 to 2011. There were 197 cPTC and 119 fvPTC tumors, including completely encapsulated (n = 46), well circumscribed (n = 46), and infiltrative (n = 27). Clinicopathologic data were compared between groups.

RESULTS:
fvPTC patients had larger tumors than cPTC patients (1.6 cm vs. 1.2 cm, p = 0.001), but age, sex, and family history did not differ. Thirty-one percent of cPTC tumors had extrathyroidal extension compared to 0 % of completely encapsulated, 0 % of well-circumscribed, and 52 % of infiltrative fvPTC tumors (p < 0.05). Central lymph node metastasis occurred in 50 % of cPTC compared to 0 % in completely encapsulated, 20 % in well-circumscribed, and 72 % in infiltrative fvPTC tumors (p < 0.05). Notably, lymph node metastasis was significantly lower in completely encapsulated than in well-circumscribed tumors, without a difference in the median number of nodes sampled. There were no differences in lymphovascular invasion or extranodal extension.

CONCLUSIONS:
Like cPTC tumors, infiltrative fvPTC tumors have aggressive clinicopathologic features and thus should be treated similarly. Conversely, completely encapsulated and well-circumscribed tumors have less aggressive features compared to cPTC and are more self-limiting; however, well-circumscribed tumors still have a notable incidence of lymph node metastasis. Clinicians should consider this variability in their management algorithm for fvPTC.

PMID: 25297901


Complication rates of central compartment dissection in papillary thyroid cancer.

Kwan WY1, Chow TL, Choi CY, Lam SH.

Author information
Abstract

BACKGROUND:
The benefits of central compartment dissection (CCD) in papillary thyroid carcinoma (PTC) are still debatable and should be weighed against its potential risks. We aim to compare the complication rates in total thyroidectomy with and without CCD for patients with PTC.

METHODS:
This is a retrospective study on prospectively collected data from our cancer registry over a 15-year period. Patients with pathologically proven PTC treated with total thyroidectomy alone or with CCD were included. CCD was performed at the operating surgeon's discretion. A total of 105 patients were included and divided into two groups for analysis: group A - total thyroidectomy alone (51 patients, 49%) and group B - total thyroidectomy with CCD (54 patients, 51%). The operative complications between the two groups were then evaluated.

RESULTS:
Overall, 6.9% and 0.98% patients had transient and permanent recurrent laryngeal nerve palsies, respectively. About 19.0% and 2.9% patients had transient and permanent hypoparathyroidism, respectively and 27.6% patients had parathyroid glands found to be included in the resected specimen. Complication rates in terms of transient or permanent recurrent laryngeal nerve palsy or hypoparathyroidism did not differ significantly between groups A and B. Within group B, 41 patients had unilateral CCD and 12 had bilateral CCD. Transient hypoparathyroidism was more frequent in bilateral CCD (50% versus 12.2%, P = 0.01).

CONCLUSIONS:
Total thyroidectomy with prophylactic unilateral CCD is a safe procedure for PTC without added complication rates compared with total thyroidectomy alone. It is recommended for patients with PTC and clinically negative neck lymph nodes.

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KEYWORDS:
carcinoma; lymph node excision/methods; papillary/surgery; thyroid neoplasms/surgery; treatment outcome

PMID: 23890372 Makale sayfası


Should central lymph node dissection be considered for all papillary thyroid microcarcinoma?

Chang YW¹, Kim HS¹, Kim HY¹, Lee JB¹, Bae JW¹, Son GS².

Author information

Abstract

BACKGROUND:
Central lymph node dissection (CLND) in patients with papillary thyroid microcarcinoma (PTMC) is still controversial. The aim of this study was to examine the risk factors and the incidence of central lymph node metastases (CLNMs) in patients with PTMC who underwent thyroidectomy and CLND.

PATIENTS AND METHODS:
Between 2002 and 2013, 613 patients were enrolled who underwent thyroidectomy with routine CLND for PTMC at the Korea University Medical Center, Ansan Hospital and risk factors and the incidence of CLNM were analyzed. In addition, we also evaluated the complications after thyroidectomy with CLND.
RESULTS:
Out of 613 patients, 239 (39.0%) were found to have CLNM. Male sex (p = 0.012), tumor size ≥ 0.5 cm (p = 0.001), capsular invasion or extrathyroidal extension (p = 0.029), and multifocality (p = 0.004) were independent risk factors for CLNM. Among the 69 patients who had PTMC without these risk factors, CLNM was identified in 12 (17.4%). In this study group, two (0.3%) had permanent recurrent laryngeal nerve injury, two (0.3%) had persistent hypocalcemia, and two (0.3%) developed postoperative hemorrhage.

CONCLUSION:
CLNM in PTMC is highly prevalent in male sex, tumor size ≥ 0.5 cm, extrathyroidal extension, and multifocality. Even in PTMC patients without these risk factors, the incidence of CLNM is rather higher than expected, and the complication rate of thyroidectomy with CLND is acceptable. Thus, CLND should be considered in all patients with PTMC.

KEYWORDS:
central lymph node; papillary thyroid cancer; papillary thyroid microcarcinoma


Retrospective evaluation of the incidental finding of 403 papillary thyroid microcarcinomas in 2466 patients undergoing thyroid surgery for presumed benign thyroid disease.

Slijepcevic N1, Zivaljevic V2,3, Marinkovic J4,5, Sipetic S6,7, Diklic A8,9, Paunovic I10,11.

Abstract

BACKGROUND:
The aim of our study was to investigate the incidence of papillary thyroid microcarcinoma (PTMC) in patients operated for benign thyroid diseases (BTD) and its relation to age, sex, extent of surgery and type of BTD.

METHODS:
Retrospective study of 2466 patients who underwent thyroid surgery for BTD from 2008 to 2013. To determine independent predictors for PTMC we used three separate multivariate logistic regression models (MLR).

RESULTS:
There were 2128 (86.3%) females and 338 (13.7%) males. PTMC was diagnosed in 345 (16.2%) females and 58 (17.2%) males. Age ranged from 14 to 85 years (mean 54 years). Sex and age were not related to the incidence of PTMC. The overall incidence of PTMC was 16.3%. The highest incidence was in Hashimoto thyroiditis (22.7%, χ²(2) = 10.80, p < 0.001); and in patients with total/near-total thyroidectomy (17.7%, χ²(2) = 7.05, p < 0.008). The lowest incidence (6.6%, χ²(2) = 9.96, p < 0.001) was in a solitary hyperfunctional thyroid nodule (SHTN). According to MLR, Hashimoto thyroiditis (OR 1.54, 95% CI 1.15-2.05, p < 0.001) was an independent predictor. Since the extent of surgery was an independent predictor (OR 1.45, 95% CI 1.10-1.92, p = 0.009) for all BTD, and sex and age were not; when the MLR model was adjusted for them, Graves disease (OR 0.72, 95% CI 0.53-0.99, p < 0.041) also proved to be an independent predictor.

CONCLUSIONS:
Sex and age are not statistically related to the incidence of PTMC in BTD. The incidence of PTMC is higher in Hashimoto thyroiditis and patients with total/near-total thyroidectomy; and lower in patients with a SHTN and Graves disease.

PMID: 25925164 Makale sayfası


Papillary thyroid carcinoma: does the association with Hashimoto’s thyroiditis affect the clinicopathological characteristics of the disease?

Girardi FM1, Barra MB2, Zettler CG2. 

Author information

Abstract

INTRODUCTION:
Papillary carcinoma is the most common malignant thyroid neoplasm. The effect of the concurrent presence of Hashimoto's thyroiditis and papillary thyroid carcinoma remains controversial.

OBJECTIVE:
To evaluate the association between Hashimoto's thyroiditis and clinicopathological parameters in thyroid papillary carcinoma cases, based on an historical institutional cohort analysis.

METHODS:
Cross-sectional study obtained from a historical cohort, including all cases submitted to thyroidectomy for papillary thyroid carcinoma in a single institution during an 11-year period study.

RESULTS:
A total of 417 patients with papillary thyroid carcinoma were enrolled; 148 (35.4%) also had Hashimoto's thyroiditis. A female predominance among cases associated to Hashimoto's thyroiditis was observed. The thyroid tumor, in cases associated with Hashimoto's thyroiditis, had a smaller mean diameter, lower frequency of extra-thyroid extension, and earlier clinicopathological staging.

CONCLUSIONS:
A high proportion of papillary thyroid carcinoma cases are associated with Hashimoto's thyroiditis. There are associations among these cases with several histopathological factors already recognized for their prognostic value, which by themselves could impact outcomes.

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KEYWORDS:
Carcinoma papilar; Neoplasias da glândula tireoide; Papillary carcinoma; Prognosis; Prognóstico; Thyroid neoplasms

PMID: 25458258 Makale sayfası


Malignant risk stratification of thyroid FNA specimens with indeterminate cytology based on molecular testing.

Paskaš S1, Janković J, Živaljević V, Tatić S, Božić V, Nikolić A, Radojković D, Savin S, Cvejić D.
**BACKGROUND:**
Fine-needle aspiration (FNA) has been employed for many years for examining thyroid nodules, and the cytology of aspirates is the primary determinant for whether thyroidectomy is indicated. Fifteen to thirty percent of thyroid nodules, not being clearly benign or malignant, fall into an indeterminate category. The main goals of molecular diagnostics for thyroid nodules are to prevent unnecessary surgery in patients with benign nodules and to stop patients with malignant nodules from being subjected to repeated operations.

**METHODS:**
This study was designed to evaluate the diagnostic utility of 4 markers in thyroid FNA cytology via testing for the BRAF V600E mutation and the expression of microRNA-221, microRNA-222, and galectin-3 protein in FNA samples with indeterminate cytology.

**RESULTS:**
A predictor model distinguishing benign samples from malignant samples on the basis of the 4 aforementioned markers was formulated. This decision model provided a sensitivity of 73.5%, a specificity of 89.8%, and a diagnostic accuracy of 75.7%. The positive predictive value was 80.6%, and the negative predictive value was 85.5%; this suggested that the prediction had good reliability.

**CONCLUSIONS:**
One hundred twenty FNA samples were examined, and 62 nodules were classified as benign with the proposed diagnostic algorithm. This resulted in a reduction of the initial 120 patients to 58 and thus decreased by half the number of persons undergoing surgery. Cancer (Cancer Cytopathol) 2015. © 2015 American Cancer Society.

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**KEYWORDS:**
BRAF; fine-needle aspirates; galectin-3; indeterminate cytology; microRNA 221 (miR-221); microRNA 222 (miR-222); thyroid cancer

PMID: 25924719 [Makale sayfasi]
clinically on postoperative laryngoscopic examination. Laryngeal surface electrodes were successfully utilized to identify and monitor SLN function intraoperatively. IONM using laryngeal surface electrodes enables analysis of waveform morphology and latency in addition to threshold and amplitude data obtained with the traditional NIM system, potentially improving the performance of nerve monitoring during thyroid surgery.

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KEYWORDS:
external branch of superior laryngeal nerve; nerve monitoring and stimulation; thyroid surgery

PMID: 25425500  Makale sayfası


RAS mutations in indeterminate thyroid nodules are predictive of the follicular variant of papillary thyroid carcinoma.

An JH¹, Song KH, Kim SK, Park KS, Yoo YB, Yang JH, Hwang TS, Kim DL.

Abstract

OBJECTIVE:
RAS mutations are the most common mutations in thyroid nodules with indeterminate cytology by fine-needle aspiration cytology (FNAC), and are mutually exclusive with BRAF mutations. However, the diagnostic utility of RAS mutation analysis is uncertain. We evaluated the diagnostic utility of RAS mutation analysis in indeterminate thyroid nodules.

DESIGN, PATIENTS, AND MEASUREMENTS:
A total of 155 thyroid nodules (90 benign and 65 indeterminate) negative for BRAF(V) (600E) mutations on FNAC were analysed for mutations in RAS codon 61 using pyrosequencing methods. We evaluated diagnostic accuracy of RAS mutation for predicting thyroid malignancy based on the surgical pathologic diagnosis.

RESULTS:
Among the 65 BRAF(V) (600E) -negative indeterminate thyroid nodules identified by FNAC, 25 (38.5%) exhibited point mutations in RAS 61 consisting of 18 NRAS 61 (72%), and 7 HRAS 61 (28%) mutations. In contrast, only five of 90 (5.6%) nodules with benign cytology had RAS mutations. Only two of 25 (8.0%) RAS 61(+) indeterminate nodules exhibited malignant ultrasonographic features. Of the 15 patients with RAS 61(+) -indeterminate nodules who underwent thyroid surgery, 14 (93.3%) were diagnosed as malignant, including 13 follicular variant of papillary thyroid carcinomas (FVPTC), and one follicular thyroid carcinoma (FTC). The average tumour size was 1.79 ± 0.62 cm. Multifocality was seen in 28.6% of cases, with 7.1% exhibiting extrathyroidal extension; no lymph node or distant metastases were evident. Based on the surgical pathologic diagnosis results, preoperative RAS 61 mutation analysis on FNAC exhibited 93.3% sensitivity, 75.0% specificity, 93.3% positive predictive value, 75.0% negative predictive value and 89.5% diagnostic accuracy for predicting malignancies.

CONCLUSION:
Our results suggest that RAS mutation analysis holds great promise as a preoperative diagnostic tool for predicting FVPTC in cytologically and sonographically indeterminate nodules negative for BRAF mutations.

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PMID: 25109485  Makale sayfası
A cut-off value of basal serum calcitonin for detecting macroscopic medullary thyroid carcinoma.

Kwon H¹, Kim WG, Choi YM, Jang EK, Jeon MJ, Song DE, Baek JH, Ryu JS, Hong SJ, Kim TY, Kim WB, Shong YK.

Abstract

OBJECTIVE:
Serum calcitonin (CT) level is used to detect medullary thyroid carcinoma (MTC), but the cut-off level is unclear. We aimed at identifying the optimal cut-off value of basal serum CT levels for detecting MTC.

DESIGN AND PATIENTS:
We retrospectively enrolled patients with hypercalcitoninemia (≥2·9 pmol/l) who had undergone thyroid ultrasonography (US) and subsequent work-up between 2001 and 2013 at Asan Medical Center. We divided patients into four groups: proven MTC (group 1, n = 93), pathologically proven non-MTC after surgery (group 2, n = 57), benign single nodule by cytology (group 3, n = 68) and patients without nodules on US (group 4, n = 24).

MEASUREMENT:
Basal serum CT levels were evaluated.

RESULTS:
The median CT level of group 1 (119·5 pmol/l) was significantly higher than those of other groups (4·0, 3·8 and 3·8 pmol/l, P < 0·001). When we adopted 19·0 pmol/l of CT level as a cut-off value, the sensitivity, specificity, and positive and negative predictive values were 77·4%, 98·7%, 97·3% and 87·8%, respectively. When we compared 29·2 pmol/l (100 pg/ml) and 19·0 pmol/l (65 pg/ml) as cut-off values, 19·0 pmol/l was more sensitive and accurate than 29·2 pmol/l. Factors associated with hypercalcitoninemia in non-MTC groups were autoimmune thyroiditis, chronic kidney disease, proton pump inhibitors and other malignancies. Serum CT levels tended to decrease spontaneously in non-MTC groups.

CONCLUSION:
Basal serum CT levels higher than 19·0 pmol/l can be a useful cut-off value for detecting macroscopic MTC, even though values below 19·0 pmol/l cannot exclude the presence of MTC like small volume MTC or premalignant C-cell hyperplasia.

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PMID: 25041034

Differentiated thyroid cancer patients with a previous indeterminate (Thy 3) cytology have a better prognosis than those with suspicious or malignant FNAC reports.


Abstract
The prognosis of differentiated thyroid cancers (DTC) read at cytology as indeterminate and classified as Thy 3 according to the British Thyroid Association has recently been suggested to be good. To obtain robust information about this potential novelty, in this study we retrospectively reviewed DTC with a prior fine-needle aspiration cytology (FNAC) of Thy 3, Thy 4 or Thy 5 presently followed up at two institutes. Patients with no FNAC before surgery were excluded and a series of 284 DTC was enrolled in the study. Of these, 53 had Thy 3, 108 Thy 4, and 123 had Thy 5 prior to surgery. At histology, 280 (98.6%) papillary and 4 follicular (1.4%) cancers were found. Overall, the less aggressive cancer forms were prevalent in all three groups. The lower TNM stages (I and II) were more frequent in the Thy 3 group (96.2%) than in the other cases (76.6%) (p < 0.001). Neck lymph node metastasis at diagnosis was found in 3.8% of Thy 3, 18.5% of Thy 4, and 26% of Thy 5 cases. At follow-up, a 16.2% recurrence rate was recorded, ranging from 1.9% in Thy 3 group to 19.5% for Thy 4 and Thy 5 (p < 0.001). According to the Kaplan-Meier curve, Thy 3 was thus a favorable prognostic factor compared with Thy 4 and Thy 5 (OR = 0.079, p < 0.001, 95%CI 0.01-0.59). At multivariate analysis, Thy 3 was an independent predictor of good prognosis (OR = 0.06, p = 0.03, 95%CI 0.01-0.80). In conclusion, DTC with a preoperative Thy 3 cytology have a better prognosis than those with Thy 4 and Thy 5 due to less aggressive tumor types and lower TNM stage at diagnosis.

PMID: 25323658

Predictive factors of contralateral paratracheal lymph node metastasis in unilateral papillary thyroid carcinoma.

Wei T1, Chen R1, Zou X1, Liu F1, Li Z1, Zhu J2.

Author information

Abstract

BACKGROUND:
Most of unilateral papillary thyroid carcinoma (PTC) metastasize to ipsilateral paratracheal lymph nodes (LNs) while some had contralateral paratracheal LN involved. The aim of this study was to analyze the predictive factors of contralateral paratracheal LN metastasis in unilateral PTC.

METHODS:
Data on 332 patients with unilateral PTC who underwent total/near total thyroidectomy and bilateral central neck dissection (CND) with/without lateral neck dissection were collected retrospectively. Patients' demographics, the extent of surgeries, and the pathological status of LNs and primary tumor were analyzed.

RESULTS:
A total of 332 patients (67 male and 265 female) were included. Contralateral paratracheal LN metastasis was found in 68 (68/332, 20.5%) patients. Tumor size (>1 cm) (P < .001), capsular/extracapsular invasion (P < .001), pretracheal/prelaryngeal LN metastasis (P < .001), lateral neck LN metastasis (P < .001) and ipsilateral paratracheal LN metastasis (P < .001) was significantly associated with contralateral paratracheal LN metastasis on univariate analysis. Multivariate analysis showed that tumor size (>1 cm) (P = .013), capsular/extracapsular invasion (P = .009), pretracheal/prelaryngeal LN metastasis (P = .021) and lateral neck LN metastasis (P = .002) were independent risk factors of contralateral paratracheal LN metastasis.

CONCLUSION:
Primary tumor size >1 cm, capsular/extracapsular invasion, pretracheal/prelaryngeal LN metastasis and lateral neck LN metastasis are predictive factors of contralateral paratracheal LN metastasis in unilateral PTC, which may help to determine the optimal extent of CND in patients with PTC.
Breach of the thyroid capsule and lymph node capsule in node-positive papillary and medullary thyroid cancer: Different biology.

Machens A¹, Dralle H².

Author information

Abstract

AIMS:
The higher incidence of extranodal growth (breach of a lymph node capsule) in the presence of extrathyroidal extension (breach of the thyroid capsule) in papillary thyroid cancer prompted conclusions that the biology of thyroid cancer is conferred to the lymph nodes, causing invasion of perinodal tissues. This study aimed at quantifying the independent contributions of clinical-pathological factors to extranodal growth in thyroid cancer.

METHODS:
Multivariate analyses of 1250 patients operated on for node-positive papillary (PTC; 702 patients) or node-positive medullary thyroid cancer (MTC; 548 patients), 138 and 130 of whom harbored extranodal growth.

RESULTS:
After correction for multiple testing, extranodal growth correlated with number of lymph node metastases (means of 17.0 vs. 10.1 nodes for PTC, 20.6 vs. 13.4 nodes for MTC; each P < 0.001) and male gender (49 vs. 35% for PTC, P = 0.005; 62 vs. 46% for MTC; P = 0.002); and in MTC also with extrathyroidal extension (46 vs. 30%; P = 0.002). On multivariate analysis, independent determinants of extranodal growth were number of lymph node metastases (odds ratios of 2.1, 3.7 and 3.7 for PTC (P ≤ 0.01) and 2.7, 3.3, and 4.0 for MTC (P ≤ 0.004) looking at 6-10, 11-20 and >20 involved nodes against a 1-5 node baseline) and male gender (odds ratio 1.6 for PTC, 1.7 for MTC; each P = 0.02), but not extrathyroidal extension.

CONCLUSIONS:
In PTC and MTC, extranodal growth develops independently from extrathyroidal extension. This finding argues against mere transference of primary tumor characteristics to lymph nodes, pointing more to accrual of invasive properties by nodal tumor deposits.

KEYWORDS:
Distant metastasis; Extranodal growth; Extrathyroidal extension; Lymph node metastases; Medullary thyroid carcinoma; Papillary thyroid carcinoma; Primary tumor diameter
Differences in the characteristics of papillary thyroid microcarcinoma ≤5 mm and >5 mm in diameter.

Kim E', Choi JY, Koo do H, Lee KE, Youn YK.

Abstract

BACKGROUND:
The behavior and optimal management of papillary thyroid microcarcinomas (PTMCs) after thyroidectomy remain unclear. The purpose of this study was to compare the clinicopathologic features and tumor recurrence rates of patients with PTMCs ≤5 mm and >5 mm in diameter after total thyroidectomy.

METHODS:
A group of patients with PTMCs ≤5 mm (n=83) has been compared to a group with >5 mm (n=122). All of these patients had conventional type PTMCs and were followed up for 5 years. Both the histology and the outcome have been compared.

RESULTS:
Sex (p=.014) and extrathyroidal extension (p=.003) of patients in the ≤5 mm and >5 mm groups differed significantly. Two and 5 patients from these groups, respectively, experienced tumor recurrence within 5 years (2.4% vs 4.1%; p=.634).

CONCLUSION:
The clinicopathologic features of PTMCs ≤5 mm and >5 mm are similar, except for sex distribution and extrathyroidal extension. The 5-year recurrence rate in the 2 groups did not differ significantly.

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KEYWORDS:
clinicopathological features; papillary thyroid microcarcinoma; recurrence; surgery; total thyroidectomy

PMID: 24596325

Number of tumor foci as predictor of lateral lymph node metastasis in papillary thyroid carcinoma.

Kim HJ', Park HK, Byun DW, Suh K, Yoo MH, Min YK, Kim SW, Chung JH.

Abstract

BACKGROUND:
The purpose of this study was to determine the clinicopathologic characteristics of patients with papillary thyroid carcinoma (PTC) by the number of tumor foci.

METHODS:
A retrospective analysis of 2095 patients with PTC was performed. The study population was divided into 4 groups based on the number of tumor foci: N1 (1 tumor focus), N2 (2 foci), N3 (3 foci), and N4 (4 or more foci).

RESULTS:
An increasing number of tumor foci was significantly associated with older age at diagnosis (p = .006), cervical lymph node metastasis (p < .001), and advanced TNM stage of disease (p = .001) at initial surgery.
The multivariate adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for the N2, N3, and N4 groups compared to the N1 group for lateral lymph node metastasis were OR 1.53 (95% CI, 1.05-2.22), OR 2.57 (95% CI, 1.50-4.42), and OR 2.88 (95% CI, 1.42-5.84), respectively.

CONCLUSION:
An increase in the number of tumor foci was strongly associated with older age at diagnosis, cervical lymph node metastasis, and advanced TNM stage of PTC. The number of tumor foci independently predicted lateral lymph node metastasis.

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KEYWORDS:
lymph node metastasis; multifocality; papillary thyroid carcinoma

PMID: 24590814  Makale sayfasi


The significance and the predictive factors of microscopic lymph node metastasis in patients with clinically node negative papillary thyroid cancer: A retrospective Cohort Study.

Noda S¹, Onoda N², Morisaki T², Kashiwagi S², Takashima T², Hirakawa K².

Author information

Abstract

BACKGROUND:
The management of pathological lateral node involvement (pN1b) from papillary thyroid cancer (PTC) are controvertial.

METHODS:
A consecui te series of 246 patients, diagnosed with clinically node negative (cN0) PTC who had undergone surgery with prophyrcatic lateral node dissection, and without postoperative radioactive iodine administration from 2001 to 11, were reviewed to clarify the significance of pN1b.

RESULTS:
Eighty-five (35%) patients had pN1b disease. One-half and 30% had pN1b in younger (age less than 45) and older patients (age 45 or over), respectively. Tumor size (≥21mm) could predict pN1b disease in older patients. Patients with pN1b disease recurred more frequently (9 cases, 10.6%) than those without (4 cases, 2.4%), and 2 cases with pN1b died of the disease.

CONCLUSIONS:
pN1b disease was commonly found in patients with PTC even when they were diagnosed clinically as node negative. pN1b disease with prognostic meaning was often found in the older patients with larger PTC indicating the necessity for adjuvant treatments.

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KEYWORDS:
microscopic node metastasis; predictive factor; thyroid cancer

PMID: 26079502  Makale sayfasi
Surgical treatment for dominant malignant nodules of the isthmus of the thyroid gland: A case control study.

Karatzas T¹, Charitoudis G², Vasileiadis D³, Kapetanakis S³, Vasileiadis P³.

Author information

Abstract

BACKGROUND:
Appropriate surgical treatment of papillary thyroid carcinomas (PTC) located in the isthmus remains controversial. The aim of this study was to evaluate the clinicopathological characteristics of PTC of the isthmus compared to tumors located in the thyroid lobes, to identify differences between PTC and microcarcinomas of the isthmus, and to use these findings to establish total thyroidectomy as an appropriate surgical resection for treating these tumors.

METHODS:
We retrospectively analyzed 2239 patients subjected to total thyroidectomy. PTC was diagnosed in 575 patients, of whom 521 had dominant malignant nodule located in thyroid lobes and 54 had a dominant carcinoma located in the isthmus. Patients with isthmic PTC were divided in Group A (n = 27) with PTC >10 mm and Group B (n = 27) with microcarcinoma ≤10 mm.

RESULTS:
In univariate analysis, multifocality (p = 0.019), lymph node metastasis (p < 0.001), mean tumor size (p = 0.028) and age ≥45 (p = 0.036) were significantly associated with PTC with dominant nodule in the isthmus. Additional analysis of PTC groups (>10 mm vs ≤10 mm) in isthmus showed that multifocality, bilaterality, histological subtype and lymph node metastasis were not significantly different between the two groups.

CONCLUSIONS:
Our results suggest that PTCs located in the isthmus were more likely to be associated with multifocal disease, lymph node involvement and capsule invasion, than carcinomas in other thyroid regions. Therefore, total thyroidectomy could be considered as an appropriate surgical treatment for papillary carcinomas located in the isthmus regardless of size.

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KEYWORDS:
Malignant; Nodule; Surgical treatment; Thyroid isthmus; Total thyroidectomy

PMID: 25900600 Makale sayfası

Detection of Thyroid Papillary Carcinoma Lymph Node Metastases Using One Step Nucleic Acid Amplification (OSNA): Preliminary Results.


Author information

Abstract
Purpose: One Step Nucleic Acid Amplification (OSNA) has been previously proposed for the diagnosis of lymph node metastases (LNMs) from several malignant conditions by quantifying the number of copies of cytokeratin 19 mRNA. Our aim was to evaluate the results obtained by OSNA in the lymph nodes of patients with papillary thyroid carcinoma (PTC) by comparing our results with the findings observed using standard pathological examination.

MATERIALS AND METHODS:
Fifty human lymph nodes (from five patients with diagnosed PTC) were studied. Each node was divided into two: one half was used for molecular study ("OSNA-node"), and the other half was used for conventional staining with hematoxylin and eosin ("HE-non-OSNA node"). Three cytological imprints using Papanicolaou and May-Grunwald-Giemsa stains were obtained from both node halves. The results from each technique were compared, and ROC analysis was performed.

RESULTS:
The OSNA study showed 22 positive samples for LNM (44%), which demonstrate a high concordance rate with the results observed using conventional pathological examination (cytology of "OSNA-node" and HE of "Non-OSNA node") with specificity and sensitivity values greater than 86% and 89%, respectively. However, both comparisons differed in the number of copies of mRNA as the best cut-off (260 copies in the first case and 93 in the second case).

CONCLUSIONS:
The OSNA results for the detection of LNM in patients with PTC are comparable with those observed using conventional techniques. However, its quantitative nature could be useful to more accurately detect lymph node involvement.

KEYWORDS:
OSNA; lymph node metastases; papillary thyroid carcinoma

PMID: 25536089

Long-term Results of Observation vs Prophylactic Selective Level VI Neck Dissection for Papillary Thyroid Carcinoma at a Cancer Center.

Ywata de Carvalho A¹, Chulam TC¹, Kowalski LP¹.

Abstract

IMPORTANCE:
The indication for prophylactic central neck dissection in papillary thyroid cancer (PTC) is controversial.

OBJECTIVE:
To compare long-term results of observation vs prophylactic selective level VI neck dissection for PTC.

DESIGN, SETTING, AND PARTICIPANTS:
We performed a retrospective cohort study of 812 patients with PTC who were treated from January 1, 1996, through January 1, 2007, at the Department of Head and Neck Surgery and Otorhinolaryngology of A. C. Camargo Cancer Center. A group of 580 consecutive patients with previously untreated PTCs and without lymph node metastasis were eligible for the study. We collected and analyzed retrospective data from February 1, 2012, through August 31, 2013.

INTERVENTIONS:
One hundred two patients (group A) underwent total thyroidectomy with elective central neck dissection; 478 patients (group B) underwent total thyroidectomy alone.

**MAIN OUTCOMES AND MEASURES:**
Absence of difference in rates of locoregional control and rates of major complications in group A.

**RESULTS:**
In group A, the rate of occult metastatic disease was 67.2%. Patients in group A exhibited higher rates of temporary hypocalcemia (46.1% vs 32.2%; *P* = .004) and permanent hypoparathyroidism (11.8% vs 2.3%; *P* < .001). We also found a significantly higher incidence of temporary (11.8% vs 6.1%; *P* = .04) and permanent (5.9% vs 1.5%; *P* = .02) recurrent laryngeal nerve dysfunction in group A. The overall recurrence rate at level VI was 1.9%.

**CONCLUSIONS AND RELEVANCE:**
Although the risk for occult lymph node metastasis reached 67.2% in a selected group of patients, elective central neck dissection for patients with PTC increased the risk for complications and did not contribute to a decrease in local recurrence rates.

PMID: 25997016

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**Management of thyroid nodules incidentally discovered on MIBI scanning for primary hyperparathyroidism.**


**Author information**

**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
Prognostic indicators in well-differentiated thyroid carcinoma when controlling for stage and treatment.

Krook KA¹, Fedewa SA, Chen AY.

Abstract

OBJECTIVES/HYPOTHESIS:
The incidence of thyroid carcinoma is rising. Few studies have examined patient characteristics that influence survival when adjusting for treatment and tumor stage/extent.

STUDY DESIGN:
Retrospective analysis was performed using the Surveillance Epidemiology and End Results registry data among patients diagnosed with well-differentiated thyroid (WDT) carcinoma during 1988-2009.

METHODS:
Kaplan-Meir survival curves were used to estimate 5- and 10-year cause-specific and overall survival differences by sociodemographics, clinical characteristics, and treatment. Multivariate Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

RESULTS:
A total of 83,985 patients were identified with WDT carcinoma. Blacks had higher hazard of death at 5 years (HR, 1.67; 95% CI, 1.42-1.96) and 10 years (HR, 1.57; 95% CI, 1.37-1.80) when compared to Caucasians, but there were no significant differences in cause-specific deaths. Hispanics had higher overall and cause-specific 5-year and 10-year hazard of death (5-year cause-specific: HR, 1.56; 95% CI, 1.23-1.99). Age was the most significant predictor of cause-specific and overall survival, with risk increasing in a nonlinear fashion. After age 45 years, the HR for 5- and 10-year cause-specific survival rose drastically, reaching an HR of 153 for individuals aged 85 years and older (HR, 153.45; 95% CI, 97.84-240.67).

CONCLUSIONS:
Age was the strongest factor associated with WDT cancer in our study. African Americans had worse overall survival, although only Hispanics had a significantly worse cause-specific survival. These factors should be taken into account in counseling patients and treatment planning.

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KEYWORDS:
Thyroid carcinoma; outcomes; race; survival

PMID: 25583017  Mälale sayfası

Prediction Table and Nomogram as Tools for Diagnosis of Papillary Thyroid Carcinoma: Combined Analysis of Ultrasonography, Fine-Needle Aspiration Biopsy, and BRAF V600E Mutation.

Kim SK¹, Lee JH, Woo JW, Park I, Choe JH, Kim JH, Kim JS.

Abstract
Although ultrasonography (US)-guided fine-needle aspiration biopsy (FNAB) is the most reliable diagnostic modality for evaluating thyroid nodules, 10% to 40% of FNAB samples yield indeterminate findings. The BRAF V600E mutation, a highly specific molecular marker for papillary thyroid carcinoma (PTC), well known for its prognostic value, has dubious diagnostic value because of its low sensitivity. Novel strategies are clearly needed to distinguish PTC, which represents the majority of thyroid malignancies, from other thyroid nodules. The records of 3297 patients with surgically proven PTC were retrospectively reviewed. A prediction table and nomogram were designed using a combination of diagnostic parameters for US, FNAB, and the BRAF V600E mutation. For the nomogram, parameters were proportionally assigned 0 to 100 points according to their regression coefficient for PTC. The probability of PTC for thyroid nodules with intermediate-risk (IR) US and atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) FNAB was significantly dependent on BRAF V600E mutation status based on our prediction table (negative, 29.2% vs positive, 87.5%; P < 0.001). By our nomogram, the probability of PTC for thyroid nodules with IR US, AUS/FLUS FNAB, and positive BRAF V600E mutation was approximately 85% to 90%. We strongly recommend preoperative evaluation of the BRAF V600E mutation in indeterminate thyroid nodules. The prediction table and nomogram developed in this study could help clinicians and patients easily assess the probability of PTC in the preoperative period.

PMID: 26020381  Makale sayfası


Parathyroid Localization and Preservation during Transcervical Resection of Substernal Thyroid Glands.

Heineman TE¹, Kadkade P², Kutler DI³, Cohen MA³, Kuhel W¹.

Author information

Abstract

OBJECTIVE:
The feasibility of parathyroid preservation during thyroidectomy has not been well documented for cases in which the thyroid gland extends into the mediastinum.

STUDY DESIGN:
Retrospective chart review.

SETTING:
Tertiary academic referral center.

SUBJECTS AND METHODS:
In this retrospective cohort study, 70 consecutive patients who had substernal thyroid glands treated with a transcervical thyroidectomy between 1993 and 2013 were compared with 286 thyroidectomies that did not entail substernal extension within that same time period. All localized parathyroid glands were confirmed histologically.

RESULTS:
Of 160 possible parathyroid glands in the substernal cases, 119 (74%) were histologically confirmed intraoperatively (67 superior and 52 inferior). In nonsubsternal cases, 725 (89%) were histologically confirmed (372 superior and 353 inferior). There was a statistically significant difference between the substernal and nonsubsternal cases in the total number of glands found (P < .0001) and the number of superior and inferior glands that were identified (P = .009 and < .0001).

CONCLUSIONS:
Even when the thyroid gland extends into the mediastinum, it is often possible, although with reduced efficiency, to identify and preserve the parathyroid glands.


**KEYWORDS:**
goiter; hypoparathyroidism; parathyroid; substernal; thyroidectomy

PMID: 25847147 [Makale sayfası]


High TPOAb Levels (>1300 IU/mL) Indicate Multifocal PTC in Hashimoto's Thyroiditis Patients and Support Total Thyroidectomy.

**Dong S**, **Xia Q**, **Wu YJ**. 

**Abstract**

**OBJECTIVE:**
We aimed to identify whether thyroid peroxidase antibodies (TPOAb) are indicative of multifocal papillary thyroid cancer (PTC) in Hashimoto's thyroiditis (HT) patients and may help to determine necessity for total thyroidectomy.

**STUDY DESIGN:**
Retrospective cohort study.

**SETTING:**
Teaching hospital.

**SUBJECTS:**
A total of 808 consecutive patients with HT alone or with HT and unifocal or multifocal PTC were included.

**METHODS:**
Preoperative thyroid function tests, TPOAb determination, preoperative ultrasonography, intraoperative frozen biopsy, and postoperative routine pathologic examination to confirm thyroid nodules were performed for all patients. Patients with nodules or malignancy potential on ultrasound and fine-needle aspiration cytology were included. Patients with hyperthyroidism, concomitant chronic disease, a history of other malignant tumors, or history of major diseases were excluded. All patients underwent surgery, and HT and PTC were confirmed by postoperative pathologic results.

**RESULTS:**
No significant differences were found in age and sex between groups (P > .05). TPOAb ≤1300 IU/mL were more prevalent in the HT + unifocal PTC group than in the other groups (99.57% vs 15.52% and 60.75%, P < .001). TPOAb >1300 IU/mL were more prevalent in the HT + multifocal PTC group than in the other groups (84.48% vs 0.43% and 39.25%; P < .001). Compared to the other groups, the HT + multifocal PTC group had higher percentages of patients with elevated thyroid-stimulating hormone and positive central lymph node (LN) metastasis (elevatedthyroid-stimulating hormone: 8.7% vs 3.2% and 6.5%, P = .008; positive central LN metastasis: 74.57% vs 67.38% and 0%, P < .001).

**CONCLUSION:**
High TPOAb levels (>1300 IU/mL) are definitive indicators of multifocal PTC in HT patients, which may support surgical treatment with total thyroidectomy.
Preoperative Serum Thyrotropin to Thyroglobulin Ratio Is Effective for Thyroid Nodule Evaluation in Euthyroid Patients.

Wang L¹, Li H¹, Yang Z¹, Guo Z¹, Zhang Q².

Author information

Abstract

OBJECTIVE:
This study was designed to assess the efficiency of the serum thyrotropin to thyroglobulin ratio for thyroid nodule evaluation in euthyroid patients.

STUDY DESIGN:
Cross-sectional study.

SETTING:
Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China.

SUBJECTS AND METHODS:
Retrospective analysis was performed for 400 previously untreated cases presenting with thyroid nodules. Thyroid function was tested with commercially available radioimmunoassays. The receiver operating characteristic curves were constructed to determine cutoff values. The efficacy of the thyrotropin:thyroglobulin ratio and thyroid-stimulating hormone for thyroid nodule evaluation was evaluated in terms of sensitivity, specificity, positive predictive value, positive likelihood ratio, negative likelihood ratio, and odds ratio.

RESULTS:
In receiver operating characteristic curve analysis, the area under the curve was 0.746 for the thyrotropin:thyroglobulin ratio and 0.659 for thyroid-stimulating hormone. With a cutoff point value of 24.97 IU/g for the thyrotropin:thyroglobulin ratio, the sensitivity, specificity, positive predictive value, positive likelihood ratio, and negative likelihood ratio were 78.9%, 60.8%, 75.5%, 2.01, and 0.35, respectively. The odds ratio for the thyrotropin:thyroglobulin ratio indicating malignancy was 5.80. With a cutoff point value of 1.525 µIU/mL for thyroid-stimulating hormone, the sensitivity, specificity, positive predictive value, positive likelihood ratio, and negative likelihood ratio were 74.0%, 53.2%, 70.8%, 1.58, and 0.49, respectively. The odds ratio indicating malignancy for thyroid-stimulating hormone was 3.23.

CONCLUSION:
Increasing preoperative serum thyrotropin:thyroglobulin ratio is a risk factor for thyroid carcinoma, and the correlation of the thyrotropin:thyroglobulin ratio to malignancy is higher than that for serum thyroid-stimulating hormone.


KEYWORDS:
thyroglobulin; thyroid carcinoma; thyroid function test; thyroid nodule evaluation; thyrotropin
Thyroid incidentalomas detected on 18F-fluorodeoxyglucose-positron emission tomography/computed tomography: Thyroid Imaging Reporting and Data System (TIRADS) in the diagnosis and management of patients.

Yoon JH\textsuperscript{1}, Cho A\textsuperscript{2}, Lee HS\textsuperscript{3}, Kim EK\textsuperscript{1}, Moon HJ\textsuperscript{1}, Kwak JY\textsuperscript{4}.

Abstract

BACKGROUND:
Our aim was to evaluate the role of the Thyroid Imaging Reporting and Data System (TIRADS) in the risk stratification of thyroid incidentalomas detected on 18F-fluorodeoxyglucose-positron emission tomography/computed tomography (18F-FDG-PET/CT) scans.

METHODS:
Eighty-seven thyroid nodules in 84 patients showing incidentally detected increased uptake on 18F-FDG-PET/CT who also had ultrasonography (US)-guided fine needle aspiration performed were included. On review of the US images, a TIRADS category was assigned to each thyroid nodule based on the number of suspicious US features. The correlation between the TIRADS category and the standard uptake values (SUV) on 18F-FDG-PET/CT were calculated and compared.

RESULTS:
Of the 87 thyroid nodules, 47 (54%) were benign, and 40 (46%) were malignant. The malignancy rate of the TIRADS categories were as follows: 9% for category 3, 15% for category 4a, 39% for category 4b, 72% for category 4c, and 100.0% for category 5. Combining the TIRADS with the SUV showed increased specificity and positive predictive value but decreased sensitivity and negative predictive value compared with TIRADS alone (all P < .05). The area under the receiver operating characteristics curve value of TIRADS was the greatest, comparable with the combined TIRADS and SUV (0.737 to 0.724, P = .788).

CONCLUSION:
TIRADS may be applied in the risk stratification of thyroid incidentalomas detected on 18F-FDG-PET/CT. Considering the high malignancy rate of thyroid incidentalomas showing increased 18F-FDG uptake, ultrasonography-guided fine needle aspiration is mandatory even if there are no suspicious features present on US.

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BACKGROUND:
The recently introduced Afirma gene expression classifier (AGEC) provides binary results (benign or suspicious) to guide management of cytologically indeterminate thyroid nodules. The AGEC is intended to reduce unnecessary surgeries for benign nodules, and management algorithms favor surgery for suspicious results. Limited data is available on the performance of this test for Hürthle cell nodules (HCNs). We hypothesized that a predominance of Hürthle cells leads to an increased rate of suspicious AGEC results with a potential for overtreatment, despite a relatively low risk of malignancy.

METHODS:
The pathology databases from three tertiary care facilities were queried from 2010 to 2014 for fine needle aspirates (FNAs) diagnosed as suspicious for Hürthle cell neoplasm (SHCN) or atypia of undetermined significance/follicular lesion of undetermined significance concerning for Hürthle cell neoplasm (AFHCN). Cytology diagnoses were rendered internally prior to AGEC testing. The patient demographics, FNA diagnosis, AGEC result, surgical procedure, and pathologic outcome were recorded.

RESULTS:
Our cohort consisted of 134 patients with HCNs. Prior to AGEC availability, 62 patients were treated: 81% (50/62) of patients had surgery, and 34% (17/50) of the resected index nodules were malignant. After introduction of the AGEC, 72 patients underwent AGEC testing: 65% (47/72) of patients had surgery, and 13% (6/46) of the resected nodules were malignant. Thirty-two percent (23/72) of patients had a benign AGEC result and were not sent to surgery, and 4% (3/72) had surgery despite a benign AGEC result with benign final pathology; whereas 63% (45/72) of patients had suspicious AGEC results, 96% of these patients (43/45) underwent surgery, and 14% (6/43) of these index nodules were malignant.

CONCLUSIONS:
While 32% of tested patients avoided surgery based on a benign AGEC, 86% of suspicious AGEC patients had unnecessary surgery, reflecting a substantially lower rate of malignancy from what was previously reported for all indeterminate nodules. Given the approximate pre-test malignancy risk of 25-35% for an FNA diagnosis of SHCN or AFHCN, a suspicious AGEC diagnosis does not increase the probability of malignancy in an HCN, and patients should be counseled accordingly.

PMID: 25962906

Surgical management of laryngeal invasion by papillary thyroid carcinoma: a retrospective analysis.

Moritani S

BACKGROUND:
Papillary thyroid carcinoma (PTC) has an excellent prognosis. Although rare, PTC invasion into the upper aerodigestive tract can adversely affect patient prognosis and quality of life. This study investigated the impact of tumor excision on the prognosis and postoperative status of patients with PTC invasion of the larynx.

METHODS:
Data on PTC patients who underwent surgery at the author’s institution between April 1981 and March 2010 were retrospectively reviewed, and 55 patients with thyroid cartilage invasion were enrolled. Curative resection was performed for all patients, and laryngeal function was preserved or reconstructed when possible.
RESULTS:
Of the 55 patients, 40 and 15 patients had superficial and intraluminal invasion of the larynx, respectively. The 10-year disease-specific survival rates were 81.0% and 61.4% in patients who underwent surgery for superficial and intraluminal invasion of the larynx, respectively. Only two patients (3.6%) had an isolated locoregional recurrence in the larynx. Four patients (7.3%) underwent total laryngectomy during the initial surgery or surgery for laryngeal recurrence. Permanent stoma remained in 26 patients (47%): 14 with laryngeal invasion, and 12 with invasion of other aerodigestive structures. The number of invaded aerodigestive structures including the larynx was correlated with the presence of permanent stoma.

CONCLUSIONS:
In many patients, PTC invasion of the larynx remained at the thyroid cartilage or paraglottic space. Most patients did not require total laryngectomy. Good locoregional control was achieved with surgical tumor excision in patients with laryngeal invasion. Distant metastases were the major cause of death in patients with PTC invasion of the larynx.

PMID: 25757392

Usefulness of core needle biopsy for thyroid nodules with macrocalcifications: comparison with fine-needle aspiration.

Yi KS\textsuperscript{1,2}, Kim JH\textsuperscript{1}, Na DG\textsuperscript{1}, Seo H\textsuperscript{1}, Min HS\textsuperscript{4,5}, Won JK\textsuperscript{4}, Yun TJ\textsuperscript{1}, Ryoo I\textsuperscript{6}, Kim SC\textsuperscript{7}, Choi SH\textsuperscript{1}, Sohn CH\textsuperscript{1}.

Author information

Abstract

BACKGROUND:
This study was performed to determine the benefits of core needle biopsy (CNB), as compared with fine-needle aspiration (FNA), for the diagnosis of thyroid nodules with macrocalcifications.

MATERIALS AND METHODS:
The institutional review board approved this retrospective study, and informed consent was waived. From February 2010 to March 2012, the study included 147 thyroid nodules with macrocalcification of 145 consecutive patients who underwent simultaneous FNA and CNB for each nodule. Diagnostic accuracy and inconclusive diagnoses, including nondiagnostic reading and atypia of undetermined significance or follicular lesion of undetermined significance reading were compared among FNA, CNB, and a combination of FNA and CNB (FNA/CNB) using McNemar's test; the benefits of CNB were calculated.

RESULTS:
Compared to FNA, CNB and FNA/CNB showed fewer inconclusive diagnoses (FNA vs. CNB: 62/147 [42.2\%] vs. 14/147 [9.5\%], p<0.001; FNA vs. FNA/CNB: 62/147 [42.2\%] vs. 14/147 [9.5\%], p<0.001), resulting in the avoidance of repeat FNA or diagnostic surgery in 48 of 62 patients (77.4\%, respectively in CNB and FNA/CNB) who would have undergone these procedures if only FNA was performed. Compared to FNA, FNA/CNB showed higher sensitivity and accuracy (sensitivity: 23/32 [71.9\%] vs. 31/32 [96.9\%], p=0.008; accuracy: 77/86 [89.5\%] vs. 85/86 [98.8\%], p=0.008), resulting in avoidance of delayed surgery in eight of nine patients (88.9\%) with thyroid cancer in whom the surgery would have been missed if FNA only had been performed.

CONCLUSION:
In the workup of thyroid nodules with macrocalcification, compared with FNA alone, FNA/CNB decreases inconclusive diagnoses and increases sensitivity, thereby reducing repeated FNA procedures, diagnostic surgeries, and delayed therapeutic surgeries.

Pre-operative ultrasound diagnosis of nodal metastasis in papillary thyroid carcinoma patients according to nodal compartment.

Lee YJ¹, Kim DW², Park HK³, Kim do H⁴, Jung SJ⁵, Oh M⁶, Bae SK⁷.

Author information

Abstract

The aim of this study was to assess the accuracy of ultrasound (US) and individual US features in the diagnosis of nodal metastasis in patients with papillary thyroid carcinoma (PTC) with respect to nodal compartment. US diagnoses and individual US features of nodal metastases with respect to nodal compartment were investigated in 184 consecutive PTC patients who underwent pre-operative US. Histopathologic results were used as a reference standard. One hundred thirty-six of 368 (37.0%) central compartments contained one or more metastatic nodes, whereas 44 of 48 (91.7%) lateral compartments had one or more metastatic nodes. The malignancy rates of suspicious US diagnoses in the central and lateral compartments were 66.3% (53/80) and 93.3% (42/45), respectively. The central and lateral compartments differed significantly in nodal composition, echogenicity, calcification, shape, hilar echogenicity and vascularity. The accuracy of US in the diagnosis of nodal metastases from PTC was lower in the central compartment than in the lateral compartment.

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KEYWORDS:
Compartment; Lymph node; Metastasis; Neck; Papillary thyroid carcinoma; Ultrasound


The clinical prognosis of patients with cN0 papillary thyroid microcarcinoma by central neck dissection.

Zhang L¹, Liu Z², Liu Y³, Gao W⁴, Zheng C⁵.

Author information

Abstract

BACKGROUND:
Central lymph node metastasis of papillary thyroid microcarcinoma (PTMC) is common; however, prophylactic central lymph node dissection (CLND) is still controversial because of the possible increased morbidity. The purpose of this study is to determine the clinical outcome of patients with cN0 PTMC by central neck dissection.

METHODS:
A retrospective cohort study was conducted on patients with PTMC without preoperative evidence of lymph node disease (cN0), and the outcomes were compared between patients undergoing total thyroidectomy (TT) alone (group A) and patients undergoing TT with CLND (group B).

RESULTS:
In this study, 242 patients with cN0 PTMC were included. Group A had 108 patients and group B had 134 patients. During a follow-up of over 60 months, the long-term postoperative complications were equivalent between the two groups. In group B, the presence of involved central neck lymph nodes upstaged 16% of patients to stage III disease, which necessitated additional postoperative radioactive iodine treatment. More patients had recurrences in group A. The rate of reoperation in the central compartment was higher in group A than in group B (8.3% vs 2.2%, P < 0.01).

CONCLUSIONS:
Prophylactic CLND does not increase long-term postoperative complications and reduces the risk of recurrence in the central compartment.

PMID: 25889385 Makale sayfası
Suspicious sonographic and cytological findings in patients with subacute thyroiditis: Two case reports.

Park HK¹, Kim DW, Lee YJ, Ha TK, Kim do H, Bae SK, Jung SJ.

**Author information**

**Abstract**

We here report on two cases of suspicious cytological findings upon ultrasound (US)-guided fine-needle aspiration (US-FNA) in patients with subacute thyroiditis (SAT). A 46-year-old woman who underwent US-FNA for a suspicious thyroid nodule in the right lobe at a local clinic was referred to our hospital for surgical treatment. Based on the cytology results, total thyroidectomy was performed. The histopathology findings confirmed the presence of SAT in the right lobe and absence of thyroid malignancy. A 40-year-old woman with a thyroid nodule in the left lobe with suspicious cytological findings upon US-FNA was referred to our hospital for surgical treatment. However, neck US revealed typical sonographic findings of SAT. On follow-up US 3 months later, near complete disappearance of the typical sonographic findings of SAT was observed, while a hypoechoic solid thyroid nodule in the left upper lobe was clearly visualized. Accordingly, US-FNA was performed for the hypoechoic thyroid nodule. Papillary thyroid carcinoma was suspected on the basis of the cytology findings; histopathologically, SAT was confirmed in both thyroid lobes and a papillary thyroid carcinoma was confirmed in the left lobe.

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**KEYWORDS:**
cytology; malignancy; subacute thyroiditis; thyroid; ultrasound

PMID: 25350937  Makale sayfası
The Role of Radionuclide Imaging in the Surgical Management of Primary Hyperparathyroidism.

Hindié E¹, Zanotti-Fregonara P², Tabarin A³, Rubello D⁴, Morelec I⁵, Wagner T⁶, Henry JF⁷, Taïeb D⁸.

Author information

Abstract

Primary hyperparathyroidism is a frequent and potentially debilitating endocrine disorder for which surgery is the only curative treatment. The modalities of parathyroid surgery have changed over the last 2 decades, as conventional bilateral neck exploration is no longer the only surgical approach. Parathyroid scintigraphy plays a major role in defining the surgical strategy, given its ability to orient a targeted (focused) parathyroidectomy and to recognize ectopic locations or multiglandular disease. This review, which represents a collaborative effort between nuclear physicians, endocrinologists, and endocrine surgeons, emphasizes the importance of performing imaging before any surgery for primary hyperparathyroidism, even in the case of conventional bilateral neck exploration. We discuss the advantages and drawbacks of targeted parathyroidectomy and the performance of various scintigraphic protocols to guide limited surgery. We also discuss the optimal strategy to localize the offending gland before reoperation for persistent or recurrent hyperparathyroidism. Finally, we describe the potential applications of novel PET tracers, with special emphasis on 18F-fluorocholine.

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KEYWORDS:
11C-methionine; 18F-fluorocholine; MIBI; PET/CT; SPECT/CT; dual-tracer; hyperparathyroidism; parathyroid subtraction imaging

PMID: 25858040


Li Y¹, Jian WH², Guo ZM³, Li QL⁴, Lin SJ⁴, Huang HY⁵.

Author information

Abstract

OBJECTIVE:

To investigate the ability of carbon nanoparticles (CNs) to identify lymph nodes and protect parathyroid glands during thyroid cancersurgery.

DATA SOURCES:

English and Chinese literature in PubMed, ClinicalTrials.gov, EMBASE, the Cochrane Database of Systematic Reviews, the China Biology Medicine Database, the China Master's and Doctoral Theses Full-Text Database, the China National Knowledge Infrastructure, the WANFANG database, and the Cqvip database (from January 2009 to July 2014).
REVIEW METHODS:
Studies were included if they were randomized controlled trials or nonrandomized controlled trials for thyroidectomy and central neck dissections that compared the use of CNs with methylene blue or a blank control in patients undergoing initial thyroid cancer surgery. The primary outcomes were the number of retrieved central lymph nodes and the accidental parathyroid removal rate.

RESULTS:
This meta-analysis identified 11 randomized controlled trials and 4 nonrandomized controlled trials comprising 1055 patients. Compared with the outcomes of the blank controls, the use of CNs resulted in an average of 2.71 more lymph nodes removed per patient (weighted mean difference = 2.71, 95% confidence interval [CI] = 1.68-3.74, P < .001), a 23% lower rate of accidental parathyroid removal (odds ratio = 0.23, 95% CI = 0.10-0.54, P = .0008), and similarly reduced rates of transient hypoparathyroidism and hypocalcemia. Compared with methylene blue, the use of CNs resulted in an average of 1.50 more lymph nodes removed per patient (weighted mean difference = 1.50, 95% CI = 0.11-2.89, P = .03) and a 5% reduction in the rate of accidental parathyroid removal (odds ratio = 0.05, 95% CI = 0.01-0.29, P = .0007).

CONCLUSION:
CNs partially improve the extent and accuracy of neck dissection and preserve the normal anatomic structure and physiologic function of the parathyroid glands during thyroid cancer surgery.


KEYWORDS:
carbon nanoparticles; lymph node; methylene blue; parathyroid; thyroid cancer

PMID: 25897006
Validation of intra-operative parathyroid hormone and its decline as early predictors of hypoparathyroidism after total thyroidectomy: A prospective cohort study.

Gupta S¹, Chaudhary P², Durga CK¹, Naskar D¹.

Abstract

INTRODUCTION:
Total thyroidectomy is a preferred surgical technique for benign as well as malignant thyroid pathologies, but many a times can cause hypoparathyroidism. The aim of this study is to evaluate the intra-operative parathyroid hormone (ioPTH) level and its decline as predictors for post-operative hypoparathyroidism after total thyroidectomy.

METHODS:
In this single-centre prospective cohort study, 90 patients who underwent total thyroidectomy for benign as well as malignant pathologies of thyroid gland were studied. Intra-operative parathyroid levels and at different time intervals parathyroid hormone and serum calcium levels were measured to predict hypoparathyroidism. The data was analysed using independent sample t test and p value < .05 was considered to be significant.

RESULTS:
There were 14 male and 76 female patients with a mean age of 41 years. Most common thyroid pathology for which total thyroidectomy was done was colloid goitre (62). Twenty four patients (26.66%) developed hypoparathyroidism. Intra-operative PTH was found to be most accurate predictor for diagnosing post-operative hypoparathyroidism (cut off was (11.3 pg/ml, calculated using ROC curves) and has maximum sum of sensitivity (91.7%) and specificity (97%). On taking cut off values of intra-operative PTH and PTH decline together, they were found to be most accurate predictor for permanent hypoparathyroidism.

DISCUSSION:
Early and accurate predictor of hypoparathyroidism is very important and always sought. Very early prediction during intra-operative periods can be used for auto transplantation of parathyroid gland.

CONCLUSION:
Intra-operative parathyroid hormone and its decline are accurate, reliable, and early predictor of hypoparathyroidism after total thyroidectomy.

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KEYWORDS:
Hypoparathyroidism; Intra-operative parathyroid hormone; Parathyroid hormone decline; Total thyroidectomy

PMID: 25934417 Makale sayfası
Intraoperative guidance in parathyroid surgery using near-infrared fluorescence imaging and low-dose Methylene Blue.

Tummers QR¹, Schepers A¹, Hamming JF¹, Kievit J¹, Frangioni JV², van de Velde CJ¹, Vahrmeijer AL³.

Abstract

BACKGROUND:
Identification of diseased and normal parathyroid glands during parathyroid surgery can be challenging. The aim of this study was to assess whether near-infrared (NIR) fluorescence imaging using administration of a low-dose Methylene Blue (MB) at the start of the operation could provide optical guidance during parathyroid surgery and assist in the detection of parathyroid adenomas.

METHODS:
Patients diagnosed with primary hyperparathyroidism planned for parathyroidectomy were included. Patients received 0.5 mg/kg MB intravenously directly after start of anesthesia. During the operation, NIR fluorescence imaging was performed to identify parathyroid adenomas. Imaging results were compared with a previous published feasibility study in which 12 patients received MB after intraoperative identification of the adenoma.

RESULTS:
A total of 13 patients were included in the current study. In 10 of 12 patients with a histologically proven adenoma, the adenoma was fluorescent. Mean signal to background ratio was 3.1 ± 2.8. Mean diameter of the resected lesions was 17 ± 9 mm (range 5-28 mm). Adenomas could be identified up to 145 minutes after administration, which was the longest timespan until resection. Interestingly, in 3 patients, a total of 6 normal parathyroid glands (median diameter 2.5 mm) with a signal to background ratio of 1.8 ± 0.4 were identified using NIR fluorescence imaging.

CONCLUSION:
Early administration of low-dose MB provided guidance during parathyroidectomy by identifying both parathyroid adenomas and normal parathyroid glands. In patients in whom difficult identification of the parathyroid adenoma is expected or when normal glands have to be identified, the administration of MB may improve surgical outcome.

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PMID: 25958068
Makale sayfası
Predictors of Multigland Disease in Primary Hyperparathyroidism: A Scoring System with 4D-CT Imaging and Biochemical Markers.

Sepahdari AR¹, Bahl M², Harari A³, Kim HJ¹, Yeh MW³, Hoang JK⁴.

Author information

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 Makale sayfası
Outpatient parathyroid surgery: ten-year experience: is it safe?

Flynn MB1, Quayyum M, Goldstein RE, Bumpous JM.

Abstract

Outpatient parathyroid surgery is increasing in frequency especially for patients undergoing minimally invasive operations. From January 1, 2000 to December 31, 2009, 585 operations were performed on patients with untreated primary hyperparathyroidism. Outpatient operations were performed on 43 per cent (249/585), whereas 57 per cent (336/585) were admitted. Comorbidities were present in 63 per cent of outpatients and 72 per cent of inpatients, whereas systemic complications occurred in 0.8 per cent of outpatients and 7 per cent of inpatients. Ninety-four per cent of outpatients were minimally invasive although inpatient procedures were evenly divided. Local complications were low (8% and 6%) in both groups. Using zip codes to determine distance from home to hospital, no differences were noted. Readmission rates were low (<0.5%) and the same in each group. Inpatients longer than 23 hours tended to be older with higher local and systemic complication rates. Over a decade, most patients undergoing same day parathyroid surgery had minimally invasive operations with lower comorbidities and lower systemic complications than inpatients. Minimally invasive and less complex nonminimally invasive operations can safely be performed on an outpatient basis with careful patient selection. Patient with more severe comorbidities and multiple comorbidities are less favorable candidates for outpatient surgery because of a higher risk of systemic complications.

PMID: 25975331

Operative failure rate and documentation of family history in young patients undergoing focused parathyroidectomy for primary hyperparathyroidism.

Stephen ET1, Quillo AR, Lewis KE, Harden FL, Bumpous JM, Flynn MB, Callender GG.

Abstract

Primary hyperparathyroidism in multiple endocrine neoplasia type I usually affects all parathyroid glands, making focused parathyroidectomy (FP) inappropriate. The risk of previously undiagnosed multiple endocrine neoplasia type I in a younger patient with primary hyperparathyroidism is higher than in an older patient. We hypothesized that FP may lead to a higher failure rate in younger versus older patients. A retrospective review was performed of a single-institution database of patients who underwent parathyroidectomy for primary hyperparathyroidism. Routine statistical analysis was performed, including Fisher’s exact test. A total of 635 patients were included. Operative failure occurred in 7/55 (13%) younger patients and 21/580 (4%) older patients (P = 0.007). In conclusion, operative failure occurred in a statistically significantly higher percentage of younger versus older patients undergoing FP. This is partly explained by undiagnosed multiple endocrine neoplasia syndrome type I in the younger patient group. Endocrine surgeons must make every effort to preoperatively identify multiple endocrine neoplasia syndrome type I in the younger patient population.

PMID: 26031271

Trends in the frequency and quality of parathyroid surgery: analysis of 17,082 cases over 10 years.

Abdulla AG¹, Ituarte PH, Harari A, Wu JX, Yeh MW.

Author information

Abstract

OBJECTIVE:
To examine trends in the frequency and quality of surgery for primary hyperparathyroidism (PHPT) in California during the period of 1999 to 2008.

BACKGROUND:
The quality of surgery for PHPT can be measured by the complication rate and the success rate of surgery. A fraction of patients with failed initial surgery undergo reoperation.

METHODS:
Data on patients undergoing parathyroidectomy (PTx) were obtained from the California Office of Statewide Health Planning and Development. Renal transplant recipients and dialysis patients were excluded. Hospitals were categorized by case volume: Very low: 1 to 4 operations annually; Low: 5 to 9; Medium, 10 to 19; High: 20 to 49; Very high: 50 or more. Complication rates and the percentage of cases requiring reoperation were analyzed.

RESULTS:
A total of 17,082 cases were studied. Annual case volume grew from 990 to 2746 (177% increase) over the study period, corresponding to a 147% increase in the per capita PTx rate. The proportion of cases performed by very high-volume hospitals increased from 6.4% to 20.5% (P < 0.001). The overall complication rate declined from 8.7% to 3.8% (P < 0.001). Complication rates were inversely related to hospital volume (very high volume, 3.9% vs very low volume, 5.2%, P < 0.05). Reoperation was performed in 363 patients (2.1%). The reoperation rate increased from 0.91% to 2.73% during the study period (P < 0.01). The reoperation rate was inversely and nonlinearly related to hospital volume, as described by the equation % reoperation = 100/(total hospital case volume).

CONCLUSIONS:
Surgery for PHPT has grown safer and more common over time. High-volume centers have lower rates of complication and reoperation.

PMID: 24950283  Makale sayfası


CaPThUS scoring model in primary hyperparathyroidism: can it eliminate the need for iOPTH testing?

Elfenbein DM¹, Weber S, Schneider DF, Sippel RS, Chen H.

Author information

Abstract

BACKGROUND:
The CaPThUS model was reported to have a positive predictive value of 100 % to correctly predict single-gland disease in patients with primary hyperparathyroidism, thus obviating the need for intraoperative parathyroid hormone (iOPTH) testing. We sought to apply the CaPThUS scoring model in our patient population and assess its utility in predicting long-term biochemical cure.

METHODS:
We retrospectively reviewed all parathyroidectomies for primary hyperparathyroidism performed at our university hospital from 2003 to 2012. We routinely perform ioPTH testing. Biochemical cure was defined as a normal calcium level at 6 months.

RESULTS:
A total of 1,421 patients met the inclusion criteria: 78 % of patients had a single adenoma at the time of surgery, 98 % had a normal serum calcium at 1 week postoperatively, and 96 % had a normal serum calcium level 6 months postoperatively. Using the CaPTHUS scoring model, 307 patients (22.5 %) had a score of ≥ 3, with a positive predictive value of 91 % for single adenoma. A CaPTHUS score of ≥ 3 had a positive predictive value of 98 % for biochemical cure at 1 week as well as at 6 months.

CONCLUSIONS:
In our population, where ioPTH testing is used routinely to guide use of bilateral exploration, patients with a preoperative CaPTHUS score of ≥ 3 had good long-term biochemical cure rates. However, the model only predicted adenoma in 91 % of cases. If minimally invasive parathyroidectomy without ioPTH testing had been done for these patients, the cure rate would have dropped from 98 % to an unacceptable 89 %. Even in these patients with high CaPTHUS scores, multigland disease is present in almost 10 %, and ioPTH testing is necessary.

PMID: 25212837


Parathyroid Surgery: Correlation between Preoperative Localization Studies and Surgical Outcomes.

Ebner Y¹, Garti-Gross Y¹, Margulis A¹, Levy Y², Nabrisky D³, Ophir D¹, Rotman-Pikielny P²,³.

Author information

Abstract

OBJECTIVE:
Preoperative imaging techniques have enabled minimally invasive parathyroid surgery to supersede the traditional approach to hyperparathyroidism surgery, which included cervical exploration. Cervical ultrasound (US) and sestamibi scan (MIBI) are commonly performed, but the results of these localization tests do not always match. This study correlated surgical outcomes with preoperative localization findings, including matched positive US and MIBI studies, one positive study (US or MIBI), conflicting studies or negative results.

DESIGN:
Retrospective medical record review.

PATIENTS:
169 consecutive patients who underwent parathyroidectomy from 1/2005-12/2012.

MEASUREMENTS:
correlation between surgical outcomes and preoperative localization tests.

RESULTS:
All patients (134F/35M, 59.6±13.5 years-of-age) had primary hyperparathyroidism. US and MIBI localization studies matched in 76%, whereas 10.7% had positive MIBI only and 8.3% US only. Studies were negative in 3.6% and contradictory in 1.8%. Minimally invasive parathyroidectomy (MIP) was performed in 87% of the matched group and 89% of the MIBI-only group. Surgical success rate, defined as postoperative normalization of calcium and PTH levels, was similar in patients with a single positive study (MIBI or US) vs. double matched studies (MIBI and US). Patients were followed-up for 6 weeks. Overall, pathology was consistent with adenoma in 95%.
DISCUSSION:
Parathyroidectomy success rate was similar in patients with primary HPT and MIBI-only or US-only positive localization studies compared to those with matched US/MIBI studies. The results support a clinical algorithm in which positive results from one imaging technique, either MIBI or US, are sufficient to refer a patient for parathyroid surgery. This article is protected by copyright. All rights reserved.

KEYWORDS:
Parathyroidectomy; cervical ultrasound; hyperparathyroidism; mini-invasive parathyroidectomy; sestamibi scan

PMID: 26053249 Makale sayfası


Direct Comparison of Neck Pinhole Dual-Tracer and Dual-Phase MIBI Accuracies With and Without SPECT/CT for Parathyroid Adenoma Detection and Localization.
Heiba SI1, Jiang M, Rivera J, Genden E, Inabnet W 3rd, Machac J, Kostakoglu L.
Author information
Abstract
INTRODUCTION:
There is uncertainty about accuracies of dual-phase (DP) and dual-tracer (DT) parathyroid scintigraphy with the newly added SPECT/CT. Although SPECT/CT was shown to be helpful in parathyroid adenoma (PA) localization, it may not have optimal resolution as pinhole. This study directly compared diagnostic accuracies and confidences of various imaging protocols on same patients.

PATIENTS AND METHODS:
One hundred fifty-five patients with pathologically confirmed diagnosis were included. Pinhole DP, pinhole DT, pinhole DP SPECT/CT, pinhole DT SPECT/CT, and SPECT/CT with only pinhole-delayed MIBI (D) were reviewed for accuracies and certainties of PA diagnosis/localization. Parathyroid adenomas were classified as clearly or unclearly distinguishable from thyroid. Furthermore, the contribution of pinhole DP to pinhole DT SPECT/CT was assessed.

RESULTS:
Of 153 PAs, the correct diagnosis/localization was significantly higher by pinhole DT SPECT/CT than pinhole DP SPECT/CT, SPECT/CT D, pinhole DT alone, and DP alone. Parathyroid adenomas were clearly more distinguished from thyroid in pinhole DT than DP with/without SPECT/CT. Consequently, PA diagnosis certainty was higher in pinhole DT than DP, whereas PA localization certainty was higher in both with SPECT/CT. In pinhole DT SPECT/CT, the pinhole DP addition confirmed diagnosis/localization of only 24 uncertain PAs.

CONCLUSIONS:
In this large patient group, the accuracy and certainty of PA diagnosis/localization were higher in pinhole DT SPECT/CT than all other parathyroid scintigraphy protocols. Pinhole DT better identified PA than pinhole DP, whereas SPECT/CT improved PA localization in both protocols. Pinhole DP showed limited contribution and thus should be only considered when PA diagnosis/localization is uncertain by pinhole DT SPECT/CT.

PMID: 25783516 Makale sayfası
Is local resection sufficient for parathyroid carcinoma?

Basceken SI, Genc V, Ersoz S, Sevim Y, Celik SU, Bayram IK.

OBJECTIVES:
Parathyroid carcinoma is a rare malignant disease of the parathyroid glands that appears in less than 1% of patients with primary hyperparathyroidism. In the literature, the generally recommended treatment is en bloc tumor excision with ipsilateral thyroid lobectomy. Based on our 12 years of experience, we discuss the necessity of performing thyroid lobectomy on parathyroid carcinoma patients.

RESULTS:
Eleven parathyroid carcinoma cases were included in the study. All operations were performed at the Department of Endocrine Surgery at Ankara University Medical School. Seven of the patients were male (63.6%), and the mean patient age was 48.9 ± 14.0 years. Hyperparathyroidism was the most common indication for surgery (n=10, 90.9%). Local disease was detected in 5 patients (45.5%), invasive disease was detected in 5 patients (45.5%) and metastatic disease was detected in 1 patient (9.1%). The mean follow-up period was 99.6 ± 42.1 months, and the patients’ average disease-free survival was 96.0 ± 49.0 months. During the follow-up period, only 1 patient died of metastatic parathyroid carcinoma.

CONCLUSION:
Parathyroid carcinoma has a slow-growing natural progression, and regional lymph node metastases are uncommon. Although our study comprised few patients, it nevertheless showed that in selected cases, parathyroid carcinoma could be solely treated with parathyroidectomy.

PMID: 26017790

Correlating pre-operative vitamin D status with post-thyroidectomy hypocalcemia.

Falcone TE, Stein DJ, Jumaily JS, Pearce EN, Holick MF, McAneny DB, Jalisi S, Grillone GA, Stone MD, Devaiah AK, Noordzij JP.

OBJECTIVE:
To examine the relationship between pre-operative vitamin D status and post-thyroidectomy hypocalcemia.

METHODS:
Retrospective study examining 264 total and completion thyroidectomies conducted between 2007 and 2011. Subjects included had a recorded 25-hydroxyvitamin D (25(OH)D) level within 21 days prior to or 1 day following surgery, did not have a primary parathyroid gland disorder, and were not taking 1,25-dihydroxyvitamin D3 (calcitriol) prior to surgery. Some subjects were repleted with vitamin D pre-operatively if a low 25(OH)D level (typically below 20 ng/mL) was identified. Pre-operative 25(OH)D, concurrent neck dissection, integrity of parathyroid glands, final pathology, postoperative parathyroid hormone (PTH), calcium nadir and repletion, and length of stay were examined.

RESULTS:
The mean pre-operative 25(OH)D for all subjects was 25 ng/mL, and the overall rate of post-operative hypocalcemia was 37.5%. Lower pre-operative 25(OH)D did not predict postoperative hypocalcemia (P = .96); however, it did predict the need for postoperative 1,25-dihydroxyvitamin D3 administration (P = .01). Lower postoperative PTH levels (P = .001) were associated with postoperative hypocalcemia.
CONCLUSION:
Pre-operative 25(OH)D did not predict a postoperative decrease in serum calcium, although it did predict the need for 1,25-dihydroxyvitamin D3 therapy in hypocalcemic subjects. We recommend that 25(OH)D be assessed and, if indicated, repleted pre-operatively in patients undergoing total thyroidectomy.

ABBREVIATIONS:
25(OH)D = 25-hydroxyvitamin D PTH = parathyroid hormone.

PMID: 25536969  Makale sayfasi


Real-Time Super Selective Venous Sampling in Remedial Parathyroid Surgery.

Lebastchi AH1, Aruny JE2, Donovan PI1, Quinn CE1, Callender GG1, Carling T1, Udelsman R3.

Author information

Abstract

BACKGROUND:
Remedial cervical exploration for persistent or recurrent primary hyperparathyroidism can be technically difficult, but is expedited by accurate preoperative localization. We investigated the use of real-time super selective venous sampling (sSVS) in the setting of negative noninvasive imaging modalities.

STUDY DESIGN:
We performed a retrospective analysis of a prospective database incorporating real-time sSVS in a tertiary academic medical center. Between September 2001 and April 2014, 3,643 patients were referred for surgical treatment of primary hyperparathyroidism. Of these, 31 represented remedial patients who had undergone one (n = 28) or more (n = 3) earlier cervical explorations and had noninformative, noninvasive preoperative localization studies.

RESULTS:
We extended the use of the rapid parathyroid hormone assay in the interventional radiology suite, generating near real-time data facilitating onsite venous localization by a dedicated interventional radiologist. The predictive value of real-time sSVS localization was investigated. Overall, sSVS correctly predicted the localization of the affected gland in 89% of cases. Of 31 patients who underwent sSVS, a significant rapidparathyroid hormone gradient was identified in 28 (90%), localizing specific venous drainage of a culprit gland. All patients underwent subsequent surgery and were biochemically cured, with the exception of one who had metastatic parathyroid carcinoma. Three patients with negative sSVS were also explored and cured.

CONCLUSIONS:
Preoperative parathyroid localization is of paramount importance in remedial cervical explorations. Real-time sSVS is a sensitive localization technique for patients with persistent or recurrent primary hyperparathyroidism, when traditional noninvasive imaging studies fail. These results validate the utility and benefit of real-time sSVS in guiding remedial parathyroid surgery.

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PMID: 25868412  Makale sayfasi
Modern experience with aggressive parathyroid tumors in a high-volume new England referral center.

Quinn CE¹, Healy J², Lebastchi AH³, Brown TC², Stein JÈ³, Prasad ML³, Callender GG², Carling T², Udelsman R².

Abstract

BACKGROUND:
Parathyroid carcinoma (PTCA) is an exceptionally rare malignancy, often with a clinical presentation similar to that of benign atypical parathyroid adenoma. Its low incidence portends unclear guidelines for management. Accordingly, thorough examination of clinical and pathologic variables was undertaken to distinguish between PTCA and atypical adenomas.

STUDY DESIGN:
This was a retrospective analysis of a prospective database at a tertiary academic referral center. Between September 2001 and April 2014, 3,643 patients were referred for surgical treatment of PHPT. Of these, 52 harbored aggressive parathyroid tumors: parathyroid carcinomas (n = 18) and atypical adenomas (n = 34). We analyzed the surgical and clinicopathologic tumor characteristics, and did a statistical analysis. We measured preoperative and intraoperative variables, and postoperative and pathologic outcomes.

RESULTS:
Parathyroid carcinoma patients present with significantly increased tumor size (3.5 cm vs 2.4 cm, respectively; p = 0.002), mean serum calcium (13.0 vs 11.8 mg/dL, respectively; p = 0.003) and intact parathyroid hormone (iPTH) levels (489 vs 266 pg/mL, respectively; p = 0.04), and a higher incidence of hypercalcemic crisis, compared with patients with atypical adenomas (50% vs 19%, respectively; p = 0.072). Parathyroid carcinoma more frequently lacks a distinct capsule (47.1% vs 12.9%, respectively; p = 0.03) and adheres to adjacent structures (77.8% vs 20.6%, respectively; p = 0.017). Of note, there was no significant difference in loss of parafibromin expression between groups.

CONCLUSIONS:
Clinical distinction between PTCA and atypical adenomas is of critical importance in determining the appropriate extent of resection and follow-up. Loss of parafibromin has not been shown to distinguish between PTCA and atypical adenoma; clearer definition of clinicopathologic criteria for PTCA is warranted and may lead to improved postoperative management.

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PMID: 25488353 Makale sayfası

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

Seeliger B¹, Alesina PF, Koch JA, Hinrichs J, Meier B, Walz MK.

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

**Accuracy of early-phase versus dual-phase single-photon emission computed tomography/computed tomography in the localization of Parathyroid disease.**

Mandal R1,2, Muthukrishnan A3, Ferris RL2, de Almeida JR4, Duvvuri U1,2.

**Author information**

**Abstract**

**OBJECTIVES/HYPOTHESIS:**
Preoperative localization for parathyroid disease has improved in recent years with the advent of dual-phase (99m) Tc-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
specifcity 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


Intramuscular and subcutaneous forearm parathyroid autograft hyperplasia in renal dialysis patients: A retrospective cohort study.

Hsu YC¹, Hung CJ². Author information

Abstract

BACKGROUND:
Intramuscular and subcutaneous forearm parathyroid autograft are proved to have compatible short-term outcome. However, long-term clinical courses have not been studied.

METHODS:
A single-surgeon retrospective cohort study of parathyroid autograft hyperplasia from August 1998 to January 2013 was performed. According to the location of their parathyroid autograft, patients were divided into an Intramuscular group and a Subcutaneous group. Clinical parameters were analyzed to assess the risk factors and clinical course of autograft hyperplasia.

RESULTS:
There were 888 consecutive patients who underwent total parathyroidectomy with forearm autotransplantation for renal hyperparathyroidism during the period. The median age at the time of total parathyroidectomy with forearm autotransplantation was 54.2 years (range, 12-86) and the median follow-up time was 4.0 years (range 0.1-16). Autograftectomy was performed on 29 of 888 patients. The incidence of autograftectomy was 15 of 65 in the Intramuscular group and 14 of 823 in the Subcutaneous group; the incidence of repeated autograftectomy was 4 of 65 in the Intramuscular group and 1 of 823 in the Subcutaneous group. The cumulative frequency of autograftectomy was greater in the Intramuscular group than that in the Subcutaneous group (11.6 vs 3.1% at 6 years, P < .001). The location of the autograft was the only significant factor affecting the autograftectomy frequency (P = .002). The Intramuscular group reoperation patients experienced a longer period between their first operation and the autograftectomy (6.6 vs 3.3 years, P = .003), longer operating times (79 vs 37 minutes, P = .002), and a greater level of pre-
autograftectomy systemic intact parathyroid hormone (1,044 vs 559 ng/L, P = .014) than the Subcutaneous group.

CONCLUSION:
Intramuscular parathyroid autotransplantation results in a high incidence of autograftectomy, repeated autograftectomy, and a high cumulative frequency of autograftectomy.

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PMID: 26054321  Makale sayfasi
Parathyroid gland autotransplantation after total thyroidectomy in surgical management of hypopharyngeal and laryngeal carcinomas: A case series.

**Author information**

**Abstract**

**BACKGROUND AND OBJECTIVES:**
Total thyroidectomy is indicated in most cases with postcricoid carcinoma, circumferential hypopharyngeal carcinoma and in advanced laryngeal carcinoma. Persistent hypoparathyroidism is a frequent complication after total thyroidectomy which is difficult to manage unlike hypothyroidism. This study was to assess the feasibility of parathyroid gland autotransplantation after total thyroidectomy in advanced carcinomas and their effectiveness in preventing persistent hypoparathyroidism.

**METHODS:**
This study included 26 patients with hypopharyngeal and laryngeal carcinoma presented to National Cancer Institute, Cairo University. Total thyroidectomy and total parathyroid gland excision were performed as a part of adequate oncologic surgical procedure. The parathyroid glands were identified, resected and stored in iced saline. Histological confirmation was necessary before implantation into separated muscle pockets in the anterior forearm muscles. Regular samples were drawn to assess serum parathormone and calcium levels.

**RESULTS:**
All patients experienced hypocalcaemia within 1-5 days after operation. Only one patient experienced parathyroid graft failure while the remaining patients were normocalcemic during follow up after surgery, indicating functioning parathyroid grafts.

**CONCLUSIONS:**
Parathyroid gland autotransplantation is a simple safe technique with high success rate in preventing persistent hypoparathyroidism after total thyroidectomy in surgical management of advanced hypopharyngeal and laryngeal carcinomas.

**KEYWORDS:**
Autotransplantation; Carcinoma; Hypopharyngeal; Laryngeal; Parathyroid

PMID: 25852933 [Makale sayfası]
Abstract
Spontaneous extracapsular hemorrhage is a rare but potentially life-threatening manifestation of parathyroid gland adenomas. We present a case demonstrating that even in a patient with increased bleeding tendency due to anticoagulants, combined with compression of trachea and esophagus, conservative treatment can be successful.

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PMID: 25935903 Makale sayfası
Metabolic and anatomic characteristics of benign and malignant adrenal masses on positron emission tomography/computed tomography: a review of literature.

Kandathil A¹, Wong KK, Wale DJ, Zatelli MC, Maffione AM, Gross MD, Rubello D.

Abstract

PET/CT with (18)F-fluorodeoxyglucose (FDG) or using different radiocompounds has proven accuracy for detection of adrenal metastases in patients undergoing cancer staging. It can assist the diagnostic work-up in oncology patients by identifying distant metastases to the adrenal(s) and defining oligometastatic disease that may benefit from targeted intervention. In patients with incidentally discovered adrenal nodules, so-called adrenal "incidentaloma" FDG PET/CT is emerging as a useful test to distinguish benign from malignant etiology. Current published evidence suggests a role for FDG PET/CT in assessing the malignant potential of an adrenal lesion that has been 'indeterminately' categorized with unenhanced CT, adrenalprotocol contrast-enhanced CT, or chemical-shift MRI. FDG PET/CT could be used to stratify patients with higher risk of malignancy for surgical intervention, while recommending surveillance for adrenal masses with low malignant potential. There are caveats for interpretation of the metabolic activity of an adrenal nodule on PET/CT that may lead to false-positive and false-negative interpretation. Adrenal lesions represent a wide spectrum of etiologies, and the typical appearances on PET/CT are still being described, therefore our goal was to summarize the current diagnostic strategies for evaluation of adrenal lesions and present metabolic and anatomic appearances of common and uncommon adrenal lesions. In spite of the emerging role of PET/CT to differentiate benign from malignant adrenal mass, especially in difficult cases, it should be emphasized that PET/CT is not needed for most patients and that many diagnostic problems can be resolved by CT and/or MR imaging.

PMID: 25273320

Feminizing adrenocortical tumors: Literature review.

Chentli F¹, Bekkaye I¹, Azzoug S¹.

Abstract

Feminizing adrenocortical tumors (FAT) are extremely rare tumors prevailing in males. Clinical manifestations are gynecomastia and/or other hypogonadism features in adults. They are rarer in pediatric population and their main manifestation is peripheral sexual precocity. In women genital bleeding, uterus hypertrophy, high blood pressure and/or abdomen mass may be the only manifestations. On the biological point, estrogen overproduction with or without increase in other adrenal hormones are the main abnormalities. Radiological examination usually shows the tumor, describes its limits and its eventual metastases. Adrenal and endocrine origins are confirmed by biochemical assessments and histology, but that one is unable to distinguish between benign and malignant tumors, except if metastases are already present. Immunostaining using anti-aromatase antibodies is the only tool that distinguishes FAT from other
Adrenocortical tumors. Abdominal surgery is the best and the first line treatment. For large tumors (≥10 cm), an open access is preferred to coeliosurgery, but for the small ones, or when the surgeon is experienced, endoscopic surgery seems to give excellent results. Surgery can be preceded by adrenolytic agents such as ortho paraprine dichloro diphenyl dichloroethane (Mitotane), ketoconazole or by aromatase inhibitors, but till now there is not any controlled study to compare the benefit of different drugs. New anti-estrogens can be used too, but their results need to be confirmed in malignant tumors resistant to classical chemotherapy and to conventional radiotherapy. Targeted therapy can be used too, as in other adrenocortical tumors, but the results need to be confirmed.

**KEYWORDS:**
Adrenocortical tumors; abdominal surgery; anti-steroid drugs; aromatase inhibitors; feminization; targeting therapy

PMID: 25932386 Magale sayfası


**Adrenal Incidentalomas: A Disease of Modern Technology Offering Opportunities for Improved Patient Care.**

Ioachimescu AG1, Remer EM2, Hamrahian AH3.

**Author information**

**Abstract**

Adrenal incidentalomas (AIs) are found in approximately 4% of patients undergoing abdominal imaging, with peak prevalence in the sixth and seventh decades of life. Detection of AI warrants clinical, biochemical, and radiological evaluation to establish its secretory status and risk of malignancy. Careful review of the lipid content, size, and imaging phenotype of an adrenal mass is needed to evaluate the risk for malignancy. Identification of an AI may be an opportunity to identify an underlying secretory tumor that may have been otherwise unrecognized. A practical approach to investigation and follow-up of AIs is presented in this article.

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**KEYWORDS:**
Adrenal incidentaloma; Noncontrast CT attenuation; Percentage washout; Pheochromocytoma; Tumor size

PMID: 26038204 Magale sayfası


**Adrenal myelolipoma: Controversies in its management.**

Shenoy VG1, Thota A1, Shankar R1, Desai MG1.

**Author information**

**Abstract**

Adrenal myelolipomas (AMLs) are rare, benign neoplasms of the adrenal gland with varied clinical presentations. The rarity of these tumors precludes any case-controlled or randomized study into their management. The available literature is limited to case reports and short series from referral centers. This review is an effort to put the available literature into perspective such that clinical decision making can be done with some clarity. The PubMed and Cochrane databases were searched with key words Adrenal Myelolipoma, Adrenal Incidentaloma (AI) and Adrenal Collision Tumor (ACT). From over 1300 search results, 547 relevant publications dating from 1954 to 2014 were reviewed. Details of about 1231 AMLs in
the indexed literature were analyzed. Increasing usage of imaging studies has significantly increased the
discovery of AMLs. Although AMLs are benign tumors, those measuring larger than 6 cm are prone to
rupture and hemorrhage. Thorough endocrine work-up may benefit a selected group of patients, especially
those who are hypertensive, diabetic/pre-diabetic, young patients (<50 years) and those with bilateral AML.
Regular observation is needed for AML patients who are being treated non-operatively, as many of them
may require surgery during follow-up. Although the AACE/AAES guidelines for AI (2009) exclude AML from
mandatory metabolic work-up for a newly discovered AI, we feel that a significant number of patients with
AML would benefit from metabolic work-up. In the literature, endocrine dysfunction in AML is 7% as
compared with 11% in AI. Endocrine dysfunction in AML is probably underdiagnosed.

KEYWORDS:
Adrenal collision tumors; adrenal incidentaloma; adrenal myelolipoma; adrenalectomy

PMID: 25878407  Makale sayfasi

Management of Adrenal Tumors in Pregnancy.

Eschler DC¹, Kogekar N², Pessah-Pollack R³.

Author information

Abstract

Adrenal diseases, including Cushing syndrome (CS), primary aldosteronism (PA), pheochromocytoma, and
adrenocortical carcinoma, are uncommon in pregnancy; a high degree of clinical suspicion must exist.
Physiologic changes to the hypothalamus-pituitary-adrenal axis in a normal pregnancy result in increased
cortisol, renin, and aldosterone levels, making the diagnosis of CS and PA in pregnancy challenging.
However, catecholamines are not altered in pregnancy and allow a laboratory diagnosis of
pheochromocytoma that is similar to that of the nonpregnant state. Although adrenaltumors in pregnancy
result in significant maternal and fetal morbidity, and sometimes mortality, early diagnosis and appropriate
treatment often improve outcomes.

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KEYWORDS:
Adrenal cell carcinoma; Adrenal tumor; Cushing syndrome; Hyperaldosteronism;
Pheochromocytoma; Pregnancy

PMID: 26038207  Makale sayfasi
Risk of adrenocortical carcinoma in adrenal tumours greater than 8 cm.

Abdel-Aziz TE¹, Rajeev P, Sadler G, Weaver A, Mihai R.

Abstract

BACKGROUND:
Adrenocortical cancer (ACC) is a rare malignancy. In the absence of metastatic disease, the suspicion of ACC is based on size and radiological appearance. The aim of this study was to analyse the long-term outcome of patients with large adrenal cortical tumours (>8 cm).

METHODS:
A prospective database recorded clinical, biochemical, operative and histological data on patients operated for cortical adrenal tumours between January 2000 and February 2013. Out of 130 patients operated for cortical adrenal tumours, analysis was restricted to 37 cortical tumours >8 cm.

RESULTS:
There were 31 (84 %) ACCs and 6 (16 %) benign adenomas (p < 0.01). The most common presentation was that of an abdominal mass[17 (55 %) vs. 3 (50 %), ACC vs. benign, respectively]. There was no difference in size between stage II and stage III-IV tumours; however, there was a trend for tumours to be heavier in advanced stages (920 ± 756 vs. 1,435 ± 1,022 g, p = 0.08, stage II vs. stage III-IV, respectively). No mortality was observed in patients with benign tumours during a median follow-up of 70 months (range 36-99 months). Mortality in the ACC group occurred in 17/31 (55 %) patients. Mitotane was administered in 12 (71 %) patients with stage III-IV ACCs with a 5-year survival rate 25 % compared to 20 % in patients who did not receive Mitotane. In stage II ACC, eight (57 %) patients received Mitotane with a 50 % mortality at 5 years.

CONCLUSIONS:
The high incidence of ACC in cortical tumours >8 cm underlines the need for adequate surgical resection via open surgery aiming to avoid local recurrence. Beyond surgery, the impact of other therapies is not fully characterised and the efficacy of adjuvant Mitotane treatment is yet to be proven.

PMID: 25526921

Makale sayfası
Congenital adrenal hyperplasia: current surgical management at academic medical centers in the United States.

Sturm RM¹, Durbin-Johnson B¹, Kurzrock EA¹.

Abstract

PURPOSE:
Controversy exists on the necessity for and timing of genitoplasty in girls with congenital adrenal hyperplasia. Our knowledge of surgical preferences is limited to retrospective series from single institutions and physician surveys, which suggest a high rate of early reconstruction. We evaluated current surgical treatment for congenital adrenal hyperplasia at academic centers.

MATERIALS AND METHODS:
We queried the Faculty Practice Solutions Center database to identify all female patients younger than 18 years with a diagnosis of congenital adrenal hyperplasia between 2009 and 2012. Procedures were identified by CPT codes for vaginoplasty, clitoroplasty and other genital procedures. Reconstruction type, age at surgery and surgeon volume were analyzed.

RESULTS:
We identified 2,614 females in the database with a diagnosis of congenital adrenal hyperplasia who were seen at a total of 60 institutions. Of infants younger than 12 months between 2009 and 2011 as few as 18% proceeded to surgery within a 1 to 4-year followup. Of those referred to a pediatric urologist 46% proceeded to surgery. Of patients who underwent surgery before age 2 years clitoroplasty and vaginoplasty were performed in 73% and 89%, respectively, while 68% were treated with a combined procedure. A medium or high volume surgeon was involved in 63% of cases.

CONCLUSIONS:
Many patients with congenital adrenal hyperplasia in the database did not proceed to early reconstructive surgery. Of those referred to surgeons, who were possibly the most virilized patients, about half proceeded to early surgery and almost all underwent vaginoplasty as a component of surgery. About two-thirds of the procedures were performed by medium or high volume surgeons, indicative of the surgical centralization of disorders of sexual development.

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KEYWORDS:
adrenal glands; adrenal hyperplasia; congenital; disorders of sex development; reconstructive surgical procedures; virilism

Comment in

* Editorial comment. [J Urol. 2015]

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

Hornstein I¹, Schwarz C, Ebbing S, Hoppe-Lotichius M, Otto G, Lang H, Musholt TJ.

Author information

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


Adrenal gland trauma: is extravasation an absolute indication for intervention?

Liao CH¹, Lin KJ, Fu CY, Wang SY, Yang SJ, Ouyang CH.

Author information

Abstract

BACKGROUND:
Adrenal gland trauma (AGT) is potentially devastating if unrecognized during the treatment of trauma patients. Because of the adrenal glands' rich vascularity, they often hemorrhage upon traumatic impact. However, there has been no conclusion about the indications for intervention in cases of hemorrhage after AGT.

METHODS:
We conducted a prospective collection with a retrospective review in a Level I trauma center in Taiwan. This study enrolled all of the patients who suffered from AGT from May 2008 to May 2013. We retrieved and analyzed the patient demographic data, clinical presentation, AGT grade, injury severity score, management, hospital stay, and mortality.

RESULTS:
The cohort consisted of 60 patients. The mean age was 31.0 ± 15.9 years. There were 32 patients (53.3 %) with extravasated AGT, which was associated with a high injury severity score, a high possibility of associated lung injury, and more than one accompanying trauma. Most of the patients could be treated conservatively. Five of these patients needed surgical hemostasis, and four of them needed angiographic embolization. Extravasation combined with a mean arterial pressure <70 mmHg was a predictor of the need for intervention (relative risk: 9.52, 95 % CI 1.64-55.56, p = 0.011).

CONCLUSION:
In conclusion, AGT is a rare injury with a good prognosis. Most AGT patients can be treated conservatively. Extravasation in AGT is not only a sign of hemorrhage, but also an indicator of severe associated injuries. However, extravasation in AGT does not always require further treatment. When intractable hypotension simultaneously occurs, further treatment should be considered.

PMID: 25613549 Makale sayfası


Adrenal Imaging Features Predict Malignancy Better than Tumor Size.

Yoo JY¹, McCoy KL, Carty SE, Stang MT, Armstrong MJ, Howell GM, Bartlett DL, Tublin ME, Yip L.

Author information

Abstract

INTRODUCTION:
In adrenal tumors, size ≥4 cm has been an indication for adrenalectomy due to concern for malignancy. We compared mass size to imaging features (ImF) for accuracy in diagnosing adrenal malignancy.

METHODS:
Data were retrieved for 112 consecutive patients who had adrenalectomy from January 2011 to August 2014. ImF was classified as nonbenign if HU > 10 on unenhanced CT scan or if loss of signal on out-of-phase imaging was absent on chemical-shift MRI. Indications for resection included hormonal hypersecretion, nonbenign ImF, and/or size ≥4 cm.

RESULTS:
Of 113 resected adrenals, 37 % were functional. Histologic malignancy occurred in 18 % (20/113) and included 3 adrenocortical carcinomas (ACC), 1 epithelioid liposarcoma, 1 lymphoma, 1 malignant nerve sheath tumor, and 14 adrenal metastases. Patients with malignancies were older (mean age, 60 ± 13 vs. 51 ± 14 years, p = 0.01). Malignant tumors were larger on preoperative imaging (mean 5.3 ± 3.2 vs. 3.9 ± 2.4 cm, p = 0.03). All 20 malignant masses had nonbenign ImF. In predicting malignancy, the sensitivity, specificity, NPV, and PPV of nonbenign ImF was 100, 57, 100, and 33 %, respectively. Size ≥4 cm was less predictive with sensitivity, specificity, NPV, and PPV of 55, 61, 86, and 23 %, respectively. If size ≥4 cm had been used as the sole criterion for surgery, 45 % of malignancies (9/20) would have been missed including 8 metastases and an ACC.

CONCLUSIONS:
In resected adrenal tumors, the presence of nonbenign ImF is more sensitive for malignancy than mass size (100 vs. 55 %) with equivalent specificity. Regardless of mass size, adrenalectomy should be strongly considered when non-benign ImF are present.

PMID: 26088650


The clinical course of patients with adrenal incidentaloma: is it time to reconsider the current recommendations?

Kastelan D¹, Kraljevic I², Dusek T³, Knezovic N⁴, Solak M⁵, Gardijan B⁶, Kralik M⁷, Poljicanin T⁸, Skoric Polovina T⁹, Kastelan Z¹⁰.

Author information

Abstract

OBJECTIVE:
The current guidelines for the management of adrenal incidentaloma advise hormonal and radiological follow-up of patients for 2-5 years after the initial diagnosis. However, the vast majority of adrenal incidentaloma are non-functional, benign cortical adenomas that require no treatment, so the routine application of the current strategies often results in a number of unnecessary biochemical and radiological investigations. The aim of this study was to analyse the clinical course of patients with adrenal incidentaloma and to provide a critical review of the current management strategy of the disease.

DESIGN AND METHODS:
This was a retrospective study performed in the Croatian Referral Center for adrenal gland disorders. The study included 319 consecutive patients with adrenal incidentaloma 174 of which were followed for at least 24 months.

RESULTS:
The vast majority of patients were diagnosed with benign adrenal masses whereas in about 5% of them adrenal tumor corresponded toadrenal carcinoma or metastasis. Tumor density was found to be superior to tumor size in distinguishing benign adrenal masses from malignant tumors and pheochromocytomas. During the follow-up no patient demonstrated a clinically significant increase in tumor size. In addition, no changes, either in metanephrines and normetanephrines or in the activity of renin-aldosterone axis, were observed during the follow-up. Six patients developed SCS whereas eight patients with SCS showed biochemical remission during follow-up.

CONCLUSION:
The study suggests that the risk of an adrenal mass initially diagnosed as benign and non-functional becoming malignant or hormonally active is extremely low. Therefore, the clinical management of those patients should be tailored on an individual basis in order to avoid unnecessary procedures.

PMID: 26024670

Primary adrenal leiomyosarcoma: a case report and review of literature.

Zhou Y¹, Tang Y¹, Tang J¹, Deng F¹, Gong G², Dai Y¹.

Author information

Abstract

Primary adrenal leiomyosarcoma (PAL) is an extremely rare mesenchymal tumors and originates from the smooth muscle wall of the central adrenalvein and its branches. Herein we report a case of a 49-year-old female suffering from PAL. Computed tomography revealed a well-circumscribed heterogeneously mass measuring 6×5×5 cm located in the left suprarenal areal, and a left laparoscopic adrenalectomy was underwent. Microscopic examination showed a hypercellular tumor with intersecting fascicled of spindled cells. Immunohistochemical staining showed that the cells were positive for desmin, smooth muscle actin (SMA), vimentin and negative for CD34, CD117, S100, Bcl-2 and Dog1. No oncological treatment underwent after surgery, and the patient had no recurrence or metastasis at 6 months postoperatively.

KEYWORDS:

Adrenal gland; adrenal gland neoplasms; leiomyosarcoma

PMID: 26097622


Laparoscopic hand-assisted adrenal sparing surgery for a giant adrenal myelolipoma: A case report.

Park BH¹, Lee SL, Seo KJ, Bae SR, Lee YS, Kang SH, Han CH.

Author information

Abstract

INTRODUCTION:

Adrenal myelolipoma is a rare, benign tumor. Surgical resection is advocated in case of symptomatic, large size (> 4cm), increase of size on follow-up and atypical appearance on imaging. Laparoscopic adrenalectomy is currently the gold standard operation for managing benign adrenal mass. However, to date, laparoscopic entire resection of ipsilateral adrenal gland with the tumor have been mainly reported in the literature. Under clinical circumstances, adrenal sparing surgery underused as first-line therapy for adrenal tumors.

CASE PRESENTATION:

We present a case of adrenal myelolipoma involving the right adrenal gland of a 45-year-old woman who presented with right-sided flank pain. On radiologic and endocrine evaluation, she was diagnosed with a giant adrenal myelolipoma (> 8cm). Right hand-assisted laparoscopic partial adrenalectomy was performed, and postoperative recovery was uneventful. Finally, histological examination confirmed adrenal myelolipoma. On follow-up computed tomography, there was no residual tumor and the remaining right adrenal gland.

CONCLUSION:
Our report suggests that hand-assisted laparoscopic partial adrenalectomy could be considered for appropriate removal of adrenal myelolipoma, even in giant adrenal myelolipoma.

**KEYWORDS:**
adrenal glands; adrenalectomy; hand-assisted laparoscopy; myelolipoma

**PMID:** 25990775


**Bilateral Pheochromocytomas in MEN2A Syndrome: A Two-Institution Experience.**


**Author information**

**Abstract**

**BACKGROUND:**
Bilateral pheochromocytoma (PHEO) is more frequently found in patients with multiple endocrine neoplasia 2A carrying a RET germline mutation located in codon 634 (C634). However, it is unclear whether different amino acid substitutions within C634 cause differences in bilateral PHEOs expression. We aimed to answer this by pooling data from two Asian institutions.

**METHODS:**
Sixty-seven patients had confirmed C634 germline mutation. Age-dependent penetrance of bilateral PHEO was calculated from date of birth to the date when bilateral PHEO was first diagnosed or when the contralateral gland became a PHEO (if the patient already had one adrenal gland removed). Age-dependent penetrance was estimated by the Kaplan-Meier method and compared by log-rank test.

**RESULTS:**
The 4 different amino acid substitutions included C634R (arginine) (n = 19, 28.4 %), C634Y (tyrosine) (n = 36, 38.8 %), C634G (glycine) (n = 4, 6.0 %), and C634W (tryptophan) (n = 8, 11.9 %). The age-related penetrance of PHEO was similar between C634R, C634Y, C634G, and C634W (by age 40, 69.8, 55.2, 25.0, and 56.2 %, respectively) (p = 0.529). However, the age-related penetrance of bilateral PHEO in C634R was significantly higher than C634Y (by age of 40, 59.3 % vs. 25.2 %, p = 0.046) or C634Y, C634G, and C634W combined (59.3 % vs. 21.5 %, p = 0.024). Nevertheless, the accumulative risk of bilateral PHEOs across all four C634 mutations almost approached 100 % over time.

**CONCLUSION:**
The accumulative risk of bilateral PHEOs almost reached 100 % but its onset was significantly earlier in C634R mutation. These findings implied that those with C634R mutation might benefit from earlier screening of contralateral PHEO than other C634 mutations after an unilateral adrenalectomy.

**PMID:** 26071011


**Nonfunctional adrenocortical carcinoma initially presenting as retroperitoneal hemorrhage.**

Kashiwagi S¹, Amano R², Onoda N³, Noda S⁴, Hirata K⁵, Asano Y⁶, Kurata K⁷, Miura K⁸, Yamazoe S⁹, Kimura K¹⁰, Ohsawa M¹¹, Kitagawa S¹², Hirakawa K¹³.

**Author information**

**Abstract**

**BACKGROUND:**
Acute adrenal hemorrhage is an uncommon entity. Although trauma is the most common cause of adrenal hemorrhage, non-traumatic etiologies have also been reported. We report an unusual case of a spontaneously ruptured adrenocortical carcinoma that initially presented as a critical massive retroperitoneal hemorrhage. The case was treated successfully using a combination of emergency interventional radiology and elective surgery.

**CASE PRESENTATION:**
A 47-year-old woman was transported to our hospital because of the sudden onset of severe pain in her left lower back. The shadow of a tumor-like soft mass accompanied by bleeding was observed in the upper pole of the left kidney, together with vascular leakage from the middle suprarenal artery on computed tomography. Transcatheter embolization of the left middle adrenal artery was administered based on a diagnosis of acute adrenal hemorrhage. Further observation indicated that the bleeding was caused by rupture of an adrenocortical carcinoma. Left adrenalectomy was subsequently carried out via laparotomy.

**CONCLUSIONS:**
We experienced an unusual case of acute massive adrenal hemorrhage caused by the rupture of a non-functional adrenocortical carcinoma, which was treated successfully by ambulatory transcatheter embolization therapy and elective surgery.

PMID: 25927963  Makale sayfası
NET

DERLEME


**GEP-NETS update: Interventional radiology: role in the treatment of liver metastases from GEP-NETs.**

de Baere T¹, Deschamps F², Tselikas L², Ducreux M³, Planchard D², Pearson E², Berdelou A², Leboulleux S², Elias D², Baudin E².

**Author information**

**Abstract**

Neuroendocrine tumors from gastro-pancreatic origin (GEP-NET) can be responsible for liver metastases. Such metastases can be the dominant part of the disease as well due to the tumor burden itself or the symptoms related to such liver metastases. Intra-arterial therapies are commonly used in liver only or liver-dominant disease and encompass trans-arterial chemoembolization (TACE), trans-arterial embolization (TAE), and radioembolization (RE). TACE performed with drug emulsified in Lipiodol has been used for the past 20 years with reported overall survival in the range of 3-4 years, with objective response up to 75%. Response to TACE is higher when treatment is used as a first-line therapy and degree of liver involvement is lower. Benefit of TACE over TAE is unproven in randomized study, but reported in retrospective studies namely in pancreatic NETs. RE provides early interesting results that need to be further evaluated in terms of benefit and toxicity. Radiofrequency ablation allows control of small size and numbered liver metastases, with low invasiveness. Ideal metastases to target are one metastasis <5 cm, or three metastases <3 cm, or a sum of diameter of all metastases below 8 cm. Ablation therapies can be applied in the lung or in the bones when needed, and more invasive surgery should be probably saved for large-size metastases. Even if the indication of image-guided therapy in the treatment of GEP-NET liver metastases needs to be refined, such therapies allow for manageable invasive set of treatments able to address oligometastatic patients in liver, lung, and bones. These treatments applied locally will save the benefit and the toxicity of systemic therapy for more advanced stage of the disease.

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PMID: 25385817 [Makale sayfası]


**Expert consensus for the management of advanced or metastatic pancreatic neuroendocrine and carcinoid tumors.**

Castellano D¹, Grande E, Valle J, Capdevila J, Reidy-Lagunes D, O'Connor JM, Raymond E.

**Author information**

**Abstract**

Neuroendocrine tumors (NETs) are rare tumors that have been increasing in incidence over the last 30 years with no significant changes in survival. As survival of patients with these tumors depends greatly on stage and histology, early diagnosis, classification and staging of tumors in patients in whom NETs are
suspected are of great importance. Surgery, either with curative or palliative intent, is the mainstay of treatment for localized NETs. Therapeutic options for this disease almost invariably include somatostatin analogs to alleviate the symptoms of excessive hormone secretion. Other approaches for advanced disease may include hepatic artery embolization or ablation, peptide receptor radionuclide therapy and systemic chemotherapy. Recent advances regarding the signaling pathways involved in tumor development have allowed the development of novel targeted therapies. However, due to the lack of prognostic molecular markers to identify high-risk patients and the absence of a common pathogenesis in all patients, treatment selection is often empirical. There is therefore a need to establish a consensus for the treatment of this disease and to provide evidence-based clinical recommendations and algorithms to optimize and individualize the treatment and follow-up for these patients.

PMID: 25480314
Survival prognostic factors of gastro-enteric-pancreatic neuroendocrine tumors after primary tumor resection in a single tertiary center: Comparison of gastro-enteric and pancreatic locations.

Russolillo N¹, Vigano' L², Razzore P³, Langella S⁴, Motta M³, Bertuzzo F⁴, Papotti M⁵, Ferrero A⁶.

Abstract

AIM:
This study aimed to evaluated prognostic factors of patients with GEP-NETs after primary tumor resection comparing pancreatic and gastro-enteric locations.

METHODS:
Patients undergone surgery for primary GEP-NETs between 01/2000 and 03/2012 were considered. All specimens were reclassified according to the WHO 2010 scheme.

RESULTS:
A total of 83 patients were considered: 37 pancreatic NETs (pNET) and 46 gastroenteric NETs (GE-NET). The two groups were similar in terms of age, sex and tumors size. A higher rate of patients with pNETs had Ki67 score ≥3 (64.8% vs. 39%, p = 0.027) while the rates of Mitotic Index ≥2x10HPF (62% pNET vs. 50% GE-NET, p = 0.374) and diagnosis of neuroendocrine carcinoma NEC (16.2% pNET vs. 17.3% GE-NET, p = 0.100) were similar. The rates of distant metastases (GE-NETs 30.4% vs. p-NETs 29.7%, p = 0.944) and liver metastases (19.5% GE-NET vs. 27% pNET, p = 0.421) were comparable. Radical resection was achieved in a similar proportion in both groups [33 patients (89.1%) pNET vs. 36 (78.2%) GE-NET, p = 0.393]. After a median follow-up of 47.1 months overall 3, 5 and 10-years survival rates of whole patients were 88.1%, 81.2% and 76.7%. There was not difference on 5-years overall survival between pNET (81.4%) and GE-NET (81%, p = 0.901). At multivariate analysis age ≥70 [OR 4.177 (CI 95% 1.26-13.8), p = 0.019] and NEC [OR 5.932 (CI 95% 1.81-19.40), p < 0.001] were negative prognostic factors of survival.

CONCLUSION:
Overall survival of GEP-NET after resection of primary tumors seems to be correlated to patient's age and WHO 2010 staging system but not to primary tumor site.

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KEYWORDS:
Gastro-enteric neuroendocrine tumors; Overall survival; Pancreatic neuroendocrine tumors; Surgery
Increasing incidence of duodenal neuroendocrine tumors: Incidental discovery of indolent disease?

Fitzgerald TL¹, Dennis SO², Kachare SD², Vohra NA², Zervos EE².

Abstract

BACKGROUND:
There has been a marked increase in the recognized incidence of gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Studies have often combined duodenal neuroendocrine tumors (D-NETs) with other small bowel GEP-NETs. As a result, the natural history and clinical ramifications of these D-NETs is poorly understood.

METHODS:
Patients diagnosed with duodenal "carcinoid" tumors from 1983 to 2010 were identified in the Surveillance Epidemiology and End Results tumor registry.

RESULTS:
A total of 1,258 patients were identified. The mean age was 64 years. The majority of patients were male (55.6%), white (55.6%), and had stage I disease (66.2%). Patients meeting inclusion criteria were divided into 2 cohorts: (i) era 1 patients diagnosed with GEP-NETs from 1983 to 2005, and (ii) era 2 those diagnosed from 2005 to 2010. There was a clear increase in the incidence rate of D-NETs from 0.27 per 100,000 in 1983 to 1.1 per 100,000 in 2010 (P < .001). Comparison of patients from the different eras revealed that those in era 2 were more likely than era 1 to present with stage I disease (69.9 vs 57.5%; P < .01) and less likely to present with late-stage disease. The 5-year, disease-specific survival improved for era 2 patients compared with era 1 (89.3 vs 85.2%; P = .05); however, multivariate analysis demonstrated that stage but not era was associated with disease-specific survival.

CONCLUSION:
Prognosis for D-NETs, in contrast with other small bowel NETs, is excellent. There has been a steady increase in the recognized incidence of D-NETs, coincident with the migration to earlier disease stage and improved disease-specific survival.

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Surgical Management of Small Bowel Neuroendocrine Tumors: Specific Requirements and Their Impact on Staging and Prognosis.

Pasquer A¹, Walter T, Hervieu V, Forestier J, Scoazec JY, Lombard-Bohas C, Poncet G.

Abstract

BACKGROUND:
Small bowel neuroendocrine tumors (SB-NETs) are characterized by two main features: they usually are metastatic at diagnosis and multiple in 30% of cases. As such, SB-NETs require
specific surgical management. This retrospective study examined local recurrence, survival, and prognosis of SB-NETs after adapted surgery.

METHODS:
All consecutive patients with SB-NETs who underwent resection of at least one primary tumor between 1 January 2000 and 1 January 2013 were analyzed. The preoperative morphologic workup, histologic classification, and metastatic lymph node (LN) ratio (LNs involved/removed) were recorded.

RESULTS:
The study enrolled 107 patients, 35 (33 %) of whom had multiple SB-NETs (range 1-44; mean 3.1). Preoperative imaging and perioperative surgical examination missed 61 and 33 % of SB-NETs, respectively, in contrast to pathologic examination. Of the 107 patients, 43 % had carcinoid syndrome, 70 % had metastatic disease, and 90 % had LN involvement. The median number of LNs retrieved was 12 (range 1-69). The LN ratio (LNs involved/removed) was 0.25. The highest tumoral grades were G1 (in 61 % of patients) and G2 (in 37 % of patients). Of the 107 patients, 13 (12 %) had local LN recurrence. The rate of LN recurrence-free survival at 5 years was 88 %. The median overall survival (OS) time was 128 months (range 91-165 months). In the multivariate analysis, high chromogranin A (CgA) levels and peritoneal carcinomatosis were significantly associated with shorter OS.

CONCLUSIONS:
Systematic palpation of the entire small bowel detects more multiple NETs than preoperative imaging. Systematic surgery with extensive LN resection is associated with low local recurrence. High CgA levels and carcinomatosis are linked with shorter survival.

PMID: 26014153


**Neuroendocrine tumors of the pancreas: a retrospective single-center analysis using the ENETS TNM-classification and immunohistochemical markers for risk stratification.**

**Brunner SM¹, Weber F², Werner JM³, Agha A⁴, Farkas SA⁵, Schlitt HJ⁶, Hornung M⁷.**

**Author information**

**Abstract**

**BACKGROUND:**
This study was performed to assess the 2006 introduced ENETS TNM-classification with respect to patient survival and surgical approach for patients who underwent surgery for a neuroendocrine tumor of the pancreas (PNET).

**METHODS:**
Between 2001 and 2010 38 patients after resection of a PNET were investigated regarding tumor localization and size. Further, patient survival with regards to the new TNM-classification, the operation methods and immunohistochemical markers was analyzed.

**RESULTS:**
The estimated mean survival time of the 38 patients was 91 ± 10 months (female 116 ± 9, male 56 ± 14 months; p = 0.008). The 5-year survival rate was 63.9%. Patient survival differed significantly depending on tumor size (pT1 107 ± 13, pT2 94 ± 16, pT3 44 ± 7 and pT4 18 ± 14 months; P = 0.006). Patients without lymph node metastasis survived significantly longer compared to patients with positive lymph node status (108 ± 9 vs. 19 ± 5 months; P < 0.001). However, survival in patients with and without distant metastasis did not differ significantly (92 ± 11 vs. 80 ± 23 months; P = 0.876). Further, the tumor grading significantly influenced patient survival (G1 111 ± 12, G2 68 ± 12 and G3 21 ± 14 months; P = 0.037).
CONCLUSIONS:
As part of the TNM-classification especially lymph node status and also tumor size and grading were identified as important factors determining patient survival. Further, gender was demonstrated to significantly influence survival time. If an R0 resection was achieved in patients with distant metastases patient survival was comparable to patients without metastasis.

PMID: 25928025 Makale sayfası


IF: 4.45

Long-Term Survival with Long-Acting Somatostatin Analogues Plus Aggressive Cytoreductive Surgery in Patients with Metastatic Neuroendocrine Carcinoma.

Deutsch GB, Lee JH, Bilchik AJ.

Abstract
BACKGROUND:
Long-acting somatostatin analogues (S-LAR) improve recurrence-free survival in patients with metastatic neuroendocrine tumor (NET) from gastrointestinal (GI) primary, but their impact on overall survival when combined with aggressive cytoreductive surgery is unclear.

STUDY DESIGN:
We reviewed our institutional cancer database to identify patients who underwent cytoreductive surgery for metastatic NET from GI primary between December 1997 and June 2013. Additionally, a cohort selected from 3,384 metastatic neuroendocrine cases in the SEER-Medicare database (January 2003 to December 2009) was used to verify and expand on our results.

RESULTS:
Most of the 49 patients from our institution had primary lesions in the small intestine (22 of 49 [44.9%]) or pancreas (14 of 49 [28.6%]); 37 patients (75.5%) had metastatic disease at initial diagnosis. These patients underwent 1 (32 of 49 [65.3%]), 2 (11 of 49 [22.4%]), or at least 3 (6 of 49 [12.3%]) surgical procedures; 33 patients (67.3%) underwent resection plus ablation, 19 (38.7%) underwent major hepatectomy, and 34 (69.4%) received S-LAR (29.4% administered preoperatively). Median follow-up was 112 months. Rates of 1-, 5-, 10-, and 15-year disease-specific survival (DSS) were 94%, 78%, 64%, and 31%, respectively, in the 34 patients undergoing aggressive cytoreductive surgery plus S-LAR. Of the SEER-Medicare population, 1,741 patients met inclusion criteria. The DSS for the 104 patients treated with combination therapy was 68.3% at 5 years and 60.6% at 10 years, as compared with 54.7% and 51.8%, respectively, for the 202 patients receiving cytoreductive surgery alone, and 50.0% and 36.0%, respectively, for the 342 patients receiving S-LAR alone (p < 0.0001). The group receiving neither treatment (n = 1,093) had 5-year and 10-year DSS of 34.3% and 26.3%, respectively.

CONCLUSIONS:
Long-acting somatostatin analogues combined with aggressive cytoreductive surgery improves the long-term survival of select patients with metastatic NET from GI primary.

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PMID: 26027502 Makale sayfası
Surgical therapy of neuroendocrine neoplasm with hepatic metastasis: patient selection and prognosis.


Author information

Abstract

BACKGROUND:
Patients with neuroendocrine neoplasms (NEN) develop hepatic metastases in 50-95%. The aims of this study were to evaluate the outcome/prognosis of patients following hepatic surgery and to identify predictive factors for the selection of patient that benefit from hepatic tumor resection.

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 Makale sayfası

Long-term Outcomes of Surgical Management of Pancreatic Neuroendocrine Tumors with Synchronous Liver Metastases.


Author information

Abstract

BACKGROUND:
The value of surgical resection in the management of PNET with LM is still debated. The aim of the study was to evaluate the outcomes of surgery of pancreatic neuroendocrine tumors (PNET) with liver metastases (LM).
METHODS:
Patients with PNET with synchronous LM between 2000 and 2011 from 4 high-volume Institutions were included. Patients were divided into 3 groups (curative resection, palliative resection, and no resection).

RESULTS:
Overall 166 patients were included. Eighteen patients (11%) underwent curative resection, 73 patients (43%) underwent palliative resection, and 75 patients (46%) underwent conservative treatment. The median overall survival (OS) from diagnosis was 73 months. Patients who underwent curative resection had a significantly better median OS from initial diagnosis compared with those who underwent palliative resection and those who were conservatively treated (97 vs. 89 vs. 36 months, \( p = 0.0001 \)). The median OS from diagnosis in those patients who underwent radical or palliative resection was 97 months with a 5-year survival rate of 76%. On multivariate analysis, factors associated with OS from diagnosis were the presence of bilobar metastases, tumor grading and curative resection in a first model. On a second model, curative or palliative surgery was an independent predictor of OS. Among 91 patients who underwent surgery, the presence of PNEC-G3 was the only factor independently associated with a poorer survival after surgery (median OS: 35 vs. 97 months, \( p < 0.0001 \)).

CONCLUSIONS:
Patients with LM from PNET benefit from surgical resection although surgery should be reserved to well- or moderately differentiated forms. © 2015 S. Karger AG, Basel.

PMID: 26043944
Giant malignant insulinoma.

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Author information

Abstract

Insulinomas are the most common pancreatic neuroendocrine tumors. Most insulinomas are benign, small, intrapancreatic solid tumors and only large tumors have a tendency for malignancy. Most patients present with symptoms of hypoglycemia that are relieved with the administration of glucose. We herein present the case of a 75-year-old woman who presented with an acute hypoglycemic episode. Subsequent laboratory and radiological studies established the diagnosis of a 17-cm malignant insulinoma, with local invasion to the left kidney, lymph node metastasis, and hepatic metastases. Patient symptoms, diagnostic and imaging work-up and surgical management of both the primary and the metastatic disease are reviewed.

KEYWORDS:
Giant tumor; Insulinoma; PNET

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