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	Derleme	Prospektif Makaleler	Retrospektif Makaleler	Vaka sunumu
Tiroid	18	9	80	2
Paratiroid	1	7	12	5
Adrenal		2	12	2
NET	5		15	2

TİROİD (1880 makale taranmıştır)

DERLEME

1. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. ►
2. Thyroglobulin antibody (TgAb) methods - Strengths, pitfalls and clinical utility for monitoring TgAb-positive patients with differentiated thyroid cancer. ►
3. Risk of Thyroid Cancer in Patients with Thyroiditis: A Population-Based Cohort Study. ►
4. A meta-analysis of the effect of prophylactic central compartment neck dissection on locoregional recurrence rates in patients with papillary thyroid cancer. ►
5. Thyroglobulin in the Washout Fluid of Lymph-Node Biopsy: What Is its Role in the Follow-Up of DifferentiatedThyroid Carcinoma? ►
6. Thyroid metastasectomy. ►
7. Classification of locoregional lymph nodes in medullary and papillary thyroid cancer. ►
8. Prophylactic central neck disection in papillary thyroid cancer: a consensus report of the European Society of Endocrine Surgeons (ESES). ►
9. Classification of aerodigestive tract invasion from thyroid cancer. ►
10. Multifocal papillary thyroid carcinoma-a consensus report of the European Society of Endocrine Surgeons (ESES). ►
11. Intraoperative neural monitoring in thyroid cancer surgery. ►
12. Minimally invasive follicular thyroid cancer (MIFTC)-a consensus report of the European Society of Endocrine Surgeons (ESES). ►
13. BRAF mutation status in papillary thyroid carcinoma: significance for surgical strategy. ►
14. Continuous monitoring of the recurrent laryngeal nerve in thyroid surgery: a critical appraisal. ►
15. The extent of lateral lymph node dissection in differentiated thyroid cancer in the N+ neck. ►
16. Diagnostic utility of PETCT in thyroid malignancies: an update. ►

17. Diagnostic value of B-RAF(V600E) in difficult-to-diagnose thyroid nodules using fine-needle aspiration: Systematic review and meta-analysis. ►
18. Suspicious for Papillary Thyroid Carcinoma' before and after The Bethesda System for Reporting ThyroidCytopathology: Impact of Standardized Terminology. ►

TİROİD

PROSPEKTİF

1. Cabozantinib in progressive medullary thyroid cancer. ►
2. Stimulated thyroglobulin at recombinant human TSH-aided ablation predicts disease-free status one year later. ►
3. How can we screen voice problems effectively in patients undergoing thyroid surgery? ►
4. Intact parathyroid hormone measurement at 24 hours after thyroid surgery as predictor of parathyroid function at long term. ►
5. Ultrasonographic elastography of thyroid nodules: is adding strain ratio to colour mapping better? ►
6. Cytological diagnosis of thyroid nodules in Hashimoto thyroiditis in elderly patients. ►
7. "The Diagnostic Accuracy of Thyroid Nodule Fine-Needle Aspiration Cytology Following Thyroid Surgery: a Case-Control Study" ►
8. Superior laryngeal nerve quantitative intraoperative monitoring is possible in all thyroid surgeries. ►
9. Sutureless thyroidectomy with energy-based devices: Cerrahpasa experience. ►

TİROİD

RETROSPEKTİF

1. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. ►
2. Prognostic nomograms to predict oncological outcome of thyroid cancers. ►
3. Potential utility of rituximab for Graves' orbitopathy. ►
4. Targeted next-generation sequencing panel (ThyroSeq) for detection of mutations in thyroid cancer. ►
5. Determination of the Optimal Time Interval for Repeat Evaluation following a Benign Thyroid Nodule Aspiration. ►
6. The Effect of Extent of Surgery and Number of Lymph Node Metastases on Overall Survival in Patients with Medullary Thyroid Cancer. ►
7. Is thyroid cancer recurrence risk increased after transplantation? ►
8. Molecular and histopathologic characteristics of multifocal papillary thyroid carcinoma. ►
9. Oncologic Outcomes After Completion Thyroidectomy for Patients with Well-Differentiated Thyroid Carcinoma. ►
10. The Role of Thyroidectomy in Metastatic Disease to the Thyroid Gland. ►
11. Radioactive Iodine Remnant Uptake After Completion Thyroidectomy: Not Such a Complete Cancer Operation. ►
12. Influence of descriptive terminology on management of atypical thyroid fine-needle aspirates. ►
13. Malignancy rate in thyroid nodules classified as Bethesda Category III (AUS/FLUS). ►

14. Serum Thyroglobulin Improves the Sensitivity of the McGill Thyroid Nodule Score for Well-Differentiated ThyroidCancer. ►

15. Aggressive variants of papillary thyroid microcarcinoma are associated with extrathyroidal spread and lymph-node metastases: a population-level analysis. ►

16. Serum Thyroglobulin Improves the Sensitivity of the McGill Thyroid Nodule Score for Well-Differentiated ThyroidCancer. ►

17. A Pre-operative Nomogram for the Prediction of Ipsilateral Central Compartment Lymph Node Metastases in Papillary Thyroid Cancer. ►

18. Prognostic implications of papillary thyroid carcinoma with tall cell features. ►

19. Outcomes of patients with differentiated thyroid cancer risk-stratified according to the American thyroidassociation and Latin American thyroid society risk of recurrence classification systems. ►

20. Long-term outcomes of total thyroidectomy versus thyroid lobectomy for papillary thyroid microcarcinoma: comparative analysis after propensity score matching. ►

21. The Role of Survivin in Thyroid Tumors: Differences of Expression in Well-Differentiated, Non-Well-Differentiated, and Anaplastic Thyroid Cancers. ►

22. Tumor classification in Well-Differentiated Thyroid Carcinoma and Sentinel Lymph Node Biopsy Outcomes: a Direct Correlation. ►

23. Impact of Molecular Screening for Point Mutations and Rearrangements in Routine Air-Dried Fine-Needle Aspiration Samples of Thyroid Nodules. ►

24. Ultrasensitive serum thyroglobulin measurement is useful for the follow-up of patients treated with total thyroidectomy without radioactive iodine ablation. ►

25. Are prognostic scoring systems of value in patients with follicular thyroid carcinoma? ►

26. The cytologic category of oncocytic (Hurthle) cell neoplasm mostly includes low-risk lesions at histology: an institutional experience. ►

27. Familial vs sporadic papillary thyroid carcinoma: a matched-case comparative study showing similar clinical/prognostic behaviour. ►

28. Thyroid fine-needle aspiration reporting rates and outcomes before and after Bethesda implementation within a combined academic and community hospital system. ►

29. Should "indeterminate" diagnoses be used for thyroid fine-needle aspirates of nodules smaller than 1 cm? ►

30. Nodule size is an independent predictor of malignancy in mutation-negative nodules with follicular lesion of undetermined significance cytology. ►

31. Total thyroidectomy for Graves' disease: compliance with American Thyroid Association guidelines may not always be necessary. ►

32. The utility of routine preoperative cervical ultrasonography in patients undergoing thyroidectomy for differentiated thyroid cancer. ►

33. Decreasing the dose of radioiodine for remnant ablation does not increase structural recurrence rates in papillarythyroid carcinoma. ►

34. Observation of clinically negative central compartment lymph nodes in papillary thyroid carcinoma. ►

35. Cost analysis of thyroid lobectomy and intraoperative frozen section versus total thyroidectomy in patients with a cytologic diagnosis of "suspicious for papillary thyroid cancer". ►

36. The impact of surgical volume on patient outcomes following thyroid surgery. ►

37. Routine prophylactic central neck dissection for low-risk papillary thyroid cancer: a cost-effectiveness analysis. ►

38. A multi-institutional international study of risk factors for hematoma after thyroidectomy. ►

39. The long-term impact of routine intraoperative nerve monitoring during thyroid and parathyroid surgery. ►

40. Treatments for complications of tracheal sleeve resection for papillary thyroid carcinoma with tracheal invasion. ►

41. Ultrasonographic features associated with malignancy in cytologically indeterminate thyroid nodules. ►

42. Prognostic significance of patient age in minimally and widely invasive follicular thyroid carcinoma: Investigation of three age groups. ►

43. Metastatic papillary thyroid cancer with lateral neck disease: pattern of spread by level. ►

44. Surgical extent of central lymph node dissection in clinically node-negative papillary thyroid cancer. ►

45. Thyroid autoimmunity and risk of malignancy in thyroid nodules submitted to fine-needle aspiration cytology. ►

46. A core needle biopsy provides more malignancy-specific results than fine-needle aspiration biopsy in thyroidnodules suspicious for malignancy. ►

47. Candidates for Limited Lateral Neck Dissection among Patients with Metastatic Papillary Thyroid Carcinoma. ►

48. Comparison Between Preconsultation Ultrasonography and Office Surgeon-Performed Ultrasound in Patients with Thyroid Cancer. ►

49. Optimal Timing of Surgery for Differentiated Thyroid Cancer in Pregnant Women. ►

50. Prophylactic Level II Neck Dissection Guided by Frozen Section for Clinically Node-Negative Papillary Thyroid Carcinoma: Is It Useful? ►

51. Results of Intraoperative Neuromonitoring in Thyroid Surgery and Preoperative Vocal Cord Paralysis. ►

52. Trends in Incidentally Identified Thyroid Cancers Over a Decade: A Retrospective Analysis of 2,090 Surgical Patients. ►

53. Role of Preoperative Basal Calcitonin Levels in the Timing of Prophylactic Thyroidectomy in Patients With Germline RET Mutations. ►

54. Candidates for Limited Lateral Neck Dissection among Patients with Metastatic Papillary Thyroid Carcinoma. ►

55. Lobectomy and Prophylactic Central Neck Dissection for Papillary Thyroid Microcarcinoma: Do Involved Lymph Nodes Mandate Completion Thyroidectomy? ►

56. Reoperative Experience with Papillary Thyroid Cancer. ►

57. Size discrepancy between sonographic and pathological evaluation of solitary papillary thyroid carcinoma. ►

58. Encapsulation Status of Papillary Thyroid Microcarcinomas is Associated with the Risk of Lymph Node Metastases and Tumor Multifocality. ►

59. Risk factors contributing to the difference in prognosis for papillary versus micropapillary thyroid carcinoma. ►

60. Can increased tumoral vascularity be a quantitative predicting factor of lymph node metastasis in papillary thyroidmicrocarcinoma? ►

61. Biochemical persistence in thyroid cancer: is there anything to worry about? ►

62. Should patients with remnants from thyroid microcarcinoma really not be treated with iodine-131 ablation? ►

63. Nodal recurrence in the lateral neck after total thyroidectomy with prophylactic central neck dissection for papillary thyroid cancer. ►

64. Pre-operative ultrasound identification of thyroiditis helps predict the need for thyroid hormone replacement afterthyroid lobectomy. ►

65. Epidermal growth factor receptor overexpression is a marker for adverse pathologic features in papillary thyroid carcinoma. ►

66. Nondiagnostic fine-needle aspirations of the thyroid: is the risk of malignancy higher? ►

67. Predictive value of nodal metastases on local recurrence in the management of differentiated thyroid cancer. Retrospective clinical study. ►

68. Diagnostic utility of BRAFV600E mutation testing in thyroid nodules in elderly patients. ►

69. Follow-up of atypia and follicular lesions of undetermined significance in thyroid fine needle aspiration cytology. ►

70. Molecular Features of Follicular Variant Papillary Carcinoma of Thyroid: Comparison of Areas With or Without Classical Nuclear Features. ►

71. What do we leave behind after neartotal and subtotal thyroidectomy: just the tissue or the disease? ►

72. The relationship between thyroid volume and malignant thyroid disease. ►

73. Should level V be included in lateral neck dissection in treating papillary thyroid carcinoma? ►

74. Anti-thyroid antibodies as a predictor of thyroid cancer. ►

75. Comparison of surgical completeness between robotic total thyroidectomy versus open thyroidectomy. ►

76. Sex is not an independent risk factor for survival in differentiated thyroid cancer. ►

77. Comparison of surgical completeness between robotic total thyroidectomy versus open thyroidectomy. ►

78. Rates of thyroid malignancy by FNA diagnostic category. ►

79. Does thyroid surgery for Graves' disease improve health-related quality of life? ►

80. Total thyroidectomy as primary definitive treatment for graves' hyperthyroidism. ►

TİROİD

Vaka sunumu

1. Coexistence of Graves' disease, papillary thyroid carcinoma and unilateral benign struma ovarii: case report and review of the literature. ►
2. A case of apathetic thyroid storm with resultant hyperthyroidism-induced hypercalcemia. ►

PARATİROİD (461 makale taranmıştır)

DERLEME

1. The Final Intraoperative Parathyroid Hormone Level: How Low Should It Go? ►

PARATİROİD

PROSPEKTİF

1. Primary hyperparathyroidism and metabolic risk factors, impact of parathyroidectomy and vitamin D supplementation, and results of a randomized double-blind study. ►
2. A novel optical approach to intraoperative detection of parathyroid glands. ►
3. The role of contrast-enhancend ultrasonography (CEUS) in comparison with 99mTechnetium-sestamibi scintigraphy for localization diagnostic of primary hyperparathyroidism. ►
4. Laterality of central venous sampling: lack of effect on the accuracy of intraoperative parathyroid hormonemonitoring. ►

5. Intact parathyroid hormone measurement at 24 hours after thyroid surgery as predictor of parathyroidfunction at long term. ►
6. The effectiveness of low-dose versus high-dose 99mTc MIBI protocols for radioguided surgery in patients with primary hyperparathyroidism. ►
7. Can the use of intraoperative intact parathyroid hormone monitoring be abandoned in patients with hyperparathyroidism? ►

PARATİROİD

RETROSPEKTİF

1. Parathyroid Surgery in the Elderly: Should Minimally Invasive Surgery Be Abandoned? ►
2. Negative Parafibromin Staining Predicts Malignant Behavior in Atypical Parathyroid Adenomas. ►
3. Minimal benefit to subsequent intraoperative parathyroid hormone testing after all four glands have been identified. ►
4. Factors in conversion from minimally invasive parathyroidectomy to bilateral parathyroid exploration for primary hyperparathyroidism. ►
5. Do giant parathyroid adenomas represent a distinct clinical entity? ►
6. Minimally invasive resection for mediastinal ectopic parathyroid glands. ►
7. Primary hyperparathyroidism in pregnancy. ►
8. Radioguided Parathyroidectomy Succesful in 98.7% Of Selected Patients. ►
9. Intraoperative parathyroid hormone level in parathyroidectomy: which patients benefit from it? ►
10. The unequal distribution of parathyroid neoplasms in male patients. ►

11. Surgery for primary hyperparathyroidism in patients with preoperatively negative sestamibi scan and discordant imaging studies: the usefulness of intraoperative parathyroid hormone monitoring. ►
12. Fine needle aspiration cytology of parathyroid lesions. ►

PARATİROİD

VAKA SUNUMU

1. Denosumab for Management of Parathyroid Carcinoma-Mediated Hypercalcemia. ►
2. Deliberate total parathyroidectomy: a potentially novel therapy for tumor-induced hypophosphatemic osteomalacia. ►
3. A rare cystic lesion of the neck: parathyroid cyst. ►
4. A rare case of double parathyroid lipoadenoma with hyperparathyroidism. ►
5. False-Positive Result in 18F-Fluorocholine PET/CT Due to Incidental and Ectopic Parathyroid Hyperplasia. ►

ADRENAL (1268 makale taranmıştır)

PROSPEKTİF

1. Analysis of circulating microRNAs in adrenocortical tumors. ►
2. Prospective Study to Compare Peri-operative Hemodynamic Alterations following Preparation forPheochromocytoma Surgery by Phenoxybenzamine or Prazosin. ►

ADRENAL

RETROSPEKTİF

1. The characterization of pheochromocytoma and its impact on overall survival in multiple endocrine neoplasia type 2. ►
2. One-year progression-free survival of therapy-naive patients with malignant pheochromocytoma and paraganglioma. ►
3. Robotic versus laparoscopic adrenalectomy for pheochromocytoma. ►
4. Multimodality imaging findings of pheochromocytoma with associated clinical and biochemical features in 53 patients with histologically confirmed tumors. ►
5. Retroperitoneal Laparoendoscopic Single-Site Adrenalectomy for Pheochromocytoma: Our Single Center Experiences. ►
6. Perioperative, functional, and oncologic outcomes of partial adrenalectomy for multiple ipsilateral pheochromocytomas. ►
7. Laparoendoscopic single-site retroperitoneoscopic adrenalectomy for pheochromocytoma: case selection, surgical technique, and short-term outcome. ►
8. Laparoscopic adrenal surgery: ten-year experience in a single institution. ►
9. Preoperative workup in the assessment of adrenal incidentalomas: outcome from 282 consecutive laparoscopic adrenalectomies. ►
10. Adrenal hemorrhagic pseudocyst as the differential diagnosis of pheochromocytoma--a review of the clinical features in cases with radiographically diagnosed pheochromocytoma. ►
11. FDG PET in the evaluation of phaeochromocytoma: a correlative study with MIBG scintigraphy and Ki-67 proliferative index. ►

12. Role of preoperative adrenergic blockade with doxazosin on hemodynamic control during the surgical treatment of pheochromocytoma: a retrospective study of 48 cases. ►

ADRENAL

VAKA SUNUMU

1. Phaeochromocytoma crisis: two cases of undiagnosed phaeochromocytoma presenting after elective nonrelated surgical procedures. ►
2. Adrenocortical carcinoma initially presenting with hypokalemia and hypertension mimickinghyperaldosteronism: a case report. ►

NET (481 makale taranmıştır)

DERLEME

1. Systemic therapeutic strategies for GEP-NETS: what can we expect in the future? ►
2. Incidence of gastroenteropancreatic neuroendocrine tumours: a systematic review of the literature. ►
3. Evaluating neuroendocrine tumors progression and therapeutic response: state of the art. ►
4. Somatostatin receptor PET/CT in neuroendocrine tumours: update on systematic review and meta-analysis. ►
5. Reassessment of the Current American Joint Committee on Cancer Staging System for PancreaticNeuroendocrine Tumors. ►

NET

RETROSPEKTİF

1. Pattern and clinical predictors of lymph node involvement in nonfunctioning pancreatic neuroendocrine tumors(NF-PanNETs). ►
2. Analysis of 320 gastroenteropancreatic neuroendocrine tumors identifies TS expression as independent biomarker for survival. ►
3. Grading of well-differentiated pancreatic neuroendocrine tumors is improved by the inclusion of both Ki67 proliferative index and mitotic rate. ►
4. Enucleation and Limited Pancreatic Resection Provide Longterm Cure for Insulinoma in Multiple Endocrine Neoplasia Type 1? ►
5. Long-term Follow-up of Asymptomatic Pancreatic Neuroendocrine Tumors in Multiple Endocrine Neoplasia Type I Syndrome. ►
6. Second cancers in patients with neuroendocrine tumors. ►
7. Sporadic nonfunctioning pancreatic neuroendocrine tumors: Prognostic significance of incidental diagnosis. ►
8. Fine Needle Aspiration of Oncocytic Variants of Pancreatic Neuroendocrine Tumor: A Report of Three Misdiagnosed Cases. ►
9. Small bowel tumors detected and missed during capsule endoscopy: Single center experience. ►
10. Clinically detected gastroenteropancreatic neuroendocrine tumors are on the rise: Epidemiological changes in Germany. ►
11. Long-term follow up of endoscopic resection for type 3 gastric NET. ►
12. Surveillance Strategy for Rectal Neuroendocrine Tumors According to Recurrence Risk Stratification. ►

13. Analysis of risk factors for recurrence after curative resection of well-differentiated pancreatic neuroendocrine tumors based on the new grading classification. ►
14. Elevated Ki-67 labeling index in 'synchronous liver metastases' of well differentiated enteropancreaticneuroendocrine tumor. ►
15. Predicting aggressive behavior in nonfunctioning pancreatic neuroendocrine tumors. ►

NET

VAKA SUNUMU

1. Giant insulinoma: a report of 3 cases and review of the literature. ►
2. Synchronous appearance of a high-grade neuroendocrine carcinoma of the ampulla vater and sigmoid colon adenocarcinoma. ►

TİROİD

DERLEME / METAANALİZ

1. J Clin Endocrinol Metab. 2013 Nov 25. [Epub ahead of print] **IF:7.02**

The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis.

Brito JP, Gionfriddo MR, Al Nofal A, Boehmer KR, Leppin AL, Reading C, Callstrom M, Elraiyah TA, Prokop LJ, Stan MN, Hassan Murad M, Morris JC, Montori VM.
Author information

Abstract

Context:Significant uncertainty remains surrounding the diagnostic accuracy of sonographic features used to predict the malignant potential of thyroidnodulesObjective:To summarize the available literature related to the accuracy of thyroid nodule ultrasound (US) in the prediction of thyroidcancer.Methods:We searched multiple databases and reference lists for cohort studies that enrolled adults with thyroid nodules with reported diagnostic measures of sonography. A total of 14 relevant US features were analyzed.Results:We included 31 studies between 1985 and 2012 (number of nodules studied 18,288; average size 15 mm). The frequency of thyroid cancer was 20%. The most common type of cancer was papillarythyroid cancer (84%). The US nodule features with the highest diagnostic odds ratio (DOR) for malignancy was being "taller than wider" [11.14 (95% CI, 6.6-18.9)]. Conversely, the US nodule features with the highest DOR for benign nodules was spongiform appearance [12 (95% CI, 0.61-234.3)]. Heterogeneity across studies was substantial. Estimates of accuracy depended on the experience of the physician interpreting the US, the type of cancer and nodule (indeterminate), and type of reference standard. In a threshold model, spongiform appearance and cystic nodules were the only two features that, if present, could have avoided the use of fine-needle aspiration biopsy.Conclusions:Low to moderate quality evidence suggests that individual ultrasound features are not accurate predictors of thyroid cancer. Two features-cystic content and spongiform appearance-, however, might predict benign nodules but this has limited applicability to clinical practice due to their infrequent occurrence.

PMID: 24276450

2. Best Pract Res Clin Endocrinol Metab. 2013 Oct;27(5):701-12. doi: 10.1016/j.beem.2013.07.003. Epub 2013 Aug 12. **IF:5.65**

Thyroglobulin antibody (TgAb) methods - Strengths, pitfalls and clinical utility for monitoring TgAb-positive patients with differentiated thyroid cancer.

Spencer C, Fatemi S.
Author information

Abstract

Thyroglobulin autoantibodies (TgAb) are detected at diagnosis or during treatment in approximately 25% of patients with differentiated thyroid cancer (DTC). When present, TgAb interferes with thyroglobulin (Tg) measurement causing falsely low or undetectable Tg immunometric assay (IMA) values that can mask disease. Guidelines mandate that every Tg test have TgAb measured simultaneously and quantitatively by immunoassay and not a recovery test. The propensity and magnitude of TgAb-Tg interference relates to both Tg and TgAb concentrations and the class of Tg method used. Because the TgAb trend reflects

changes in thyroid tissue mass, TgAb concentrations serve as a surrogate post-operative DTC tumor marker. A rising, or de novo appearance of TgAb may indicate recurrence, whereas a progressive decline suggests successful treatment. This review focuses on the technical limitations of current TgAb methods, characteristics of TgAb interference with different classes of Tg method, and the clinical value of monitoring TgAb trends as a surrogate DTC tumor marker.

KEYWORDS:

Tg interference, TgAb methods, differentiated thyroid cancer (DTC), thyroglobulin autoantibodies (TgAb)

PMID: 24094640 http://dx.doi.org/10.1016/j.beem.2013.07.003

3. Ann Surg Oncol. 2013 Nov 8. [Epub ahead of print] **IF:4.33**

Risk of Thyroid Cancer in Patients with Thyroiditis: A Population-Based Cohort Study.

Liu CL, Cheng SP, Lin HW, Lai YL.
Author information

Abstract

BACKGROUND:
The causative relationship between autoimmune thyroiditis and thyroid cancer remains a controversial issue. The aim of this population-based study was to investigate the risk of thyroid cancer in patients with thyroiditis.

METHODS:
From the Longitudinal Health Insurance Database 2005 (LHID2005) of Taiwan, we identified adult patients newly diagnosed with thyroiditis between 2004 and 2009 (n = 1,654). The comparison cohort (n = 8,270) included five randomly selected age- and sex-matched controls for each patient in the study cohort. All patients were followed up from the date of cohort entry until they developed thyroid cancer or to the end of 2010. Multivariate Cox regression was used to assess the risk of developing thyroid cancer. A total of 1,000 bootstrap replicates were created for internal validation.

RESULTS:
A total of 35 patients developed thyroid cancer during the study period, of whom 24 were from the thyroiditis cohort and 11 were from the comparison cohort (incidence 353 and 22 per 100,000 person-years, respectively). After adjusting for potential confounding factors, the hazard ratio (HR) for thyroid cancer in patients with thyroiditis was 13.24 (95 % CI 6.40-27.39). Excluding cancers occurring within 1 year of follow-up, the HR remained significantly increased (6.64; 95 % CI 2.35-18.75). Hypothyroidism was not an independent factor associated with the occurrence of thyroidcancer.

CONCLUSIONS:
We found an increased risk for the development of thyroid cancer after a diagnosis of thyroiditis, independent of comorbidities.

PMID: 24201747

4. Ann Surg Oncol. 2013 Oct;20(11):3477-83. doi: 10.1245/s10434-013-3125-0. Epub 2013 Jul 12. **IF:4.33**

A meta-analysis of the effect of prophylactic central compartment neck dissection on locoregional recurrence rates in patients with papillary thyroid cancer.

Wang TS, Cheung K, Farrokhyar F, Roman SA, Sosa JA.
Author information

Abstract

BACKGROUND:
It is not known whether prophylactic central compartment neck dissection (pCCND) in conjunction with total thyroidectomy decreases rates of locoregional recurrence in patients with papillary thyroid cancer (PTC).

METHODS:
A meta-analysis was performed of reported recurrence rates of clinically node-negative PTC in patients treated with total thyroidectomy (TT) alone, or TT and pCCND. The primary outcome was locoregional recurrence of PTC.

RESULTS:
Eleven studies capturing 2,318 patients met the inclusion criteria. Overall, the recurrence rate for patients undergoing TT/pCCND was 3.8 % [95 % confidence interval (CI) 2.3-5.8]. In the six comparative studies, which included 1,740 patients, 995 patients undergoing TT and 745 patients undergoing TT/pCCND, the overall recurrence rate was 7.6:7.9 % in the TT group and 4.7 % in the TT/pCCND group. The relative risk of recurrence was 0.59 (95 % CI 0.33-1.07), favoring a lower recurrence rate in the TT/pCCND arm. The number of patients that would need to be treated (NNT) in order to prevent a single recurrence is 31. The relative risk for permanent hypocalcemia was 1.82 (95 % CI 0.51-6.5) and for permanent recurrent laryngeal nerve injury was 1.14 (95 % CI 0.46-2.83).

CONCLUSIONS:
There was no difference in recurrence or long-term complication rates between patients undergoing TT or TT/pCCND. There was a trend toward lower recurrence rates in TT/pCCND patients, with a NNT of 31 patients. On the basis of these data, routine pCCND might be considered in the hands of high-volume surgeons treating patients with clinically node-negative PTC.

PMID: 23846784 http://dx.doi.org/10.1245/s10434-013-3125-0

5. Thyroid. 2013 Oct 29. [Epub ahead of print] **IF:3.84**

Thyroglobulin in the Washout Fluid of Lymph-Node Biopsy: What Is its Role in the Follow-Up of DifferentiatedThyroid Carcinoma?

Torres MR, Nóbrega Neto SH, Rosas RJ, Martins AL, Ramos AL, da Cruz TR.
Author information

Abstract

Background: The clinical evaluation of enlarged local lymph nodes (LNs) is difficult at the beginning and throughout the follow-up of differentiatedthyroid carcinoma (DTC). Although the examination of samples collected from LNs by fine-needle aspiration biopsy cytology (FNAB-C) is extremely specific for the diagnosis of metastases, its sensitivity is low, especially in paucicellular samples. Summary: The measurement of thyroglobulin (Tg) in the fine-needle aspiration biopsy (FNAB) washout fluid (FNAB-Tg) increases the diagnostic performance of cytology to up to 100% sensitivity and specificity. However, the application of FNAB-Tg is currently hindered by the absence of methodological standardization, a lack of definite cutoff points, and the ongoing debate regarding its accuracy in nonthyroidectomized patients, those with elevated serum Tg, and those with circulating anti-Tg antibodies. Conclusion: FNAB-Tg improves the

diagnostic performance of FNAB-C in LN metastases, even when the latter is unable to diagnose the metastases. For that reason, FNAB-Tg should be included in the monitoring of DTC.

PMID: 24044517

6. J Surg Oncol. 2014 Jan;109(1):36-41. doi: 10.1002/jso.23452. Epub 2013 Oct 4. **IF:2.97**

Thyroid metastasectomy.

Montero PH, Ibrahimpasic T, Nixon IJ, Shaha AR.
Author information

Abstract

Metastases to the thyroid gland are uncommon. Renal, lung, breast, and colon cancer and melanoma are the most common primary diseases implicated. Few retrospective series have been reported. Treatment decisions must be individualized, and will depend on the state of systemic disease. Selected patients could benefit from surgical treatment. Although most patients selected for surgery will not be cured, the aim of surgery is to avoid the complications of uncontrolled central neck disease. J. Surg. Oncol. 2014 109:36-41. © 2013 Wiley Periodicals, Inc.

KEYWORDS:

metastasectomy, metastasis, thyroid cancer, thyroid neoplasms/secondary, thyroid surgery

PMID: 24122778 http://dx.doi.org/10.1002/jso.23452

7. Langenbecks Arch Surg. 2013 Dec 5. [Epub ahead of print] **IF:2.21**

Classification of locoregional lymph nodes in medullary and papillary thyroid cancer.

Musholt TJ.
Author information

Abstract

BACKGROUND:
Among the various thyroid malignancies, medullary and papillary thyroid carcinomas are characterized by predominant locoregional lymph node metastases that may cause morbidity and affect patient survival. Although lymph node metastases are frequently detected, the optimal strategy aiming at the removal of all tumor tissues while minimizing the associated surgical morbidity remains a matter of debate.

PURPOSE:
A uniform consented terminology and classification is a precondition in order to compare results of the surgical treatment of thyroidcarcinomas. While the broad distinction between central and lateral lymph node groups is generally accepted, the exact boundaries of these neck regions vary significantly in the literature. Four different classification systems are currently used. The classification system of the American Head and Neck Society and the corresponding classification system of the Union for International Cancer Control (UICC) are based on observations of squamous cell carcinomas and appointed to needs of head and neck surgeons. The classification of the Japanese Society for Thyroid Diseases and the compartment classification acknowledge the distinctive pattern of metastasis in thyroid carcinomas.

CONCLUSIONS:
Comparison of four existing classification systems reveals underlying different treatment concepts. The compartment system meets the necessities of thyroid carcinomas and is used worldwide in studies describing the results of lymph node dissection. Therefore, the German Association of Endocrine Surgery has recommended using the latter system in their recently updated guidelines on thyroid carcinoma.

PMID: 24306103

8. Langenbecks Arch Surg. 2013 Dec 19. [Epub ahead of print] **IF:2.21**

Prophylactic central neck disection in papillary thyroid cancer: a consensus report of the European Society of Endocrine Surgeons (ESES).

Sancho JJ, Lennard TW, Paunovic I, Triponez F, Sitges-Serra A.
Author information

Abstract

BACKGROUND:
There remains still no clear answer as to whether or not prophylactic central compartment neck dissection (pCCND) is indicated for the treatment of patients with papillary thyroid cancer.

METHODS:
The published studies, including single cohort, comparative studies and meta-analysis, were critically appraised. Aspects beyond postoperative complications and loco-regional recurrence rates in the analysis, as the impact of pre- and post-ablation thyroglobuline levels, multifocality, bilaterality and additional risk factors for recurrence, were also considered.

RESULTS:
Thirty studies and five meta-analyses were assessed. The lack of randomized clinical trials on the subject and the heterogeneity of study populations are the main limiting factors to draw clear conclusions, and a comprehensive list of bias sources has been identified. Recent comparative studies and systematic reviews all associate the pCCND with higher proportions of temporary postoperative hypocalcemia but not with significantly higher permanent hypoparathyroidism, recurrent laryngeal nerve injury or permanent vocal cord paralysis. The risk of recurrence appears to be reduced after pCCND, and the number of patients needed to treat to avoid a recurrence is between 20 and 31.

CONCLUSIONS:
It is suggested that routine level 6 prophylactic dissections should be risk-stratified. Larger tumours (T3, T4), patients aged 45 years and older or 15 years and younger, male patients, patients with bilateral or multifocal tumours, and patients with known involved lateral lymph nodes could all be candidates for routine unilateral level 6 dissection. The operation should be limited to surgeons who have the available expertise and experience.

PMID: 24352594

9. Langenbecks Arch Surg. 2013 Nov 24. [Epub ahead of print] **IF:2.21**

Classification of aerodigestive tract invasion from thyroid cancer.

Brauckhoff M.
Author information

Abstract

BACKGROUND:
Widely invasive extrathyroidal thyroid cancer invading the aerodigestive tract (ADT) including larynx, trachea, hypopharynx, and/or esophagus occurs in 1-8 % of patients with thyroid cancer and is classified as T4a (current UICC/AJCC system). The T4a stage is associated with impaired tumor-free survival and increased disease-specific mortality. Concerning prognosis and outcome, further subdivisions of the T4a stage, however, have not been made so far.

METHODS:
This study is based on a systematic review of the relevant literature in the PubMed database.

RESULTS:

Retrospective studies suggest a better outcome in patients with invasion of the trachea or the esophagus when compared to laryngeal invasion. Regarding surgical strategies, ADT invasion can be classified based on a three-dimensional assessment determining surgical resection options. Regardless of the invaded structure, tumor infiltration of the ADT can be subdivided into superficial, deep extraluminal, and intraluminal invasion. In contrast to superficial ADT invasion, allowing tangential incomplete wall resection (shaving/extramucosal esophagus resection), deeper wall and intraluminal invasions require complete wall resection (either window or sleeve). Based on the Dralle classification (types 1-6), particularly airway invasion, can be further classified according to the vertical and horizontal extents of tumor invasion.

CONCLUSIONS:
The Dralle classification can be considered as a reliable subdivision system evaluated regarding surgical options as well as oncological outcome. However, further studies determining the prognostic impact of this technically oriented classification system are required.

PMID: 24271275

10. Langenbecks Arch Surg. 2013 Nov 22. [Epub ahead of print] **IF:2.21**

Multifocal papillary thyroid carcinoma-a consensus report of the European Society of Endocrine Surgeons (ESES).

Iacobone M, Jansson S, Barczyński M, Goretzki P.
Author information

Abstract

BACKGROUND:
Multifocal papillary thyroid carcinoma (MPTC) has been reported in literature in 18-87 % of cases. This paper aims to review controversies in the molecular pathogenesis, prognosis, and management of MPTC.

METHODS:
A review of English-language literature focusing on MPTC was carried out, and analyzed in an evidence-based perspective. Results were discussed at the 2013 Workshop of the European Society of Endocrine Surgeons devoted to surgery of thyroid carcinoma.

RESULTS:
Literature reports no prospective randomized studies; thus, a relatively low level of evidence may be achieved.

CONCLUSIONS:
MPTC could be the result of either true multicentricity or intrathyroidal metastasis from a single malignant focus. Radiation and familial nonmedullary thyroid carcinoma are conditions at risk of MPTC development. The prognostic importance of multifocal tumor growth in PTC remains controversial. Prognosis might be impaired in clinical MPTC but less or none in MPTC <1 cm. MPTC can be diagnosed preoperatively by FNAB and US, with low sensitivity for MPTC <1 cm. Total or near-total thyroidectomy is indicated to reduce the risk of local recurrence. Prophylactic central node dissection should be considered in patients with total tumor diameter >1 cm, or in cases with high number of cancer foci. Completion thyroidectomy might be necessary when MPTC is diagnosed after less than near-total thyroidectomy. Radioactive iodine ablation should be considered in selected patients with MPTC at increased risk of recurrence or metastatic spread.

PMID: 24263684

11. Langenbecks Arch Surg. 2013 Nov 27. [Epub ahead of print] **IF:2.21**

Intraoperative neural monitoring in thyroid cancer surgery.

Randolph GW, Kamani D.
Author information

Abstract

BACKGROUND:
Intraoperative neural monitoring (IONM) has increasingly garnered the attention of the surgeons performing thyroid and parathyroid surgery around the world. Current studies suggest a majority of general and head and neck surgeons utilize neural monitoring in their thyroid surgical case load in both the US and Germany.

PURPOSE:
We aim to present an up-to-date review of the application of IONM specifically focusing on its utility in thyroid cancer surgery. Neural monitoring is discussed particularly as it relates to neural prognosis, the issues of staged thyroid surgery for thyroid cancer, and new horizons in the monitoring of the superior laryngeal nerve (SLN) and prevention of neural injury through continuous vagal neural monitoring.

CONCLUSION:
IONM, as it relates to thyroid surgery, has obtained a widespread acceptance as an adjunct to the gold standard of visual nerve identification. The value of IONM in prognosticating neural function and in intraoperative decision making regarding proceeding to bilateral surgery is also well-known. Initial data on recent extensions of IONM in the form of SLN monitoring and continuous vagal nerve monitoring are promising. Continuous vagal nerve monitoring expands the utility of IONM by providing real-time electrophysiological information, allowing surgeons to take a corrective action in impending neural injury.

PMID: 24281845

12. Langenbecks Arch Surg. 2013 Nov 14. [Epub ahead of print] **IF:2.21**

Minimally invasive follicular thyroid cancer (MIFTC)-a consensus report of the European Society of Endocrine Surgeons (ESES).

Dionigi G, Kraimps JL, Schmid KW, Hermann M, Sheu-Grabellus SY, De Wailly P, Beaulieu A, Tanda ML, Sessa F.
Author information

Abstract

BACKGROUND:
This paper aims to review controversies in the management of minimally invasive follicular thyroid carcinoma (MIFTC) and to reach an evidence-based consensus.

METHOD:
MEDLINE search of the literature was conducted using keywords related to MIFTC. The search term was identified in the title, abstract, or medical subject heading. Available literature meeting the inclusion criteria were assigned the appropriate levels of evidence and recommendations in accordance with accepted international standards. Results were discussed at the 2013 Workshop of the European Society of Endocrine Surgeons devoted to MIFTC.

RESULTS:
Published papers on MIFTC present inadequate power with a III-IV level of evidence and C grade of recommendation. Several issues demanded a comparison of published studies from different medical reports regarding MIFTC definition, specimen processing, characteristics, diagnosis, prognoses, and therapy. As a consequence, it is difficult to make valuable statements on MIFTC with a sufficient recommendation rating. MIFTC diagnosis requires clearer, unequivocal, and reproducible criteria for

pathologist, surgeons, and endocrinologists to use in the management of these patients. If the distinction between MIFTC and WIFTC cannot be made, an expert in thyroid pathologist should be consulted.

CONCLUSION:
According to published papers, the following conclusions can be drawn. (a) Candidates for hemithyroidectomy are MIFTC with exclusive capsular invasion, patients <45 years old at presentation, tumor size <40 mm, without vascular invasion, and without any node or distant metastases. (b) Candidates for total thyroidectomy are MIFTC in patients ≥45 years at presentation, tumor size ≥40 mm, vascular invasion present, positive nodes, and positive distant metastases. (c) In the absence of clinical evidence for lymph node metastasis, patients with MIFTC do not require prophylactic lymph node dissection. (d) Radio iodine ablation is indicated in elderly patients (>45 years), large tumor size (>40 mm), extensive vascular invasion, presence of distant synchronous or metachronous metastasis, positive nodes, and if recurrence is noted at follow-up.

PMID: 24233345

13. Langenbecks Arch Surg. 2013 Dec 30. [Epub ahead of print] **IF:2.21**

BRAF mutation status in papillary thyroid carcinoma: significance for surgical strategy.

Miccoli P, Basolo F.
Author information

Abstract

BACKGROUND:
BRAF mutation is probably the only molecular marker acting as a risk factor that is available before surgery: for this reason, soon after it became quite widespread, it seemed an important tool as a guide towards an individualized surgical therapy in papillary thyroid carcinoma.

PURPOSE:
Capsule invasion, multifocality, and lymph node involvement are the most important parameters influencing the choice of surgical strategy in front of small papillary cancers and, in more detail, of micro papillary carcinomas. The relationship between these parameters and the BRAF mutation are closely examined through the more recent literature. Capsular invasion seems to show the strongest correlation with the mutation and this has important correlations, thus suggesting that a more aggressive local surgery might be advisable, whereas the correlation between the mutation and lymph node involvement would be weaker, at least according to the most recent studies.

CONCLUSIONS:
The personalization of surgical therapy, today, seems easier to achieve thanks to molecular testing. In particular, an important result could be in the short term reduction in the number of completion thyroidectomies following simple lobectomies. Also, post operative radioactivated iodine therapies should be more carefully evaluated and tailored according to BRAF status. A possible flow chart for the decision of the therapeutic approach is proposed in accordance to the results of the literature.

PMID: 24375266

14. Int J Surg. 2013 Dec;11 Suppl 1:S44-6. doi: 10.1016/S1743-9191(13)60014-X. **IF:1.73**

Continuous monitoring of the recurrent laryngeal nerve in thyroid surgery: a critical appraisal.

Dionigi G[1], Donatini G[2], Boni L[1], Rausei S[1], Rovera F[1], Tanda ML[3], Kim HY[4], Chiang FY[5], Wu CW[5], Mangano A[1], Rulli F[6], Alesina PF[7], Dionigi R[1].
Author information

Abstract

BACKGROUND AND PURPOSE:
Intraoperative neuromonitoring (IONM) contributes in several ways to recurrent laryngeal nerve (RLN) protection. Notwithstanding these advantages, surgeons must be aware that the current, intermittent, mode of IONM (I-IONM) has relevant limitations. To overcome these I-IONM limitations, a continuous IONM (C-IONM) technology has been proposed.

METHODS:
A PubMed indexed literature review of the current limitations of I-IONM is presented and a commentary about C-IONM is provided presenting the preliminary results of research on this topic.

MAIN FINDINGS:
I-IONM, despite the advantages it produces, presents some important limitations; to overcome these drawbacks a C-IONM technology has been introduced.

CONCLUSIONS:
RLN traction injury is still the most common cause of RLN injury and is difficult to avoid with the application of I-IONM in thyroidsurgery. C-IONM is useful to prevent the imminent traction injury by detecting progressive decreases in electromyographic amplitude combined with progressive latency increases. C-IONM seems to be a technological improvement. Likely, C-IONM by vagal nerve stimulation should enhance the standardization process, RLN intraoperative information, documentation, protection, training, and research in modern thyroid surgery. Although C-IONM is a promising technology at the cutting edge of research in thyroid surgery, we need more studies to assess in an evidence-based way all its advantages.

KEYWORDS:

C-IONM, Continuous intraoperative neuromonitoring, IONM, Thyroid surgery

PMID: 24380551 http://dx.doi.org/10.1016/S1743-9191(13)60014-X

15. Eur Arch Otorhinolaryngol. 2013 Nov;270(11):2947-52. doi: 10.1007/s00405-013-2434-z. Epub 2013 Mar 22. **IF:1.59**

The extent of lateral lymph node dissection in differentiated thyroid cancer in the N+ neck.

Kumar S, Burgess C, Moorthy R.
Author information

Abstract

The management of the lateral neck in metastatic differentiated thyroid cancer (DTC) varies widely. Most groups advocate dissection of nodal levels II-IV but many perform a more extensive dissection. We aimed to asses whether there was any evidence for a modified radical neck dissection over a selective neck dissection by looking at the extent to which DTC metastases to levels I and V. We performed a review of the current literature including adult and paediatric patients who underwent a lateral neck dissection for metastatic DTC. The primary endpoint was histological confirmation of metastases in nodal levels I and V. 650 abstracts were identified and reviewed. 23 papers were included in the study. The incidence of level V

metastases during routine level V dissection in patients with DTC is 20 % and the incidence of level I metastases during routine level I dissection in patients with DTC is 8 %. Histologically proven metastases were found in 22.5 % of level V neck dissection of which 2.5 % were pre-operatively suspected of metastases. 20 % had histologically proven metastases to level I of which 12 % were pre-operatively suspected of metastases. Our study has shown a 20 % incidence of level V metastases in the N+ neck suggesting that level V should be part of a planned neck dissection. Evidence is lacking for routine dissection of level I. A future prospective study is required to asses the question of risk factors for lateral nodal metastases, recurrence and survival.

PMID: 23519682 http://dx.doi.org/10.1007/s00405-013-2434-z

16. Ann Nucl Med. 2013 Oct;27(8):681-93. doi: 10.1007/s12149-013-0740-6. Epub 2013 Jun 26. **IF:1.63**

Diagnostic utility of PETCT in thyroid malignancies: an update.

Palaniswamy SS, Subramanyam P.
Author information

Abstract
The primary clinical application of (18)F FDG PET/CT ((18)Fluorine labeled flurodeoxyglucose positron emission tomography/computed tomography) in differentiated thyroid carcinoma is in the identification of active disease in thyroglobulin (Tg) positive (>10 ng/ml), whole body iodine scan negative patients. The impact of FDG PET/CT in diagnosis, surveillance, cure, and progression-free survival of differentiated thyroid carcinoma patients remains to be seen. Five main indications of FDG PET/CT in thyroid cancer have been recommended by revised American thyroid association guidelines 2009. This review aims to provide a complete picture of PET imaging in thyroid malignancies and enumerates each indication with literature review. This review also highlights recent advances in targeted molecular imaging. Currently differentiated thyroid cancer is best imaged using conventional single photon emission computed tomography-based radioiodine tracers ((123)I/(131)I). Although the utility of FDG PET in well differentiated thyroidcancer patients who are iodine negative but with raised Tg is well established, evidence is emerging on the advantages of FDG PET/CT in other histological types of thyroid malignancy, such as Hurthle cell, medullary, and the anaplastic malignancies. Novel PET radiotracers, such as (124)Iodine ((124)I), (18)F-DOPA (3,4-dihydroxy-L-phenylalanine), and (68)Ga-DOTA peptides are revolutionizing the way thyroid malignancies are imaged. Newer concepts on targeted molecular imaging and theranostics are ushering in new possibilities for imaging and treating thyroid cancer.

PMID: 23801405 http://dx.doi.org/10.1007/s12149-013-0740-6

17. Diagn Cytopathol. 2014 Jan;42(1):94-101. doi: 10.1002/dc.23044. Epub 2013 Oct 25. **IF:1.21**

Diagnostic value of B-RAF(V600E) in difficult-to-diagnose thyroid nodules using fine-needle aspiration: Systematic review and meta-analysis.

Jia Y, Yu Y, Li X, Wei S, Zheng X, Yang X, Zhao J, Xia T, Gao M.
Author information

Abstract
Fine-needle aspiration (FNA) is routinely used in the preoperative evaluation of thyroid nodules. However, approximately 5-20% of thyroid nodules are considered indeterminate or suspicious cases that do not meet clinical standards. The B-RAF(V600E) mutation has been reported in FNA specimens. We conducted a systematic review to evaluate the diagnostic value of testing for B-RAF(V600E) in thyroid nodules that are difficult to diagnose by FNA. A systematic literature search was performed from January 1, 2002 to June

30, 2012. Articles were obtained by searching two electronic databases (MEDLINE and EMBASE), hand searching selected journals, and contacting authors. Article quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. Sensitivity, specificity, and other measures of accuracy were pooled using random effects models. Summary receiver operating characteristic (SROC) curves were used to summarize overall diagnostic accuracy. A total of 16 studies incorporating 1131 patients were included in a meta-analysis on diagnostic accuracy of B-RAF(V600E) tests. Pooled sensitivity was 0.60 (95% confidence interval [CI]: 0.556-0.634), pooled specificity was 0.99 (95% CI 0.976-0.997), and the area under the curve of the SROC curve was 0.8376. Q index value was 0.7696. Our data suggest a potentially useful adjunct to evaluating thyroid nodules that are difficult to diagnose. The B-RAF(V600E) test has a high positive predictive value and could help clinicians formulate a more individualized treatment schedule. When supplemented with other noninvasive test methods, the B-RAF(V600E) test could be a powerful adjunct with extensive clinical applications. Diagn. Cytopathol. 2014;42:94-101. © 2013 Wiley Periodicals, Inc.

KEYWORDS:

BRAFV600E, fine-needle aspiration, thyroid nodule

PMID: 24167125 http://dx.doi.org/10.1002/dc.23044

18. Acta Cytol. 2013 Nov 1. [Epub ahead of print] **IF:0.93**

'Suspicious for Papillary Thyroid Carcinoma' before and after The Bethesda System for Reporting ThyroidCytopathology: Impact of Standardized Terminology.

Olson MT, Boonyaarunnate T, Atlinboga AA, Ali SZ.
Author information

Abstract

Background: The high-risk 'suspicious for papillary thyroid carcinoma' (SPTC) is a clinically relevant diagnosis in the cytological interpretation ofthyroid aspirates. While The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has provided invaluable terminology standardization, a performance comparison for this diagnostic category has not been performed. Therefore, this study evaluates the SPTC diagnosis before and after the introduction of TBSRTC in a large meta-analysis and at a single institution. Materials and Methods: The meta-analysis analyzed publications of SPTC or similar diagnoses before and after the introduction of TBSRTC. Similarly our own institutional experience was analyzed for the 8 years surrounding the introduction of TBSRTC. A correlation of the cytopathology and surgical pathology diagnoses was performed. Results: The introduction of TBSRTC coincided with a significant decrease in the fraction of cases called SPTC in the meta-analysis (4.5-3.1%, $p < 0.00001$) and in the institutional review (1.7-0.9%, $p = 0.005$). Meanwhile, the malignancy risk for those cases increased significantly in the meta-analysis from 62.5 to 80.5% ($p < 0.00001$) and trended upwards in the institutional review from 69 to 79% ($p = 0.4$). The follow-up rate was similar in both time periods in the meta-analysis and the institutional review. Conclusions: The introduction of TBSRTC coincided with a decrease in the fraction of cases called SPTC and an increase in the malignancy risk associated with that diagnosis. © 2013 S. Karger AG, Basel.

PMID: 24192286

TİROİD

PROSPEKTİF

1. J Clin Oncol. 2013 Oct 10;31(29):3639-46. doi: 10.1200/JCO.2012.48.4659. Epub 2013 Sep 3.

IF:15.18

Cabozantinib in progressive medullary thyroid cancer.

Elisei R, Schlumberger MJ, Müller SP, Schöffski P, Brose MS, Shah MH, Licitra L, Jarzab B, Medvedev V, Kreissl MC, Niederle B, Cohen EE, Wirth LJ, Ali H,Hessel C, Yaron Y, Ball D, Nelkin B, Sherman SI.
Author information

Abstract

PURPOSE:
Cabozantinib, a tyrosine kinase inhibitor (TKI) of hepatocyte growth factor receptor (MET), vascular endothelial growth factor receptor 2, and rearranged during transfection (RET), demonstrated clinical activity in patients with medullary thyroid cancer (MTC) in phase I.

PATIENTS AND METHODS:
We conducted a double-blind, phase III trial comparing cabozantinib with placebo in 330 patients with documented radiographic progression of metastatic MTC. Patients were randomly assigned (2:1) to cabozantinib (140 mg per day) or placebo. The primary end point was progression-free survival (PFS). Additional outcome measures included tumor response rate, overall survival, and safety.

RESULTS:
The estimated median PFS was 11.2 months for cabozantinib versus 4.0 months for placebo (hazard ratio, 0.28; 95% CI, 0.19 to 0.40; P < .001). Prolonged PFS with cabozantinib was observed across all subgroups including by age, prior TKI treatment, and RET mutation status (hereditary or sporadic). Response rate was 28% for cabozantinib and 0% for placebo; responses were seen regardless of RET mutation status. Kaplan-Meier estimates of patients alive and progression-free at 1 year are 47.3% for cabozantinib and 7.2% for placebo. Common cabozantinib-associated adverse events included diarrhea, palmar-plantar erythrodysesthesia, decreased weight and appetite, nausea, and fatigue and resulted in dose reductions in 79% and holds in 65% of patients. Adverse events led to treatment discontinuation in 16% of cabozantinib-treated patients and in 8% of placebo-treated patients.

CONCLUSION:
Cabozantinib (140 mg per day) achieved a statistically significant improvement of PFS in patients with progressive metastatic MTC and represents an important new treatment option for patients with this rare disease. This dose of cabozantinib was associated with significant but manageable toxicity.

Comment in

- How to incorporate new tyrosine kinase inhibitors in the treatment of patients with medullary thyroid cancer. [J Clin Oncol. 2013]

PMID: 24002501 http://dx.doi.org/10.1200/JCO.2012.48.4659

2. J Clin Endocrinol Metab. 2013 Nov;98(11):4364-72. doi: 10.1210/jc.2013-2267. Epub 2013 Sep 13. **IF:7.02**

Stimulated thyroglobulin at recombinant human TSH-aided ablation predicts disease-free status one year later.

Melo M, Costa G, Ribeiro C, Carrilho F, Martins MJ, da Rocha AG, Sobrinho-Simões M, Carvalheiro M, Soares P.
Author information

Abstract

CONTEXT:
Thyroglobulin (Tg) levels measured at the time of remnant ablation after thyroid hormone withdrawal (THW) were shown to have prognostic value in predicting disease-free status.

OBJECTIVES:
Our objectives were to determine whether stimulated Tg levels, measured at the time of remnant ablation performed under recombinant human TSH (rhTSH) stimulation, has value in predicting absence of detectable disease 1 year after radioiodine therapy and to compare the results obtained with this approach with a cohort of patients submitted to ablation after THW.

DESIGN:
This was a prospective observational study.

SETTING AND PATIENTS:
The study included 293 consecutive patients treated for a differentiated thyroid carcinoma with no initial evidence of distant metastasis. All patients were submitted to a total or near-total thyroidectomy, followed by ablation either under rhTSH (n = 151) or endogenous TSH stimulation (n = 142). Patients with positive Tg antibodies were excluded.

MAIN OUTCOME MEASURES:
The predictive value of Tg at ablation was assessed by receiver operating characteristic curve analysis.

RESULTS:
In the rhTSH group, 96 patients (73.3%) were considered disease-free at 1 year. Stimulated Tg at ablation after rhTSH was found to be an independent prognostic indicator of disease persistence 12 months later. The highest-accuracy cutoff value for absence of detectable disease was defined as 7.2 ng/mL, with a negative predictive value of 90%. In the THW group, Tg at ablation also proved to have independent predictive value. Using the same threshold (7.2 ng/mL), the negative predictive value of Tg was 95% in the THW group.

CONCLUSIONS:
When rhTSH was used, stimulated Tg at ablation had independent predictive value for disease-free status 1 year later. A low stimulated Tg at rhTSH-aided ablation may be considered a favorable prognosis factor.

PMID: 24037891 http://dx.doi.org/10.1210/jc.2013-2267

3. Thyroid. 2013 Nov;23(11):1437-44. doi: 10.1089/thy.2013.0262. Epub 2013 Sep 20. **IF:3.84**

How can we screen voice problems effectively in patients undergoing thyroid surgery?

Park JO, Bae JS, Chae BJ, Kim CS, Nam IC, Chun BJ, Shim MR, Hwang YS, Kim MS, Sun DI.
Author information

Abstract

BACKGROUND:

Voice problems following thyroid surgery are well known, and perioperative voice analysis in patients undergoing thyroidectomy no longer seems optional. However, multiple means of assessing vocal function are time-consuming, require specific instruments and specialists, and increase costs. Therefore, we designed this study to develop an efficient and cost-effective screening tool for detecting voice disorders following thyroidectomy.

METHODS:
We developed the Perioperative Voice-Screening Protocol for Thyroid Surgery (PVST) using the Thyroidectomy-Related Voice Questionnaire (TVQ) to provide a cost-effective diagnostic flow chart for patients following thyroidectomy. The TVQ is a simple questionnaire that was developed at our institution and has already demonstrated its effectiveness in detecting pre- and postthyroidectomy voice-related disorders in our previous studies. To investigate the PVST, we enrolled 242 subjects who underwent thyroidectomy and let them follow the PVST. All subjects underwent a voice work-up by a voice specialist to verify the predictive value of the protocol.

RESULTS:
Using PVST, we could effectively screen for abnormal preoperative laryngeal findings with sensitivity and specificity of 82.1% and 50.5%, respectively, especially laryngeal benign mucosal disease with sensitivity and specificity of 100% and 45.6%, respectively. We could also screen for postoperative voice-related problems with sensitivity and specificity of 100% and 50.4% for detecting vocal-cord palsy, and 66.7% and 51.2% for detecting a low-pitched voice, respectively. If all 242 patients followed the protocol, US $42,768 would be saved, and the PVST was estimated to decrease costs by 43.5%.

CONCLUSIONS:
The PVST is a reliable and cost-effective perioperative screening tool that enables thyroid surgeons to detect patients with voice problems in their routine outpatient clinic for early and appropriate referral to voice specialists.

PMID: 23829579 http://dx.doi.org/10.1089/thy.2013.0262

4. Am J Surg. 2013 Nov;206(5):783-9. doi: 10.1016/j.amjsurg.2013.01.038. Epub 2013 Jul 5. **IF:2.39**

Intact parathyroid hormone measurement at 24 hours after thyroid surgery as predictor of parathyroid function at long term.

Julián MT, Balibrea JM, Granada ML, Moreno P, Alastrué A, Puig-Domingo M, Lucas A.
Author information

Abstract

BACKGROUND:
There is no consensus about the usefulness of postoperative intact parathyroid hormone (iPTH) determination to predict permanent hypoparathyroidism (pHPP). We evaluated the value of calcium (Ca2+) and iPTH concentration at 24 hours after total thyroidectomy (TT) for predicting pHPP.

METHODS:
Ca2+ and iPTH levels from 70 consecutive patients who underwent TT were measured at 24 hours and 6 months after TT.

RESULTS:
Five patients (7.1%) developed pHPP. An iPTH concentration ≤5.8 pg/mL at 24 hours after TT identified patients at risk for pHPP (sensitivity, 100%; specificity, 81.5%), but it was not accurate enough to predict its development (positive predictive value, 30%). Conversely, an iPTH level >5.8 pg/mL predicted normal parathyroid function at 6 months (negative predictive value, 100%). Compared with iPTH, a postoperative Ca2+ level ≤1.95 mmol/L was 60% sensitive and 78.5% specific to predict pHPP.

CONCLUSIONS:
An iPTH concentration >5.8 pg/mL on the first postoperative day rules out pHPP with much better diagnostic accuracy than Ca2+. Postoperative iPTH could be helpful in identifying patients at risk for developing pHPP.

KEYWORDS:

Permanent hypoparathyroidism, Postoperative hypocalcemia, Total thyroidectomy

PMID: 23835208 http://dx.doi.org/10.1016/j.amjsurg.2013.01.038

5. Clin Radiol. 2013 Dec;68(12):1241-6. doi: 10.1016/j.crad.2013.06.023. Epub 2013 Aug 20. **IF:2.15**

Ultrasonographic elastography of thyroid nodules: is adding strain ratio to colour mapping better?

Chong Y, Shin JH, Ko ES, Han BK.
Author information

Abstract

AIM:
To determine the diagnostic performance of colour mapping and strain ratio for characterizing malignant thyroid nodules on ultrasonographic (US) elastography.

MATERIALS AND METHODS:
The study was approved by the institutional review board and written informed consent was obtained. One hundred and thirty-one patients with 142 thyroid nodules >0.5 cm were prospectively enrolled between July 2010 and January 2011. Seven radiologists performed US elastography (iU22 Vision 2010; Philips, Seattle, WA, USA) using colour mapping and strain ratio for thyroid nodules blinded to the cytopathological results. Diagnostic performances of colour mapping alone, strain ratio alone, colour mapping and strain ratio, and colour mapping or strain ratio were compared using receiver operating characteristic (ROC) curve analysis.

RESULTS:
Of the 142 nodules, 69 (48.6%) were benign and 73 (51.4%) were malignant. Colour mapping of elastography showed a more frequent blue colour in malignant nodules than in benign nodules (65.8% versus 24.6%, $p < 0.0001$). A higher ratio than 1.21 as the best cut-off value was found in 65.8% of malignant nodules and 46.4% of benign nodules ($p = 0.030$). Area under the ROC curve (AUC) of colour mapping alone was significantly greater than that of colour mapping or strain ratio (AUC = 0.706 versus AUC = 0.63, $p = 0.0195$) and similar to that of colour mapping and strain ratio (AUC = 0.673, $p = 0.1364$).

CONCLUSION:
US elastography is helpful to predict malignant thyroid nodules. However, adding strain ratio to colour mapping does not improve performance compared to colour mapping alone.

PMID: 23969150 http://dx.doi.org/10.1016/j.crad.2013.06.023

6. BMC Surg. 2013 Oct 8;13 Suppl 2:S41. doi: 10.1186/1471-2482-13-S2-S41. Epub 2013 Oct 8. **IF:2.06**

Cytological diagnosis of thyroid nodules in Hashimoto thyroiditis in elderly patients.

Caleo A, Vigliar E, Vitale M, Crescenzo V, Cinelli M, Carlomagno C, Garzi A, Zeppa P.

Abstract

BACKGROUND:

Long standing Hashimoto Thyroiditis (HT) causes shrinking and atrophy of the thyroid, but may also lead to diffuse enlargement of the gland and/or formation of nodules. These nodules should be differentiated from papillary thyroid carcinoma (PTC) and primary thyroidal non-Hodgkin lymphoma (PTL), which are possible complications of HT, and require pre-surgical diagnoses and different treatments.

METHODS:

Thirty-four elderly patients (≥ 65 yrs) with HT and diffuse or nodular enlargement of the thyroid underwent ultrasound (US)-guided FNC. Smears were routinely stained and evaluated; additional passes were used for flow cytometry (FC) assessment of lymphoid infiltrate in 6 cases.

RESULTS:

The cytological diagnosis was HT in 12 cases with prevalence of Hurtle cells in 2 cases, PTC in 1 case and PTL in 2 cases. FC assessed the reactive, non-lymphomatous nature of the lymphoid infiltrate in 5 cases and demonstrated light chain restriction, hence the lymphomatous nature of the lymphoid infiltrate in 2 cases of PTL.

CONCLUSIONS:

FNC plays a key role in the clinical surveillance and pre-surgical diagnosis of diffuse enlargement and nodular presentation of HT in elderly patients. FNC can correctly diagnose HT, PTC and PTL indicating the need for surgery and its extension in suspicious or neoplastic cases, leaving other cases to the medical treatment and clinical surveillance.

PMID: 24266923 http://dx.doi.org/10.1186/1471-2482-13-S2-S41

7. Endocr Pathol. 2013 Nov 22. [Epub ahead of print] **IF:1.77**

"The Diagnostic Accuracy of Thyroid Nodule Fine-Needle Aspiration Cytology Following Thyroid Surgery: a Case-Control Study"

Onal ED, Saglam F, Sacikara M, Ersoy R, Guler G, Cakir B.
Author information

Abstract

Thyroid surgery may cause regional scarring and some degree of fibrotic process which may extend into the perithyroidal soft tissues. This may result in problems when collecting thyroid fine-needle aspiration biopsy (FNAB) samples and evaluating the cellular abnormalities. This study aimed to determine if a history of thyroid surgery is a risk factor for nondiagnostic (ND) FNAB results. Patients with ≥1 discrete nodular lesion of the thyroidwho underwent FNAB were included. The patients with a history of thyroid surgery constituted group 1, and the others constituted group 2. The factors which may influence FNAB results, including age, gender, presence of Hashimoto's thyroiditis, and ultrasound characteristics, were also evaluated. Group 1 included 123 patients with 200 nodules, and group 2 included 132 patients with 200 nodules. The two groups were similar with respect to demographic characteristics of the patients and ultrasonographic features of the nodules including diameter, content (cystic or solid), echogenicity, margin, and calcifications ($P > 0.05$). In all, 176 (44 %) of the participants had ND FNAB results. The median time interval betweenthyroid surgery and FNAB was 15 years [range, 1-45 years; interquartile range (IQR) 13 years]. Significantly more nodules in group 1 had ND FNAB results than in group 2 [98 (49 %) vs 78

(39 %), respectively, P = 0.028]. Multivariate analysis revealed that history of thyroid surgery was independently associated with ND FNAB [odds ratio (OR) 1.55, 95 % confidence interval (CI) 1-2.33, P = 0.033]. A history of thyroid surgery increases the risk of initial ND FNAB.

PMID: 24264435

8. Laryngoscope. 2013 Oct 1. doi: 10.1002/lary.24446. [Epub ahead of print] **IF:1.32**

Superior laryngeal nerve quantitative intraoperative monitoring is possible in all thyroid surgeries.

Darr EA, Tufano RP, Ozdemir S, Kamani D, Hurwitz S, Randolph G.
Author information

Abstract

Short Running Title: SLN Intraoperative monitoring parameters Objective: To report and compare normative external branch of the superior laryngeal nerve EMG data to analogous recurrent laryngeal nerve and vagus nerve data using standard monopolar and a novel bipolar stimulator probe. Study Design: Prospective multiple tertiary center study Method: A prospective study of quantitative analysis of normative EMG data of external branch of the superior laryngeal nerve, Recurrent Laryngeal Nerve and Vagus Nerves using a standard monopolar and a novel bipolar stimulator probe along with cricothyroid muscle twitch response during external branch of the superior laryngeal nerve stimulation using a novel endotracheal tube during thyroidsurgery were analyzed. Preoperative and postoperative laryngeal exams were normal in all cases. Results: In 100% of cases, external branch of the superior laryngeal nerve was identified as well as quantifiable EMG response was observed. EMG amplitude did not change despite extensive nerve dissection and multiple nerve stimulations. External branch of the superior laryngeal nerve amplitude was similar for left and right sides, for patients under age 50 and aged 50 or older, for both genders and with monopolar and bipolar stimulators. Conclusions: Intraoperative neural monitoring may be used to safely assist in external branch of the superior laryngeal nerve identification during thyroid surgery in 100% of patients. This new endotracheal tube allows for quantifiable external branch of the superior laryngeal nerve EMG activity in 100% of cases. Monopolar and bipolar stimulator probes produce similar EMG data.

KEYWORDS:

External branch of superior laryngeal nerve identification (EBSLN), Intraoperative nerve monitoring (IONM), Recurrent laryngeal nerve, electrophysiologic parameters

PMID: 24115215 http://dx.doi.org/10.1002/lary.24446

9. Updates Surg. 2013 Dec;65(4):301-7. doi: 10.1007/s13304-013-0231-2. Epub 2013 Aug 29.

IF:1.13

Sutureless thyroidectomy with energy-based devices: Cerrahpasa experience.

Teksoz S, Bukey Y, Ozcan M, Arikan AE, Ozyegin A.
Author information

Abstract

Total thyroidectomy makes up the majority of all thyroidectomy cases. Energy-based advanced vessel-sealing devices which were developed in recent years for the control of vascular pedicles allowed significant progress in thyroid surgery. This study is designed to compare the efficiency and safety of the

two energy-based vessel-sealing devices (Ligasure™ LF1212 and Harmonic FOCUS(®)) in sutureless thyroidectomy. Two hundred and forty-five consecutive patients underwent sutureless total thyroidectomy. Patients were randomized for the Ligasure™ LF1212 (n = 126) or Harmonic FOCUS(®) (n = 119). The parameters of demographics, surgical indications, morbidity, incision length, duration of operation, weight of specimen, amount of drainage, postoperative pain, hospital stay, and histopathology of specimen were recorded. Mean duration of operation was 37.98 ± 14.98 min (16-92 min) and was significantly shorter for Harmonic FOCUS(®) ($p < 0.001$). Mean hospital stay was 1.09 ± 0.3 (1-3) days. Morbidity rate was 9.8 % in total, whereas no mortality was observed. In terms of morbidity rates, no significant difference was determined between the two groups ($p = 0.476$). In both groups, there was no need for extra analgesic application other than the routine given after surgery. According to our experience, sutureless thyroidectomy can be performed with low morbidity rates in secure and efficient way.

PMID: 23990508 http://dx.doi.org/10.1007/s13304-013-0231-2

TİROİD

RETROSPEKTİF

1. JAMA Intern Med. 2013 Oct 28;173(19):1788-96. doi: 10.1001/jamainternmed.2013.9245. **IF:13.51**

Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study.

Smith-Bindman R, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, Jin C, Kornak J.
Author information

Abstract

IMPORTANCE:
There is wide variation in the management of thyroid nodules identified on ultrasound imaging.

OBJECTIVE:
To quantify the risk of thyroid cancer associated with thyroid nodules based on ultrasound imaging characteristics.

METHODS:
Retrospective case-control study of patients who underwent thyroid ultrasound imaging from January 1, 2000, through March 30, 2005. Thyroid cancers were identified through linkage with the California Cancer Registry.

RESULTS:
A total of 8806 patients underwent 11,618 thyroid ultrasound examinations during the study period, including 105 subsequently diagnosed as having thyroid cancer. Thyroid nodules were common in patients diagnosed as having cancer (96.9%) and patients not diagnosed as having thyroid cancer (56.4%). Three ultrasound nodule characteristics--microcalcifications (odds ratio [OR], 8.1; 95% CI, 3.8-17.3), size greater than 2 cm (OR, 3.6; 95% CI, 1.7-7.6), and an entirely solid composition (OR, 4.0; 95% CI, 1.7-9.2)--were the only findings associated with the risk of thyroid cancer. If 1 characteristic is used as an indication for biopsy, most cases of thyroid cancer would be detected (sensitivity, 0.88; 95% CI, 0.80-0.94), with a high false-positive rate (0.44; 95% CI, 0.43-0.45) and a low positive likelihood ratio (2.0; 95% CI, 1.8-2.2), and 56 biopsies will be performed per cancer diagnosed. If 2 characteristics were required for biopsy, the sensitivity and false-positive rates would be lower (sensitivity, 0.52; 95% CI, 0.42-0.62; false-positive rate, 0.07; 95% CI, 0.07-0.08), the positive likelihood ratio would be higher (7.1; 95% CI, 6.2-8.2), and only 16 biopsies will be performed per cancer diagnosed. Compared with performing biopsy of all thyroid nodules larger than 5 mm, adoption of this more stringent rule requiring 2 abnormal nodule characteristics to prompt biopsy would reduce unnecessary biopsies by 90% while maintaining a low risk of cancer (5 per 1000 patients for whom biopsy is deferred).

CONCLUSIONS AND RELEVANCE:
Thyroid ultrasound imaging could be used to identify patients who have a low risk of cancer for whom biopsy could be deferred. On the basis of these results, these findings should be validated in a large prospective cohort.

Comment in

- The importance, and important limitations, of ultrasound imaging for evaluating thyroid nodules. [JAMA Intern Med. 2013]

PMID: 23978950 http://dx.doi.org/10.1001/jamainternmed.2013.9245

2. J Clin Endocrinol Metab. 2013 Dec;98(12):4768-75. doi: 10.1210/jc.2013-2318. Epub 2013 Oct 23.

IF:7.02

Prognostic nomograms to predict oncological outcome of thyroid cancers.

Pathak KA, Mazurat A, Lambert P, Klonisch T, Nason RW.
Author information

Abstract

Context: Thyroid cancers represent a conglomerate of diverse histological types with equally variable prognosis. There is no reliable prognostic model to predict the risks of relapse and death for different types of thyroid cancers. Objective: The purpose of this study was to build prognostic nomograms to predict individualized risks of relapse and death of thyroid cancer within 10 years of diagnosis based on patients' prognostic factors. Design: Competing risk subhazard models were used to develop prognostic nomograms based on the information on individual patients in a population-basedthyroid cancer cohort followed up for a median period of 126 months. Analyses were conducted using R version 2.13.2. The R packages cmprsk10, Design, and QHScrnomo were used for modeling, developing, and validating the nomograms for prediction of patients' individualized risks of relapse and death of thyroid cancer. Setting: This study was performed at CancerCare Manitoba, the sole comprehensive cancer center for a population of 1.2 million. Patients: Participants were a population-based cohort of 2306 consecutive thyroid cancers observed in 2296 patients in the province of Manitoba, Canada, during 1970 to 2010. Main Outcome Measures: Outcomes were discrimination (concordance index) and calibration curves of nomograms. Results: Our cohort of 570 men and 1726 women included 2155 (93.4%) differentiated thyroid cancers. On multivariable analysis, patient's age, sex, tumor histology, T, N, and M stages, and clinically or radiologically detectable posttreatment gross residual disease were independent determinants of risk of relapse and/or death. The individualized 10-year risks of relapse and death of thyroid cancer in the nomogram were predicted by the total of the weighted scores of these determinants. The concordance indices for prediction of thyroid cancer-related deaths and relapses were 0.92 and 0.76, respectively. The calibration curves were very close to the diagonals. Conclusions: We have successfully developed prognostic nomograms for thyroid cancer with excellent discrimination (concordance indices) and calibration.

PMID: 24152685 http://dx.doi.org/10.1210/jc.2013-2318

3. J Clin Endocrinol Metab. 2013 Nov;98(11):4291-9. doi: 10.1210/jc.2013-1804. Epub 2013 Sep 5.

IF:7.02

Potential utility of rituximab for Graves' orbitopathy.

Salvi M, Vannucchi G, Beck-Peccoz P.
Author information

Abstract

CONTEXT:

B-Cell contribution to autoimmunity has been emphasized since the use of B-cell depleting therapies. B cells produce autoantibodies but also activate CD4+ T cells and inflammation and are important antigen-presenting cells. Several cell surface markers are targets on which B cell-depleting agents can act directly.

EVIDENCE ACQUISITION:

Targeting of CD20+ cells removes B lymphocytes in all intermediate stages of B-cell maturation, activated memory B, and short-lived plasma cells by depleting their immediate precursors. Rituximab (RTX) has been used off-label in various autoimmune disorders but is approved for clinical use only in non-Hodgkin's lymphoma and rheumatoid arthritis. The rationale of RTX use in Graves' disease is that blockade of pathogenic autoantibody generation might bring about Graves' hyperthyroidism remission.

EVIDENCE SYNTHESIS:

To date, RTX has been used in 43 patients with active Graves' orbitopathy (GO). Disease has become inactive in as many as 39 (91%), has not changed in three, and worsened in one patient. In most patients, proptosis and eye motility have been shown to improve. Side effects have been reported in about one-third of patients, usually infusion-related reactions. Because RTX does not seem to modify circulating TSH receptor antibodies, its effect may result from the blockade of antigen presentation by B cells after anti-CD20-induced lysis.

CONCLUSIONS:
Although evidence from controlled trials is needed before proposing RTX as a novel therapeutic tool in this disease, collected data suggest that RTX does significantly affect the activity and severity of GO. Controlled studies will also help decide whether RTX is to be used in any patients with active GO or only in those with otherwise unresponsive disease of a severe degree. The data reported on RTX therapy in GO suggest that B-cell depletion may be pursued shortly after diagnosis, and not only as a therapeutic option when standard immunosuppression has failed.

PMID: 24009135 http://dx.doi.org/10.1210/jc.2013-1804

4. J Clin Endocrinol Metab. 2013 Nov;98(11):E1852-60. doi: 10.1210/jc.2013-2292. Epub 2013 Aug 26. **IF:7.02**

Targeted next-generation sequencing panel (ThyroSeq) for detection of mutations in thyroid cancer.

Nikiforova MN, Wald AI, Roy S, Durso MB, Nikiforov YE.
Author information

Abstract

OBJECTIVES:
Next-generation sequencing (NGS) allows for high-throughput sequencing analysis of large regions of the human genome. We explored the use of targeted NGS for simultaneous testing for multiple mutations in thyroid cancer.

DESIGN:
A custom panel (ThyroSeq) was designed to target 12 cancer genes with 284 mutational hot spots. Sequencing was performed to analyze DNA from 228 thyroid neoplastic and nonneoplastic samples including 105 frozen, 72 formalin-fixed, and 51 fine-needle aspiration samples representing all major types of thyroid cancer.

RESULTS:
Only 5-10 ng of input DNA was sufficient for successful analysis of 99.6% of samples. The analytical accuracy for mutation detection was 100% with the sensitivity of 3%-5% of mutant allele. ThyroSeq DNA assay identified mutations in 19 of 27 of classic papillary thyroid carcinomas (PTCs) (70%), 25 of 30 follicular variant PTCs (83%), 14 of 18 conventional (78%) and 7 of 18 oncocytic follicular carcinomas (39%), 3 of 10 poorly differentiated carcinomas (30%), 20 of 27 anaplastic (ATCs) (74%), and 11 of 15 medullary thyroid carcinomas (73%). In contrast, 5 of 83 benign nodules (6%) were positive for mutations. Most tumors had a single mutation, whereas several ATCs and PTCs demonstrated two or three mutations. The most common mutations detected were BRAF and RAS followed by PIK3CA, TP53, TSHR, PTEN, GNAS, CTNNB1, and RET. The BRAF mutant allele frequency was 18%-48% in PTCs and was lower in ATCs.

CONCLUSIONS:
The ThyroSeq NGS panel allows simultaneous testing for multiple mutations with high accuracy and sensitivity, requires a small amount of DNA and can be performed in a variety of thyroid tissue and fine-needle aspiration samples, and provides quantitative assessment of mutant alleles. Using this approach, the point mutations were detected in 30%-83% of specific types of thyroid cancer and in only 6% of benign thyroid nodules and were shown to be present in the majority of cells within the cancer nodule.

Comment in

- Cancer: Next-generation sequencing for detecting thyroid cancer. [Nat Rev Endocrinol. 2013]

PMID: 23979959 http://dx.doi.org/10.1210/jc.2013-2292

5. J Clin Endocrinol Metab. 2013 Nov 25. [Epub ahead of print] **IF:7.02**

Determination of the Optimal Time Interval for Repeat Evaluation following a Benign Thyroid Nodule Aspiration.

Nou E, Kwong N, Alexander LK, Cibas ES, Marqusee E, Alexander EK.
Author information

Abstract

Introduction:The optimal timing for repeat evaluation of a cytologically benign thyroid nodule >1cm is uncertain. Arguably, the most important determinant is the disease-specific mortality resulting from an undetected thyroid cancer. Presently, there exists no data which evaluate this important endpoint.Methods:We studied the long-term status of all patients evaluated in our thyroid nodule clinic between 1995-2003 with initially benign FNA cytology. The follow up interval was defined from time of initial benign FNA to any one of the following: thyroidectomy, death, or the most recent clinic visit documented anywhere in our healthcare system. We sought to determine the optimal timing for repeat assessment based upon identification of falsely benign malignancy, and most important, disease related mortality due to a missed diagnosis.Results:1,369 patients with 2,010 cytologically benign nodules were followed for an average of 8.5yrs (range 0.25-18yrs). 30 deaths were documented, though zero attributed to thyroidcancer. 18 false negative thyroid malignancies were identified, and removed at a mean 4.5yrs (range 0.3-10 years) after initial benign aspiration. None had distant metastasis, and all are alive presently at an average of 11yrs following initial falsely benign FNA. Separate analysis demonstrates that patients with initially benign nodules who subsequently sought thyroidectomy for compressive symptoms did so an average of 4.5yrs later.Conclusions:An initially benign FNA confers negligable mortality risk during long-term follow up despite a low risk of identifying several such nodules as thyroid cancer. As such malignancies appear adequately treated despite detection at a mean 4.5yrs following falsely benign cytology, these data support a recommendation for repeat thyroid nodule evaluation 2-4yrs after initial benign FNA.

PMID: 24276452

6. J Clin Endocrinol Metab. 2013 Nov 25. [Epub ahead of print] **IF:7.02**

The Effect of Extent of Surgery and Number of Lymph Node Metastases on Overall Survival in Patients with Medullary Thyroid Cancer.

Esfandiari NH, Hughes DT, Yin H, Banerjee M, Haymart MR.
Author information

Abstract

Context:Total thyroidectomy with central lymph node dissection is recommended in patients with medullary thyroid cancer (MTC). However, the relationship between disease severity and extent of resection on overall survival remains unknown.Objective:To identify the effect of surgery on overall survival in MTC patients.Methods:Using data from 2,968 patients with MTC diagnosed between 1998-2005 from the National Cancer Database, we determined the relationship between number of cervical lymph nodes metastases, tumor size, distant metastases and extent of surgery on overall survival in patients with MTC.Results:Older patient age [5.69 (3.34-9.72)], larger tumor size [2.89 (2.14-3.90)], presence of distant

metastases [5.68 (4.61-6.99)], and number of positive regional lymph nodes [for ≥ 16 lymph nodes, 3.40 (2.41-4.79)] were independently associated with decreased survival. Overall survival for patients with cervical lymph nodes resected and negative, cervical lymph nodes not resected, 1-5, 6-10, 11-16 and ≥ 16 cervical lymph nodes metastases was 90%, 76%, 74%, 61%, 69% and 55% respectively. There was no difference in survival based on surgical intervention in patients with tumor size ≤ 2 cm without distant metastases. In patients with tumor size > 2.0 cm and no distant metastases, all surgical treatments resulted in a significant improvement in survival compared to no surgery (P< 0.001). In patients with distant metastases, only total thyroidectomy with regional lymph node resection resulted in a significant improvement in survival (P<0.001).Conclusions:The number of lymph node metastases should be incorporated into MTC staging. Extent of surgery in patients with MTC should be tailored to tumor size and distant metastases.

PMID: 24276457

7. J Clin Endocrinol Metab. 2013 Oct;98(10):3981-8. doi: 10.1210/jc.2013-1357. Epub 2013 Jul 24.

IF:7.02

Is thyroid cancer recurrence risk increased after transplantation?

Tisset H, Kamar N, Faugeron I, Roy P, Pouteil-Noble C, Klein M, Mourad G, Drui D, Do Cao C, Leenhardt L, Allix I, Bonichon F, Morelon E, Leboulleux S, Kelly A,Niccoli P, Toubert ME, Frimat L, Vantyghem MC, Bournaud C, Schlumberger M, Borson-Chazot F; TUTHYREF network.

Author information

Abstract

CONTEXT:
An increased cancer mortality is reported in transplanted patients.

OBJECTIVE:
This multicentric study aimed to investigate the rate of thyroid cancer recurrence after transplantation.

RESULTS:
Sixty-eight patients (35 male/33 female) with a history of both thyroid cancer and organ transplantation were recruited via two nationwide French networks. Histological analysis identified 58 papillary (88%), 5 follicular (7.5%), and 3 poorly differentiated cancer cases (4.5 %). Thirty-one patients (52%) presented high recurrence risk tumors. In the 36 patients with thyroid cancer diagnosed after transplantation, the 5-year disease-free survival (DFS) was 74.7% (SE: 7.3%). One patient died after progression of a poorly differentiated cancer. Persistent disease was observed in six high-risk patients. One of them underwent a second transplantation and disease remained stable after 5 years of follow-up. Thyroid cancer had been diagnosed before transplantation in 32 patients. One patient with cystic fibrosis and thyroid lung metastases at the time of lung transplantation underwent a 4-year remission. For the 31 patients in remission at the time of transplantation, the 5-year DFS was 93.1% (SE: 4.8%). Two patients with local recurrence presented subsequent remission. For the entire study population, the 5-year and 9-year DFS were 81.9% (SE: 5.5%) and 75.6% (SE: 7.9%), respectively. Recurrence or persistent disease occurred in patients with high-risk tumors.

CONCLUSIONS:
The prognosis of thyroid cancer does not seem to be altered by transplantation. This suggests that a history of thyroid cancer should not be considered a contraindication.

PMID: 23884779 http://dx.doi.org/10.1210/jc.2013-1357

8. Am J Surg Pathol. 2013 Oct;37(10):1586-91. doi: 10.1097/PAS.0b013e318292b780.v **IF:5.53**

Molecular and histopathologic characteristics of multifocal papillary thyroid carcinoma.

Bansal M, Gandhi M, Ferris RL, Nikiforova MN, Yip L, Carty SE, Nikiforov YE.
Author information

Abstract

Papillary thyroid carcinoma (PTC) is frequently multifocal, which can represent either intraglandular spread from a single primary tumor or multiple synchronous primary tumors (MSPTs). To distinguish and characterize these entities, we investigated whether multifocal PTCs contain genetically similar or different mutations and have particular histopathologic characteristics. In 60 cases of PTC with 2 to 4 discrete tumor foci, each focus was tested for BRAF, NRAS, HRAS, and KRAS point mutations and RET/PTC1 and RET/PTC3 rearrangements and analyzed for various histopathologic features. Overall, BRAF mutations were found in 43% of tumors, RAS in 27%, and RET/PTC in 2%. Four different patterns of mutation occurrence were identified: (i) 2 foci containing different mutations (30%); (ii) 1 tumor containing a mutation and another carrying no mutations (32%); (iii) both/all tumors containing the same mutation (25%); (iv) all tumors having no mutations (13%). The 30% of cases with 2 different mutations represent a group of tumors that are unequivocally MSPT. These tumors more commonly occurred in different lobes, although they could be located as close as 0.6 cm from each other. Moreover, MSPTs typically demonstrated distinct histologic variants/microscopic features, were encapsulated or had a smooth border, and showed no microscopic peritumoral dissemination. In conclusion, we demonstrate that at least 30% of multifocal PTCs represent unequivocal MSPTs that develop through distinct molecular alterations and that as many as 60% of multifocal PTCs are likely MSPTs. Histopathologically, MSPTs are typically located in different lobes, have distinct growth patterns, and do not show microscopic peritumoral dissemination.

PMID: 23797723 http://dx.doi.org/10.1097/PAS.0b013e318292b780.v

9. Ann Surg Oncol. 2013 Dec 24. [Epub ahead of print] **IF:4.33**

Oncologic Outcomes After Completion Thyroidectomy for Patients with Well-Differentiated Thyroid Carcinoma.

Untch BR, Palmer FL, Ganly I, Patel SG, Michael Tuttle R, Shah JP, Shaha AA.
Author information

Abstract

BACKGROUND:

At our institution, thyroid lobectomy is employed as a definitive operation for unifocal intrathyroidal low risk cancers and thus completion thyroidectomy is rarely performed. The purpose of this study was to identify the indications for selective completion thyroidectomy and to report oncologic outcomes.

METHODS:

A retrospective review was performed to identify patients who underwent planned completion thyroidectomy for well-differentiated thyroidcarcinoma (WDTC) from 2001 to 2010 based on initial lobectomy pathology. Assessment for risk of recurrence was based on the American ThyroidAssociation Initial Risk Stratification.

RESULTS:

During the 10-year study period, 79 patients underwent completion thyroidectomy for WDTC. Forty-four (56 %) patients were low risk and 35 (44 %) were intermediate risk. Completion thyroidectomy was recommended for 64 patients, whereas 15 patients were given an option of surveillance but ultimately decided to have surgery. Patients in the "recommended group" had more T3 tumors and fewer T1a tumors ($p = 0.005$ and 0.006, respectively). These patients also were more likely to be intermediate risk ($p = 0.008$) and to present with aggressive histology ($p = 0.002$). The rate of contralateral tumors ($n = 27$) was similar

between both groups (35 and 33 %, respectively). Contralateral cancers were micropapillary in 24 of 27 (89 %) patients, 10 (40 %) of whom had multifocal disease. There were two pulmonary recurrences and no local-regional recurrences (median follow-up of 42.3 months).

CONCLUSIONS:
Completion thyroidectomy is infrequent and performed for a select group of intermediate and low risk WDTCs at our institution with low recurrence rates. Incidental multifocal and unifocal contralateral cancers are common after completion thyroidectomy.

PMID: 24366419

10. Ann Surg Oncol. 2013 Oct 1. [Epub ahead of print] **IF:4.33**

The Role of Thyroidectomy in Metastatic Disease to the Thyroid Gland.

Romero Arenas MA, Ryu H, Lee S, Morris LF, Grubbs EG, Lee JE, Perrier ND.
Author information

Abstract

BACKGROUND:
Whether thyroidectomy for metastases to the thyroid is associated with a survival benefit remains debatable; in general, palliation and disease control are accepted goals in this setting. We evaluated the clinical features and overall survival of patients with thyroid metastasis treated by thyroid resection or nonoperatively.

METHODS:
This retrospective analysis included 90 patients identified with metastasis to the thyroid confirmed pathologically via thyroidectomy (n = 31) or fine-needle aspiration biopsy (n = 59). Overall survival was calculated by the Kaplan-Meier method, and differences between groups were calculated by Pearson's χ^2 coefficient.

RESULTS:
The most common primary malignancies were renal cell (20 %), head and neck (19 %), and lung (18 %). The median time from primary tumor diagnosis to thyroid metastasis diagnosis was 37.4 months (range 0-210 months). Most metastases (69 %) were metachronous, and 12 % were isolated. The median follow-up after diagnosis of thyroid metastasis was 11.5 months (range 0-112 months). Median overall survival was longer in thyroidectomy patients compared to the fine-needle aspiration group (34 vs. 11 months, $P < 0.0001$). Patients with renal cell primary tumors were more likely to undergo thyroidectomy than patients with other primary tumors (78 vs. 24 %, $P < 0.0001$). Nearly all patients with lung primary tumors died within 24 months of thyroid metastasis diagnosis, and thyroidectomy was only offered to three patients.

CONCLUSIONS:
Thyroidectomy was safe for selected patients with metastatic disease to the thyroid. Patients with metachronous or renal cell metastasis to the thyroid and whose primary tumor is/was treatable may be appropriate candidates for resection. Lung cancer metastasis to thethyroid is generally an ominous sign.

PMID: 24081800

11. Ann Surg Oncol. 2013 Dec 31. [Epub ahead of print] **IF:4.33**

Radioactive Iodine Remnant Uptake After Completion Thyroidectomy: Not Such a Complete Cancer Operation.

Oltmann SC, Schneider DF, Leverson G, Sivashanmugam T, Chen H, Sippel RS.
Author information

Abstract

BACKGROUND:
Given limitations in preoperative diagnostics, thyroid lobectomy followed by completion thyroidectomy (CT) for differentiated thyroidcancer (DTC) may be required. It is unclear whether resection quality by CT differs from that by total thyroidectomy (TT). Additional surgeon or patient factors may also influence the "completeness" of resection. This study evaluated how CT and surgeon volume influence the adequacy of resection as measured by radioactive iodine (RAI) remnant uptake.

METHODS:
A retrospective review of a prospectively collected thyroid database was queried for patients treated for DTC with TT or CT followed by RAI ablation. CT patients were matched 1:2 by age, sex, and tumor size to TT patients. Surgeon volume, time to completion, and continuity of surgeon care were reviewed.

RESULTS:
Over 18 years, 45 patients with DTC had CT and RAI. Mean age was 48 ± 2 years, and 76 % were female, with a tumor size of 2.7 ± 0.3 cm. CT had higher remnant uptake than TT (0.07 vs. 0.04 %; p = 0.04). CT performed by a high-volume surgeon had much lower remnant uptakes (0.06 vs. 0.22 %; p = 0.04). Remnant uptake followed a stepwise decrease with involvement of a high-volume surgeon for part or all of the surgical management (p = 0.11). Multiple regression analysis found CT (p = 0.02) and surgeon volume (p = 0.04) to significantly influence uptake after controlling for other factors.

CONCLUSIONS:
Single-stage TT provides a better resection based on smaller thyroid remnant uptakes than CT for patients with thyroid cancer. If a staged operation for cancer is necessary, surgeon volume may affect the completeness of resection.

PMID: 24378987

12. Cancer Cytopathol. 2013 Nov 7. doi: 10.1002/cncy.21367. [Epub ahead of print] **IF:4.01**

Influence of descriptive terminology on management of atypical thyroid fine-needle aspirates.

Vivero M, Renshaw AA, Krane JF.
Author information

Abstract

BACKGROUND:
The Bethesda System category of atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) is used to classify a variety of mild abnormalities in thyroid FNAs. Modifying terminology is often added to FNA reports, but it is unknown whether specific phrases affect clinical management. To answer this question, the authors correlated treatment of patients who had initial AUS/FLUS diagnoses from Baptist Hospital (Miami, Fla) (BH) and Brigham and Women's Hospital (Boston, Mass) (BWH) with the language used in pathology reports.

METHODS:
In total, 146 FNAs from BH, including 115 women and 31 men with a median age of 53 years (range, 21-79 years), and 300 FNAs from BWH, including 241 women and 59 men with a median age of 66 years (range, 10-85 years), were included. FNA reports were evaluated for predetermined descriptive phrases and were correlated with subsequent management.

RESULTS:

More patients with available follow-up underwent excision at BH than at BWH (86% vs 8%; P < .001), and fewer underwent a repeat biopsy (14% vs 92%; P < .001). Qualifiers associated with differing malignancy risk affected patient management (P < .05) at BH, but not at BWH. Reports indicating a scant or limited specimen increased rebiopsy rates at BH (100% vs 4.8%; P < .05), but not at BWH (93% vs 91%; P = .67), as did explicit recommendation for rebiopsy at BH (35% vs 14%; P = .03). No other phrases affected patient management (P > .05).

CONCLUSIONS:
In practice settings that follow The Bethesda System management guidelines, descriptive report terminology does not modify patient treatment. In less standardized settings, terminology associated with differing risk of malignancy on subsequent excision, pathologist recommendations, and phrases indicative of limited sampling significantly alter patient management. Cancer (Cancer Cytopathol) 2013;. © 2013 American Cancer Society.

KEYWORDS:

Bethesda, atypical, fine-needle aspiration, terminology, thyroid

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13. Thyroid. 2013 Dec 16. [Epub ahead of print] **IF:3.84**

Malignancy rate in thyroid nodules classified as Bethesda Category III (AUS/FLUS).

Ho AS, Sarti EE, Jain KS, Wang H, Nixon IJ, Shaha AR Md, Shah JP, Kraus D, Ghossein R Md, Fish S, Wong RJ, Lin O, Morris LG.
Author information

Abstract

Background: The Bethesda System for thyroid cytopathology is the standard for interpreting fine needle aspiration (FNA) specimens. The Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS) category, known as Bethesda Category III, has been ascribed a malignancy risk of 5-15%, but the probability of malignancy in AUS/FLUS specimens remains unclear. Our objective was to determine the risk of malignancy in thyroid FNAs categorized as AUS/FLUS. Methods: The management of 541 AUS/FLUS thyroid nodule patients between 2008-2011 was analyzed. Clinical and radiologic features were examined as predictors for surgery. Target AUS/FLUS nodules were correlated with surgical pathology. Results: Of patients with an FNA initially categorized as AUS/FLUS, 64.7% (350/541) underwent immediate surgery, 17.7% (96/541) had repeat FNA, and 17.6% (95/541) were observed. Repeat FNA cytology was unsatisfactory in 5.2% (5/96), benign in 42.7% (41/96), AUS/FLUS in 38.5% (37/96), suspicious for follicular neoplasm in 5.2% (5/96), suspicious for malignancy in 4.2% (4/96), and malignant in 4.2% (4/96). Of nodules with two consecutive AUS/FLUS diagnoses that were resected, 26.3% (5/19) were malignant. Among all index AUS/FLUS nodules (triaged to surgery, repeat FNA, or observation), malignancy was confirmed on surgical pathology in 26.6% (95% CI, 22.4-31.3). Among AUS/FLUS nodules triaged to surgery, the malignancy rate was 37.8% (95% CI, 33.1-42.8). Incidental cancers were found in 22.3% of patients. On univariate logistic regression analysis, factors associated with triage to surgery were younger patient age (p < 0.0001), increasing nodule size (p < 0.0001), and nodule hypervascularity (p = 0.032). Conclusions: Malignancy rates in nodules with AUS/FLUS cytology are higher than previously estimated, with 26.6-37.8% of AUS/FLUS nodules harboring cancer. These data imply that Bethesda Category III nodules may have a higher risk of malignancy than traditionally believed, and that guidelines recommending repeat FNA or observation merit reconsideration.

PMID: 24341462

14. Thyroid. 2013 Dec 16. [Epub ahead of print] **IF:3.84**

Serum Thyroglobulin Improves the Sensitivity of the McGill Thyroid Nodule Score for Well-Differentiated ThyroidCancer.

Scheffler P, Forest VI, Leboeuf R, Florea AV, Tamilia M, Sands NB, Hier MP, Mlynarek AM, Payne RJ.
Author information

Abstract
Background: The McGill Thyroid Nodule Score (MTNS) is a scoring system elaborated to help physicians to assess the preoperative risk that athyroid nodule is malignant. It uses 22 different known risk factors for thyroid cancer (radiation exposure, microcalcifications on ultrasound, positive HBME-1 stain on biopsy, etc) and attributes a percentage risk that the nodule is malignant. Recently, preoperative thyroglobulin (Tg) levels has been shown to correlate with the risk of malignancy. The aim of this study was to incorporate Tg levels into the already established MTNS. Methods: This is a retrospective analysis of 184 thyroidectomy patients at the McGill University Thyroid Cancer Centre. Patients with preoperative Tg levels were included in the study, and patients with incidental papillary microcarcinoma without extrathyroidal extent on final pathology were excluded. MTNS scores were calculated for all patients. Preoperative Tg levels of 75ng/mL added 1 point to the MTNS, and levels of 187.5ng/mL added 2 points. The new score is named MTNS+. Results: Malignancy rates were calculated for each MTNS+ score. Patients with a score of 0-1 were <5% at risk of malignancy, the malignancy rate for scores from 2-3 was 14.29%, followed by 28.95% for scores from 4-6, 32.65% for scores from 7-8, 64.86% from scores from 9-11, 71.43% for scores from 12-14, 78.57% for scores from 15-18, and 92.31% for scores from 19-22. All patients (5 of 5) with an MTNS+ score of 23 or more had a malignant final pathology result. Patients with scores >8 had a relative risk of 2.5 (95% CI 1.79-3.49) of malignancy compared to patients with lower scores. MTNS+ showed good specificity at higher scores, with 89%, 96%, and 100% at scores above 11, 14, and 20, respectively. Compared to MTNS, adding Tg levels did not improve positive predictive values (PPV) or specificity, but improved sensitivity by 7.89% at scores >8, and by up to 10.48% for scores >7. Conclusion: This study shows that adding Tg to the MTNS, increases the sensitivity of this scoring system. Moreover, it suggests that a combined scoring system such as the MTNS+ can accurately stratify the risk of well-differentiated malignancy in patients with thyroid nodules.

PMID: 24341425

15. Thyroid. 2013 Oct;23(10):1305-11. doi: 10.1089/thy.2012.0563. Epub 2013 Sep 14. **IF:3.84**

Aggressive variants of papillary thyroid microcarcinoma are associated with extrathyroidal spread and lymph-node metastases: a population-level analysis.

Kuo EJ, Goffredo P, Sosa JA, Roman SA.
Author information

Abstract
BACKGROUND:
Tall cell variant (TCV) and diffuse sclerosing variant (DSV) of papillary thyroid cancer are aggressive subtypes, for which tumors ≤1 cm have not been exclusively studied.

METHODS:
The SEER database (1988-2009) was used to compare characteristics of TCV ≤1 cm (mTCV) and DSV ≤1 cm (mDSV) with classic papillary thyroid microcarcinoma (mPTC). Survival was analyzed with the Kaplan-Meier method and log-rank test, and risk factors for nodal metastases with chi-square analysis and binary logistic regression.

RESULTS:
There were 97 mTCV, 90 mDSV, and 18,260 mPTC patients. mTCV incidence increased by 79.9% (p=0.153) over the study period, while mDSV incidence decreased by 10.3% (p=0.315). Compared to classic mPTC, mTCV tended to be larger on average (7.1 mm vs. 5.3 mm, p<0.001), with higher rates of multifocality (47.2% vs. 34.0% respectively, p=0.018) and lymph-node examination (63.9% vs. 39.2% respectively, p<0.001), while in mDSV, nodal metastases were more frequent (57.1% vs. 33.1% respectively, p=0.007). Both aggressive variants had higher rates of extrathyroidal extension (27.8% mTCV vs. 13.3% mDSV vs. 6.1% mPTC, p<0.001). Aggressive variants also received radioactive iodine more frequently (39.2% mTCV vs. 40.0% mDSV vs. 29.1% mPTC, p<0.001). However, they were not statistically more likely to receive thyroidectomy over lobectomy compared to classic mPTC. There were no significant differences in overall and disease-specific survival between the histologies. In mTCV, after adjustment, extrathyroidal extension was independently associated with size >7 mm (odds ratio (OR) 4.4 [CI 1.5-13.6]) and nodal metastasis with multifocality (OR 5.4 [CI 1.3-23.4]) and extrathyroidal extension (OR 5.8 [CI 1.3-25.4]). No statistically significant predictors of extrathyroidal extension or nodal metastasis in mDSV were observed.

CONCLUSIONS:
Aggressive variants of mPTC tend to exhibit more aggressive pathologic characteristics than classic mPTC, but survival appears to be similar. Treatment with total thyroidectomy and central lymphadenectomy may be warranted if the diagnosis can be made pre- or intraoperatively.

PMID: 23600998 http://dx.doi.org/10.1089/thy.2012.0563

16. Thyroid. 2013 Dec 16. [Epub ahead of print] **IF:3.84**

Serum Thyroglobulin Improves the Sensitivity of the McGill Thyroid Nodule Score for Well-Differentiated ThyroidCancer.

Scheffler P, Forest VI, Leboeuf R, Florea AV, Tamilia M, Sands NB, Hier MP, Mlynarek AM, Payne RJ.
Author information

Abstract

Background: The McGill Thyroid Nodule Score (MTNS) is a scoring system elaborated to help physicians to assess the preoperative risk that athyroid nodule is malignant. It uses 22 different known risk factors for thyroid cancer (radiation exposure, microcalcifications on ultrasound, positive HBME-1 stain on biopsy, etc) and attributes a percentage risk that the nodule is malignant. Recently, preoperative thyroglobulin (Tg) levels has been shown to correlate with the risk of malignancy. The aim of this study was to incorporate Tg levels into the already established MTNS. Methods: This is a retrospective analysis of 184 thyroidectomy patients at the McGill University Thyroid Cancer Centre. Patients with preoperative Tg levels were included in the study, and patients with incidental papillary microcarcinoma without extrathyroidal extent on final pathology were excluded. MTNS scores were calculated for all patients. Preoperative Tg levels of 75ng/mL added 1 point to the MTNS, and levels of 187.5ng/mL added 2 points. The new score is named MTNS+. Results: Malignancy rates were calculated for each MTNS+ score. Patients with a score of 0-1 were <5% at risk of malignancy, the malignancy rate for scores from 2-3 was 14.29%, followed by 28.95% for scores from 4-6, 32.65% for scores from 7-8, 64.86% from scores from 9-11, 71.43% for scores from 12-14, 78.57% for scores from 15-18, and 92.31% for scores from 19-22. All patients (5 of 5) with an MTNS+ score of 23 or more had a malignant final pathology result. Patients with scores >8 had a relative risk of 2.5 (95% CI 1.79-3.49) of malignancy compared to patients with lower scores. MTNS+ showed good specificity at higher scores, with 89%, 96%, and 100% at scores above 11, 14, and 20, respectively. Compared to MTNS, adding Tg levels did not improve positive predictive values (PPV) or specificity, but improved sensitivity by 7.89% at scores >8, and by up to 10.48% for scores >7. Conclusion: This study shows that adding Tg to the MTNS, increases the sensitivity of this scoring system. Moreover, it suggests that a

combined scoring system such as the MTNS+ can accurately stratify the risk of well-differentiated malignancy in patients with thyroid nodules.

PMID: 24341425

17. Thyroid. 2013 Oct 1. [Epub ahead of print] **IF:3.84**

A Pre-operative Nomogram for the Prediction of Ipsilateral Central Compartment Lymph Node Metastases in Papillary Thyroid Cancer.

Thompson AM, Turner RM, Hayen A, Aniss A, Jalaty S, Learoyd DL, Sidhu S, Delbridge L, Yeh MW, Clifton-Bligh R, Sywak M.
Author information

Abstract

Background Central compartment lymph node metastases in papillary thyroid carcinoma (PTC) are difficult to detect pre-operatively and the role of routine or prophylactic central compartment lymph node dissection (CLND) in managing PTC remains controversial. The aim of this project was to create a nomogram able to predict the occurrence of central compartment lymph node metastasis using readily available pre-operative clinical characteristics. Methods Records from patients undergoing total thyroidectomy and lymph node dissection for PTC in the period 1968-2012 were analysed. Nodal status was based on results of serial H&E examination. Age, sex, tumor size, tumor site and multifocality were included in a multivariable logistic regression model to predict lymph node metastasis. A coefficient-based nomogram was developed and validated using an external patient cohort. Results The study population included 914 patients (80% females) with an average central compartment nodal yield of 8 per patient. Central compartment lymph node metastases were present in 390 patients (42.7%). The variables with the strongest predictive value were age (p<0.001), male sex (p<0.001), increasing tumor size (p<0.001) and tumor multifocality (p<0.05). The nomogram had good discrimination with a concordance index of 76.4% (95%CI 73.3% to 79.4%), supported by an external validation point estimate of 61.5% (95%CI 49.5% to 73.6%). An online calculator and smartphone application were developed for point of care use. Conclusions A validated nomogram utilizing readily available preoperative variables has been developed to give a predicted probability of central lymph node metastases in patients presenting with PTC. This nomogram may help guide surgical decision making in PTC.

PMID: 24083952

18. Thyroid. 2013 Nov 21. [Epub ahead of print] **IF:3.84**

PROGNOSTIC IMPLICATIONS OF PAPILLARY THYROID CARCINOMA WITH TALL CELL FEATURES.

Ganly I, Ibrahimpasic T, Rivera M, Nixon I, Palmer FL, Patel SG, Tuttle RM Md, Shah JP, Ghossein R Md.
Author information

Abstract

Background: The prognostic implications of the diagnosis of a papillary thyroid carcinoma (PTC) with tall cell features (TCF) are unknown. Methods: All PTC patients identified between 1985 and 2005 were analyzed histologically. Classical PTC (cPTC) were defined as having <30% tall cells, PTC TCF (30-49% tall cells), tall cell variant (TCV) (>50% tall cells). All cPTC, PTC TCF and TCV > 1 cm in size were included. Results: 453 patients satisfied the inclusion criteria (288 cPTC, 31 PTC TCF and 134 TCV). cPTC patients were younger than their PTC TCF and TCV counterparts (p<0.0002). There was an increase in tumor size from cPTC to PTC TCF and TCV (p=0.05). Extensive extra-thyroid extension and positive margins were more often present in TCV and PTC TCF than in cPTC . (p=0.0001, 0.03 respectively).

Overall pathologic tumor (pT) stage was more advanced in TCV and PTC TCF than in cPTC (p<0.0001). Total thyroidectomy and radioactive iodine therapy were more often performed and administered on TCV patients than on their PTC TCF and cPTC counterparts (p=0.001, p=0.0001 respectively). Median follow up was 9.3 years. 10 year disease specific survival (DSS) was lower in TCV (96%) and PTC TCF (91%) than in cPTC (100%) (p<0.001). 10 year distant recurrence free (RFS) survival was higher in cPTC (98%) than in PTC TCF (89%) and TCV (96%) (p=0.03). In multivariate analysis, the presence of >5 positive nodes and extra-nodal extension were the only independent prognostic factors of neck and distant RFS respectively. Four (2.4%) of 165 PTC with TCF and PTC TCV developed poorly differentiated or anaplastic carcinoma in their recurrence while none of 288 classical PTC transformed into higher grades (p=0.017). Conclusions: 1) PTC TCF and TCV have similar clinico-pathologic features that are more aggressive than cPTC 2) PTC TCF and TCV have similar DSS and distant RFS but poorer than cPTC 3) PTC TCF are currently being treated like cPTC less aggressively than TCV 4) PTC TCF and PTC TCV have a higher rate of high grade transformation than cPTC. 5) Consideration should be given to use a 30% tall cells threshold to diagnose TCV.

PMID: 24262069

19. Thyroid. 2013 Nov;23(11):1401-7. doi: 10.1089/thy.2013.0011. Epub 2013 Jul 25. **IF:3.84**

Outcomes of patients with differentiated thyroid cancer risk-stratified according to the American thyroidassociation and Latin American thyroid society risk of recurrence classification systems.

Pitoia F, Bueno F, Urciuoli C, Abelleira E, Cross G, Tuttle RM.
Author information

Abstract

OBJECTIVES:
The aims of this study were to validate the proposed Latin American Thyroid Society (LATS) risk of recurrence stratification system and to compare the findings with those of the American Thyroid Association (ATA) risk of recurrence stratification system.

SUBJECTS AND METHODS:
This study is a retrospective review of papillary thyroid cancer patients treated with total thyroidectomy and radioactive iodine at a single experienced thyroid cancer center and followed according to the LATS management guidelines. Each patient was risk-stratified using both the LATS and ATA staging systems. The primary endpoints were (i) the best response to initial therapy defined as either remission (stimulated thyroglobulin [Tg] <1 ng/mL, negative ultrasonography) or persistent disease (biochemical and/or structural), and (ii) clinical status at final follow-up defined as no evidence of disease (suppressed Tg <1 ng/mL, negative ultrasonography), biochemical persistent disease (suppressed Tg >1 ng/mL in the absence of structural disease), structural persistent disease (locoregional or distant metastases), or recurrence (biochemical or structural disease identified after a period of no evidence of disease).

RESULTS:
One hundred seventy-one papillary thyroid cancer patients were included (mean age 45 ± 16 years, followed for a median of 4 years after initial treatment). Both the ATA and LATS risk stratification systems provided clinically meaningful graded estimates with regard to (i) the likelihood of achieving remission in response to initial therapy, (ii) the likelihood of having persistent structural disease in response to initial therapy and at final follow-up, (iii) the likely locations of the persistent structural disease (locoregional vs. distant metastases), (iv) the likelihood of recurrence, and (v) the likelihood of being no evidence of disease at final follow-up. The likelihood of having persistent biochemical evidence of disease was not significantly different across the staging categories.

CONCLUSIONS:

Both the ATA and LATS risk of recurrence systems effectively risk-stratify patients with regard to multiple important clinical outcomes. When used in conjunction with a staging system that predicts disease-specific mortality, either of these systems can be used to guide risk-adapted individualized initial management recommendations.

PMID: 23517313 http://dx.doi.org/10.1089/thy.2013.0011

20. Thyroid. 2013 Nov;23(11):1408-15. doi: 10.1089/thy.2012.0463. Epub 2013 Jul 17. **IF:3.84**

Long-term outcomes of total thyroidectomy versus thyroid lobectomy for papillary thyroid microcarcinoma: comparative analysis after propensity score matching.

Lee J, Park JH, Lee CR, Chung WY, Park CS.
Author information

Abstract

AIMS:
The objectives of this study were to compare long-term outcomes after total thyroidectomy (TT) or thyroid lobectomy (LT) in a large cohort of patients with papillary thyroid microcarcinoma (PTMC), and to determine whether tumor size (≤0.5 cm vs. >0.5 cm) has a significant impact on the extent of surgery.

METHODS:
We evaluated 2014 patients with PTMC who underwent TT with central compartment node dissection (CCND; n = 1015) or LT with CCND (n = 999) between March 1986 and December 2006 and for whom complete follow-up data were available for at least 5 years (median 11.8 years, range 5-26 years). Using propensity score matching to reduce the impact of treatment selection bias and potential confounding in an observational study, we compared overall survival and disease-free survival in the overall cohort and in patients with tumors ≤0.5 cm and >0.5 cm in size.

RESULTS:
After adjustment for differences in baseline clinicopathologic risk factors, we observed no significant differences between the LT and the TT groups in the risk of death (hazard ratio for the LT group 1.05, 95% confidence interval [CI] 0.71-1.47, p = 0.890) and locoregional recurrence (hazard ratio for the LT group 3.08 [CI 1.99-8.05], p = 0.194) in the overall matched cohort. Similar results were observed when we compared LT and TT in patients with tumors ≤0.5 cm and >0.5 cm.

CONCLUSIONS:
The long-term rates of death and locoregional recurrence were similar in patients with PTMC who underwent LT with CCND and those who underwent TT with CCND. Therefore, completion thyroidectomy may not be recommended unless recurrence after LT is definitely detected in low-risk PTMC patients, and close follow-up is adequate in these patients. Moreover, tumor size greater than or less than 0.5 cm was not a significant determinant of the extent of surgery in patients with PTMC.

PMID: 23509895 http://dx.doi.org/10.1089/thy.2012.0463

21. Thyroid. 2013 Dec 13. [Epub ahead of print] **IF:3.84**

The Role of Survivin in Thyroid Tumors: Differences of Expression in Well-Differentiated, Non-Well-Differentiated, and Anaplastic Thyroid Cancers.

Pannone G, Santoro A, Pasquali D, Zamparese R, Mattoni M, Russo G, Landriscina M, Piscazzi A, Toti P, Cignarelli M, Muzio LL, Bufo P.
Author information

Abstract

Background: Survivin is involved in human cancer and is responsible for aggressive biological behavior and poor clinical outcomes in several human malignancies. Thus, we hypothesized that the upregulation of survivin protein expression may be enhanced in parallel with transition toward a poorly differentiated phenotype in human thyroid carcinomas. Methods: The expression of survivin was evaluated, using a standard linked streptavidin-biotin horseradish peroxidase technique technique, in a series of 56 human thyroid carcinomas (42 papillary, 4 poorly differentiated, and 10 anaplastic carcinomas) and thyroid carcinoma cell lines at different degrees of differentiation. Results: The cytoplasmic expression of survivin protein was significantly upregulated in all thyroid tumors. A statistically significant association was found between nuclear survivin expression and anaplasticthyroid cancer (mean±SD: well-differentiated thyroid cancer, 1.22±20.21; non-well-differentiated thyroid cancer, 34.00±25.17; anaplastic thyroidcancer, 56.50±22.10; p<0.001). Nuclear staining of survivin has been shown in poorly differentiated and anaplastic thyroid carcinomas, and this is likely due to the upregulation of the ΔEx3 survivin splicing variant, as shown in poorly differentiated/anaplastic thyroid carcinoma cell lines. Of note, selected thyroid tumors characterized by a mixed population of differentiated and undifferentiated neoplastic cells, likely progressing from well to poorly differentiated and anaplastic phenotypes, exhibited cytoplasmic expression of survivin in differentiated fields and nuclear protein staining in poorly differentiated and anaplastic areas. This expression profile provides substantial added value to conventional clinical markers in predicting anaplastic cancer. The cut-off for distinguishing thyroids that developed ATC from those that remained differentiated was >30% of nuclear survivin expression. The receiver operating characteristic (ROC) area was 0.92, with a p-value of <0.0001. Conclusions: Upregulation of survivin expression may be a molecular marker of dedifferentiation in thyroid epithelial carcinomas, likely being responsible for survival responses of tumor cells and, thus, favoring progression toward a poorly differentiated phenotype.

PMID: 24117205

22. Thyroid. 2013 Nov 8. [Epub ahead of print] **IF:3.84**

Tumor classification in Well-Differentiated Thyroid Carcinoma and Sentinel Lymph Node Biopsy Outcomes: a Direct Correlation.

Maniakas A, Forest VI, Jozaghi Y, Saliba J, Hier MP, Mlynarek A, Tamilia M, Payne RJ.
Author information

Abstract

Objective: Predicting locoregional metastasis in well-differentiated thyroid carcinoma (WDTC) is a challenge for thyroid cancer surgeons. Sentinel lymph node biopsy (SLNB) has been shown to be an effective predictive tool. To our knowledge, Primary Tumor (T) classification has yet to be studied with regard to SLNB. We hypothesized that larger primary tumors would correlate with the rate of malignancy in SLNBs. Methods: A retrospective chart review was conducted on patients operated for WDTC at the McGill Thyroid Cancer Center over a 36 month period. Patients who underwent a total thyroidectomy and SLNB for WDTC were included in this study. Results: 311 patients were included and separated into two groups (236 negative and 75 positive SLNBs). Among patients with negative SLNBs, 65% had T1 primary tumors, 17% T2, 16% T3 and 2% T4, whereas 18% of patients with positive SLNBs had T1 primary tumors,

5% T2, 45% T3 and 32% T4 (p<0.001). Patients <45 years old had a higher rate of positive SLNs (36% in <45 years old vs. 17% in ≥45 years old) (p<0.001). Conclusions: Age (<45 years old) and higher T category were found to be associated with a higher rate of positive SLNBs.

PMID: 24199963

23. Thyroid. 2013 Oct 29. [Epub ahead of print] **IF:3.84**

Impact of Molecular Screening for Point Mutations and Rearrangements in Routine Air-Dried Fine-Needle Aspiration Samples of Thyroid Nodules.

Eszlinger M, Krogdahl A, Münz S, Rehfeld C, Precht Jensen EM, Ferraz C, Bösenberg E, Drieschner N, Scholz M, Hegedüs L, Paschke R.
Author information

Abstract
Background: The diagnostic limitations of thyroid fine-needle aspiration (FNA), such as the indeterminate category, can be partially overcome by molecular analyses. However, until now, rearrangements have only been detected in fresh FNA material and the number of follicular thyroidcarcinomas (FTCs) was rather low in previous studies. We aimed at investigating the impact of point mutations and rearrangement detection in a set of routine air-dried FNA smears with a higher percentage of FTCs. Methods: RNA and DNA was extracted from 310 FNAs (164 indeterminate, 57 malignant, 89 benign) and corresponding formalin-fixed paraffin-embedded tissue (156 follicular adenomas [FAs], 32 FTCs, 44 papillary thyroidcarcinomas [PTCs], 9 follicular variant PTCs, and 69 goiters). PAX8/PPARG and RET/PTC rearrangements were detected by qPCR, BRAF and RAS mutations by high-resolution melting PCR and by pyrosequencing. Results: Forty-seven mutations were detected in the FNAs: 22 BRAF, 13 NRAS, and 3 HRAS mutations, 8 PAX8/PPARG, and one RET/PTC-rearrangement. While the presence of a BRAF and RET/PTC mutation was associated with cancer in 100% of samples each, the presence of a RAS and PAX8/PPARG mutation was associated with cancer in only 12% and 50% of samples, respectively. In the indeterminate group 4 of 25 carcinomas were identified by molecular FNA screening, which increased the sensitivity from 67% (cytology alone) to 75% (cytology plus molecular screening). Conclusion: Molecular screening for point mutations and rearrangements is feasible in air-dried FNAs. Although the impact of detecting point mutations and rearrangements in FNAs has most likely been overestimated in previous studies, molecular FNA analyses improve presurgical diagnostics. The detection of BRAF mutations in FNA may improve the choice of surgery and postsurgical treatment. Further data are necessary to elucidate the true impact of detecting RAS and PAX8/PPARG mutations in FNAs. The inclusion of additional rare somatic mutations and miRNA markers might further improve the impact of molecular FNA diagnostics.

PMID: 23837487

24. Eur J Endocrinol. 2013 Oct 4;169(5):689-93. doi: 10.1530/EJE-13-0386. Print 2013 Nov. **IF:3.64**

Ultrasensitive serum thyroglobulin measurement is useful for the follow-up of patients treated with total thyroidectomy without radioactive iodine ablation.

Nascimento C, Borget I, Troalen F, Al Ghuzlan A, Deandreis D, Hartl D, Lumbroso J, Chougnet CN, Baudin E, Schlumberger M, Leboulleux S.
Author information

Abstract
CONTEXT:
Thyroglobulin (Tg) measurement is a major tool for the follow-up of differentiated thyroid cancer (DTC) patients; however, in patients who do not undergo radioactive iodine (RAI) ablation, normal ultrasensitive Tg levels measured under levothyroxine treatment (usTg/l-T4) are not well defined.

OBJECTIVE AND DESIGN:
This single-center retrospective study assessed usTg/l-T4 level in 86 consecutive patients treated with total thyroidectomy without RAI ablation for low-risk DTC (n=77) or for tumors of uncertain malignant potential (TUMP) (n=9).

RESULTS:
DTCS were classified as PT1, PT2, and PT3 in 75, 1, and 1 case respectively and PN0, PN1, and PNX in 40, 6, and 31 respectively. following surgery, ten patients had TG antibodieS (TGAB). Among those without TGAB, the first USTG/L-T4 determination obtained at a mean time of 9 months after surgery was 0.1NG/ML in 62% of cases, 0.3NG/ML in 82% of cases, 1NG/ML in 91%, and 2NG/ML in 96% of cases. after a median follow-up of 2.5 years (range: 0.6-7.2 years), one patient had persistent disease with an usTg/l-T4 at 11 ng/ml and an abnormal neck ultrasonography (US) and two patients had usTg/l-T4 level >2 ng/ml (3.9 and 4.9 ng/ml) with a normal neck US. Within the first 2 years following total thyroidectomy without RAI ablation, usTg/l-T4 level is ≤2 ng/ml in 96% of the cases.

CONCLUSION:
After total thyroidectomy, sensitive serum Tg/l-T4 level is ≤2 ng/ml in most patients and can be used for patient follow-up.

PMID: 23939918 http://dx.doi.org/10.1530/EJE-13-0386

25. Eur J Endocrinol. 2013 Oct 21;169(6):821-7. doi: 10.1530/EJE-13-0372. Print 2013 Dec. **IF:3.64**

Are prognostic scoring systems of value in patients with follicular thyroid carcinoma?

Ríos A, Rodríguez JM, Ferri B, Matínez-Barba E, Febrero B, Parrilla P.
Author information

Abstract

PURPOSE:
Most prognostic systems for differentiated carcinoma have been designed for papillary carcinoma.

OBJECTIVE:
To analyze the value of the existing prognostic systems for evaluating follicular carcinoma and to determine whether any of them have a better predictive effect.

METHODS:
A total of 66 follicular carcinomas were analyzed. The following prognostic systems were studied: EORTC, AGES, AMES, MACIS, TNM, and NTCTCS.

RESULTS:
The AGES and AMES systems did not demonstrate a good prognostic correlation. In the EORTC system, the rate of disease-free patients was 89% in group 1, 75% in group 2, 69% in group 3, and 0% in group 4. The MACIS system showed 83, 60, 67, and 0% of disease-free patients respectively. The TNM system showed 81, 71, 50, and 0% of disease-free patients respectively. Finally, the NTCTCS system demonstrated 100, 84, 53, and 0% of disease-free patients respectively. Cox's regression analysis was used to calculate the proportion of variation in survival time explained (PVE). The prognostic classification system with the greatest survival prediction was EORTC at 67.64% of PVE, followed by TNM at 62.5% of PVE, and MACIS at 57.82% of PVE.

CONCLUSIONS:
MACIS and TNM are good prognostic systems for evaluating follicular thyroid carcinoma, although the one with the most prognostic value was the EORTC system.

PMID: 24050927 http://dx.doi.org/10.1530/EJE-13-0372

26. Eur J Endocrinol. 2013 Oct 1;169(5):649-55. doi: 10.1530/EJE-13-0431. Print 2013 Nov. **IF:3.64**

The cytologic category of oncocytic (Hurthle) cell neoplasm mostly includes low-risk lesions at histology: an institutional experience.

Rossi ED, Martini M, Straccia P, Raffaelli M, Pennacchia I, Marrucci E, Lombardi CP, Pontecorvi A, Fadda G.
Author information

Abstract

DESIGN:
The cytological diagnosis of oncocytic/Hurthle cell neoplasms (OCN) represents a challenge with which cytopathologists face up to in their practice. The majority of these lesions undergo surgery for a definitive characterization of the nature mainly due to their more aggressive behavior than other malignant follicular lesions. In this study, we aimed at the evaluation of the effective malignant rate in a large cohort of OCNs.

METHODS:
From January 2008 to December 2011, we analyzed 150 cyto-histological OCNs and 64 benign oncocytic/Hurthle lesions (BOL). Both groups of patients were analyzed for clinical and cyto-histological parameters. All the nodules were sampled under sonographic guidance and processed with the liquid-based cytological method.

RESULTS:
In agreement with literature, we found a significant correlation only with female gender in both OCN (P=0.0160) and BOL groups. The 64 BOLs were histologically diagnosed as 15 Hashimoto thyroiditis (HT), 45 hyperplastic nodules in HT, and four papillary thyroid carcinomas (PTC, 6.2%). The 150 OCNs resulted in 141 (94%) oncocytic adenomas and nine (6%) malignant lesions. The latter group included five oncocytic carcinomas (OCC), three oncocytic variants of PTC, and one macrofollicular PTC featured by mild nuclear clearing with a dispersive cellular pattern. The malignant rate was respectively 6.2% in BOLs without any OCC whereas 3.3% OCC diagnosed in the OCN category.

CONCLUSIONS:
Our OCNs mostly resulted in histological adenomas with a lower rate of malignancy than in other series. Some morphological parameters (nuclear clearing, dysplasia, and dispersive cellular pattern) might be helpful in stratifying OCN patients into different risks of malignancy.

PMID: 23985131 http://dx.doi.org/10.1530/EJE-13-0431

27. Eur J Endocrinol. 2013 Dec 21;170(2):323-9. doi: 10.1530/EJE-13-0865. Print 2014. **IF:3.64**

Familial vs sporadic papillary thyroid carcinoma: a matched-case comparative study showing similar clinical/prognostic behaviour.

Pinto AE, Silva GL, Henrique R, Menezes FD, Teixeira MR, Leite V, Cavaco BM.
Author information

Abstract

OBJECTIVE:
Familial non-medullary thyroid cancer has been proposed as an aggressive clinical entity. Our aim in this study is to investigate potential distinguishing features as well as the biological and clinical aggressiveness of familial vs sporadic papillary thyroid carcinoma (PTC). We assessed clinicopathological characteristics, outcome measures and DNA ploidy.

DESIGN:
A matched-case comparative study.

METHODS:

A series of patients with familial PTC (n=107) and two subgroups, one with three or more affected elements (n=32) and another including index cases only (n=61), were compared with patients with sporadic PTC (n=107), matched by age, gender, pTNM disease extension and approximate follow-up duration. Histological variant, extrathyroidal extension, vascular invasion, tumour multifocality and bilateral growth were evaluated. Ploidy pattern was analysed in available samples by DNA flow cytometry. The probabilities of disease-free survival (DFS) and overall survival (OS) were estimated according to the Kaplan-Meier (K-M) method.

RESULTS:
No patient with familial PTC died of disease during follow-up (median, 72 months), contrarily to five patients (4.7%) (P=0.06) with sporadic PTC (median, 90 months). There was a significantly higher tumour multifocality in familial PTC (index cases subgroup) vs sporadic PTC (P=0.035), and a trend, in the familial PTC cohort with three or more affected elements, to show extrathyroidal extension (P=0.054) more frequently. No difference was observed in DNA ploidy status. The K-M analyses showed no significant differences between both entities in relation to DFS or OS.

CONCLUSION:
Apart from multifocality, familial PTC appears to have similar clinical/prognostic behaviour when compared with sporadic forms of the disease.

PMID: 24272198 http://dx.doi.org/10.1530/EJE-13-0865

28. Arch Pathol Lab Med. 2013 Nov;137(11):1664-8. doi: 10.5858/arpa.2012-0366-OA. **IF:3.27**

Thyroid fine-needle aspiration reporting rates and outcomes before and after Bethesda implementation within a combined academic and community hospital system.

Harvey AM, Mody DR, Amrikachi M.
Author information

Abstract

CONTEXT:
The current study compares data from our hospital system before and after the 2008 implementation of the Bethesda System for Reporting Thyroid Cytology (BSRTC).

OBJECTIVE:
To show the effects the BSRTC has had on the reporting rates and outcomes for thyroid lesions.

DESIGN:
A search for thyroid fine-needle aspiration biopsies (FNABs) was performed for 2002-2005 (before BSRTC) and 2009-2011 (after BSRTC). Diagnostic outcomes were reviewed for cases with available follow-up.

RESULTS:
For 2002-2005, cytology reports for 3302 thyroid FNABs were reviewed, and 309 (9.4%) were classified as suspicious. For 2009-2011, cytology reports for 3432 thyroid FNABs were reviewed; 72 (2.1%) were classified as "atypia of undetermined significance or follicular lesion of undetermined significance" (AUS/FLUS), and 142 (4.1%) were classified as suspicious. Follow-up material was available for 31 AUS/FLUS cases (43.0%), and 6 of these cases (19%) were malignant. Follow-up material was available for 60 cases (42.3%) classified as suspicious, and 23 of these cases (38%) were malignant.

CONCLUSIONS:
The AUS/FLUS rate of 2.1% at our institution is at the lower range of the <7% recommended by the BSRTC, and our rate of 19% for risk of malignancy for AUS/FLUS is slightly above the BSRTC recommendation of 5% to 15%. Implementation of the BSRTC did not significantly affect our institution's reporting rates, most likely because an essentially similar classification system was employed before implementation of the BSRTC.

PMID: 24168507 http://dx.doi.org/10.5858/arpa.2012-0366-OA

29. Arch Pathol Lab Med. 2013 Nov;137(11):1627-9. doi: 10.5858/arpa.2012-0575-OA. **IF:3.27**

Should "indeterminate" diagnoses be used for thyroid fine-needle aspirates of nodules smaller than 1 cm?

Renshaw AA, Gould EW.
Author information

Abstract

CONTEXT:
The Bethesda System for thyroid fine-needle aspirates does not account for the size of the lesion that is aspirated.

OBJECTIVE:
To determine whether the size of the lesion would be helpful in order to reduce indeterminate thyroid aspirations.

DESIGN:
We correlated the results of all thyroid aspirations and surgical resection for the last 16 years at our institutions.

RESULTS:
A total of 9080 cases were aspirated and 1393 resections were performed. Of those resected, a total of 236 (17%) were classified as atypical follicular cells of undetermined significance, and 256 (18%) were classified as suspicious for a follicular/Hürthle cell neoplasm. A total of 52 incidental papillary carcinomas were identified in these indeterminate cases at resection (52 of 492; 11%). Thirty-seven (16%) atypical follicular cells of undetermined significance cases and 21 (8%) suspicious for a follicular/Hürthle cell neoplasm cases were for nodules smaller than 1 cm in diameter. When cases subtyped as atypical, a papillary carcinoma cannot be ruled out, were removed (13 cases), the remaining 24 and 21 aspirates identified 3 tumors each (13% and 14%), all papillary carcinomas. Together, the incidence of identified carcinomas was not significantly different than that of incidental carcinomas (13% versus 11%, P = .48). The rate of identified carcinomas was significantly less than for similar indeterminate cases smaller than 1 cm (excluding cases of atypical, papillary carcinoma cannot be ruled out) (88 of 330 cases; 27%; P = .05).

CONCLUSIONS:
For nodules smaller than 1 cm in our series, indeterminate aspirates without features of papillary carcinomas have the same risk of malignancy as benign aspirates.

PMID: 24168500 http://dx.doi.org/10.5858/arpa.2012-0575-OA

30. Surgery. 2013 Oct;154(4):730-6; discussion 736-8. doi: 10.1016/j.surg.2013.05.015. **IF:3.19**

Nodule size is an independent predictor of malignancy in mutation-negative nodules with follicular lesion of undetermined significance cytology.

Mehta RS, Carty SE, Ohori NP, Hodak SP, Coyne C, LeBeau SO, Tublin ME, Stang MT, Johnson JT, McCoy KL, Nikiforova MN, Nikiforov YE, Yip L.
Author information

Abstract

BACKGROUND:
In thyroid nodule fine-needle aspiration (FNA) cytology, the atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS) category has a 5-15% malignancy risk that increases to 85-99% when mutation testing for BRAF, RAS, RET/PTC, or PAX8/PPARγ is positive. However, negative

testing does not exclude malignancy. The study objective was to identify clinical and imaging features that predict cancer in mutation-negative AUS/FLUS thyroid nodules.

METHODS:
All patients were reviewed (April 2007 to April 2009) who had AUS/FLUS cytology, negative prospective molecular testing of FNA, and histopathology.

RESULTS:
Of the 230 nodules, 12 (5.2%) were malignant in 11 of 190 patients, and known clinical risk factors for thyroid cancer did not predict malignancy. On preoperative imaging, ≥1 suspicious ultrasound feature was identified in 33% of nodules and occurred regardless of histology (P = .23). Malignant mutation-negative AUS/FLUS nodules were larger than benign nodules (mean maximum diameter, 33.6 vs 24.0 mm; P = .007). On multivariate analysis, nodule size remained an independent predictor of malignancy (odds ratio, 1.043; P = .018). We observed no malignancies in 88 mutation-negative AUS/FLUS nodules <18.5 mm.

CONCLUSION:
Size is an independent predictor of malignancy in mutation-negative AUS/FLUS nodules and the risk increased 4.3% with every millimeter increase in nodule size. Selected patients with small, mutation-negative AUS/FLUS thyroid nodules may be managed with ultrasound surveillance in lieu of thyroidectomy.

PMID: 24074409 http://dx.doi.org/10.1016/j.surg.2013.05.015

31. Surgery. 2013 Nov;154(5):1009-15. doi: 10.1016/j.surg.2013.04.064. Epub 2013 Sep 26. **IF:3.19**

Total thyroidectomy for Graves' disease: compliance with American Thyroid Association guidelines may not always be necessary.

Shinall MC Jr, Broome JT, Nookala R, Shinall JB, Kiernan C, Parks L 3rd, Solórzano CC.
Author information

Abstract

BACKGROUND:
Total thyroidectomy (TT) is the preferred operative approach to Graves' disease. Current guidelines of the American ThyroidAssociation call for the administration of potassium iodide (KI) and achievement of euthyroid state before operation. Small numbers and a mixture of operative approaches spanning several decades hinder previous operative series. We present the outcomes for TT at a single high-volume center.

METHODS:
A retrospective cohort study was conducted on 165 patients undergoing TT for Graves' disease from July 2007 to May 2012.

RESULTS:
Mean age was 43 years (range, 17-78), and 128 patients (78%) were female. A total of 95% of patients were on methimazole or propylthiouracil, and 42% remained hyperthyroid at time of TT. Only 3 (2%) patients received KI. Mean operative time was 132 minutes (range, 59-271). Mean gland size and blood loss were 41 g (range, 8-180) and 55 mL (range, 10-1050), respectively. No patient developed thyroid storm. Median follow-up was 7.5 months. Temporary and permanent hypocalcemia developed in 51 (31%) and 2 patients (1.2%), respectively. Temporary and permanent recurrent laryngeal nerve paresis occurred in 12 (7%) and one (0.6%) patient, respectively. Sixty-one (37%) patients experienced at least one complication. On multivariate analysis, patient age younger than 45 years (odds ratio 2.93, 95% confidence interval 1.39-6.19) and obesity (odds ratio 2.11, 95% confidence interval 1.00-4.43) were associated with the occurrence of complications.

CONCLUSION:

This high-volume surgeon experience demonstrates no appreciable detriment to patient outcomes when recommendations of the American Thyroid Association for routine use of KI and euthyroid state before thyroidectomy are not met. Transient hypocalcemia and hoarseness are frequent complications of TT for Graves' disease, resolving within 6 months in most patients. Age younger than 45 years and obesity are risk factors for postoperative complications.

PMID: 24075271 http://dx.doi.org/10.1016/j.surg.2013.04.064

32. Surgery. 2013 Oct;154(4):697-701; discussion 701-3. doi: 10.1016/j.surg.2013.06.040. Epub 2013 Sep 5. **IF:3.19**

The utility of routine preoperative cervical ultrasonography in patients undergoing thyroidectomy for differentiated thyroid cancer.

O'Connell K, Yen TW, Quiroz F, Evans DB, Wang TS.
Author information

Abstract

BACKGROUND:
Preoperative ultrasonography (US) is recommended in all patients with differentiated thyroid cancer (DTC) to evaluate for clinically occult metastatic lymphadenopathy. The purpose of this study was to examine the influence of preoperative US findings on the initial operative management of patients with DTC.

METHODS:
This is a retrospective review of 70 patients with biopsy-proven DTC who underwent total thyroidectomy between February 2010 and January 2012. All patients underwent preoperative cervical US (thyroid, central, and lateral neck lymph node compartments).

RESULTS:
Palpable lateral neck adenopathy was thought to be present in 5 (7%) of the 70 patients, but confirmed by US in only 3; 2 patients avoided lateral compartment neck dissection (LCND). Of 65 patients with no palpable lymphadenopathy, 14 (22%) had abnormal lymphadenopathy on preoperative US. All 14 patients underwent total thyroidectomy with central compartment neck dissection (CCND); 12 patients with abnormal US findings in the lateral compartment(s) also underwent LCND. Metastatic disease was confirmed in 13 (93%) of the 14 patients: 13 of 14 who underwent CCND and 11 (92%) of 12 who underwent LCND.

CONCLUSION:
This study confirms the importance of preoperative, high-quality cervical US in patients with DTC because it changed the operative management in 16 of 70 patients (23%); 13 had a more complete operation for pathologically confirmed, clinically occult, lymph node metastases, 2 avoided nontherapeutic LCND, and 1 had false-positive US results.

PMID: 24011674 http://dx.doi.org/10.1016/j.surg.2013.06.040

33. Surgery. 2013 Dec;154(6):1337-44; discussion 1344-5. **IF:3.19**

Decreasing the dose of radioiodine for remnant ablation does not increase structural recurrence rates in papillarythyroid carcinoma.

Kruijff S, Aniss AM, Chen P, Sidhu SB, Delbridge LW, Robinson B, Clifton-Bligh RJ, Roach P, Gill AJ, Learoyd D, Sywak MS.

Abstract

BACKGROUND:
Our aim was to compare the rate of structural recurrence between patients who had lesser doses of radioactive iodine (RAI) and those who had traditional greater doses for remnant ablation after total thyroidectomy for papillary thyroid carcinoma (PTC).

METHODS:
A retrospective cohort study of patients who had undergone thyroidectomy and RAI for PTC was undertaken. We divided the cohort into those who had < or =3 GBq (75 mCi) RAI (group A) and those who had >3 GBq (75 mCi) RAI (group B). The primary outcome measure was the rate of structural recurrence.

RESULTS:
Of 1,171 patients with PTC from 1990 to 2012 who were followed for a mean of 60 months, 970 with T1–T3 tumors underwent RAI in addition to thyroidectomy. The mean first dose of RAI was 2.5 GBq (68 mCi) for group A (n = 153) and 4.7 GBq (127 mCi) for group B (n = 817; P < .001). The overall rate of recurrence was 8%. When corrected for T stage, the recurrence rates were not different for T1 tumors (2% group A versus 4% group B; P = .54) nor for T2 and T3 tumors (P = .36 and .55, respectively). On multivariate analysis, the dose of RAI was not an independent predictor for structural recurrence.

CONCLUSION:
Decreasing the dose of RAI at initial ablation for patients with pT1–pT3 PTC does not seem to be associated with an increased risk of structural cancer recurrence.

PMID: 24383104

34. Surgery. 2013 Dec;154(6):1166-72; discussion 1172-3. doi: 10.1016/j.surg.2013.04.035. **IF:3.19**

Observation of clinically negative central compartment lymph nodes in papillary thyroid carcinoma.

Nixon IJ, Ganly I, Patel SG, Morris LG, Palmer FL, Thomas D, Tuttle RM, Shah JP, Shaha AR.
Author information

Abstract

BACKGROUND:
The role of prophylactic central neck dissection in the management of papillary thyroid cancer (PTC) is controversial. We report our experience of an observational approach to the cN0 neck in PTC.

METHODS:
We reviewed 1,129 patients with PTC who had total thyroidectomy between 1986 and 2005. In that group, 470 patients were pN1; 384 had benign nodes removed (pN0); and the remaining 275 had no nodes removed (pNx). The pNx group formed the cohort for this study.

RESULTS:
With a median follow-up of 70 months, the 10-yr disease-specific survival was 100%. We found 4 patients who had evidence of radioactive iodine uptake on scans performed during follow-up without diagnostic cytology. All subsequently received radioactive iodine and are considered disease free. Three patients had biopsy-proven lateral-neck recurrence and underwent neck dissection; 1 patient developed a low-level thyroglobulin suspicious for recurrence; and 1 patient had a subcentimeter level VI node suspicious for

recurrence, which has been observed. Therefore, the rate of structural recurrence in the central neck was 0.4% (1/275), and the rate of reoperation on the central neck was 0.

CONCLUSION:
Our results suggest that properly selected patients can be managed safely with observation of the central neck rather than prophylactic central neck dissection, which has a higher complication rate.

PMID: 24238042 http://dx.doi.org/10.1016/j.surg.2013.04.035

35. Surgery. 2013 Dec;154(6):1307-13; discussion 1313-4. doi: 10.1016/j.surg.2013.06.031. **IF:3.19**

Cost analysis of thyroid lobectomy and intraoperative frozen section versus total thyroidectomy in patients with a cytologic diagnosis of "suspicious for papillary thyroid cancer".

Leiker AJ, Yen TW, Cheung K, Evans DB, Wang TS.
Author information

Abstract

BACKGROUND:
The optimal operation for a patient with a thyroid nodule "suspicious for papillary thyroid cancer (PTC)" on fine-needle aspiration (FNA) is unclear. This study examines the incremental cost-utility of thyroid lobectomy with intraoperative frozen section (thyroid lobectomy) versus total thyroidectomy.

METHODS:
Cost-utility analysis was performed for patients with a cytologic diagnosis of "suspicious for PTC" on FNA. Patients underwent either initial total thyroidectomy or thyroid lobectomy and, if needed, completion thyroidectomy. The incremental cost-utility ratio (ICUR; US$/quality-adjusted-life-year [QALY]), was determined from a societal perspective.

RESULTS:
The base-case ICUR of thyroid lobectomy is $90,776/QALY, strongly favoring total thyroidectomy as a more cost-effective modality. On sensitivity analyses, the model is sensitive to the accuracy of frozen section and to the rate of injury to the recurrent laryngeal nerve (RLN). Thyroidlobectomy is more cost-effective only if both frozen section and final pathology are benign in ≥92% of patients (ICUR $47,959/QALY at 92%). With increasing rates of unilateral (>5%) or bilateral (>2%) RLN injury associated with total thyroidectomy, there is a trend toward thyroid lobectomy being more cost effective ($53,127 and $51,325/QALY, respectively).

CONCLUSION:
In our model, initial total thyroidectomy is cost-effective for patients with a single thyroid nodule suspicious for PTC on FNA. Our results strongly support total thyroidectomy for initial treatment; thyroid lobectomy is preferred only when complications reach unacceptable levels.

PMID: 24238049 http://dx.doi.org/10.1016/j.surg.2013.06.031

36. Surgery. 2013 Dec;154(6):1346-52; discussion 1352-3. doi: 10.1016/j.surg.2013.04.068. **IF:3.19**

The impact of surgical volume on patient outcomes following thyroid surgery.

Kandil E, Noureldine SI, Abbas A, Tufano RP.
Author information

Abstract

BACKGROUND:
This study aimed to evaluate the effects of indications for thyroidectomy on patient outcomes and to examine the impact of surgical volume on these outcomes.

METHODS:
The nationwide inpatient sample was used to identify all patients who underwent total thyroidectomy (TT) between 2000 and 2009. We examined the effects of surgeon volume and hospital characteristics on predicting patient outcomes. Univariate and multivariate analyses were used to examine the effects of the indication for surgical care on postoperative outcomes.

RESULTS:
Overall, 46,261 procedures were identified. Patients with Graves disease had the highest postoperative complications (17.5%) compared to patients undergoing TT for other benign (13.9%) and malignant (13.2%) thyroid disease (P < .001). After stratification by surgeon volume, Graves disease was found to be a significant predictor of postoperative complications in surgeries performed by low- and intermediate-volume surgeons (P < .05). However, Graves disease was not a significant predictor of postoperative complications when performed by high volume surgeons (P = .81). Hospital volume had an inconsistent and marginal protective effect on postoperative outcomes.

CONCLUSION:
Surgery for Graves disease is associated with a higher risk for complications when performed by less experienced surgeons. This finding should prompt recommendations for increasing surgical specialization and referrals to high-volume surgeons in the management of Graves disease.

PMID: 24238052 http://dx.doi.org/10.1016/j.surg.2013.04.068

37. Surgery. 2013 Dec;154(6):1148-5; discussion 1154-5. **IF:3.19**

Routine prophylactic central neck dissection for low-risk papillary thyroid cancer: a cost-effectiveness analysis.

Zanocco K, Elaraj D, Sturgeon C.

Abstract

BACKGROUND:
Routine prophylactic central neck dissection (pCND) after total thyroidectomy (TTX) for low-risk papillary thyroid cancer (PTC) offers the potential to decrease disease recurrence but may increase operative complications. We hypothesized that routine pCND is not cost-effective in low-risk PTC.

METHODS:
A Markov transition-state model was constructed to compare TTX with and without pCND. Outcome probabilities, utilities, and costs were estimated on the basis of literature review. The threshold for cost-effectiveness was $100,000 per quality-adjusted life year. Sensitivity analysis was used to examine model uncertainty.

RESULTS:
pCND cost $10,315 and produced an effectiveness of 23.785 quality-adjusted life years. This strategy was more costly and less effective than TTX without pCND and was therefore dominated. pCND became cost-effective when the probability of recurrence increased from 6% to 10.3%, cost of reoperation for recurrence

increased from $8,900 to $26,120, or added probabilities of recurrent laryngeal nerve injury and hypoparathyroidism due to pCND were less than 0.20% and 0.18% during 2-way sensitivity analysis. Monte Carlo simulation showed that pCND was not cost-effective in 97.3% of iterations.

CONCLUSION:
Routine pCND for low-risk PTC is not cost-effective unless the recurrence rate is greater than 10.3%. Application of pCND should be individualized based on risk of recurrence and added complications.

Comment in

- Is routine prophylactic central neck dissection indicated for low-risk papillary thyroid cancer: can we determine cost-effectiveness if we are unsure about its effectiveness and safety? [Surgery. 2013]

PMID: 24383082

38. Surgery. 2013 Dec;154(6):1283-89; discussion 1289-91. doi: 10.1016/j.surg.2013.06.032. Epub 2013 Oct 25. **IF:3.19**

A multi-institutional international study of risk factors for hematoma after thyroidectomy.

Campbell MJ, McCoy KL, Shen WT, Carty SE, Lubitz CC, Moalem J, Nehs M, Holm T, Greenblatt DY, Press D, Feng X, Siperstein AE, Mitmaker E, Benay C,Tabah R, Oltmann SC, Chen H, Sippel RS, Brekke A, Vriens MR, Lodewijk L, Stephen AE, Nagar S, Angelos P, Ghanem M, Prescott JD, Zeiger MA, Aragon Han P, Sturgeon C, Elaraj DM, Nixon IJ, Patel SG, Bayles SW, Heneghan R, Ochieng P, Guerrero MA, Ruan DT.
Author information

Abstract

BACKGROUND:
Cervical hematoma can be a potentially fatal complication after thyroidectomy, but its risk factors and timing remain poorly understood.

METHODS:
We conducted a retrospective, case-control study identifying 207 patients from 15 institutions in 3 countries who developed a hematoma requiring return to the operating room (OR) after thyroidectomy.

RESULTS:
Forty-seven percent of hematoma patients returned to the OR within 6 hours and 79% within 24 hours of their thyroidectomy. On univariate analysis, hematoma patients were older, more likely to be male, smokers, on active antiplatelet/anticoagulation medications, have Graves' disease, a bilateral thyroidectomy, a drain placed, a concurrent parathyroidectomy, and benign pathology. Hematoma patients also had more blood loss, larger thyroids, lower temperatures, and higher blood pressures postoperatively. On multivariate analysis, independent associations with hematoma were use of a drain (odds ratio, 2.79), Graves' disease (odds ratio, 2.43), benign pathology (odds ratio, 2.22), antiplatelet/anticoagulation medications (odds ratio, 2.12), use of a hemostatic agent (odds ratio, 1.97), and increased thyroid mass (odds ratio, 1.01).

CONCLUSION:
A significant number of patients with a postoperative hematoma present >6 hours after thyroidectomy. Hematoma is associated with patients who have a drain or hemostatic agent, have Graves' disease, are actively using antiplatelet/anticoagulation medications or have large thyroids. Surgeons should consider these factors when individualizing patient disposition after thyroidectomy.

PMID: 24206619 http://dx.doi.org/10.1016/j.surg.2013.06.032

39. Surgery. 2013 Oct;154(4):704-11; discussion 711-3. doi: 10.1016/j.surg.2013.06.039. Epub 2013 Sep 3. **IF:3.19**

The long-term impact of routine intraoperative nerve monitoring during thyroid and parathyroid surgery.

Snyder SK, Sigmond BR, Lairmore TC, Govednik-Horny CM, Janicek AK, Jupiter DC.
Author information

Abstract

BACKGROUND:
Despite widespread use of intraoperative nerve monitoring (IONM) as an adjunct to visual identification of the recurrent laryngeal nerve (RLN), published studies have shown little or no benefit. No long-term studies exist detailing the effect of experience gained from IONM on the rate of RLN injury. The aim of this study was to evaluate the impact of IONM feedback on surgical outcomes over time at a single institution.

METHODS:
We conducted retrospective analysis of prospectively gathered data for 1,936 patients including 3,435 nerves at risk between March 2004 and September 2011. Each RLN was analyzed for the specific, unilateral operative procedure that placed the nerve at risk of injury. The primary outcome measures included temporary vocal cord palsy and permanent vocal cord paralysis or paresis as determined by intraoperative loss of RLN function and postoperative laryngoscopy. Additional measures included instances where IONM assisted the surgeon's localization of the RLN.

RESULTS:
Of the 3,435 nerves at risk, 105 (3.06%) were injured, 4 had permanent paralysis (0.12%), and 7 had paresis (0.20%). Over time, a decrease in RLN injury was seen per successive operative year for thyroid lobectomy with paratracheal lymph node dissection with or without parathyroidectomy (odds ratio, 0.98; 95% confidence interval, 0.97-1.00; P = .04); the rate of nerve injury stabilized after 20 months of continued use of nerve monitoring. IONM particularly assisted the surgeon with identification of 108 nerves at risk (3.14%) with aberrant anatomy, and with identification of 236 nerves at risk (6.87%) during difficult dissections.

CONCLUSION:
With experience, routine use of IONM during thyroid and parathyroid operations significantly decreased the incidence of injury to the RLN for thyroid lobectomy with paratracheal lymph node dissection and provided useful assistance with RLN identification for 10% of nerves at risk.

PMID: 4008089 http://dx.doi.org/10.1016/j.surg.2013.06.039

40. Eur J Surg Oncol. 2013 Dec 25. pii: S0748-7983(13)00955-4. doi: 10.1016/j.ejso.2013.12.008. [Epub ahead of print] **IF:3.07**

Treatments for complications of tracheal sleeve resection for papillary thyroid carcinoma with tracheal invasion.

Lin S[1], Huang H[2], Liu X[3], Li Q[4], Yang A[5], Zhang Q[6], Guo Z[7], Chen Y[8].
Author information

Abstract

OBJECTIVE:
To evaluate the treatment, prognosis, and complications of differentiated thyroid carcinoma with tracheal invasion. We report our outcomes from a single center using a tracheal sleeve resection.

PATIENTS AND METHODS:

Retrospective analysis of clinicopathological data on tracheal sleeve resection in patients with thyroid cancer and accompanying tracheal invasion from January 2009 to July 2012. The postoperative complications were analyzed and the literature was reviewed.

RESULTS:
Nineteen patients with thyroid carcinoma and accompanying tracheal invasion underwent tracheal sleeve resection followed by end-to-end anastomosis. The median survival time was 22 months. Five patients (5/19) developed postoperative complications. The major complications included bilateral recurrent laryngeal nerve paralysis (2 cases), tracheal anastomotic stenosis (1 case), esophageal fistula (2 cases), and anastomotic dehiscence (2 cases). The treatment for these complications included partial posterior cordectomy by CO_2 laser for bilateral recurrent laryngeal nerve paralysis; CO_2 laser treatment followed by postoperative external beam radiotherapy (EBRT) (20 Gy/10 times) for tracheal anastomotic stenosis, femoral anterior dissociative flap to repair esophageal fistula, and a T-tube positioned in the wound in cases of anastomotic dehiscence.

CONCLUSIONS:
Tracheal sleeve resection remain a safe option with less morbidity and perioperative complications for the management of patients with differentiated thyroid carcinoma accompanied by intratracheal invasion.

KEYWORDS:

CO(2) laser, Complication, Sleeve resection, Thyroid carcinoma, Tracheal invasion

PMID: 24388407 http://dx.doi.org/10.1016/j.ejso.2013

41. Eur J Surg Oncol. 2013 Dec 14. pii: S0748-7983(13)00924-4. doi: 10.1016/j.ejso.2013.11.015. [Epub ahead of print] **IF:3.07**

Ultrasonographic features associated with malignancy in cytologically indeterminate thyroid nodules.

Batawil N[1], Alkordy T[2].
Author information

Abstract

CONTEXT:
Thyroid nodules with indeterminate cytology usually are treated with surgery, but most are benign. Neck ultrasonography has varied results in predicting malignancy.

OBJECTIVE:
To evaluate the predictive value of ultrasonography and the frequency of malignancy in patients who had indeterminate thyroid nodules.

DESIGN:
Retrospective study.

SETTING:
University hospital.

PATIENTS:
There were 78 patients who had thyroid nodules that were diagnosed on cytology (fine needle aspiration) as a follicular lesion (atypia of undetermined significant) or follicular neoplasm. Ultrasonography was available in 69 patients (88%).

INTERVENTION AND MAIN OUTCOME MEASURES:
Diagnostic fine needle aspiration (cytology), ultrasonography, and surgical pathology of thyroidnodules.

RESULTS:

Fine needle aspiration was indeterminate in all patients, with follicular lesions in 60 patients (77%) and follicular neoplasm in 18 patients (23%). Ultrasonography showed micro calcification in 6 patients (9%), irregular border in 15 patients (22%), size ≥ 3 cm in 31 patients (45%), and hypoechogenicity in 43 patients (62%). Surgical pathology showed that the nodules were benign in 50 patients (64%) and malignant in 28 patients (36%). Malignancy was significantly associated with male sex (relative risk, 2.3), solid nodule structure (relative risk, 2.6), and irregular border (relative risk, 3.6). Compared with other ultrasonographic characteristics, irregular borders had the highest specificity (93%), positive predictive value (80%), and accuracy (78%) for malignancy.

CONCLUSIONS:
The frequency of malignancy is high in indeterminate thyroid nodules. Based on the limited accuracy or predictive value of ultrasonographic risk factors, surgery is the treatment of choice for indeterminate thyroid nodules.

KEYWORDS:

Carcinoma, Cytology, Fine needle aspiration, Imaging

PMID: 24373298 http://dx.doi.org/10.1016/j.ejso.2013.11.015

42. Endocr J. 2013 Dec 28. [Epub ahead of print] **IF:2.88**

Prognostic significance of patient age in minimally and widely invasive follicular thyroid carcinoma: Investigation of three age groups.

Ito Y, Miyauchi A, Tomoda C, Hirokawa M, Kobayashi K, Miya A.
Author information

Abstract

Follicular thyroid carcinoma (FTC) is the second most common malignancy arising from follicular cells. It is classified into two categories based on the degree of invasion: widely and minimally invasive FTC. Here we focused on the prognostic value of patient age in FTC. We enrolled 292 minimally invasive and 79 widely invasive FTC patients who underwent initial surgery between 1983 and 2007. We classified these patients into three groups based on patient age: < 20 years (children and adolescents), 20-44 years (young adults) and ≥ 45 years (middle-aged or older), and compared their prognoses disease-free survival (DFS) and cause-specific survival (CSS). Among the minimally invasive FTC patients, those aged ≥ 45 years showed a poorer DFS and CSS than those < 45 years. In the subset of patients < 45 years, the DFS of patients < 20 years tended to be poorer than those aged 20-44 years, but none of the patients < 20 years died of FTC. Among the patients with widely invasive FTC, only three were younger than 20 years old. Two patients showed carcinoma recurrence, but neither died of FTC. In minimally invasive FTC, the DFS showed a biphasic pattern, but the CSS became poorer with increasing age. In widely invasive FTC, similar to minimally invasive FTC, patients < 20 years might be likely to show recurrence but are unlikely to die of FTC, although studies using larger number of patients are necessary before drawing any conclusions.

PMID: 24390055

43. Head Neck. 2013 Oct;35(10):1439-42. doi: 10.1002/hed.23149. Epub 2012 Sep 10. **IF:2.85**

Metastatic papillary thyroid cancer with lateral neck disease: pattern of spread by level.

Merdad M, Eskander A, Kroeker T, Freeman JL.
Author information

Abstract

BACKGROUND:
Currently, there is no clear consensus on the extent of this lateral neck dissection required in papillary thyroid cancer (PTC) with lateral neck metastasis. The purpose of this study was to review our experience with metastatic PTC, and identify the pattern of lymphatic spread to the lateral neck.

METHODS:
A retrospective medical chart review of PTC patients treated with lateral neck dissection (levels II-Vb) at our institution between January 2004 and 2011. A total of 185 patients underwent 248 selective lateral neck dissections.

RESULTS:
Levels II, III, IV, and Vb were respectively involved in 49.3%, 76.6%, 61.6%, and 29.2% of cases.

CONCLUSION:
We advocate for a routine excision of levels II, III, IV, and Vb in PTC with metastasize to any lateral neck level. Although we have routinely dissected level IIb, it may be appropriate to omit its dissection, as well as level Va, when there are no clinical, radiologic, or intraoperative evidence of disease involving these sublevels.

KEYWORDS:

lateral, level, metastasis, neck dissection, papillary cancer, thyroid

PMID: 22965902 http://dx.doi.org/10.1002/hed.23149

44. Head Neck. 2013 Nov;35(11):1616-20. doi: 10.1002/hed.23197. Epub 2013 Jan 16. **IF:2.85**

Surgical extent of central lymph node dissection in clinically node-negative papillary thyroid cancer.

Kim WW, Park HY, Jung JH.
Author information

Abstract

BACKGROUND:
The indications for elective bilateral central node dissection for patients with unilateral papillary thyroid carcinoma (PTC) who are clinically node negative are still not verified. We investigated the predictive factors of lymph node metastasis and formulated guidelines for surgical extent.

METHODS:
From 2004 to 2009, 325 patients diagnosed with unilateral PTC who had undergone total thyroidectomy with bilateral central lymph node dissection (CLND) were enrolled retrospectively.

RESULTS:
Central node metastasis was found in 45.2%, ipsilateral and contralateral lymph node metastasis was found in 40.0% and 16.0%, respectively. Tumor size larger than 1.0 cm and extrathyroidal extension were significant factors in predicting ipsilateral node metastasis ($p = .004$, $< .001$, respectively), and extrathyroidal extension and ipsilateral lymph node metastasis predicted contralateral node metastasis in multivariable analysis ($p = .039$, $< .001$, respectively).

CONCLUSION:

Elective bilateral central node dissection may be considered in unilateral PTC with extrathyroidal extension or ipsilateral node metastasis.

KEYWORDS:

cancer, extent, lymph node dissection, papillary, thyroid

PMID: 23322499 http://dx.doi.org/10.1002/hed.23197

45. Head Neck. 2013 Dec 24. doi: 10.1002/hed.23587. [Epub ahead of print] **IF:2.85**

Thyroid autoimmunity and risk of malignancy in thyroid nodules submitted to fine-needle aspiration cytology.

Grani G, Calvanese A, Carbotta G, D'Alessandri M, Nesca A, Bianchini M, Del Sordo M, Vitale M, Fumarola A.
Author information

Abstract

Background. Whether the risk of cancer is increased in patients with chronic autoimmune thyroiditis is a controversial issue. Methods. Between May 2005 and October 2012, 3777 FNACs were performed on 2562 patients. Serum FT4, TSH, anti-thyroglobulin (TgAb) and anti-thyroperoxidase (TPOAb) antibodies were determined. Results. Patients with suspicious cytology were younger and presented smaller maximum lesion diameter. In patients with TgAb positivity, suspicious citology was detected more frequently (9.4%) than patients without TgAb (5.7%; p=0.04). No significant difference was recorded between benign and suspicious cytology, in positive TPOAb rate. Risk factors for suspicious cytology were younger age (OR 0.94), smaller maximum diameter (0.95), single lesion (1.85), microcalcifications (3.45), and TgAb (1.74). Mixed solid/fluid content resulted as being protective factor (0.34). According to multivariate logistic regression analysis, age, mixed content, and microcalcification confirmed significance. Conclusions. Thyroid nodule malignancy in patients with Hashimoto's thyroiditis is not more frequent than in patients without thyroiditis. Head Neck, 2013.

KEYWORDS:

Biopsy, Fine-Needle, Hashimoto Disease, Thyroid Neoplasms, autoimmunity, cytology

PMID: 24375752 http://dx.doi.org/10.1002/hed.23587

46. J Clin Pathol. 2013 Dec;66(12):1046-50. doi: 10.1136/jclinpath-2013-201559. Epub 2013 Jul 17.

IF:2.82

A core needle biopsy provides more malignancy-specific results than fine-needle aspiration biopsy in thyroidnodules suspicious for malignancy.

Hakala T, Kholová I, Sand J, Saaristo R, Kellokumpu-Lehtinen P.
Author information

Abstract

BACKGROUND AND AIMS:

The most commonly used diagnostic method for the preoperative diagnosis of thyroid nodules is ultrasound-guided fine-needle aspiration biopsy (FNA), which often yields non-diagnostic or non-definitive

results and seldom produces definite malignant diagnoses. To improve upon the malignancy-specific sensitivity, we tested core needle biopsies (CNBs) of thyroid lesions taken from surgical specimens.

MATERIAL AND METHODS:
52 consecutive patients with malignant or malignant-suspicious thyroid nodules were referred to Tampere University Hospital between May 2010 and December 2011. Preoperative FNAs were categorised as follicular neoplasm (48%), suspicion for malignancy (46%) or malignancy (6%). Intraoperative FNA and CNB samples were acquired from surgical specimens removed during surgery. The results of the needle biopsies were compared with the final pathological diagnosis.

RESULTS:
CNBs had a high definitive sensitivity for malignancy (61%, CI 41% to 78%) whereas the definitive sensitivity for malignancy of FNAs was significantly lower (22%, CI 10% to 42%). CNB was not beneficial in the diagnosis of follicular thyroid lesions. When all suspected follicular tumours were excluded, the definitive sensitivity of CNB rose to 70% (CI 48% to 86%).

CONCLUSIONS:
CNB may be beneficial for the diagnosis of papillary thyroid carcinoma and other non-follicular thyroid lesions. CNB may be considered as an additional diagnostic procedure in cases with FNA suspicious for malignancy.

KEYWORDS:

CYTOLOGY, HEAD AND NECK CANCER, HISTOPATHOLOGY, THYROID, THYROID CANCER

PMID: 23863219 http://dx.doi.org/10.1136/jclinpath-2013-201559

47. World J Surg. 2013 Dec 12. [Epub ahead of print] **IF:2.47**

Candidates for Limited Lateral Neck Dissection among Patients with Metastatic Papillary Thyroid Carcinoma.

Kang BC, Roh JL, Lee JH, Cho KJ, Gong G, Choi SH, Nam SY, Kim SY.
Author information

Abstract

BACKGROUND:
Papillary thyroid carcinoma (PTC) is associated with an excellent prognosis but frequently spreads to regional lymph nodes. The extent of neck dissection, particularly routine level II or V lymphadenectomy, is still controversial as it may lead to spinal accessory nerve injury and associated postoperative morbidities. We assessed the diagnostic value of preoperative ultrasonography (US) plus computed tomography (CT) for detecting metastatic lymph nodes and for identifying predictors of level II or V metastasis in patients with PTC.

METHODS:
The results of US and CT were compared with histopathologic findings at various neck levels in 209 previously untreated PTC patients with lateral cervical nodal metastases who underwent total thyroidectomy with central and lateral neck dissection. Clinicopathologic predictors for level II or V metastases were identified.

RESULTS:
Pathologic metastases to level II and V were observed in 53.6 and 25.4 % of patients, respectively. Occult metastases were found in 34.5 and 16.8 %, respectively. The sensitivities of US plus CT for levels II and V were 64.6 and 50.9 %, respectively. Image-based, isolated lateral level IV involvement and macroscopic extranodal extension were independently associated with level II metastasis or either level II or V metastasis ($p < 0.01$). Macroscopic extranodal extension was also independently associated with level V metastasis ($p = 0.001$).

CONCLUSIONS:
Patients with image-based, isolated lateral level IV involvement and no macroscopic extranodal extension are potential candidates for limited level III-IV dissection or prophylactic level II lymphadenectomy omission. Level V lymphadenectomy may be omitted in patients without macroscopic extranodal extension.

PMID: 24337241

48. World J Surg. 2013 Oct 19. [Epub ahead of print] **IF:2.47**

Comparison Between Preconsultation Ultrasonography and Office Surgeon-Performed Ultrasound in Patients with Thyroid Cancer.

Carneiro-Pla D, Amin S.
Author information

Abstract

BACKGROUND:
Cervical ultrasonography (US) is mandatory before surgery for thyroid cancer and recommended for thyroid nodule evaluation. Therefore, most patients undergo thyroid ultrasound before surgical evaluation. Several US findings are critical for adequate surgical planning but they are often not mentioned on preconsultation US. The goal of this study is to compare the preconsultation US findings with surgeon-performed US (SUS) and describe the changes in management as a consequence of SUS findings in patients with thyroid cancer.

METHODS:
The charts of 194 consecutive patients with thyroid cancer (2007-2013) from a single institution were reviewed. Preconsultation US and SUS reports were available for 136 patients. Mention of nodes, local invasion, thyroid nodule features/location, and presence of intrathoracic extension was recorded and changes in preoperative and/or operative management based on SUS findings were described.

RESULTS:
From 136 patients with the diagnosis of thyroid cancer, SUS changed the management of 61 (45 %) patients by identifying preoperatively central and/or lateral node metastasis, indicating preoperative biopsy of suspicious thyroid lesions/nodes, and pointing out thyroid intrathoracic extension. When compared to SUS, the preconsultation US failed to mention node status in 101 (74 %) patients, suspicious nodule features in 60/111 (54 %) patients with suspicious lesions, bilateral thyroid lesions in 19/88 (22 %) patients with bilateral nodules, local invasion in 5/5 (100 %), and intrathoracic extension in 5/5 (100 %) cases.

CONCLUSION:
Surgeon-performed US changed the operative management of patients with thyroid cancer by demonstrating additional and distinct information compared to preconsultation US in almost half of the patients. Ultrasound is more accurate and critical in the evaluation of patients withthyroid cancer when performed by the surgeon.

PMID: 24142328

49. World J Surg. 2013 Nov 19. [Epub ahead of print] **IF:2.47**

Optimal Timing of Surgery for Differentiated Thyroid Cancer in Pregnant Women.

Uruno T, Shibuya H, Kitagawa W, Nagahama M, Sugino K, Ito K.
Author information

Abstract

BACKGROUND:

Differentiated thyroid cancer (DTC) is the second most common cancer diagnosed in pregnant women, but there is no consensus as to whether surgery should be performed during pregnancy or after delivery.

METHODS:
We retrospectively reviewed the records of 45 patients with DTC operated on during pregnancy or within 1 year after delivery, and we compared the clinicopathological features and outcomes of the patients operated during pregnancy (group A, n = 24) and the patients operated after delivery (group B, n = 21).

RESULTS:
All 45 patients were histologically diagnosed with well-differentiated papillary thyroid cancer. Nineteen (79 %) of the 24 patients in group A underwent thyroidectomy during the second trimester. No complications associated with surgery or general anesthesia were reported in either group. There were no significant differences between the two groups in terms of age, tumor size, incidence of lymph node metastasis, or incidence of extrathyroidal extension. No distant metastases were detected in any of the patients. Two small for date infants (8.3 %) and 2 heavy for date infants (8.3 %) were delivered in group A, but only 1 small for date infant (4.7 %) was delivered in group B. There were no miscarriages, and none of the infants in either group had birth defects. Because 3 patients in group A and 1 patient in group B experienced a local recurrence, salvage surgeries were performed.

CONCLUSIONS:
Although thyroid surgery was performed safely in the second trimester, surgery after delivery was also acceptable. Surgery after delivery is recommended for most patients with non-aggressive DTC.

PMID: 24248429

50. World J Surg. 2013 Nov 15. [Epub ahead of print] **IF:2.47**

Prophylactic Level II Neck Dissection Guided by Frozen Section for Clinically Node-Negative Papillary Thyroid Carcinoma: Is It Useful?

Hartl DM, Al Ghuzlan A, Borget I, Leboulleux S, Mirghani H, Schlumberger M.
Author information

Abstract

BACKGROUND:
Prophylactic lateral neck dissection (PLND) is generally not performed for papillary thyroid carcinoma (PTC). When performed, occult metastases are found in up to 50 % of patients, although the incidence of occult level II nodes seems low. Our aim was to evaluate frozen section analysis-oriented elective level II PLND in patients with clinically node-negative (cN0) PTC.

METHODS:
This retrospective study included patients with cN0 PTC treated with total thyroidectomy and prophylactic bilateral central and lateral neck dissection of ipsilateral levels III and IV. Frozen section analysis of PLND III and IV was performed. If positive, the PLND was extended to level II. We measured the accuracy of frozen section analysis, the incidence of occult level II metastasis, and oncologic outcomes.

RESULTS:
A total of 295 patients were included. For frozen section analysis, the sensitivity was 71.0 %, specificity 99.6 %, positive predictive value 97.8 %, negative predictive value 92.4 %, overall accuracy 93.2 %. Definitive analysis found lateral node metastases in 63 of the 295 (21 %) patients. Extension to level II was performed in 27 of 46 cases (59 %). Level II contained metastatic nodes in 12 of 27 (44 %) patients. There was no difference in total doses of ^{131}I administered to patients with or without level II disease. Even when extension of PLND to level II was not performed, no cases of recurrent or persistent disease in level II occurred.

CONCLUSIONS:

Frozen section analysis was highly accurate. The rate of occult metastases in level II was low. Detection of additional metastases in level II did not modify subsequent treatment or the rate of recurrence and is not useful for routine application.

PMID: 2423190

51. World J Surg. 2013 Dec 18. [Epub ahead of print] **IF:2.47**

Results of Intraoperative Neuromonitoring in Thyroid Surgery and Preoperative Vocal Cord Paralysis.

Lorenz K, Abuazab M, Sekulla C, Schneider R, Nguyen Thanh P, Dralle H.
Author information

Abstract

BACKGROUND:
Systematic studies of intermittent intraoperative neuromonitoring (IONM) have shown that IONM enhances recurrent laryngeal nerve (RLN) identification via functional assessment, but does not significantly reduce rates of vocal cord (VC) paralysis (VCP). The reliability of functional nerve assessment depends on the preoperative integrity of VC mobility. The present study was therefore performed to analyze the validity of IONM in patients with pre-existing VC paralysis.

METHODS:
Of 8,128 patients, 285 (3.5 %) with preoperative VCP underwent thyroid surgery using standardized IONM of the RLN and vagus nerves (VNs). VC function was assessed by pre- and postoperative direct videolaryngoscopy. Quantitative parameters of IONM in patients with VCP were compared with IONM in patients with intact VC function. Clinical symptoms and surgical outcomes of patients with pre-existing VCP were analyzed.

RESULTS:
A total of 244 patients revealed negative, and 41 revealed positive IONM on the side of the VCP. VCP with positive IONM revealed significantly lower amplitudes of VN and RLN than intact VN ($p = 0.010$) and RLN ($p = 0.011$). Symptoms of patients with VCP included hoarseness (25 %), dyspnea (29 %), stridor (13 %), and dysphagia (13 %); 13 % were asymptomatic. New VCP occurred in five patients, ten needed tracheostomy for various reasons, and one patient died.

CONCLUSIONS:
Patients with pre-existing VCP revealed significantly reduced amplitude of ipsilateral VN and RLN, indicating retained nerve conductivity despite VC immobility. Preoperative laryngoscopy is therefore indispensable for reliable IONM and risk assessment, even in patients without voice abnormalities.

PMID: 24346632

52. World J Surg. 2013 Dec 20. [Epub ahead of print] **IF:2.47**

Trends in Incidentally Identified Thyroid Cancers Over a Decade: A Retrospective Analysis of 2,090 Surgical Patients.

Bahl M, Sosa JA, Nelson RC, Esclamado RM, Choudhury KR, Hoang JK.
Author information

Abstract

BACKGROUND:
The aim of this study was to describe trends in the incidence of incidental thyroid cancers and compare their characteristics with clinically presenting cancers.

METHODS:

We performed a retrospective review of patients with thyroid cancer who underwent thyroid surgery from 2003 to 2012. Patients' initial presentation was categorized as incidental (on imaging or final surgical pathology) or clinical (palpable or symptomatic) cancer. Characteristics of incidental and clinical cancers were compared.

RESULTS:
Of the 2,090 patients who underwent thyroid surgery, 680 (33 %) were diagnosed with cancer. One hundred ninety (28 %) were incidental cancer, of which 101 were detected on imaging studies and 89 were detected on analysis of the surgical pathology specimens. The incidence ofthyroid cancer increased by 7.6-fold from 2003 to 2012. The proportion of incidental cancers on imaging did not increase, but incidental cancers found on pathology steadily increased from 6 % in 2003 to 20 % in 2012. 84 % of the cancers were papillary cancer, and the proportion of papillary cancer was similar for both clinical and incidental cancers. Clinical cancers were larger than incidental cancers on imaging (2.2 vs. 1.8 cm, $p = 0.02$). Incidental cancers on imaging were less likely to have lateral compartment nodal metastases (7 vs. 13 %, $p < 0.001$).

CONCLUSIONS:
Thyroid cancer diagnoses have increased at our institution, but the proportion of incidental cancers identified on imaging relative to clinical cancers has been stable over a decade and is not the sole explanation for the observed increase in thyroid cancer diagnoses. Incidental cancers on imaging are smaller in size and less likely to have lateral compartment nodal metastases than clinical cancers.

PMID: 24357246

53. World J Surg. 2013 Dec 20. [Epub ahead of print] **IF:2.47**

Role of Preoperative Basal Calcitonin Levels in the Timing of Prophylactic Thyroidectomy in Patients With Germline RET Mutations.

Lifante JC, Blanchard C, Mirallié E, David A, Peix JL.
Author information

Abstract

BACKGROUND:
The American Thyroid Association (ATA) published recommendations for the timing of prophylactic surgery for medullary thyroidcarcinoma based on the specific mutation, patient age, family history, and serum calcitonin levels. The aim of this study was to assess the role of preoperative basal calcitonin (prebCt) levels in predicting the presence of medullary carcinoma of the thyroid in patients with RET mutations.

METHODS:
We conducted a retrospective study in two endocrine surgery departments. Between 1986 and 2012, a total of 32 patients with RET mutations underwent prophylactic thyroidectomy. The patients were stratified into four ATA risk levels: A, B, C, and D.

RESULTS:
All of the patients were biologically cured. Microcarcinoma was observed in the final pathology report for four of the 20 patients with normal prebCt (25 %) and for nine of the 12 patients with elevated prebCt (75 %). In the level A group, four patients with normal prebCt and one patient with elevated prebCt presented with microcarcinoma. In the level C group, one patient with normal prebCt and six of the seven patients with elevated prebCt (86 %) presented with microcarcinoma.

CONCLUSIONS:
PrebCt can predict the presence of microcarcinoma according to surgical pathological analysis. Patients with microcarcinoma can be biochemically and clinically cured using prophylactic thyroidectomy.

PMID: 24357249

54. World J Surg. 2013 Dec 12. [Epub ahead of print] **IF:2.47**

Candidates for Limited Lateral Neck Dissection among Patients with Metastatic Papillary Thyroid Carcinoma.

Kang BC, Roh JL, Lee JH, Cho KJ, Gong G, Choi SH, Nam SY, Kim SY.
Author information

Abstract

BACKGROUND:
Papillary thyroid carcinoma (PTC) is associated with an excellent prognosis but frequently spreads to regional lymph nodes. The extent of neck dissection, particularly routine level II or V lymphadenectomy, is still controversial as it may lead to spinal accessory nerve injury and associated postoperative morbidities. We assessed the diagnostic value of preoperative ultrasonography (US) plus computed tomography (CT) for detecting metastatic lymph nodes and for identifying predictors of level II or V metastasis in patients with PTC.

METHODS:
The results of US and CT were compared with histopathologic findings at various neck levels in 209 previously untreated PTC patients with lateral cervical nodal metastases who underwent total thyroidectomy with central and lateral neck dissection. Clinicopathologic predictors for level II or V metastases were identified.

RESULTS:
Pathologic metastases to level II and V were observed in 53.6 and 25.4 % of patients, respectively. Occult metastases were found in 34.5 and 16.8 %, respectively. The sensitivities of US plus CT for levels II and V were 64.6 and 50.9 %, respectively. Image-based, isolated lateral level IV involvement and macroscopic extranodal extension were independently associated with level II metastasis or either level II or V metastasis ($p < 0.01$). Macroscopic extranodal extension was also independently associated with level V metastasis ($p = 0.001$).

CONCLUSIONS:
Patients with image-based, isolated lateral level IV involvement and no macroscopic extranodal extension are potential candidates for limited level III-IV dissection or prophylactic level II lymphadenectomy omission. Level V lymphadenectomy may be omitted in patients without macroscopic extranodal extension.

PMID: 24337241

55. World J Surg. 2013 Dec 4. [Epub ahead of print] **IF:2.47**

Lobectomy and Prophylactic Central Neck Dissection for Papillary Thyroid Microcarcinoma: Do Involved Lymph Nodes Mandate Completion Thyroidectomy?

Lee CR, Son H, Lee S, Kang SW, Jeong JJ, Nam KH, Chung WY, Park CS.
Author information

Abstract

BACKGROUND:
The present study was designed to investigate the necessity of completion thyroidectomy for patients who underwent thyroidlobectomy for low-risk papillary thyroid microcarcinoma (PTMC) that was later pathologically diagnosed as central lymph node (CLN) metastasis.

METHODS:
Between 1986 and 2001, we assessed 551 patients who underwent thyroidectomy with prophylactic ipsilateral central compartment neck dissection, and 409 patients were followed-up completely. Thyroid lobectomy were performed in 281 and 128 patients, respectively. The patients were

divided into two groups according to CLN metastasis. Clinicopathological profiles and follow-up details were investigated by retrospective chart review.

RESULTS:
The CLN-positive and -negative groups were comprised of 43 (15.2 %) and 238 patients (84.8 %), respectively. The mean ages of the two groups were not significantly different ($p > 0.05$). The mean tumor size of the CLN-positive group (6.8 mm) was significantly larger than that of the CLN-negative group (5.6 mm; $p < 0.05$). Microscopic capsular invasion was significantly higher in the CLN-positive group (51.2 vs. 23.9 %; $p < 0.05$). Overall, 21 patients (7.4 %, 21/281) experienced recurrence. Among these, 2 (4.7 %, 2/43) and 19 (8.0 %, 19/238) were in the CLN-positive and -negative groups, respectively. There was no significant correlation between CLN metastasis and tumor recurrence.

CONCLUSIONS:
Postoperative recurrence was lower in the CLN-positive group, and there was no significant correlation between CLN metastasis and tumor recurrence. Our results suggest that it is not necessary to perform completion thyroidectomy for PTMC patients who have undergone thyroidlobectomy and who have been pathologically diagnosed with CLN metastasis.

PMID: 24305923

56. World J Surg. 2013 Dec 4. [Epub ahead of print] **IF:2.47**

Reoperative Experience with Papillary Thyroid Cancer.

Onkendi EO, McKenzie TJ, Richards ML, Farley DR, Thompson GB, Kasperbauer JL, Hay ID, Grant CS.
Author information

Abstract

BACKGROUND:
Intense postoperative monitoring has resulted in increasing detection of patients with recurrent papillary thyroid cancer (PTC). Our goals included quantifying successful reoperation, and analyzing surgical complications and reasons for relapse.

METHODS:
From 1999 to 2008, a total of 410 patients underwent reoperation for PTC relapse. We analyzed post-reoperative disease outcomes, reasons for relapse, and complications.

RESULTS:
Bilateral reoperative thyroidectomy was performed in 13 (3 %) patients; lobectomy, 34 (8 %); central neck (VI) soft tissue local recurrence excision, 47 (11.5 %); bilateral VI node dissection, 107 (26 %); unilateral VI dissection, 112 (27 %); levels II-V dissection, 93 (23 %); levels III-V, 86 (21 %); lateral single- or two-compartment dissection, 51 (12 %); and node picking, 20 (5 %) of level VI and 53 (13 %) lateral neck. Complications occurred in 6 %; including hypoparathyroidism, 3 %; unintentional recurrent laryngeal nerve (RLN) paralysis, 3 %; phrenic nerve injury, 0.5 %; spinal accessory nerve injury, 0.5 %; and chyle leak in 1.6 %. Of 380 (93 %) patients with follow-up (mean 5.2 years); 274 (72 %) patients are alive with no structural evidence of disease, 38 % developed disease relapse (mean 2.1 years), 42 (11 %) died from PTC, and 55 (14 %) are alive with disease. The reason for relapse was a false negative pre-reoperative ultrasound (US) in 18 (5 %), nodal recurrence in the operative field in 37 (10 %), a combination of these two reasons in 10 (3 %), and disease virulence (local or systemic recurrence) in 81 (21 %).

CONCLUSIONS:
Although 72 % of patients were rendered structurally disease free after reoperation, nearly 40 % suffered additional relapse. Improved surgical technique or preoperative localization might positively affect 15-20 %; at least 20 % reflect the biologic aggressiveness of the disease.

PMID: 24305931

57. Eur J Radiol. 2013 Nov;82(11):1899-903. doi: 10.1016/j.ejrad.2013.07.002. Epub 2013 Aug 12.

IF:2.46

Size discrepancy between sonographic and pathological evaluation of solitary papillary thyroid carcinoma.

Bachar G, Buda I, Cohen M, Hadar T, Hilly O, Schwartz N, Shpitzer T, Segal K.
Author information

Abstract

BACKGROUND:
Sonographic size of suspicious thyroid lesions is an essential parameter in the evaluation of thyroid nodules, determining the need for needle biopsy and has impact on the extent of surgery. Limited data is available on the correlation between the size of the thyroid nodule on sonography and the actual size measured during histological examination. The aim of the present study was to compare these two modalities and to discuss the potential clinical implications of the findings in the study population.

METHODS:
The database of Rabin Medical Center was reviewed for all patients with histologically proven papillary carcinoma of the thyroid treated bythyroid surgery between 2005 and 2010.

RESULTS:
292 patients with papillary thyroid carcinoma were included. The mean sonographic size of the nodule was 2.19 ± 1.15 cm. The mean pathological diameter was 1.69 ± 1.09 cm. Discrepancies between tumor histological diameter and the sonographically measurement were more prominent in tumors larger than 1.5 cm. Nonetheless, 18.8% of thyroid nodules that were measured by US as larger than 1cm, were found to be smaller than 1cm on final pathology. Similarly, 7.2% of nodules evaluated by sonography were determined as being larger than 4 cm, while their definitive size was smaller than 4 cm.

CONCLUSIONS:
We noted a significant discrepancy between the preoperative sonographic and the pathologic size measurements for papillarythyroid carcinoma. The sonographic evaluation misclassifies both patients with small and large thyroid tumors, and consequently exposes them to unnecessary workup and more extensive operation. This discrepancy between the ultrasound findings and actual tumor size should be taken into account in clinical practice and help guide the evaluation and treatment of patients with thyroid nodules.

KEYWORDS:

Fine needle aspiration, Papillary carcinoma, Pathology, Size, Sonography, Thyroid

PMID: 23948454 http://dx.doi.org/10.1016/j.ejrad.2013.07.002

58. Horm Metab Res. 2013 Dec 19. [Epub ahead of print] **IF:2.40**

Encapsulation Status of Papillary Thyroid Microcarcinomas is Associated with the Risk of Lymph Node Metastases and Tumor Multifocality.

Cupisti K[1], Lehwald N[1], Anlauf M[2], Riemer J[2], Werner TA[1], Krieg A[1], Witte J[1], Chanab A[1], Baldus SE[2], Krausch M[1], Raffel A[1], Herdter C[1], Schott M[3], Knoefel WT[1].
Author information

Abstract

The management of papillary microcarcinoma (PMC) of the thyroid is controversial, especially after partial thyroid resection for benign thyroid disease. In order to detect prognostic factors for PMC, we

analyzed 116 patients with PMC for encapsulation status and lymph node metastases. Between 10/1992 and 12/2010, 116 patients with PMC have been operated in our department (87 females, 29 males, median age 49 years). Eighty per cent of PMCs were diagnosed postoperatively. Seventy-six patients (66%) received a more extended resection with either thyroidectomy, near total thyroidectomy, or Dunhill operation either primarily or after completion operation, whereas 40 patients (34%) had only partial resection. Fifty patients (43%) received radioiodine (RIA) ablation. Lymph node metastases were found in 21 patients (18%). Univariate analysis showed four risk factors to be significantly associated with the risk of lymph node metastasis ($p<0.05$): male gender, younger age, age group<50 years and nonencapsulation of the tumor. Multivariate analysis demonstrated statistical significance for gender and tumor capsulation status. The tumor capsulation status also correlated with tumor multifocality. Our data show that the risk of lymph node metastases is significantly higher in partially or nonencapsulated PMC than in encapsulated specimens. We therefore suggest that the WHO classification should be extended to a compulsory notification of the encapsulation status in PMC.

PMID: 24356791

59. Am J Surg. 2013 Oct;206(4):586-93. doi: 10.1016/j.amjsurg.2013.02.008. Epub 2013 Jun 19.

IF:2.39

Risk factors contributing to the difference in prognosis for papillary versus micropapillary thyroid carcinoma.

Karatzas T, Vasileiadis I, Kapetanakis S, Karakostas E, Chrousos G, Kouraklis G.
Author information

Abstract

BACKGROUND:
The aggressiveness of papillary thyroid carcinoma (PTC) was evaluated by comparing conventional PTC with papillary thyroid microcarcinoma (PTMC). Risk factors associated with differences in clinical and pathologic features were analyzed to provide appropriate surgical management.

METHODS:
A total of 539 patients with papillary carcinoma who underwent total thyroidectomy were retrospectively reviewed. The median follow-up period was 32 months.

RESULTS:
Of 539 patients, 311 (57.7%) had PTMC, and 228 (42.3%) had conventional PTC. No differences between patients with PTMC and those with PTC were observed in age, gender, and multifocality. PTMC was associated with less frequent bilaterality ($P = .002$), lymph node metastasis ($P < .001$), thyroid capsule invasion ($P < .001$), and disease recurrence ($P < .001$), and a higher rate of incidental diagnosis ($P = .001$). There was no statistically significant difference between the prevalence of lymph node metastasis at diagnosis and disease recurrence rate between nonincidental PTMC and conventional PTC ($P > .05$).

CONCLUSIONS:
Incidental PTMC had significantly fewer aggressive tumor features. Nonincidental PTMC presented with aggressive characteristics similar to those of conventional PTC and should be treated likewise. The authors suggest routine total thyroidectomy followed by an adequate exploration of the central neck compartment as a safe treatment.

KEYWORDS:

Papillary thyroid carcinoma, Papillary thyroid microcarcinoma, Prognosis, Risk factors

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60. Endocrine. 2013 Dec 24. [Epub ahead of print] **IF:2.24**

Can increased tumoral vascularity be a quantitative predicting factor of lymph node metastasis in papillary thyroidmicrocarcinoma?

Shin HJ, Kim EK, Moon HJ, Yoon JH, Han KH, Kwak JY.
Author information

Abstract

The aim of the present study was to evaluate the clinical implications of the vascular index (VI) as a predicting factor for central and lateral lymph node metastasis (LNM) in patients with papillary thyroid microcarcinoma (PTMC). From January 2011 to October 2011, 588 patients (495 females, 93 males) who were diagnosed with PTMC were included. Clinicopathologic characteristics of patients and ultrasound (US) features of the lesions including VI were evaluated retrospectively. The VI was measured with QLAB 7.0 quantification software using preoperative Doppler US images. Univariate and multivariate analysis were used to assess predictive factors of LNM. From 588 patients, 140 patients (23.8 %) had central LNM and 26 patients (4.4 %) had lateral LNM on pathologic results. The presence of lateral LNM [odds ratio (OR) 5.46; 95 % confidence interval (CI) = 2.19-13.64], bilaterality (OR 2.16; 95 % CI 1.17-4.01), and increased tumor size (OR 1.15; 95 % CI 1.04-1.28) were significant independent factors for predicting central LNM. The presence of central LNM (OR 5.58; 95 % CI 2.22-14.04), upper third location of malignancy (OR 2.50; 95 % CI 1.01-6.21), and tumor size (OR 1.34; 95 % CI 1.03-1.73) were significant independent factors for predicting lateral LNM. However, the VI was not a significant predicting factor for both central and lateral LNM. Therefore, the VI of PTMC may not be useful for predicting central and lateral LNM in patients with PTMC.

PMID: 24366642

61. Endocrine. 2013 Nov 28. [Epub ahead of print] **IF:2.24**

Biochemical persistence in thyroid cancer: is there anything to worry about?

Fabián P, Erika A, Hernán T, Fernanda B, Carolina U, Graciela C.
Author information

Abstract

To evaluate the outcome of differentiated thyroid cancer (DTC) patients with biochemical persistence of disease (BP) after initial treatment (total thyroidectomy with or without lymph node dissection (LND) and thyroid remnant ablation). BP was defined as suppressed thyroglobulin (Tg) levels <1 ng/ml and rhTSH-stimulated thyroglobulin (St-Tg) >1ng/ml, with no evidence of structural disease. Structural persistence/recurrence (SPR): clinically identifiable disease. We reviewed 278 records of DTC patients. Tg-Ab positive patients (n = 73) were excluded and 32 were included in the analysis (median age 45 years, range 18-77 years); risk of recurrence ATA was: low in 38 %, Intermediate in 47 %, and high in 15 % of patients. All subjects had Tg levels <1 ng/ml under thyroid hormone therapy. Patients were divided into three groups: Group 1: St-Tg 1-2 ng/ml, n = 6; Group 2: St-Tg 2-10 ng/ml, n = 17; Group 3: St-Tg > 10 ng/ml, n = 9. In 5/32 (16 %) patients, SPR was observed after a median follow-up of 6 years (range 2-23 years). In Group 1: all patients were considered with no evidence of disease after a median follow-up of 2 years (range 1-2.5 years). In Group 2: 13/17 (76.5 %) patients continued with only a BP after a median follow-up of 4 years (range 2-10 years) and 4/17 (23.5 %) patients with intermediate risk of recurrence had a structural persistence (lymph nodes metastasis) diagnosed between 1 and 3.5 years after initial assessment. Following LND, all of them remained with BP after a median of 2 years (range 1.5-5 years). In Group 3: 8/9 (89 %) patients had BP after a median follow-up of 7 years (range 2-23 years) and 1/9 (11 %) had a SPR diagnosed 28 months after initial assessment, LND was indicated but he continued with BP,

5 years after the second surgery. Most patients with DTC and BP present an indolent course of the disease. In these patients the diagnosis of the structural recurrence did not change the outcome because all of them continued with BP.

PMID: 24287799

62. Endocrine. 2013 Oct;44(2):426-33. doi: 10.1007/s12020-013-9935-9. Epub 2013 Mar 28. **IF:2.24**

Should patients with remnants from thyroid microcarcinoma really not be treated with iodine-131 ablation?

Gallicchio R, Giacomobono S, Capacchione D, Nardelli A, Barbato F, Nappi A, Pellegrino T, Storto G.
Author information

Abstract
Remnant ablation by radioiodine is generally not recommended in patients presenting uni- or multifocal cancer <1 cm, in the absence of other higher risk features. We retrospectively studied low-risk patients (pts) with differentiated thyroid cancer (DTC) less than 1 cm recruited for radioiodine therapy (RAI). Methods: 91 pts (79 women, age 48.4 ± 12 yrs) with DTC were enrolled for RAI. Patients underwent pre-therapy ultrasonography (US), those with suspected/ambiguous lymph-nodes were excluded and proposed for cytology. Treated pts underwent post-therapeutic whole body scan (WBSt) completed by neck/chest SPECT/CT, when necessary (e.g. evidence of uptake outside of thyroid bed). A target lesion on SPECT/CT was defined as an identifiable lymph-nodal site presenting a matched significant iodine uptake. The patients were followed up for 14 ± 2 months thereafter. Results: All pts/cancers were pT1. The mean histological diameter was 0.68 ± 0.23 cm. Six patients were excluded because of suspected nodal involvement at US. Thirty (35 %) out of 85 pts had suspicious WBSt as per lymph-nodal involvement which was confirmed at the subsequent SPECT/CT acquisition in most part of pts (26/30; 86 %). Overall detected target lesions was 34, and nine (26 %) had interim positive fine needle cytology. Conclusions: a significant part of low risk DTC patients, for whom RAI is not recommended, presents an incidental suspicion of lymph-nodal involvement at WBSt confirmed by subsequent SPECT/CT. Such setting would have not been treated by I-131.

Comment in

- Should patients with papillary microcarcinoma undergo radioiodine ablation? [Endocrine. 2013]

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63. Langenbecks Arch Surg. 2013 Nov 9. [Epub ahead of print] **IF:2.21**

Nodal recurrence in the lateral neck after total thyroidectomy with prophylactic central neck dissection for papillary thyroid cancer.

Barczyński M, Konturek A, Stopa M, Nowak W.
Author information

Abstract
PURPOSE:
The aim of this study was to examine risk factors for nodal recurrence in the lateral neck (NRLN) in patients with papillary thyroid cancer (PTC) who underwent total thyroidectomy with prophylactic central neck dissection (TT + pCND).

METHODS:
This was a retrospective cohort study of patients with PTC who underwent TT + pCND. Data of all patients treated over a 10-year period (between 1998 and 2007) were analysed. The primary outcome was prevalence of NRLN within the 5-year follow-up after initial surgery. Predictors of NRLN were determined in the univariable and multivariable analysis.

RESULTS:
Of 760 patients with PTC included in this study, 44 (6.0 %) developed NRLN. In the univariable analysis, the following factors were identified to be associated with an increased risk of NRLN: positive/negative lymph node ratio ≥0.3 (odds ratio (OR) 14.50, 95 % confidence interval (CI) 7.21 to 29.13; p < 0.001), central lymph node metastases (OR 7.47, 95 % CI 3.63 to 15.38; p < 0.001), number of level VI lymph nodes <6 in the specimen (OR 2.88, 95 % CI 1.21 to 6.83; p = 0.016), extension through the thyroid capsule (OR 2.55, 95 % CI 1.21 to 5.37; p = 0.013), localization of the tumour within the upper third of the thyroid lobe (OR 2.35, 95 % CI 1.27 to 4.34; p = 0.006) and multifocal lesions (OR 1.85, 95 % CI 1.01 to 3.41; p = 0.048).

CONCLUSIONS:
Central lymph node metastases together with positive to negative lymph node ratio ≥0.3 represent the strongest independent prognostic factors for the PTC recurrence in the lateral neck.

PMID: 24213969

64. Endocr Pract. 2013 Nov-Dec;19(6):1015-20. doi: 10.4158/EP12334.OR. **IF:2.12**

Pre-operative ultrasound identification of thyroiditis helps predict the need for thyroid hormone replacement afterthyroid lobectomy.

Morris LF, Iupe IM, Edeiken-Monroe BS, Warneke CL, Hansen MO, Evans DB, Lee JE, Grubbs EG, Perrier ND.
Author information

Abstract

Objective: To evaluate whether pre-operative thyroiditis identified by ultrasound (US) could help predict the need for thyroid hormone replacement (THR) following thyroid lobectomy.Methods: Data from patients who underwent thyroid lobectomy in 2006-2011, were not taking THR pre-operatively, and had ≥1 month of follow-up were reviewed retrospectively. THR was prescribed for relatively elevated thyroid-stimulating hormone (TSH) and hypothyroid symptoms. The Kaplan-Meier method was used to estimate the percentage of patients who required THR at 6, 12, 18, and 24 months postoperatively, and Cox proportional hazards regression models were used to evaluate prognostic factors for requiring post-thyroid lobectomy THR.Results: During follow-up, 45 of 98 patients required THR. Median follow-up among patients not requiring THR was 11.6 months (range, 1.2 to 51.3 months). Six months after thyroid lobectomy, 22% of patients were taking THR (95% confidence interval [CI], 15-32%); the proportion increased to 46% at 12 months (95% CI, 36-57%) and 55% at 18 months (95% CI, 43-67%). On univariate analysis, significant prognostic factors for postoperative THR included a pre-operative TSH level >2.5 μ international units [IU]/mL (hazard ratio [HR], 2.8; 95% CI, 1.4-5.5; P = .004) and pathology-identified thyroiditis (HR, 2.4; 95% CI, 1.3-4.3; P = .005). Patients with both pre-operative TSH >2.5 μIU/mL and US-identified thyroiditis had a 5.8-fold increased risk of requiring postoperative THR (95% CI, 2.4-13.9; P<.0001).Conclusion: A pre-operative TSH level >2.5 μIU/mL significantly increases the risk of requiring THR after thyroid lobectomy. Thyroiditis can add to that prediction and guide pre-operative patient counseling and surgical decision making. US-identified thyroiditis should be reported and post-thyroid lobectomy patients followed long-term (≥18 months).

PMID: 24013973 http://dx.doi.org/10.4158/EP12334

65. J Surg Res. 2013 Nov;185(1):217-24. doi: 10.1016/j.jss.2013.05.003. Epub 2013 May 23. **IF:2.08**

Epidermal growth factor receptor overexpression is a marker for adverse pathologic features in papillary thyroid carcinoma.

Fisher KE, Jani JC, Fisher SB, Foulks C, Hill CE, Weber CJ, Cohen C, Sharma J.
Author information

Abstract

BACKGROUND:
Epidermal growth factor receptor (EGFR) overexpression (EGFR-H) is implicated in thyroid carcinoma disease progression; however, the clinicopathologic significance of EGFR-H in tumors that harbor EGFR and/or v-Raf murine sarcoma viral oncogene homolog B1 (BRAF)(V600E) mutations is unknown.

METHODS:
Tissue microarrays from 81 patients who had undergone thyroidectomy for carcinoma from 2002-2011 were scored for EGFR expression using immunohistochemistry. Somatic mutations in EGFR exons 19 and 21 and BRAF were analyzed. Correlations between the EGFR immunohistochemistry, EGFR, and BRAF(V600E) mutations and the clinicopathologic features were assessed.

RESULTS:
EGFR-H was detected in 39.5% of carcinomas (n = 32) from patients with papillary (PTC, 46.2%, n = 18), follicular (29.6%, n = 8), and anaplastic (100.0%, n = 6) but not medullary (0.0%, n = 9) thyroid carcinoma. BRAF(V600E) mutations were identified in 22.2% of the carcinoma cases (n = 18, 15 PTCs and 3 anaplastic thyroid carcinomas). No somatic EGFR mutations were detected in any subtype. On PTC univariate analysis, EGFR-H correlated with increasing stage, extrathyroid extension, tumor capsule invasion, adverse pathologic features (any demonstration of extrathyroid extension, tumor capsule invasion, lymphovascular invasion, lymph node metastasis, and/or distant metastasis), and BRAF(V600E) mutations. On multivariate analysis, EGFR-H correlated with BRAF(V600E) mutations. In BRAF wild-type PTCs, the correlation between EGFR-H and adverse pathologic features approached statistical significance (P = 0.065).

CONCLUSIONS:
EGFR-H could be an important biomarker for aggressive PTCs, particularly in BRAF wild-type PTCs. Despite EGFR-H in PTC, follicular thyroid carcinoma, and anaplastic thyroid carcinoma by immunohistochemistry, somatic EGFR mutations were absent. Therefore, future investigations of EGFR should consider histologic and immunohistochemical methods, in addition to molecular profiling of thyroid carcinomas. This multimodal approach is particularly important for future clinical trials testing anti-EGFR therapy.

KEYWORDS:

BRAF, Carcinoma, EGFR, Immunohistochemistry, Molecular, Papillary, Thyroid

PMID: 23746767 http://dx.doi.org/10.1016/j.jss.2013.05.003

66. J Surg Res. 2013 Oct;184(2):746-50. doi: 10.1016/j.jss.2013.02.018. Epub 2013 Mar 4. **IF:2.08**

Nondiagnostic fine-needle aspirations of the thyroid: is the risk of malignancy higher?

Coorough N, Hudak K, Jaume JC, Buehler D, Selvaggi S, Rivas J, Sippel R, Chen H.
Author information

Abstract

BACKGROUND:
Nondiagnostic fine-needle aspirations (FNAs) pose a dilemma in the management of patients with thyroid nodules. In most cases, these patients undergo either repeat FNA or surgical resection. However, a significant number of patients will only be observed, assuming that the risk of malignancy is low. Therefore, the purpose of this study was to determine whether the risk of malignancy is higher in patients with thyroid nodules and nondiagnostic FNAs.

METHODS:
We reviewed reports from 4286 consecutive FNA biopsies performed on patients with thyroid nodules at our institution between 2002 and 2010. We divided FNAs into two categories: diagnostic and nondiagnostic. We collected demographic, follow-up, and pathology data from both groups and then analyzed them with analysis of variance and chi-square tests.

RESULTS:
Of the 4286 FNAs, 259 were classified as nondiagnostic (6%). We saw no significant differences in age or gender between patients with diagnostic versus nondiagnostic FNAs. Of the patients with nondiagnostic FNAs, 62 underwent diagnostic thyroidectomy (24%), 74 had a repeat FNA (29%), and 123 had observation only (47%); thus, 136 patients had a cytologic or pathologic diagnosis. Patients with nondiagnostic FNAs had a significantly higher rate of all types of thyroid cancer, compared with those with diagnostic FNAs (12% versus 5%, respectively; $P < 0.001$). Impressively, the chance of papillary thyroid cancer was twofold higher in patients with nondiagnostic FNAs.

CONCLUSIONS:
The percentage of nondiagnostic FNA at our institution during this period (6%) was relatively low. However, the incidence of malignancy in these patients was significantly higher. Therefore, we recommend that patients with thyroid nodules and nondiagnostic FNAs undergo either repeat biopsy or diagnostic thyroidectomy.

KEYWORDS:

Fine-needle aspiration, Thyroid

PMID: 23490138 http://dx.doi.org/10.1016/j.jss.2013.02.018

67. BMC Surg. 2013 Oct 8;13 Suppl 2:S3. doi: 10.1186/1471-2482-13-S2-S3. Epub 2013 Oct 8.

IF:2.06

Predictive value of nodal metastases on local recurrence in the management of differentiated thyroid cancer. Retrospective clinical study.

Conzo G, Docimo G, Pasquali D, Mauriello C, Gambardella C, Esposito D, Tartaglia E, Della Pietra C, Napolitano S, Rizzuto A, Santini L.

Abstract

BACKGROUND:

The significance of nodal metastases, very common in papillary thyroid cancer, and the role of lymph node dissection in the neoplasm management, are still controversial. The impact of lymph node involvement on local recurrence and long-term survival remains subject of active research. With the aim to better analyze the predictive value of lymph node involvement on recurrence and survival, we investigated the clinico-pathological patterns of local relapse following total thyroidectomy associated with lymph node dissection, for clinical nodal metastases papillarythyroid cancer, in order to identify the preferred surgical treatment.

METHODS:

Clinical records, between January 2000 and December 2006, of 69 patients undergoing total thyroidectomy associated with selective lymph node dissection for clinical nodal metastases papillary thyroid cancer, were retrospectively evaluated. Radioiodine ablation, followed by ThyroidStimulating Hormone suppression therapy was recommended in every case. In patients with loco regional lymph nodal recurrence, a repeated lymph node dissection was carried out. The data were compared with those following total thyroidectomy not associated with lymph node dissection in 210 papillary thyroid cancer patients without lymph node involvement, at preoperative ultrasonography and intra operative inspection.

RESULTS:

Incidence of permanent hypoparathyroidism (iPTH < 10 pg/ml) and permanent monolateral vocal fold paralysis were respectively 1.4 % (1/69) and 1.4% (1/69), similar to those reported after total thyroidectomy "alone". The rate of loco regional recurrence, with positive cervical lymph nodes, following 8 year follow-up, was 34.7% (24/69), higher than that reported in patients without nodal metastases (4.2%). A repeated lymph node dissection was carried out without significant complications.

CONCLUSIONS:

Nodal metastases are a predictor of local recurrence, and a higher rate of lymph node involvement is expected after therapeutic lymph node dissection associated with total thyroidectomy. The prognostic significance of nodal metastases on long-term survival remains unclear, and more prospective randomized trials are requested to better evaluate the benefits of different therapeutic approaches.

PMID: 24267409 http://dx.doi.org/10.1186/1471-2482-13-S2-S3

68. BMC Surg. 2013 Oct 8;13 Suppl 2:S37. doi: 10.1186/1471-2482-13-S2-S37. Epub 2013 Oct 8.

IF:2.06

Diagnostic utility of BRAFV600E mutation testing in thyroid nodules in elderly patients.

Guerra A, Di Crescenzo V, Garzi A, Cinelli M, Carlomagno C, Pepe S, Zeppa P, Tonacchera M, Vitale M.

Abstract

BACKGROUND:

Thyroid cancer is a rare disease characterized by the subtle appearance of a nodule. Fine-needle cytology (FNC) is the first diagnostic procedure used to distinguish a benign from a malignant nodule. However, FNC yields inconclusive results in about 20% of cases. BRAFV600E mutation is the most frequent genetic

alteration in papillary thyroid carcinoma (PTC); its high prevalence makes this oncogene a useful marker to refine inconclusive FNC results. However, the prevalence of the BRAFV600E mutation depends on detection methods, geographical factors, and age. The aim of this study is to determine the prevalence of BRAFV600E mutation and its utility as a diagnostic tool in elderly subjects.

METHODS:
FNC from 92 PTC patients were subjected to the analysis of BRAF mutation by pyrosequencing and direct sequencing; age-dependent prevalence was also determined.

RESULTS:
BRAF mutation analysis was successful in all FNC specimens. BRAFV600E was documented in 62 (67.4%) and in 58 (63.0%) PTCs by pyrosequencing and direct sequencing, respectively. BRAFV600E prevalence did not correlate with patient's age at diagnosis. Twenty out of 32 PTCs (62.5%) were correctly diagnosed by BRAF mutation analysis in inconclusive FNC results.

CONCLUSIONS:
Detection of BRAFV600E in cytology specimens by pyrosequencing is a useful diagnostic adjunctive tool in the evaluation of thyroidnodules also in elderly subjects.

PMID: 24267957 http://dx.doi.org/10.1186/1471-2482-13-S2-S37

69. Cytopathology. 2013 Dec;24(6):385-90. doi: 10.1111/cyt.12021. Epub 2012 Oct 18. **IF:2.05**

Follow-up of atypia and follicular lesions of undetermined significance in thyroid fine needle aspiration cytology.

Dincer N, Balci S, Yazgan A, Guney G, Ersoy R, Cakir B, Guler G.
Author information

Abstract

OBJECTIVE:
To report our experience of atypia of undetermined significance (AUS)/follicular lesion of undetermined significance (FLUS) rate and outcome.

METHODS:
Among 7658 patients with 19 569 nodules, 524 (2.7%) nodules were diagnosed as AUS/FLUS on fine needle aspiration (FNA). After exclusion of patients with simultaneous nodules that were suspicious for follicular neoplasm or malignancy or that were malignant, 368 (4.8%) patients were diagnosed as AUS/FLUS. The outcome of 146 patients who had undergone surgery or repeated fine needle aspirate at the time of preparation of this study was evaluated. The original FNAs were matched to repeated FNAs and thyroidectomy or diagnostic lobectomy specimens.

RESULTS:
Seventy-two (19.6%) of the 368 patients had directly undergone surgery, either a lobectomy or a thyroidectomy: of these, 27 (37.5%) had neoplastic nodules (21 were malignant). Seventy-four (20.1%) of the 368 patients had repeat FNA. On second FNA, 47 of 74 (63.5%) were benign, three were suspicious for follicular neoplasm, one was malignant and 23 (31.1%) were non-diagnostic. Four patients had a third FNA: two were AUS/FLUS, one was malignant and one non-diagnostic. One patient had a fourth FNA, which was diagnosed as AUS/FLUS. Sixteen (21.6%) of 74 patients with repeat FNA had surgery: three of these had neoplastic nodules (two were malignant). Overall, 88 of the 368 (23.9%) patients had a thyroidectomy of which 30 (34.1%) were neoplastic and 23 (26.1%) malignant. The neoplastic rate for patients who were once diagnosed with AUS/FLUS was 8.2% and the malignancy rate 6.3%. The malignancy rate for patients on follow-up at the time we prepared the study was 15.7% (23/146); 222 remained on follow-up without surgery or repeat FNA or were managed elsewhere.

CONCLUSIONS:

Although in this category repeat FNA is expected rather than excision, we suggest evaluation of all AUS/FLUS patients in multidisciplinary meetings to decide management and recommend follow-up of all patients with this diagnosis.

KEYWORDS:

AUS/FLUS, Bethesda classification, fine needle aspiration cytology, follow-up, thyroid

PMID: 23078633 http://dx.doi.org/10.1111/cyt.12021

70. Endocr Pathol. 2013 Nov 27. [Epub ahead of print] **IF:1.77**

Molecular Features of Follicular Variant Papillary Carcinoma of Thyroid: Comparison of Areas With or Without Classical Nuclear Features.

Guney G, Tezel GG, Kosemehmetoglu K, Yilmaz E, Balci S, Ersoy R, Cakir B, Guler G.
Author information

Abstract

We aimed to compare the genetic background of different areas in follicular variant papillary thyroid carcinomas (FVPTC) with or without classical nuclear changes. Sixteen cases of FVPTC were included in our study. All tumors were well demarcated from surrounding thyroid tissue and had both areas with nuclear features (WNF) and areas without nuclear features (WONF) of papillary carcinoma. DNA is obtained by laser microdissection from WNF and WONF areas of each case. Point mutations for NRAS codon 61, HRAS codon 61, and BRAF were investigated by direct sequencing. In 11 cases, reverse transcription PCR was performed for the presence of PAX8-PPARγ and RET/PTC1-3 gene rearrangements. Point mutation for NRAS codon 61 was also studied in 15 colloidal nodules. Seven cases (44 %) showed at least one mutation; two cases (13 %) revealed the same mutation in both WNF and WONF areas, while in the rest only WNF areas were mutated. None of the studied 11 cases demonstrated RET/PTC1-3 gene rearrangement and in only one case PAX8-PPARγ gene rearrangement was found. Six cases (38 %) showed NRAS codon 61 mutation, involving only WNF areas in five cases and both WNF and WONF areas in one case. Neither HRAS codon 61 nor BRAF mutations were present. Fifteen colloidal nodules were also wild type for NRAS codon 61. Our findings suggest that NRAS codon 61 point mutations and PAX8-PPARγ gene rearrangement play a role in the FVPTC pathogenesis and may be established before the morphological/phenotypical features fully develop.

PMID: 24277231

71. Int J Clin Exp Med. 2013 Oct 25;6(10):922-9. **IF:1.73**

What do we leave behind after neartotal and subtotal thyroidectomy: just the tissue or the disease?

Karakoyun R, Bülbüller N, Koçak S, Habibi M, Gündüz U, Erol B, Oner O, Aslaner A, Sürer D, Ozdemir S, Gülkesen H.
Author information

Abstract

Selection of multinodular goiter (MNG) surgery procedure is stilll under discussion. Subtotal thyroidectomy (STT) and neartotal thyroidectomy (NTT) are preferred surgical procedures. However, it is uncertain whether the remnant tissue contains pathological findings or not after these procedures. We aimed to evaluate and comparison the pathologic findings in remnant tissue after NTT and STT. Thyroid tissue samples of 50 patients who underwent TT for MNG disease between January 2010 and August 2011 in our

clinic were evaluated. Before the dissection of the thyroid tissue subtotal and neartotal margins were marked in both right and left lobes. After the resection of the specimen, the tissue was excised from the subtotal and neartotal margin marked during the surgery. The pathologic findings of the main tissue, the residual subtotal and neartotal tissues were evaluated and compared. All patients were followed-up 1 year. 43 (86%) females and 7 (14%) males with an average age of 50.5 (23-77) were included in the study. Incidental papillary thyroid cancer was detected in 5 patients (10%). Pathologic findings were present in 31 patients (62%) of subtotal residual tissue and 28 of the patients (56%) of neartotal residual tissue. Papillary microcarcinoma was detected in 3 (9.7%) of subtotal residual tissues and 2 (7.1%) of neartotal residual tissues. There is no significant difference between subtotal and neartotal tissues in terms of existence of pathological findings ($p>0.05$). There is no significant difference between the neartotal and subtotal residual tissues contralateral of dominant nodule ($p>0.05$). 2 of the patients (4%) had temporary hypocalcemia, 1 patient (2%) had seroma and 1 patient (2%) had recurrent laryngeal nerve injury. There are high rates of microscopic pathological findings on residual tissues both after STT and NTT. The neartotal and subtotal residual tissues contralateral to the large nodule also had high levels of pathologic findings.

KEYWORDS:

Total thyroidectomy, multinodular goiter, neartotal thyroidectomy, residual tissue, subtotal thyroidectomy

PMID: 24260598

72. Med Oncol. 2014 Jan;31(1):814. doi: 10.1007/s12032-013-0814-2. Epub 2013 Dec 12. **IF:1.71**

The relationship between thyroid volume and malignant thyroid disease.

Duran AO, Anil C, Gursoy A, Nar A, Altundag O, Inanc M, Bozkurt O, Tutuncu NB.
Author information

Abstract

The present retrospective study aimed to investigate the relationship between thyroid volume and prevalence of thyroid cancer. We investigated the data of 3,850 patients who underwent fine-needle aspiration biopsy (FNAB). Biopsy results were evaluated as diagnostic or nondiagnostic, and diagnostic results were classified as benign, malignant, and indeterminate. We included 2,672 patients who underwent FNAB firstly in our hospital and evaluated as diagnostic biopsy except subgroup of indeterminate. We obtained cytologic data, levels of serum thyroid-stimulating hormone (TSH), and thyroid volumes of those patients retrospectively. Among 2,672 patients with thyroid nodule, 2,562 (95.9 %) patients had benign cytology and 110 (%4,1) patients had malignant cytology. There was no correlation between the malignancy and gender ($p = 0.935$), and patients with malignant cytology were younger (52 vs 59, $p < 0.001$). Also, TSH levels were higher in patients with malignant than benign cytology ($p = 0.017$). Median volume of right part, left part, and total thyroid for patients who had malignant cytology was significantly lower than patients who had benign cytology (8.3, 7.1, 15.9 vs 10.8 ml, 9.0 mml, 20.6 ml, respectively, $p \leq 0.001$ for all parameters). The results demonstrated that thyroid cancer prevalence was higher in patients with low thyroid volume. According to our results, thyroid volume should be considered as a risk factor for malignancy in the evaluation of thyroid nodules.

PMID: 24338169 http://dx.doi.org/10.1007/s12032-013-0814-2

73. World J Surg Oncol. 2013 Nov 25;11:304. doi: 10.1186/1477-7819-11-304. **IF:1.37**

Should level V be included in lateral neck dissection in treating papillary thyroid carcinoma?

Zhang XJ, Liu D, Xu DB, Mu YQ, Chen WK.
Author information

Abstract

BACKGROUND:
The study was designed to explore the regular patterns of level V lymph node metastasis (LNM) in papillary thyroid carcinoma (PTC), and to indicate whether level V should be included in the management of lateral neck dissection when treating PTC.

METHODS:
This retrospective study consisted of 330 patients diagnosed with PTC from January 1994 to July 2009 who underwent an operation that included therapeutic lateral neck dissection (levels II to V). The patterns of lateral neck LNM were analyzed and the relevant risk factors of level V LNM were analyzed with univariate and multivariate analysis, respectively.

RESULTS:
All the patients underwent lateral neck dissection at levels II to V. The predominant site of metastasis was level III (247/330 (74.8%)), followed by level IV (233/330 (70.6%)), and level II (215/330 (65.3%)). Simultaneous multilevel involvement (level II, III, and IV) of lymphatic metastases presented in 46.1% (152/330) of the cases. Level V showed 28.8% (95/330) of nodal metastasis. Multivariate analysis showed that level V LNM was significantly associated with location (whole thyroid), gross extrathyroidal extension and simultaneous multilevel involvement (level II, III and IV). ($P < 0.05$).

CONCLUSIONS:
Due to relatively high rate of level V involvement and its correlation with location (whole thyroid), gross extrathyroidal extension and multilevel involvement, we consider that it may be more rational to include level V in the therapeutic lateral neck dissection when treating PTC, especially for those who have any one of these three independent risk factors.

PMID: 24274694 http://dx.doi.org/10.1186/1477-7819-11-304

74. ANZ J Surg. 2013 Dec 3. doi: 10.1111/ans.12453. [Epub ahead of print] **IF:1.35**

Anti-thyroid antibodies as a predictor of thyroid cancer.

Wong SL, Grodski S, Yeung MJ, Serpell JW.
Author information

Abstract

BACKGROUND:
Recent literature has suggested an association between autoimmune thyroiditis and papillary thyroid cancer. The aims of this study were to evaluate if positive thyroid antibodies are associated with thyroid carcinoma and to examine the role of thyroid antibodies in the management of thyroid nodules.

METHODS:
This is a database study of all patients undergoing thyroidectomy with recorded preoperative thyroid antibodies (autoantibodies to thyroglobulin and/or thyroid peroxidase) levels from 2010 to 2012. We analysed preoperative thyroid antibody levels, fine needle aspiration cytology (FNAC) results, type of thyroid surgery and final histopathology.

RESULTS:

There were 960 patients who underwent thyroidectomy with recorded preoperative thyroid antibodies. Of 960 patients, 784 had preoperative FNAC of thyroid nodules. Final histopathology showed 758 benign and 202 malignant cases. As expected, there was a strong association between raised thyroid antibodies and lymphocytic thyroiditis on histology (P = 0.0001) (two-sided probability). Overall, positive thyroidantibodies were not found to be a predictor of thyroid carcinoma (P = 0.161) (two-sided probability). However, in patients with benign FNAC, positivethyroid antibodies increased the risk of thyroid malignancy (odds ratio 2.16; 95% confidence interval 1.11 to 4.21, P = 0.027) (two-sided probability).

CONCLUSION:
Patients with positive thyroid antibodies have a greater risk of malignancy in those with benign FNAC. We recommend routine thyroidantibody assessment in addition to FNAC as part of the assessment of thyroid nodules.

KEYWORDS:

anti-thyroid antibodies, autoimmune thyroiditis, fine needle aspirate cytology, thyroid cancer, thyroid nodule

PMID: 24299506 http://dx.doi.org/10.1111/ans.12453

75. Laryngoscope. 2013 Nov 7. doi: 10.1002/lary.24511. [Epub ahead of print] **IF:1.32**

Comparison of surgical completeness between robotic total thyroidectomy versus open thyroidectomy.

Tae K, Song CM, Ji YB, Kim KR, Kim JY, Choi YY.
Author information

Abstract

OBJECTIVES/HYPOTHESIS:
The aim of this study was to investigate the surgical completeness of robotic total thyroidectomy compared with conventional open thyroidectomy.

STUDY DESIGN:
Retrospective, case-control study.

METHODS:
We studied 245 patients with papillary thyroid carcinoma who underwent total thyroidectomy and postoperative radioactive iodine (RAI) ablation. Of these, 62 patients underwent robotic thyroidectomy by a gasless unilateral axillo-breast (GUAB) or axillary (GUA) approach, and 183 underwent conventional open thyroidectomy. We analyzed serum TSH-stimulated thyroglobulin (Tg) and RAI uptake at the time of RAI remnant ablation to compare surgical completeness in the two groups.

RESULTS:
Tumor characteristics and complications did not differ between the two groups except TNM stage. The mean TSH-stimulated Tg at the first RAI ablation was significantly higher in the robotic group (10.20 ± 9.98 ng/ml) than in the open group (3.85 ± 6.79 ng/ml) (P <0.001). In subgroup analysis of the robotic group by the period in which operations took place, TSH-stimulated Tg was significantly higher than in the open group in the first (13.28 ± 11.91 ng/ml) and second (10.45 ± 9.30 ng/ml) periods, but there was no significant difference in the third period (6.00 ± 6.26 ng/ml, P = 0.141). The RAI uptake rate at the first RAI ablation did not differ between the two groups, and TSH-stimulated Tg after RAI ablation was similar.

CONCLUSION:
The surgical completeness of robotic total thyroidectomy by a GUAB/GUB approach is comparable to that of open thyroidectomy, if performed by experienced robotic thyroid surgeons in properly selected patients.

LEVEL OF EVIDENCE:
3b. Laryngoscope, 2013.

KEYWORDS:

Robotic thyroidectomy, endoscopic thyroidectomy, gasless unilateral axillary approach, gasless unilateral axillo-breast approach, papillarythyroid carcinoma

PMID: 24338236 http://dx.doi.org/10.1002/lary.24511

76. Laryngoscope. 2013 Nov;123(11):2913-9. doi: 10.1002/lary.24018. Epub 2013 Apr 5. **IF:1.32**

Sex is not an independent risk factor for survival in differentiated thyroid cancer.

Oyer SL, Smith VA, Lentsch EJ.
Author information

Abstract

OBJECTIVES/HYPOTHESIS:
To determine the impact of sex on disease-specific survival (DSS) in differentiated thyroid cancer.

STUDY DESIGN:
Retrospective analysis of population database.

METHODS:
Adult patients with papillary thyroid carcinoma (PTC) or follicular thyroid carcinoma (FTC) were identified from the Surveillance, Epidemiology, and End Results Database between 1988 and 2003. Patients were grouped according to tumor type (PTC or FTC), with age, sex, tumor size, extension, and nodal or distant metastases recorded. The Kaplan-Meier method was used to compare DSS based on sex in each group.

RESULTS:
We identified 36,725 patients, of which 77% were female and 23% were male. PTC represented 91.3% of patients and FTC the remaining 8.7%. Males with PTC and FTC were diagnosed at an older age and were significantly more likely to present with advanced-stage disease. In patients ≥45 years old, DSS was similar in male and female patients; however, in patients <45 years old, DSS was significantly worse in males. When compared by stage, DSS was similar among male and female patients with stage II PTC; however, males with stage I PTC had a minimally reduced DSS. Stage-stratified analysis revealed no DSS difference between male and female patients with FTC.

CONCLUSIONS:
Male sex does not portray an independent survival risk in differentiated thyroid cancer when survival is compared by disease stage. Men present at a later age with more advanced disease, which may explain their poorer survival seen in some studies.

KEYWORDS:

Differentiated thyroid cancer, Epidemiology, Surveillance, and End Results database, sex, survival

PMID: 23564257 http://dx.doi.org/10.1002/lary.24018

77. Laryngoscope. 2013 Nov 7. doi: 10.1002/lary.24511. [Epub ahead of print] **IF:1.32**

Comparison of surgical completeness between robotic total thyroidectomy versus open thyroidectomy.

Tae K, Song CM, Ji YB, Kim KR, Kim JY, Choi YY.
Author information

Abstract

OBJECTIVES/HYPOTHESIS:
The aim of this study was to investigate the surgical completeness of robotic total thyroidectomy compared with conventional open thyroidectomy.

STUDY DESIGN:
Retrospective, case-control study.

METHODS:
We studied 245 patients with papillary thyroid carcinoma who underwent total thyroidectomy and postoperative radioactive iodine (RAI) ablation. Of these, 62 patients underwent robotic thyroidectomy by a gasless unilateral axillo-breast (GUAB) or axillary (GUA) approach, and 183 underwent conventional open thyroidectomy. We analyzed serum TSH-stimulated thyroglobulin (Tg) and RAI uptake at the time of RAI remnant ablation to compare surgical completeness in the two groups.

RESULTS:
Tumor characteristics and complications did not differ between the two groups except TNM stage. The mean TSH-stimulated Tg at the first RAI ablation was significantly higher in the robotic group (10.20 ± 9.98 ng/ml) than in the open group (3.85 ± 6.79 ng/ml) (P <0.001). In subgroup analysis of the robotic group by the period in which operations took place, TSH-stimulated Tg was significantly higher than in the open group in the first (13.28 ± 11.91 ng/ml) and second (10.45 ± 9.30 ng/ml) periods, but there was no significant difference in the third period (6.00 ± 6.26 ng/ml, P = 0.141). The RAI uptake rate at the first RAI ablation did not differ between the two groups, and TSH-stimulated Tg after RAI ablation was similar.

CONCLUSION:
The surgical completeness of robotic total thyroidectomy by a GUAB/GUB approach is comparable to that of open thyroidectomy, if performed by experienced robotic thyroid surgeons in properly selected patients.

LEVEL OF EVIDENCE:
3b. Laryngoscope, 2013.

KEYWORDS:

Robotic thyroidectomy, endoscopic thyroidectomy, gasless unilateral axillary approach, gasless unilateral axillo-breast approach, papillarythyroid carcinoma

PMID: 24338236 http://dx.doi.org/10.1002/lary.24511

78. J Otolaryngol Head Neck Surg. 2013 Dec 20;42(1):61. doi: 10.1186/1916-0216-42-61. **IF:1.25**

Rates of thyroid malignancy by FNA diagnostic category.

Williams BA, Bullock MJ, Trites JR, Taylor SM, Hart RD.
Author information

Abstract

BACKGROUND:
Fine needle aspiration (FNA) of thyroid nodules is a cornerstone of surgical decision making in thyroid cancer. The most widely utilized system for reporting thyroid FNA results is the Bethesda System, which includes predicted malignancy rates for each FNA category. To date there have been few studies to determine whether these predictions are widely applicable.

METHODS:
All thyroid FNA results at the Queen Elizabeth II Health Science Centre from 2006-2010 were included in this study. The results were tabulated by FNA category and the health records were reviewed to determine whether the patient went on to have surgery and the result of surgical histopathology. Rates of malignancy were calculated and compared to published values.

RESULTS:
A total of 1491 thyroid FNAs were included in the study, representing 1117 individual patients with available health records. The majority of these FNAs were Benign, but the proportion of Unsatisfactory FNAs was higher than predicted while Malignant and Suspicious for Malignancy were lower than predicted. Surgery was performed on 388 patients and 110 were positive for malignancy (28%). The malignancy rate for each FNA category was higher than predicted based on literature values.

CONCLUSIONS:
The proportions of FNA diagnoses and the rates of malignancy for each FNA category at our institution were not consistent with predicted values. It is important for clinicians to base their surgical recommendations on institution specific malignancy rates, not solely on literature values.

PMID: 24359603 http://dx.doi.org/10.1186/1916-0216-42-61

79. Surg Today. 2013 Dec;43(12):1398-405. doi: 10.1007/s00595-012-0442-z. Epub 2012 Dec 11.

IF:1.12

Does thyroid surgery for Graves' disease improve health-related quality of life?

Scerrino G, Morfino G, Paladino NC, Di Paola V, Amodio E, Gulotta G, Bonventre S.
Author information

Abstract

PURPOSE:
Graves' disease can induce alterations of the psychosocial well-being that negatively influence the overall well-being of patients. Among the current treatments, surgery has limited indications, and its impact on the health-related quality of life has not been well clarified. The aim of this study was to assess the impact of surgery on the quality of life.

METHODS:
Fifty-seven patients who underwent total thyroidectomy for Graves' disease in our surgical unit between April 2002 and December 2009 were administered a questionnaire concerning four issues: organic alterations and clinical manifestations, neurovegetative system disturbances, impairment of daily activities, psychosocial problems. Patients were retrospectively questioned after thyroidectomy about the presence of these symptoms in both the pre and postoperative periods.

RESULTS:
There was a significant improvement after surgery in all four areas. Organic manifestations and psychosocial problems had higher average improvements, as did some aspects of the neurovegetative system and difficulties in undertaking daily activities. There were no reports of a worsening of symptoms.

CONCLUSIONS:
Surgery resolved the hyperthyroidism in 100 % of cases, and was associated with a quality of life improvement of about 70 % in the patients. Surgery can therefore provide an immediate and effective resolution of Graves' disease, with benefits in health-related quality of life.

PMID: 23229839 http://dx.doi.org/10.1007/s00595-012-0442-z

80. Am Surg. 2013 Dec;79(12):1283-8. **IF:0.98**

Total thyroidectomy as primary definitive treatment for graves' hyperthyroidism.

Snyder S, Govednik C, Lairmore T, Jiang DS, Song J.
Author information

Abstract

The objective of this study was to compare the results of total thyroidectomy (TT) for hyperthyroidism secondary to Graves' disease (GD) with TT for other benign thyroid diseases to determine if TT should be considered more often as first-line therapy for GD. Seven hundred eighty patients underwent TT for benign disease: 203 for GD, 56 for other hyperthyroidisms, and 521 for other benign diseases from March 1, 2003, to December 31, 2009. The perioperative results of these three groups were compared for demographics, blood loss, operative time, complications, and hospitalization. There were no significant differences among the three groups except the patients with GD were more likely to be younger (42 vs 56 vs 57 years; $P < 0.001$), have more blood loss (154 vs 99 vs 110 mL; $P = 0.05$), and were more likely to develop permanent hypoparathyroidism (1.0 vs 1.8 vs 0%; $P = 0.03$) when compared with other causes of hyperthyroidism and other benign thyroid diseases. Permanent recurrent laryngeal nerve injury did not occur in the GD group (0 vs 0 vs 0.4% nerves at risk; $P = 0.69$) with transient recurrent laryngeal nerve injury occurring in 1.7 versus 2.7 versus 3.1 per cent nerves at risk ($P = 0.35$). The lack of a euthyroid state preoperatively had no influence on surgical outcomes or complications. Eighty percent of the TTs for GD were done as same-day outpatient procedures. TT offers a safe, low-risk, and rapid cure for GD to justifiably be considered as a reasonable first-line therapy in selected patients with Graves' hyperthyroidism.

PMID: 24351357

TİROİD

Vaka sunumu

1. Metabolism. 2013 Oct;62(10):1350-6. doi: 10.1016/j.metabol.2013.05.013. Epub 2013 Jun 24.

IF:3.28

Coexistence of Graves' disease, papillary thyroid carcinoma and unilateral benign struma ovarii: case report and review of the literature.

Anastasilakis AD, Ruggeri RM, Polyzos SA, Makras P, Molyva D, Campennì A, Gkiomisi A, Balaris C, Fotiadis PP, Tuccari G, Papachatzopoulos S.
Author information

Abstract

BACKGROUND:
Struma ovarii is a rare cause of hyperthyroidism, while coexistence with Graves' disease has been scarcely reported.

PATIENT FINDINGS:
We report a patient with Graves' disease and unilateral benign functioning struma ovarii, accompanied by ascites, pleural effusion and elevated cancer antigen-125 (CA-125) levels. In subsequent thyroidectomy, incidental papillary thyroid carcinoma was also identified. The functionality of struma ovarii tissue in our patient was supported by the immunohistochemical identification of TSH receptors (TSHR), which may stimulate growth and thyroid hormone production in the presence of circulating TSHR stimulating antibodies (TSHR-Ab).

REVIEW OF THE LITERATURE:
A systematic review of reported cases of coexistent Graves' disease and struma ovarii was performed.

CONCLUSIONS:
The diagnosis of struma ovarii may be masked by Graves' disease and, therefore, be delayed for several years. Furthermore, ascites, pleural effusion and increased CA-125 may result from a benign struma ovarii. The presence of TSHR in the struma ovarii tissue along with their absence in the surrounding ovarian tissue indirectly suggests that struma ovarii is functional. It is unclear whether TSHR-Ab play a role in the development of thyroid carcinomas in such patients.

KEYWORDS:

CA-125, CT, Hyperthyroidism, Meigs syndrome, Pleural effusion, TFTs, TG-Ab, TPO-Ab, TSH, TSH receptor, TSHR, TSHR-Ab, Thyroid cancer, US, cancer antigen-125, computed tomography, thyroglobulin autoantibodies, thyroid function tests, thyroid peroxidase autoantibodies, thyrotropin, thyrotropin receptors, thyrotropin receptors autoantibodies, ultrasound

PMID: 23806737 http://dx.doi.org/10.1016/j.metabol.2013.05.013

2. Am J Med Sci. 2013 Oct;346(4):338-40. doi: 10.1097/MAJ.0b013e31828ffcbc. **IF:1.39**

A case of apathetic thyroid storm with resultant hyperthyroidism-induced hypercalcemia.

Parker KI, Loftley A, Charles C, Hermayer K.
Author information

Abstract

Thyroid storm is a complication of thyrotoxicosis with a 20% to 30% mortality rate characterized by hyperthermia, tachycardia and altered mental status. Rarely, thyroid storm may have an apathetic presentation. The authors present a 63-year-old woman with apathetic thyrotoxicosis and hypercalcemia. The action of thyroid hormones stimulating bone resorption more than bone formation is thought to cause increased bone demineralization and, occasionally, hypercalcemia. This occurs in the absence of malignancy, prolonged immobility, hypervitaminosis D and primary hyperparathyroidism. Her thyroid storm was medically managed and her hypercalcemia was treated with intravenous fluids, calcitonin and a bisphosphonate. This case describes the presence of hypercalcemia in a patient with apathetic thyroid storm with no other factors contributing to the hypercalcemia. In addition, this patient had significant elevation in serum calcium, which possibly contributed to her symptomatology. The calcium remained normal after the thyrotoxicosis resolved, which is typical of the hypercalcemia of thyrotoxicosis.

PMID: 23608928 http://dx.doi.org/10.1097/MAJ.0b013e31828ffcbc

PARATİROİD

DERLEME

1. World J Surg. 2013 Nov 20. [Epub ahead of print] **IF:2.47**

The Final Intraoperative Parathyroid Hormone Level: How Low Should It Go?

Wharry LI, Yip L, Armstrong MJ, Virji MA, Stang MT, Carty SE, McCoy KL.
Author information

Abstract

BACKGROUND:
In minimally invasive surgery for primary hyperparathyroidism (HPT), intraoperative parathyroid hormone (IOPTH) monitoring assists in obtaining demonstrably better outcomes, but optimal criteria are controversial.

METHODS:
The outcomes of 1,108 initial parathyroid operations for sporadic HPT using IOPTH monitoring from 1997 to 2011 were stratified by final post-resection IOPTH level. All patients had adequate follow-up to verify cure.

RESULTS:
With mean follow-up of 1.8 years (range 0.5-14.3 years), parathyroidectomy using IOPTH monitoring failed in 1.2 % of cases, with an additional 0.5 % incidence of long-term recurrence at a mean of 3.2 years (range 0.8-6.8 years) postoperatively. Operative success was equally likely with a final IOPTH drop to 41-65 pg/mL vs ≤40 pg/mL (p = 1). In the 76 patients with an elevated baseline IOPTH level that did not drop to ≤65 pg/mL, surgical failure was 43 times more likely than with a drop into normal range (13 vs. 0.3 %; p < 0.001). When the final IOPTH level dropped by >50 % but not into the normal range, surgical failure was 19 times more likely (3.8 vs. 0.2 %; p = 0.015). Long-term recurrence was more likely in patients with a final IOPTH level of 41-65 pg/mL than with a level ≤40 pg/mL (1.2 vs. 0; p = 0.016).

CONCLUSIONS:
Adjunctive intraoperative PTH monitoring facilitates a high cure rate for initial surgery of sporadic primary hyperparathyroidism. A final IOPTH level that is within the normal range and drops by >50 % from baseline is a strong predictor of operative success. Patients with a final IOPTH level between 41-65 pg/mL should be followed beyond 6 months for long-term recurrence.

PMID: 24253106

PARATİROİD

PROSPEKTİF

1. Eur J Endocrinol. 2013 Oct 21;169(6):795-804. doi: 10.1530/EJE-13-0547. Print 2013 Dec.

IF:3.64

Primary hyperparathyroidism and metabolic risk factors, impact of parathyroidectomy and vitamin D supplementation, and results of a randomized double-blind study.

Norenstedt S, Pernow Y, Brismar K, Sääf M, Ekip A, Granath F, Zedenius J, Nilsson IL.
Author information

Abstract

BACKGROUND:
Vitamin D insufficiency may increase the risk for cardio metabolic disturbances in patients with primary hyperparathyroidism (PHPT).

OBJECTIVE:
To analyze the vitamin D status and indices of the metabolic syndrome in PHPT patients and the effect of vitamin D supplementation afterparathyroid adenomectomy (PTX).

DESIGN AND METHODS:
Double-blinded, randomized clinical trial (ClinicalTrials.gov identifier: NCT00982722) performed at Karolinska University Hospital, Sweden, April 2008 to November 2011. One hundred and fifty consecutive patients with PHPT (119 women) were randomized after PTX, 75 to oral treatment with calcium carbonate 1000mg daily and 75 to calcium carbonate 1000mg and cholecalciferol 1600IU daily over 12 months. Changes in metabolic profile and ambulatory blood pressure (BP) were analyzed. Main outcome measures were changes in metabolic factors, BP, and body composition.

RESULTS:
The 25-hydroxyvitamin D (25-OH-D)-level was <50nmol/l in 76% of the patients before PTX. After PTX, glucose, insulin, and IGF1 decreased, while the 25-OH-D and the IGF-binding protein 1 increased and remained unchanged at follow-up after study medication. One year of vitamin D supplementation resulted in lower parathyroid hormone (PTH) (40 (34-52) vs 49 (38-66) ng/l) and higher 25-OH-D (76 (65-93) vs 49 (40-62) nmol/l; P<0.05). Other laboratory parameters were stable compared with after PTX. Systolic BP decreased and total bone mineral content increased in both groups.

CONCLUSION:
Except for the lowering of the PTH level, no additive effect of vitamin D supplementation was seen. However, PTX proved effective in reducing insulin resistance.

PMID: 24026893 http://dx.doi.org/10.1530/EJE-13-0547

2. Surgery. 2013 Dec;154(6):1371-7; discussion 1377. doi: 10.1016/j.surg.2013.06.046. **IF:3.19**

A novel optical approach to intraoperative detection of parathyroid glands.

McWade MA, Paras C, White LM, Phay JE, Mahadevan-Jansen A, Broome JT.

Abstract

BACKGROUND:

Inadvertent removal of parathyroid glands is a challenge in endocrine operations. There is a critical need for a diagnostic tool that provides sensitive, real-time parathyroid detection during procedures. We have developed an intraoperative technique using near-infrared (NIR) fluorescence for in vivo, real-time detection of the parathyroid regardless of its pathologic state.

METHODS:

NIR fluorescence was measured intraoperatively from 45 patients undergoing parathyroidectomy and thyroidectomy. Spectra were measured from the parathyroid and surrounding neck tissues during the operation with the use of a portable, probe-based fluorescence system at 785-nm excitation. Accuracy was evaluated by comparison with histology or visual recognition by the surgeon.

RESULTS:

NIR fluorescence detected the parathyroid in 100% of patients. Parathyroid fluorescence was stronger (1.2-18 times) than that of the thyroid with peak fluorescence at 822 nm. Surrounding tissues showed no auto-fluorescence. Disease state did not affect the ability to discriminateparathyroid glands but may account for signal variability.

CONCLUSION:

NIR fluorescence spectroscopy can detect intraoperatively the parathyroid regardless of tissue pathology. The signal may be caused by calcium-sensing receptors present in the parathyroid. The signal strength and consistency indicates the simplicity and effectiveness of this method. Its implementation may limit operative time, decrease costs, and improve operative success rates.

PMID: 24238054 http://dx.doi.org/10.1016/j.surg.2013.06.046

3. Clin Hemorheol Microcirc. 2013 Oct 28. [Epub ahead of print] **IF:2.48**

The role of contrast-enhancend ultrasonography (CEUS) in comparison with 99mTechnetium-sestamibi scintigraphy for localization diagnostic of primary hyperparathyroidism.

Agha A, Hornung M, Schlitt HJ, Stroszczynski C, Jung EM.
Author information

Abstract

INTRODUCTION:

Correct preoperative detection of parathyroid gland adenoma (PA) in the case of primary hyperparathyroidism (pHPT) is the requirement for unilateral cervical exploration associated with lower morbidity. We present our experience with contrast-enhanced ultrasonography (CEUS) as diagnostic tool for the preoperative localization of PA in pHPT in comparison to the 99mTechnetium-sestamibi scintigraphy.

METHODS:

Between 8/2009-5/2013 143 patients with pHPT received surgical interventions in the Department of Surgery at the University Hospital of Regensburg. In all patients contrast-enhanced ultrasonography (CEUS) was performed as diagnostic tool for the localization of pathologicalparathyroid glands. By one experienced examiner CEUS was performed after bolus injection of 1-2.4 ml contrast agent with storage of digital cine loops from the arterial phase (15-45 s) to the late phase (3 Min). Criteria for a parathyroid adenoma were marginal hypervascularisation in the arterial phase and wash out in the late phase. 74 patients received 99mTechnetium-sestamibi scintigraphy. The sensitivity of both diagnostic tools was analyzed in comparison to the intraoperative and histological findings.

RESULTS:

CEUS revealed a sensitivity of 95.9% for the detection of pathological parathyroid glands and even of 97.1% for patients without scintigrapy in comparison to 60.8% for 99mTechnetium-sestamibi scintigraphy. Sensitivity of CEUS in patients with negative scintigraphy was 96.3%. In multivariate regression analysis detection of small PA compared to scintigraphy was better by trend but did not reach significance (p = 0.019). Follow-up with a minimum of 8 weeks showed normal serum levels of calcium and parathyroid hormone in all patients except one.

CONCLUSIONS:

CEUS represents a new diagnostic method for the localization of parathyroid gland adenomas independent on findings in scintigraphy. In the present of appropriate expertise in CEUS no further diagnostic procedures are required.

KEYWORDS:

^{99m}Technetium-sestamibi scintigraphy, Contrast-enhancend ultrasonography, diagnostic of primary hyperparathyroidism

PMID: 24165576

4. Am J Surg. 2013 Dec;206(6):883-7. doi: 10.1016/j.amjsurg.2013.07.023. Epub 2013 Oct 10.

IF:2.39

Laterality of central venous sampling: lack of effect on the accuracy of intraoperative parathyroid hormonemonitoring.

Korovin LN, Guerrero MA.

Author information

Abstract

BACKGROUND:

The purpose of this study was to determine if laterality of internal jugular vein (IJV) sampling affects the accuracy of intraoperativeparathyroid hormone (PTH) monitoring during parathyroidectomy for primary hyperparathyroidism.

METHODS:

In this study, 109 patients underwent parathyroidectomy (82 with unilateral disease, 27 with multigland disease). PTH samples were taken from both the left and the right IJV at these time points: preincision (baseline) and then at 5, 10, and, in selected patients, 20 minutes after excision. The Miami criterion was used to determine operative success.

RESULTS:

In all 109 patients combined, the mean decreases in intraoperative PTH levels were 73.8 ± 22.2% for the left IJV and 71.9 ± 23.0% for the right IJV (P = .22). The Miami criterion was met in 105 patients: in 100 (95%) left IJV samples and 99 (94%) right IJV samples (P = 1.00).

CONCLUSIONS:

No difference was found in the accuracy of intraoperative PTH monitoring between patients' left and right IJV samples. Central venous laterality did not affect fulfillment of the Miami criterion.

KEYWORDS:

Central venous sampling, Intraoperative PTH monitoring, Miami criterion, Primary hyperparathyroidism

PMID: 24119891 http://dx.doi.org/10.1016/j.amjsurg.2013.07.023

5. Am J Surg. 2013 Nov;206(5):783-9. doi: 10.1016/j.amjsurg.2013.01.038. Epub 2013 Jul 5. **IF:2.39**

Intact parathyroid hormone measurement at 24 hours after thyroid surgery as predictor of parathyroidfunction at long term.

Julián MT, Balibrea JM, Granada ML, Moreno P, Alastrué A, Puig-Domingo M, Lucas A.
Author information

Abstract

BACKGROUND:
There is no consensus about the usefulness of postoperative intact parathyroid hormone (iPTH) determination to predict permanent hypoparathyroidism (pHPP). We evaluated the value of calcium (Ca2+) and iPTH concentration at 24 hours after total thyroidectomy (TT) for predicting pHPP.

METHODS:
Ca2+ and iPTH levels from 70 consecutive patients who underwent TT were measured at 24 hours and 6 months after TT.

RESULTS:
Five patients (7.1%) developed pHPP. An iPTH concentration ≤5.8 pg/mL at 24 hours after TT identified patients at risk for pHPP (sensitivity, 100%; specificity, 81.5%), but it was not accurate enough to predict its development (positive predictive value, 30%). Conversely, an iPTH level >5.8 pg/mL predicted normal parathyroid function at 6 months (negative predictive value, 100%). Compared with iPTH, a postoperative Ca2+ level ≤1.95 mmol/L was 60% sensitive and 78.5% specific to predict pHPP.

CONCLUSIONS:
An iPTH concentration >5.8 pg/mL on the first postoperative day rules out pHPP with much better diagnostic accuracy than Ca2+. Postoperative iPTH could be helpful in identifying patients at risk for developing pHPP.

KEYWORDS:

Permanent hypoparathyroidism, Postoperative hypocalcemia, Total thyroidectomy

PMID: 23835208 http://dx.doi.org/10.1016/j.amjsurg.2013.01.038

6. Am J Surg. 2013 Oct;206(4):574-7. doi: 10.1016/j.amjsurg.2013.01.043. Epub 2013 Jul 2. **IF:2.39**

Can the use of intraoperative intact parathyroid hormone monitoring be abandoned in patients with hyperparathyroidism?

Sakimura C, Minami S, Hayashida N, Uga T, Inokuchi N, Eguchi S.
Author information

Abstract

BACKGROUND:
Ultrasound (US) and technetium-99m sestamibi scintigraphy (MIBI) are used to determine the localization of abnormal glands in cases of primary hyperparathyroidism (PHPT).

Intraoperative intact parathyroid hormone (iPTH) monitoring is a reliable examination used to cure PHPT. The aim was to assess the necessity of intraoperative iPTH monitoring.

METHODS:
Sixty patients were examined using preoperative MIBI and US. iPTH was measured at 3 time points: (1) at the start of surgery; (2) 10 minutes after gland resection; and (3) more than 60 minutes after surgery. We defined a decreased iPTH level as an iPTH measured 10 minutes after resection that was less than 50% of the preoperative level.

RESULTS:
The iPTH of 55 patients with concordant lesions decreased to within the normal range more than 60 minutes after surgery.

CONCLUSIONS:
It is not necessary to monitor intraoperative iPTH when single concordant lesions are preoperatively identified on both MIBI and US.

KEYWORDS:

Intraoperative intact parathyroid hormone monitoring, Primary hyperparathyroidism, Technetium-99m sestamibi scintigraphy, Ultrasound

PMID: 23827512 http://dx.doi.org/10.1016/j.amjsurg.2013.01.043

7. Nucl Med Commun. 2013 Dec 5. [Epub ahead of print] **IF:1.48**

The effectiveness of low-dose versus high-dose 99mTc MIBI protocols for radioguided surgery in patients with primary hyperparathyroidism.

Gencoglu EA, Aras M, Moray G, Aktas A.
Author information

Abstract

OBJECTIVE:
The aim of this study was to compare the efficacy of low-dose and high-dose Tc methoxy isobutyl isonitrile (MIBI) protocols in intraoperative localization of parathyroid adenomas by means of a gamma probe in patients with primary hyperparathyroidism (PHPT).

PATIENTS AND METHODS:
The study included 62 patients with PHPT who were divided into two groups. Group 1 consisted of 32 patients who were injected with a low dose (1 mCi) of Tc MIBI in the surgical suite 10 min before incision. Group 2 included 30 patients who were intravenously administered a high dose (15 mCi) of Tc MIBI 2 h before surgery. With the aid of a gamma probe, intraoperative localization of parathyroid adenomas was performed in both groups of patients who underwent minimally invasive parathyroidectomy. All lesions thought to be parathyroid adenomas were excised and subsequently evaluated histopathologically.

RESULTS:
All parathyroid adenomas in both groups were localized and excised by means of an intraoperative gamma probe. The sensitivity, specificity, and accuracy of low-dose and high-

dose Tc MIBI protocols in the intraoperative localization of adenomas in patients with PHPT were 100%.

CONCLUSION:
In the light of these findings, we conclude that low-dose Tc MIBI may be preferred to intraoperative identification of parathyroidadenomas by means of a gamma probe in PHPT patients because it appears to be as effective as high-dose Tc MIBI. Moreover, the low-dose protocol does not have the disadvantages of high-dose protocol.

PMID: 24323310

PARATİROİD

RETROSPEKTİF

1. Ann Surg Oncol. 2013 Dec 4. [Epub ahead of print] **IF:4.33**

Parathyroid Surgery in the Elderly: Should Minimally Invasive Surgery Be Abandoned?

Mekel M, Gilshtein H, Chapchay K, Bishara B, Krausz MM, Freund HR, Kluger Y, Eid A, Mazeh H.

Author information

Abstract

BACKGROUND:

Single adenoma is the cause of 80 % of primary hyperparathyroidism (PHPT) resulting in wide acceptance of minimally invasive parathyroidectomy (MIP). The incidence of PHPT increases with age. Little information is available regarding the prevalence of multiglandular disease (MGD) in older patients.

METHODS:

The records of 537 patients that underwent parathyroid surgery between January 2005 and October 2012 at two endocrine surgery referral centers were retrospectively reviewed. Comparison was performed between patients younger than 65 and older than 65 years of age. Clinical variables included preoperative laboratories and imaging, extent of neck exploration, number of glands excised, and intraoperative parathyroid hormone levels during surgery.

RESULTS:

There were 374 (70 %) patients in the younger age group (YG) and 163 (30 %) patients in the older age group (OG). The mean age was 50 ± 0.5 and 71 ± 0.4 years, respectively. There was no difference between the groups in terms of gender or laboratory results. MGD was significantly more common in the OG (24 % vs. 12 %; $p = 0.001$) and similarly MIP was less commonly completed in the OG (49 % vs. 68 %; $p < 0.001$). Cure rates were comparable between the OG and YG (93 % vs. 95 %; $p = 0.27$). In the OG, patients with MGD had significantly smaller glands as compared to patients with single adenomas in this group (331 ± 67 vs. 920 ± 97 mg; $p = 0.006$, respectively).

CONCLUSIONS:

MGD in PHPT was found to be more prevalent in older patients. Planning a bilateral neck exploration should be considered in older patients, especially when a relatively small gland is suggested by imaging or encountered during surgery.

PMID: 24306663

2. Ann Surg Oncol. 2013 Oct 1. [Epub ahead of print] **IF:4.33**

Negative Parafibromin Staining Predicts Malignant Behavior in Atypical Parathyroid Adenomas.

Kruijff S, Sidhu SB, Sywak MS, Gill AJ, Delbridge LW.
Author information

Abstract

BACKGROUND:
The histopathological criteria for carcinoma proposed by the World Health Organization (WHO) are imperfect predictors of the malignant potential of parathyroid tumors. Negative parafibromin (PF) and positive protein gene product 9.5 (PGP9.5) staining are markers of CDC73 mutation and occur commonly in carcinoma but rarely in adenomas. We investigated whether PF and PGP9.5 staining could be used to predict the behavior of atypical parathyroid adenomas-tumors with atypical features that do not fulfill WHO criteria for malignancy.

METHODS:
Long-term outcomes were compared across four groups: group A, WHO-positive criteria/PF-negative staining; group B, WHO^{+}/PF^{+}, group C; WHO^{-}/PF^{-}; and group D, WHO^{-}/PF^{+}.

RESULTS:
Eighty-one patients were included in the period 1999-2012: group A (n = 13), group B (n = 14), group C (n = 21), and group D (n = 33). Mortality and recurrence rates, respectively, for group A were 15 and 38 %, for group B 7 and 36 %, for group C 0 and 10 %, and for group D 0 and 0 %. The $PGP9.5^{+}$ ratios for groups A to D were 85, 78, 71, and 12 %, further informing prognosis. Five-year disease-free survival for groups A to D were 55, 80, 78, and 100 %, respectively. Tumor recurrence was significantly associated with PF (p = 0.048) and PGP9.5 (p = 0.003) staining.

CONCLUSIONS:
Although WHO criteria are essential to differentiate parathyroid carcinoma from benign tumors, the presence of negative PF staining in an atypical adenoma predicts outcome better, whereas PF-positive atypical adenomas do not recur and can be considered benign. PF-negative atypical adenomas have a low but real recurrence risk and should be considered tumors of low malignant potential.

PMID: 24081804

3. Ann Surg Oncol. 2013 Dec;20(13):4200-4. doi: 10.1245/s10434-013-3188-y. Epub 2013 Aug 14.

IF:4.33

Minimal benefit to subsequent intraoperative parathyroid hormone testing after all four glands have been identified.

Ahmed K, Alhefdhi A, Schneider DF, Ojomo KA, Sippel RS, Chen H, Mazeh H.

Author information

Abstract

BACKGROUND:

Modern tools, such as intraoperative parathyroid hormone (IoPTH) assay, reduce operative time and extent of parathyroidectomy. However, the utility of a subsequent final set of IoPTH after all four glands are visualized remains questionable. This study was designed to determine the added value of IoPTH assay following parathyroidectomy with four-gland visualization in patients with primary hyperparathyroidism (PHPT).

METHODS:

A retrospective review of patients who underwent parathyroidectomy for PHPT between July 2001 and February 2012 by two experienced endocrine surgeons was performed. Included were patients with operative reports indicating that all four parathyroid glands were identified. Following four-gland visualization a subsequent final set of IoPTH was measured to confirm cure. Cure was defined as at least 50 % fall by 5, 10, or 15 min postexcision compared with preincision levels.

RESULTS:

Of 1,838 patients that underwent parathyroidectomy, four glands were visualized in 238 cases (13 %). Of those patients meeting inclusion criteria with four glands visualized, the final set of IoPTH fell to cure criteria in 235 patients (98 %). An inadequate drop was documented in three (2 %) patients all of which were found to have multigland disease. Only in one patient (0.4 %) was a fifth parathyroid gland identified and resected. In all three cases, the subsequent final IoPTH did not affect the ultimate outcome or cure rate.

CONCLUSIONS:

When experienced surgeons visualize all four parathyroid glands, drawing a subsequent final set of IoPTH rarely changes the operative course and therefore serves a limited role.

PMID: 23943032 http://dx.doi.org/10.1245/s10434-013-3188-y

4. Surgery. 2013 Dec;154(6):1428-34; discussion 1434-5. doi: 10.1016/j.surg.2013.04.020. Epub 2013 Sep 3. **IF:3.19**

Factors in conversion from minimally invasive parathyroidectomy to bilateral parathyroid exploration for primary hyperparathyroidism.

Hughes DT, Miller BS, Park PB, Cohen MS, Doherty GM, Gauger PG.
Author information

Abstract

BACKGROUND:
Ongoing experience has documented equivalence of minimally invasive parathyroidectomy (MIP) and standard bilateral parathyroidexploration (BPE) for primary hyperparathyroidism in most patients; however, intraoperative conversion of MIP to BPE is required for multiple indications. This study analyzes the factors, predictors, and cure rates in converted MIP.

METHODS:
We retrospectively analyzed a database of 1,002 patients undergoing initial parathyroidectomy for primary hyperparathyroidism from 2008 to 2011 for rate of successful MIP, converted MIP, planned BPE, and factors leading to conversion from MIP to BPE.

RESULTS:
Of 989 included parathyroidectomies, 647 (65%) were successful MIP, 186 (19%) were converted MIP, and 156 (16%) were planned BPE. The most common indication for conversion included intraoperative parathyroid hormone (IOPTH) criteria not met (46%), localization incorrect (36%), and evidence of multigland disease (17%). Converted MIP had lower preoperative calcium and PTH and lower baseline IOPTH compared with successful MIP. Complication rates were similar; however, rates of persistent hyperparathyroidism were highest in converted MIPs (6%) versus planned BPEs (3%) and successful MIPs (2%; $P < .01$).

CONCLUSION:
Patients requiring conversion of MIP to BPE have lower preoperative serum calcium and PTH levels, a less dramatic decrease in IOPTH, and a greater rate of persistent disease than successful MIP.

PMID: 24008086 http://dx.doi.org/10.1016/j.surg.2013.04.020

5. Surgery. 2013 Oct;154(4):714-8; discussion 718-9. doi: 10.1016/j.surg.2013.05.013. Epub 2013 Aug 23. **IF:3.19**

Do giant parathyroid adenomas represent a distinct clinical entity?

Spanheimer PM, Stoltze AJ, Howe JR, Sugg SL, Lal G, Weigel RJ.
Author information

Abstract

BACKGROUND:
The size of abnormal parathyroid glands in patients with primary hyperparathyroidism (PHPT) is highly variable, but the clinical significance of giant glands is unknown.

METHODS:
We reviewed 300 consecutive patients after parathyroidectomy for PHPT. We compared patients with giant parathyroid adenomas (weight ≥95th percentile) with the remaining patients.

RESULTS:
Giant adenomas were defined as weight ≥95th percentile or 3.5 g (median, 0.61; range, 0.05-29.93). Patients with giant adenomas had a greater mean preoperative calcium level, greater mean parathyroid hormone (PTH) level, and were less likely to have multiglandular or symptomatic disease. Giant adenomas were successfully localized on imaging in 87% of patients, which was not increased over other patients (82%). There were no differences between the groups in age, gender, gland location, or the incidence of persistent or recurrent hyperparathyroidism. Finally, giant glandshad an increased incidence of symptomatic postoperative hypocalcemia, including 1 patient who required rehospitalization after removal of a giant gland.

CONCLUSION:
Giant parathyroid adenomas have a distinct presentation characterized by single gland disease and lower incidence of symptoms despite increased levels of calcium and PTH. Additionally, after resection of a giant adenoma, patients are more likely to develop symptomatic hypocalcemia.

PMID: 23978594 http://dx.doi.org/10.1016/j.surg.2013.05.013

6. Ann Thorac Surg. 2013 Oct;96(4):1229-33. doi: 10.1016/j.athoracsur.2013.05.084. Epub 2013 Aug 20. **IF:2.32**

Minimally invasive resection for mediastinal ectopic parathyroid glands.

Said SM, Cassivi SD, Allen MS, Deschamps C, Nichols FC 3rd, Shen KR, Wigle DA.
Author information

Abstract

BACKGROUND:
We reviewed our experience with ectopic mediastinal parathyroidectomy.

METHODS:
Between March 1980 and September 2010, mediastinal parathyroidectomy was performed in 33 patients with hypercalcemia secondary to hyperparathyroidism.

RESULTS:
Primary hyperparathyroidism was the main diagnosis in 32 patients (97%). Technetium-sestamibi scan was used in 23 (70%) for preoperative localization. Minimally invasive resections were performed in 18 patients (55%), and 15 (45%) underwent open surgery. The most common minimally invasive surgery approach was video-assisted thoracoscopy in 9 patients (27%); the most common open approach was median sternotomy in 11 (33%). Intraoperative parathyroid hormone monitoring was used in 22 patients (67%). The ectopic glands were intrathymic in 15 patients (45%), in the aortopulmonary window in 7 (21%), and in other intrathoracic locations in the remaining 11 (33%). Parathyroid adenomas were identified in 21 patients (64%); parathyroid hyperplasia and carcinoma were identified in 9 (27%) and 3 (9%), respectively. No early mortality occurred in either group. Reoperation was required in 1 patient in the minimally invasive surgery group because of hemothorax. Morbidity occurred in 8 patients (24%), the most common of which was hypocalcemia in 4 (12%). The mean length of stay was significantly shorter in the minimally invasive surgery group (2 versus 6 days; $p < 0.001$) but mortality and morbidity were not statistically different between the two groups ($p = 0.05$). Mean follow-up was 3 ± 3.7 years.

CONCLUSIONS:
Minimally invasive mediastinal parathyroidectomy has similar outcomes to open surgery, with significantly shorter length of hospital stay.

KEYWORDS:
13

PMID: 23968765 http://dx.doi.org/10.1016/j.athoracsur.2013.05.084

7. Endocrine. 2013 Dec;44(3):591-7. doi: 10.1007/s12020-013-9980-4. Epub 2013 May 14. **IF:2.24**

Primary hyperparathyroidism in pregnancy.

Diaz-Soto G, Linglart A, Sénat MV, Kamenicky P, Chanson P.
Author information

Abstract

Primary hyperparathyroidism (PHPT) is rarely diagnosed during pregnancy but is associated with significant maternal and fetal morbidity and mortality. Information on appropriate management is limited. We reviewed the medical literature through December 2012 for key articles on PHPT during pregnancy, focusing on large series. Clinical knowledge in this area is restricted to isolated case reports and a few retrospective studies. Diagnosis can be difficult, owing to the non-specific nature of signs and symptoms of hypercalcemia during pregnancy. Pregnant women with a calcium level over 2.85 mmol/L (11.4 mg/dL) and prior pregnancy loss are at a particularly high risk of maternal complications (hypercalcemic crisis, nephrolithiasis, pancreatitis, etc.) and fetal loss. Around one-half of neonates born to mothers with untreated PHPT have hypocalcemia and tetany. Algorithms proposed for the management of the pregnant woman with PHPT are not evidence based, reflecting the paucity of data. Treatment should thus be individually tailored. Gestational age and the severity of hypercalcemia should be taken into account when assessing the risk-benefit balance of a conservative approach (hyperhydration and vitamin D supplementation) versus parathyroid surgery. Current evidence supports parathyroidectomy as the main treatment, performed preferably during the second trimester, when the serum calcium is above 2.75 mmol/L (11 mg/dL). In the patients with mild forms of PHPT, which are nowadays the most frequent, a conservative management is generally preferred.

PMID: 23670708 http://dx.doi.org/10.1007/s12020-013-9980-4.

8. Endocr Pract. 2013 Nov 18:1-18. [Epub ahead of print] **IF:2.12**

Radioguided Parathyroidectomy Succesful in 98.7% Of Selected Patients.

Livingston CD.
Author information

Abstract

Objective: To examine an individualized approach to patients with Primary Hyperparathyroidism (PHPT) in an effort to identify factors that would differentiate patients who can be treated with Radioguided Parathyroidectomy (RP) from those that require more extensive parathyroid exploration (PE) using intraoperative parathyroid hormone (IOPTH) measurement and to compare rates of recurrence and persistent hypercalcemia.Methods: 100 patients were retrospectively studied. Patients with positive single photon emission CT (SPECT) scans underwent surgeon performed sonography (SPS) followed by RP. Patients with negative or equivocal SPECT scans underwent PE utilizing SPS as a guide and IOPTH. Success rate, recurrence and persistence rates, and rate of bilateral exploration were compared.Results: 75% of patients with PHPT had a positive SPECT scan and underwent RP, while 25% of patients had negative SPECT scan and underwent PE with IOPTH utilizing SPS as a guide. Persistent hypercalcemia was noted in one patient (1.3%) and recurrent

hypercalcemia in 2 patients (2.6%) in the RP group while none were noted in the group undergoing PE utilizing SPS and IOPTH. Overall 89% of patients were cured with unilateral surgery.Conclusion: Patients with positive SPECT scans may undergo RP with an expected cure rate of 98.7%. Patients with negative SPECT scans should undergo SPS followed by PE using IOPTH and can expect a cure rate near 100%. Properly selected patients may undergo Radioguided Parathyroidectomy with low rates of persistent (1.3%), and recurrent hypercalcemia (2.6%).

PMID: 24246353

9. J Otolaryngol Head Neck Surg. 2013 Dec 19;42(1):56. doi: 10.1186/1916-0216-42-56. **IF:1.68**

Intraoperative parathyroid hormone level in parathyroidectomy: which patients benefit from it?

Zawawi F, Mlynarek AM, Cantor A, Varshney R, Black MJ, Hier MP, Rochon L, Payne RJ.
Author information

Abstract

BACKGROUND:
Intraoperative parathyroid hormone level (IOPTH) is withdrawn during parathyroidectomy to confirm the success of the procedure. Recently, the importance of IOPTH has been put to question. The purpose of this study is to determine whether IOPTH is necessary for all patients undergoing parathyroidectomy in the presence of frozen section.

MATERIALS AND METHODS:
A cohort study of parathyroidectomies was performed in three university affiliated hospitals during 2007-2012. The patients were divided into two groups. Group 1: Patients with two preoperative concordant imaging localizing a hyperactive gland. Group 2: Patients without two concordant imaging. A comparison of benefit of IOPTH was carried out. Frozen section results were also analyzed to determine sensitivity and predictability of a parathyroid adenoma.

RESULTS:
The study considered 221 patients having parathyroidectomies for primary hyperparathyroidism (PHPT). Of them, 10 were excluded due to incomplete data. Among the remaining, 186 had 2 concordant imaging preoperatively localizing an adenoma. 93.5% of whom were found intraoperatively in that location. IOPTH was not found to be of importance in 98.92% of the preoperative localized adenomas in the presence of frozen section. IOPTH added an estimate of 30.9 minutes on average to the surgery time.

CONCLUSION:
This study demonstrates that the added operating time associated with IOPTH may not be justified for patients undergoing parathyroidectomy who have 2 concordant imaging preoperatively in the presence of frozen section. This study suggests a simple algorithm, The McGill Parathyroid Protocol (MPP), to help in approaching PHPT patients undergoing parathyroidectomy.

PMID: 24350891 http://dx.doi.org/10.1186/1916-0216-42-56

10. Am Surg. 2013 Oct;79(10):1022-5. **IF:0.99**

The unequal distribution of parathyroid neoplasms in male patients.

Goldner B, Lee B, Stabile BE.
Author information

Abstract

There is a known lesser incidence of primary hyperparathyroidism and parathyroid neoplasms in male patients. Any difference in the anatomic distribution between males and females has not been documented. Review of our institutional experience with 125 pathologically confirmed parathyroidadenomas (119) or carcinomas (six) from 2000 through 2012 was conducted. The anatomic location was identified from operative records and the distributions between males and females were compared. Ninety-two females with parathyroid neoplasms had equal anatomic distributions between left and right sides and no significant difference between superior and inferior locations (P = 0.381). In marked contrast, tumors in 33 male patients had a significant predilection for the right side (67%, P = 0.016) and inferior position (85%, P = 0.033) and most notably the right inferior position (64%, P = 0.026). For the group as a whole, inferior adenomas were significantly more common (70%, P = 0.044). All patients had postoperative normalization of serum calcium levels. Late biochemical recurrence was noted in two patients. This is the first operatively confirmed delineation of the anatomic distributions of parathyroid neoplasms in separate sexes. Based on the unexpected findings of this study, we recommend the right inferior cervical region be explored first in males with suspected parathyroid tumors of indeterminate location.

PMID: 24160792

11. Clin Med Insights Endocrinol Diabetes. 2013 Oct 23;6:63-7. doi: 10.4137/CMED.S13114. **IF:0.38**

Surgery for primary hyperparathyroidism in patients with preoperatively negative sestamibi scan and discordant imaging studies: the usefulness of intraoperative parathyroid hormone monitoring.

Calò PG, Pisano G, Loi G, Medas F, Tatti A, Piras S, Nicolosi A.
Author information

Abstract

The aim of this study was to evaluate the impact of intraoperative parathyroid hormone (PTH) monitoring on surgical strategy, intraoperative findings, and outcome in patients with negative sestamibi scintigraphy and with discordant imaging studies. We divided our 175 patients into 3 groups: group A was methoxyisobutylisonitrile (MIBI)-positive and ultrasonography positive and was concordant (114 patients), group B was MIBI-positive and ultrasonography-negative (50 patients), and group C was MIBI-and ultrasonography-negative (11 patients). The overall operative success was 99.12% in group A, 98% in group B, and 90.91% in group C, with an incidence of multiglandular disease of 3.5% in group A, 12% in group B, and 9.09% in group C. Intraoperative PTH monitoring changed the operative management in 2.63% of patients in group A and 14% in group B. The use of intraoperative PTH achieves to obtain excellent

results in the treatment of primary hyperparathyroidism in high-volume centers, even in the most difficult cases, during MIBI-negative and discordant preoperative imaging studies.

KEYWORDS:

intraoperative PTH, parathyroidectomy, primary hyperparathyroidism, sestamibi scintigraphy

PMID: 24250241 http://dx.doi.org/10.4137/CMED.S13114

12. Korean J Pathol. 2013 Oct;47(5):466-71. doi: 10.4132/KoreanJPathol.2013.47.5.466. Epub 2013 Oct 25. **IF:0.18**

Fine needle aspiration cytology of parathyroid lesions.

Heo I, Park S, Jung CW, Koh JS, Lee SS, Seol H, Choi HS, Cho SY.

Author information

Abstract

BACKGROUND:

There has been an increase in the use of fine needle aspiration cytology (FNAC) for the diagnosis of parathyroid lesions (PLs). Differentiation between a thyroid lesion and a PL is not easy because of their similar features. We reviewed parathyroid aspirates in our institution and aimed to uncover trends in diagnostic criteria.

METHODS:

We selected 25 parathyroid aspirates (from 6 men and 19 women) confirmed surgically or immunohistochemically from 2006 to 2011.

RESULTS:

Major architectural findings of PLs include scattered naked nuclei, loose clusters, a papillary pattern with a fibrovascular core, tight clusters, and a follicular pattern. These architectures were commonly admixed with one another. Cytological features included anisokaryosis, stippled chromatin, a well-defined cell border, and oxyphilic cytoplasm. Eighteen of the 25 patients were diagnosed with PL using FNAC. Seven patients had been misdiagnosed with atypical cells (n=2), benign follicular cells (n=2), adenomatous goiter (n=2) and metastatic carcinoma (n=1) in FNAC. Using clinicoradiologic data, the sensitivity of the cytological diagnosis was 86.7%. The cytological sensitivity decreased to 50% without this information.

CONCLUSIONS:

FNAC of PL is easily confused with thyroid lesions. A combination of cytological parameters and clinical data will be required to improve the diagnostic sensitivity of PLs.

KEYWORDS:

Biopsy, fine-needle, Cytology, Parathyroid lesions

PMID: 24255635 http://dx.doi.org/10.4132/KoreanJPathol.2013.47.5.466

PARATİROİD

VAKA SUNUMU

1. J Clin Endocrinol Metab. 2013 Oct 31. [Epub ahead of print] **IF:7.02**

Denosumab for Management of Parathyroid Carcinoma-Mediated Hypercalcemia.

Vellanki P, Lange K, Elaraj D, Kopp PA, El Muayed M.
Author information

Abstract

Context:Most of the morbidity and mortality from parathyroid cancer is due to PTH-mediated hypercalcemia. Classically, management mainly consists of surgical resection, chemotherapy, and alleviation of hypercalcemia using bisphosphonates and calcium receptor agonists. The use of denosumab in the treatment of parathyroid cancer-mediated hypercalcemia has not been reported.Objective:The aim of this report is to describe the effect of denosumab on parathyroid cancer-induced hypercalcemia.Subject, Measures, and Result:The patient presented at age 39 with metastatic parathyroidcancer. His calcium levels initially responded to surgery, bisphosphonates, calcium receptor agonist, and chemotherapy (dacarbazine). However, his disease progressed, and his hypercalcemia became refractory to these measures in the setting of rising PTH levels. The addition of denosumab, a humanized monoclonal antibody inhibiting receptor activator of nuclear factor κB ligand resulted in successful management of his hypercalcemia for an additional 16 months.Conclusions:Denosumab can be effective in the treatment of refractory hypercalcemia in parathyroid cancer. It may also be of potential use in settings of benign hyperparathyroid-related hypercalcemia such as parathyromatosis, where hypercalcemia is not amenable to surgery or medical therapy with bisphosphonates and calcium receptor agonists.

PMID: 24178790

2. J Clin Endocrinol Metab. 2013 Nov;98(11):4273-8. doi: 10.1210/jc.2013-2705. Epub 2013 Aug 16.
IF:7.02

Deliberate total parathyroidectomy: a potentially novel therapy for tumor-induced hypophosphatemic osteomalacia.

Bhadada SK, Palnitkar S, Qiu S, Parikh N, Talpos GB, Rao SD.
Author information

Abstract

BACKGROUND:

Tumor-induced osteomalacia (TIO) is an acquired hypophosphatemic metabolic bone disorder that can be cured by removing or ablating the offending tumor. However, when the tumor cannot be localized, lifelong therapy with oral phosphate and calcitriol or cinacalcet with close monitoring is required.

CASE REPORT:
A 56-year-old man was diagnosed with TIO in 1990. Initial therapy consisted of oral phosphate and calcitriol with symptomatic and biochemical improvement and healing of osteomalacia. Eight years later, hypercalcemic hyperparathyroidism developed, requiring subtotal parathyroidectomy with a transient increase in serum phosphate and normalization of serum calcium and PTH. Recurrent hypercalcemic hyperparathyroidism developed after 10 years of medical therapy. A deliberate total parathyroidectomy produced a prompt rise in serum phosphate into the normal range > 3.0 mg/dL and remained normal during the next 4 years of follow-up, despite continued very high serum fibroblast growth factor-23 levels throughout the 23-year follow-up.

CONCLUSION:
We report an unusual case of a TIO patient with long-term follow-up who developed recurrent hypercalcemic hyperparathyroidism on long-term oral phosphate therapy. Deliberate total parathyroidectomy normalized serum phosphate despite persistently elevated fibroblast growth factor-23 levels. Total parathyroidectomy offers a potentially novel therapy in some patients with TIO in whom medical therapy is not feasible or the tumor is unresectable.

PMID: 23956343 http://dx.doi.org/10.1210/jc.2013-2705

3. BMJ Case Rep. 2013 Oct 11;2013. pii: bcr2013200813. doi: 10.1136/bcr-2013-200813. **IF:1.58**

A rare cystic lesion of the neck: parathyroid cyst.

Kaplanoglu V, Kaplanoglu H, Cılız DS, Duran S.
Author information

Abstract

Parathyroid cysts are rarely observed neck masses. Their physical examination is not specific and preoperative diagnosis is usually difficult. Imaging findings and ultrasound-guided fine-needle aspiration with hormone analysis evaluation are important diagnostic criteria. A 48-year-old female patient admitted to our hospital with a symptom of swelling on the left side of the neck was diagnosed with parathyroid cyst by imaging methods (ultrasonography, MRI, parathyroid scintigraphy) and laboratory findings. Fine-needle aspiration biopsy was performed and because of relapse on the follow-up sclerotherapy was planned. Our aim in this study was to present the radiological findings of this case of parathyroid cyst.

PMID: 24121814 http://dx.doi.org/10.1136/bcr-2013-200813

4. Am J Med Sci. 2013 Nov;346(5):432-4. doi: 10.1097/MAJ.0b013e31829bce2e. **IF:1.39**

A rare case of double parathyroid lipoadenoma with hyperparathyroidism.

Ogrin C.
Author information

Abstract

A rare case of double lipoadenomas of parathyroid glands with hyperparathyroidism is described. A 56-year-old woman was referred for management of diabetes. Work up

revealed: serum Calcium (Ca) =11.9 mg/dl, glomerular filtration rate (GFR) = 103 ml/min/m2, parathyroid hormone (PTH) = 60 pg/ml, Phosphorus = 3.0 mg/dl, 25 hydroxy vitamin D (25 OH D) =16.5 ng/ml, 24 h urine Calcium =179 mg/day. Parathyroid sestamibi scan showed increased activity in the left thyroid and right thyroid lobe. Single photon emission computed tomography demonstrated uptake in inferior left and right thyroid lobes. Her serum calcium following successful bilateral parathyroidectomy was 9.3 mg/dl. Pathology showed double parathyroid lipoadenomas. After surgery, her serum Calcium and PTH normalized to 9.8 mg/dl and 32 pg/ml respectively. Lipoadenoma has been described as a very rare lesion of the parathyroid gland and is most commonly non-functional. PubMed search failed to reveal any case of hyperparathyroidism due to doubleparathyroid lipoadenomas.

PMID: 24157966 http://dx.doi.org/10.1097/MAJ.0b013e31829bce2e

5. Clin Nucl Med. 2013 Oct 22. [Epub ahead of print] **IF:0.86**

False-Positive Result in 18F-Fluorocholine PET/CT Due to Incidental and Ectopic Parathyroid Hyperplasia.

Cazaentre T, Clivaz F, Triponez F.
Author information

Abstract

PET/CT with F-fluorocholine (a positron-labeled choline analog) is currently used as a diagnostic tool for restaging prostate cancer patients with increasing prostate-specific antigen. We present an unusual case of a false-positive result using F-fluorocholine PET/CT because of incidental and ectopic parathyroid hyperplasia.

PMID: 24152627

ADRENAL

PROSPEKTİF

1. Lab Invest. 2013 Dec 16. doi: 10.1038/labinvest.2013.148. [Epub ahead of print] **IF:4.17**

Analysis of circulating microRNAs in adrenocortical tumors.

Szabó DR[1], Luconi M[2], Szabó PM[3], Tóth M[1], Szücs N[1], Horányi J[4], Nagy Z[1], Mannelli M[2], Patócs A[5], Rácz K[1], Igaz P[1].

Author information

Abstract

Differential diagnosis of adrenocortical adenoma (ACA) and carcinoma is of pivotal clinical relevance, as the prognosis and clinical management of benign and malignant adrenocortical tumors (ACTs) is entirely different. Circulating microRNAs (miRNAs) are promising biomarker candidates of malignancy in several tumors; however, there are still numerous technical problems associated with their analysis. The objective of our study was to investigate circulating miRNAs in ACTs and to evaluate their potential applicability as biomarkers of malignancy. We have also addressed technical questions including the choice of profiling and reference gene used. A total of 25 preoperative plasma samples obtained from patients with ACAs and carcinomas were studied by microarray and quantitative real-time PCR. None of the three miRNAs (hsa-miR-192, hsa-mir-197 and hsa-miR-1281) found as differentially expressed in plasma samples in our microarray screening could be validated by quantitative real-time PCR. In contrast, of the selected eight miRNAs reported in the literature as differentially expressed in ACT tissues, five (hsa-miR-100, hsa-miR-181b, hsa-miR-184, hsa-miR-210 and hsa-miR-483-5p) showed a statistically significant overexpression in adrenocortical cancer vs adenoma when normalized on hsa-miR-16 as a reference gene. Receiver operator characteristic analysis of data revealed that the combination of $dCT_{hsa\text{-}miR\text{-}210}$ - $dCT_{hsa\text{-}miR\text{-}181b}$ and $dCT_{hsa\text{-}miR\text{-}100}/dCT_{hsa\text{-}miR\text{-}181b}$ showed the highest diagnostic accuracy (area under curve 0.87 and 0.85, respectively). In conclusion, we have found significant differences in expression of circulating miRNAs between ACAs and carcinomas, but their diagnostic accuracy is not yet high enough for clinical application. Further studies on larger cohorts of patients are needed to assess the diagnostic and prognostic potential application of circulating miRNA markers.Laboratory Investigation advance online publication, 16 December 2013; doi:10.1038/labinvest.2013.148.

PMID: 24336071 http://dx.doi.org/10.1038/labinvest.2013.148

2. World J Surg. 2013 Nov 14. [Epub ahead of print] **IF:2.47**

Prospective Study to Compare Peri-operative Hemodynamic Alterations following Preparation forPheochromocytoma Surgery by Phenoxybenzamine or Prazosin.

Agrawal R, Mishra SK, Bhatia E, Mishra A, Chand G, Agarwal G, Agarwal A, Verma AK.
Author information

Abstract

BACKGROUND:
Prospective studies comparing the efficacy of selective versus nonselective alpha blockers for preoperative preparation ofpheochromocytoma (PCC) are lacking. In this prospective nonrandomized study, we compared the outcome of preoperative preparation with phenoxybenzamine (PBZ) and prazosin (PRZ) in terms of perioperative hemodynamic alterations.

METHODS:
The study was conducted at a tertiary referral center from July 2010 to December 2012. Thirty-two patients with PCC underwent operation after adequate preparation with PBZ (n = 15) or PRZ (n = 17). Five pediatric and adolescent patients were excluded because of different hemodynamics in this population. Perioperative monitoring was done for pulse rate (PR) and blood pressure (BP) alterations, occurrence of arrhythmias, and time taken to achieve hemodynamic stability. Groups were compared with the Mann-Whitney test, Student's t test, and the χ^2 test as applicable.

RESULTS:
Patients in the two groups were similar in age, gender, 24 h urinary metanephrine and normetanephrine levels, and type of procedure. Patients prepared with PRZ had significantly more intraoperative episodes of transient hypertension (systolic BP ≥ 160 mmHg) and hypertensive urgency (BP > 180/110 mmHg) (p 0.02, 0.03, respectively). More patients receiving PRZ suffered from transient severe hypertension (SBP ≥ 220 mmHg) (p 0.03). The PRZ group also had more median maximum SBP (233 mmHg vs PBZ 181.5 mmHg) (p = 0.01) and lesser median minimum SBP (71 mmHg vs PBZ 78 mmHg) (p 0.03). No significant differences were found between the study groups for changes in PR, postoperative BP alterations, occurrence of arrhythmias, and time taken to achieve hemodynamic stability.

CONCLUSIONS:
PBZ was found superior to PRZ in having fewer intraoperative hemodynamic fluctuations.

PMID: 24233658

ADRENAL

RETROSPEKTİF

1. J Clin Endocrinol Metab. 2013 Nov;98(11):E1813-9. doi: 10.1210/jc.2013-1653. Epub 2013 Sep 12.

IF:7.02

The characterization of pheochromocytoma and its impact on overall survival in multiple endocrine neoplasia type 2.

Thosani S, Ayala-Ramirez M, Palmer L, Hu MI, Rich T, Gagel RF, Cote G, Waguespack SG, Habra MA, Jimenez C.

Author information

Abstract

CONTEXT:

Pheochromocytoma (PHEO) occurs in 50% of patients with multiple endocrine neoplasia type 2 (MEN2). It is unknown if the presence of PHEO is associated with more aggressive medullary thyroid cancer (MTC).

OBJECTIVE:

To present our experience with MEN2 PHEO and evaluate whether PHEO impacts MTC overall survival in patients with RET codon 634 mutations.

DESIGN:

We performed a retrospective chart review of MEN2 patients at MD Anderson Cancer Center from 1960 through 2012.

PATIENTS:

The study group comprised 85 patients (group 1) with MEN2-associated PHEO. Of these, 59 patients (subgroup 1) with RET codon 634 mutations were compared to 48 patients (group 2) with RET codon 634 mutations, but without MEN2-associated PHEO.

MAIN OUTCOME MEASURES:

Of 85 patients with MEN2 and PHEO, 70 had MEN2A and 15 had MEN2B. Median age at PHEO diagnosis was 32 years. The initial manifestation of MEN2 was MTC in 60% of patients, synchronous MTC and PHEO in 34%, and PHEO in 6% of patients. Of patients, 72% had bilateral PHEO, and most tumors were synchronous (82%). Subgroup analysis of MEN2 patients with and without PHEO, who were carriers of RET codon 634, the most common mutation with PHEO, showed no significant differences in the stage of MTC at initial diagnosis. The median follow-up time for patients with PHEO was 249 months and without PHEO was 67 months ($P < .01$). Survival analyses among RET 634 carriers did not show shorter survival for patients with PHEO. The median survival time for patients with PHEO was 499 months and without PHEO was 444 months ($P < .05$).

CONCLUSIONS:

PHEO in MEN2 patients are usually bilateral and unlikely to be metastatic. Subgroup analysis of patients with RET 634 mutations with and without PHEO showed that PHEO was not associated with a more advanced stage of MTC at diagnosis or a shorter survival.

PMID: 24030942 http://dx.doi.org/10.1210/jc.2013-1653

2. J Clin Endocrinol Metab. 2013 Oct;98(10):4006-12. doi: 10.1210/jc.2013-1907. Epub 2013 Jul 24.

IF:7.02

One-year progression-free survival of therapy-naive patients with malignant pheochromocytoma and paraganglioma.

Hescot S, Leboulleux S, Amar L, Vezzosi D, Borget I, Bournaud-Salinas C, de la Fouchardiere C, Libé R, Do Cao C, Niccoli P, Tabarin A, Raingeard I, Chougnet C,Giraud S, Gimenez-Roqueplo AP, Young J, Borson-Chazot F, Bertherat J, Wemeau JL, Bertagna X, Plouin PF, Schlumberger M, Baudin E; French group of Endocrine and Adrenal tumors (Groupe des Tumeurs Endocrines-REseau NAtional des Tumeurs ENdocrines and COrtico-MEdullo Tumeurs Endocrines networks).

Author information

Abstract

CONTEXT:

The natural history of malignant pheochromocytoma or paragangliomas (MPP) remain unknown.

OBJECTIVE:

The primary aim of this study was to define progression-free survival at 1 year in therapy-naive patients with MPP. Secondary objectives were to characterize MPP and to look for prognostic parameters for progression at 1 year.

DESIGN AND SETTING:

The files of MPP followed up between January 2001 and January 2011 in two French Endocrine Networks were retrospectively reviewed. Therapy-naive patients were enrolled.

MAIN OUTCOME MEASURES:

The main outcome was progression-free survival at 1 year in therapy-naive MPP patients according to Response Evaluation Criteria In Solid Tumors 1.1 criteria.

RESULTS:

Ninety files (46 men, 44 women, mean age of 47.5 ± 15 years) were reviewed on site by one investigator. MPP characteristics were as follows: presence of an adrenal primary, a mitotic count exceeding 5 per high power field, hypertension, inherited disease, and presence of bone metastases in 50%, 22%, 60%, 49%, and 56% patients, respectively. Fifty-seven of the 90 patients with MPP (63%) were classified as therapy-naive. The median follow-up of these 57 patients was 2.4 years (range, 0.4-5.7). At 1 year, progression-free survival was 46% (CI 95: 33-59). Twenty-six of 30 (87%) patients with progression at 1 year had exhibited progressive disease at the first imaging workup performed after a median of 5.7 months. No prognostic parameter was identified.

CONCLUSIONS:

Half of the therapy-naive patients with MPP achieved stable disease at 1 year. In symptom-free patients with MPP, a wait-and-see antitumor policy seems appropriate as first line. Modality for a prospective follow-up is proposed.

PMID: 23884775 http://dx.doi.org/10.1210/jc.2013-1907

3. Ann Surg Oncol. 2013 Dec;20(13):4190-4. doi: 10.1245/s10434-013-3134-z. Epub 2013 Jul 18.

IF:4.33

Robotic versus laparoscopic adrenalectomy for pheochromocytoma.

Aliyev S, Karabulut K, Agcaoglu O, Wolf K, Mitchell J, Siperstein A, Berber E.
Author information

Abstract

BACKGROUND:
Although initial reports demonstrated the safety and feasibility of robotic adrenalectomy (RA), there are scant data on the use of this approach for pheochromocytoma. The aim of this study is to compare perioperative outcomes and efficacy of RA versus laparoscopic adrenalectomy (LA) for pheochromocytoma.

METHODS:
Within 3 years, 25 patients underwent 26 RA procedures for pheochromocytoma. These patients were compared with 40 patients who underwent 42 LA procedures before the start of the robotic program. Data were retrospectively reviewed from a prospectively maintained, IRB-approved adrenal database.

RESULTS:
Demographic and clinical parameters at presentation were similar between the groups, except for a larger tumor size in the robotic group. In both groups, skin-to-skin operative time, estimated blood loss less, and intraoperative hemodynamic parameters were similar. The conversion to open rate was 3.9 % in the robotic and 7.5 % in the laparoscopic group (p = .532). There was no morbidity or mortality in the robotic group; morbidity was 10 % (p = .041) and mortality 2.5 % in the laparoscopic group. The pain score on postoperative day 1 was lower, and the length of hospital stay shorter in the robotic group (1.2 ± .1 vs. 1.7 ± .1 days, p = .036).

CONCLUSIONS:
To our knowledge, this is the first study comparing robotic versus laparoscopic resection of pheochromocytoma. Our results show that the robotic approach is similar to the laparoscopic regarding safety and efficacy. The lower morbidity, less immediate postoperative pain, and shorter hospital stay observed in the robotic approach warrant further investigation in future larger studies.

PMID: 23864309 http://dx.doi.org/10.1245/s10434-013-3134-z

4. AJR Am J Roentgenol. 2013 Oct;201(4):825-33. doi: 10.2214/AJR.12.9576. **IF:3.25**

Multimodality imaging findings of pheochromocytoma with associated clinical and biochemical features in 53 patients with histologically confirmed tumors.

Raja A, Leung K, Stamm M, Girgis S, Low G.
Author information

Abstract

OBJECTIVE:

The purpose of this study was to determine the spectrum of imaging appearances of pheochromocytoma and the associated clinical and biochemical features.

MATERIALS AND METHODS:

In this retrospective study, a citywide pathology database (2000-2011) was searched to identify the records of patients with pheochromocytoma. The search yielded the cases of 53 patients (28 men, 25 women; mean age, 50 years). The institutional PACS and radiology information system records, hospital charts, and the provincial electronic health records of these patients were reviewed. Imaging appearances and clinical and biochemical features related to pheochromocytomas were recorded.

RESULTS:

One chart was not available for review. In the 52 cases analyzed, 40 of the patients had symptoms: 31 patients had hypertension; 10 had the triad of palpitations, diaphoresis, and headaches; and all had elevated urinary metanephrine concentrations. Seven patients had a familial syndrome, and five had bilateral pheochromocytomas. One patient had an extraadrenal pheochromocytoma, and five had malignant tumors. The mean size of pheochromocytomas was 4.0 cm. Most pheochromocytomas were heterogeneous (CT, 56%; MRI, 65%; ultrasound, 45%) and were MIBG positive (90%). Eleven of 34 (32%) pheochromocytomas had T2 signal intensity greater than that of the spleen. Most pheochromocytomas were less enhancing than the spleen (CT, 85%; MRI, 71%). Contrast-enhanced CT was performed on 33 tumors, of which 20 enhanced less than the spleen and 8 showed similar enhancement to the spleen; contrast-enhanced MRI was performed on 24 tumors, of which 12 enhanced less than the spleen and 5 showed similar enhancement to the spleen. Predominant cystic change was found in 4 of 20 (20%) ultrasound, 9 of 41 (22%) CT, and 11 of 34 (32%) MRI examinations. Eight of 34 (24%) pheochromocytomas were hemorrhagic, two (5%) had calcifications, and three of six were PET positive. Two cystic pheochromocytomas and one lipid-containing pheochromocytoma were misdiagnosed as adrenal adenomas.

CONCLUSION:

Most pheochromocytomas were heterogeneous at imaging, were MIBG positive, accompanied elevated urinary metanephrine concentrations, and were symptomatic. High T2 signal intensity was found in approximately one third of solid tumors. Atypical imaging features included homogeneity, cystic change, hemorrhage, intense enhancement, calcifications, intracellular lipid, bilaterality, and malignancy.

PMID: 24059371 http://dx.doi.org/10.2214/AJR.12.9576

5. J Endourol. 2013 Nov 9. [Epub ahead of print] **IF:2.36**

Retroperitoneal Laparoendoscopic Single-Site Adrenalectomy for Pheochromocytoma: Our Single Center Experiences.

Yuan X, Wang D, Zhang X, Cao X, Bai T.
Author information

Abstract

Abstract Objective: To evaluate the feasibility and safety of retroperitoneal laparoendoscopic single-site adrenalectomy for pheochromocytoma (LESS-PHEO) and summarize our initial experience. Patients and Methods: Between June 2009 and June 2013, 21 patients with adrenal pheochromocytomaunderwent adrenalectomy by means of LESS-PHEO in our department. Fifty-three patients with pheochromocytoma underwent conventional retrolaparoscopic adrenalectomy (RLAP-PHEO) between March 2001 and June 2013, of whom 42 were selected as a control group for a retrospective serial case-control analysis (1:2 matched-pair cohort). In the operation, the retroperitoneal space was created and dilated by blunt finger dissection and the pneumoperitoneal pressure was maintained below 10 mm Hg. As the first step, ligation of the adrenal central vein was performed. Intraoperative hemodynamic parameters, operating time, estimated blood loss, transfusion requirement, incidence of perioperative complications, visual analog pain scale (VAPS) score, time to resumption of oral intake and ambulation, and postoperative hospitalization were compared between the groups. Results: All the operations were technically successful, without reoperations or conversion to open procedures. The 24-hour postoperative VAPS score was lower in the LESS-PHEO group than in the control group (5 vs. 7; $p<0.001$). Despite a longer median operative time (167.4 minutes vs. 125.5 minutes; $p<0.001$), the patients in the LESS-PHEO group resumed oral intake sooner (1 day vs. 2 days; $p<0.001$), ambulated sooner (1 day vs. 2 days; $p<0.001$), and were discharged earlier (4 days vs. 7 days; $p<0.001$). No perioperative complications occurred in both the groups. No statistically significant differences in hemodynamic parameters or estimated blood loss were found between the groups. Conclusion: Although more training and practice are needed to shorten its operative time, LESS-PHEO, as performed by an experienced laparoscopic urologist, is a feasible and safe procedure associated with less postoperative pain and faster recovery.

PMID: 24004249

6. J Endourol. 2014 Jan;28(1):112-6. doi: 10.1089/end.2013.0298. Epub 2013 Oct 23. **IF:2.36**

Perioperative, functional, and oncologic outcomes of partial adrenalectomy for multiple ipsilateral pheochromocytomas.

Gupta GN, Benson JS, Ross MJ, Sundaram VS, Lin KY, Pinto PA, Linehan WM, Bratslavsky G.
Author information

Abstract

Abstract Objective: Managing patients with multiple adrenal masses is technically challenging. We present our experience with minimally invasive partial adrenalectomy (PA) performed for synchronous multiple ipsilateral pheochromocytomas in a single setting. Materials and Methods: We reviewed records of patients undergoing PA for pheochromocytoma at the National Cancer Institute between 1994 and 2010. Patients

were included if multiple tumors were excised from the ipsilateral adrenal gland in the same operative setting. Perioperative, functional, and oncologic outcomes of PA for multiple pheochromocytomas are shown. Results: Of 121 partial adrenalectomies performed, 10 procedures performed in eight patients for synchronous multiple ipsilateral pheochromocytomas were identified. All eight patients were symptomatic at presentation. The mean patient age was 30.6 years, median follow up was 12 months. The average surgical time was 228 minutes, average blood loss of 125 mL, and average number of tumors removed was 2.6 per adrenal. In total, 26 tumors were removed, 24 were pathologically confirmed pheochromocytomas, while two were adrenal cortical hyperplasia. After surgery, all patients had resolution of their symptoms, one patient required steroid replacement postoperatively. On postoperative imaging, one patient had evidence of ipsilateral adrenal nodule at the prior resection site 2 months postoperatively, which was consistent with incomplete resection. Conclusions: Minimally invasive surgical resection of synchronous multiple pheochromocytomas is feasible with acceptable perioperative, functional, and short-term oncologic outcomes.

PMID: 23998199 http://dx.doi.org/10.1089/end.2013

7. J Endourol. 2014 Jan;28(1):56-60. doi: 10.1089/end.2013.0318. Epub 2013 Oct 23. **IF:2.36**

Laparoendoscopic single-site retroperitoneoscopic adrenalectomy for pheochromocytoma: case selection, surgical technique, and short-term outcome.

He Y, Chen Z, Luo YC, Fang XL, Chen X.
Author information

Abstract

Abstract Purpose: To present our experience with case selection and operative skills of laparoendoscopic single-site (LESS) retroperitoneoscopic adrenalectomy for pheochromocytoma and evaluate its feasibility. Patients and Methods: Between June 2011 and December 2012, we performed LESS retroperitoneoscopic adrenalectomy for 16 patients with pheochromocytoma. In all patients, the diameter of the pheochromocytoma was less than 4.0 cm. During the operation, a single-port access was inserted through a 2.5-3.0 cm transverse incision below the tip of the 12th rib. Internally, the operative procedure duplicates the conventional retroperitoneoscopic adrenalectomy for pheochromocytoma. Results: No conversions to open surgery or standard laparoscopy with additional trocars were necessary. The mean operative duration was 68.1 minutes (range 41-125 min). The mean blood loss was negligible (<50 mL), and no patient needed blood transfusion. Intraoperative hypertension (SBP>180 mmHg) occurred in 12.5% (2/16) of the patients. No patient had sustained hypertension, and none experienced intraoperative hypotension (systolic blood pressure <80 mm Hg). The only postoperative complication was one case of pneumonia successfully treated with antibiotics. The average postoperative hospital stay was 3.1 days (range 2-5 days). All patients left the hospital with a good cosmetic appearance. Conclusions: In properly selected patients, LESS retroperitoneoscopic adrenalectomy is a feasible and safe procedure for pheochromocytoma.

PMID: 23941419 http://dx.doi.org/10.1089/end.2013.0318

8. BMC Surg. 2013 Oct 8;13 Suppl 2:S5. doi: 10.1186/1471-2482-13-S2-S5. Epub 2013 Oct 8.

IF:2.06

Laparoscopic adrenal surgery: ten-year experience in a single institution.

Conzo G, Pasquali D, Della Pietra C, Napolitano S, Esposito D, Iorio S, De Bellis A, Docimo G, Ferraro F, Santini L, Sinisi A.

Abstract

BACKGROUND:

Minimal invasive adrenalectomy has become the procedure of choice to treat adrenal tumors with a benign appearance, ≤ 6 cm in diameter and weighing < 100 g. Authors evaluated medium- and long-term outcomes of laparoscopic adrenalectomy (LA), performed for ten years in a single endocrine surgery unit.

METHODS:

We retrospectively reviewed 88 consecutive patients undergone LA for lesions of adrenal glands from 2003 to 2013. The first 30 operations were considered part of the learning curve. Doxazosin was preoperatively administered in case of pheochromocytoma (PCC), while spironolactone and potassium were employed to treat Conn's disease. Perioperative cardiovascular status modifications and surgical and medium- and long-term results were analyzed.

RESULTS:

Forty nine (55.68%) functioning tumors, and one (1.13%) bilateral adrenal disease were identified. In 2 patients (2.27%) a supposed adrenal metastasis was postoperatively confirmed, while in no patients a diagnosis of incidental primitive malignancy was performed. There was no mortality or major post operative complication. The mean operative time was higher during the learning curve. Conversion and morbidity rates were respectively 1.13% and 5.7%. Intraoperative hypertensive crises (≥180/90 mmHg) were observed in 23.5% (4/17) of PCC patients and were treated pharmacologically with no aftermath. There was no influence of age, size and operative time on the occurrence of PCC intraoperative hypertensive episodes. Surgery determined a normalization of the endocrine profile. One single PCC persistence was observed, while in a Conn's patient, just undergone right LA, a left sparing adrenalectomy was performed for a contralateral metachronous aldosteronoma.

CONCLUSIONS:

LA, a safe, effective and well tolerated procedure for the treatment of adrenal neoplasms ≤ 6 cm, is feasible for larger lesions, with a similar low morbidity rate. Operative time has improved along with the increase of the experience and of the technological development. Preoperative adrenergic blockade did not prevent PCC intraoperative hypertensive crises, but facilitated the control of the hemodynamic stability.

PMID: 24267584 http://dx.doi.org/10.1186/1471-2482-13-S2-S5

9. BMC Surg. 2013 Nov 27;13(1):57. doi: 10.1186/1471-2482-13-57. **IF:2.06**

Preoperative workup in the assessment of adrenal incidentalomas: outcome from 282 consecutive laparoscopic adrenalectomies.

Musella M, Conzo G, Milone M, Corcione F, Belli G, De Palma M, Tricarico A, Santini L, Palazzo A, Bianco P, Biondi B, Pivonello R, Colao A.

Author information

Abstract

BACKGROUND:

To confirm the efficacy of preoperative workup, the authors analyse the results of a multicentre study in a surgical series of patients diagnosed with an adrenal incidentaloma.

METHODS:

The retrospective review of a prospectively collected database was conducted. The data was obtained by six surgical units operating in the Campania Region, Italy. Five-hundred and six (506) adrenalectomies performed between 1993 and 2011 on 498 patients were analysed. Final histology in patients with a preoperative diagnosis of incidentaloma and studied according to guidelines (230/282 patients group A) was compared with final histology coming from patients presenting the same preoperative diagnosis but studied not according to guidelines (52/282 patients group B).

RESULTS:

In group A preoperative diagnosis was confirmed at final histology in 76/81 (93.8%) cases of subclinical functioning lesions presenting as an incidentaloma. The preoperative detection of pheochromocytoma and primary adrenocortical cancer (ACC) reached 91.6% and 84.6% respectively. In group B conversion rate to open surgery was higher than in group A ($p = 0.02$). One pheochromocytoma was missed at preoperative diagnosis whereas one ACC smaller than 4 centimetres (cm) and coming from an incidental lesion was discovered. In both groups a significant association between increasing dimensions of incidentaloma and cancer has been observed ($p = 0.001$).

CONCLUSIONS:

This surgical series confirm the high efficacy of suggested guidelines. A significant preoperative detection rate of adrenal lesions presenting as incidentaloma is observed. The unnecessary number of adrenalectomies performed in understudied patients, causing higher morbidity, was not associated to a higher detection rate of primary adrenocortical cancer.

PMID: 24279337 http://dx.doi.org/10.1186/1471-2482-13-57

10. J Endocrinol Invest. 2013 Oct;36(9):707-11. doi: 10.3275/8928. Epub 2013 Apr 8. **IF:1.57**

Adrenal hemorrhagic pseudocyst as the differential diagnosis of pheochromocytoma--a review of the clinical features in cases with radiographically diagnosed pheochromocytoma.

Kyoda Y, Tanaka T, Maeda T, Masumori N, Tsukamoto T.
Author information

Abstract

BACKGROUND:
Clinical diagnosis of pheochromocytoma is difficult for some adrenal tumors.

AIM:
Herein, we review clinical and pathological findings of 31 cases with radiographically diagnosed pheochromocytoma, including three cases of hemorrhagic pseudocysts (HPC).

MATERIALS/SUBJECTS AND METHODS:
Between January 1992 and December 2010, 31 patients with adrenal tumors were pre-operatively diagnosed as having pheochromocytoma by radiographic imaging, and underwent adrenalectomy. Histological examination revealed HPC in 3 patients (9.7%), and pheochromocytoma in the remaining 28 patients. We reviewed and compared the clinical features, including the biochemical and radiographic features, of HPC and pheochromocytoma cases.

RESULTS:
Biochemical testing showed no definitive excessive catecholamine secretion in any of the three patients with HPC and four (14.3%) of those with histologically proven pheochromocytoma. (131)Imetaiodobenzylguanidine scintigraphy was negative in the three with HPC, but positive in all of the four with pheochromocytoma who did not have suggestive biochemical results. All HPC patients had concomitant disease or symptoms suggestive ofpheochromocytoma, and two had received an anti-coaglant or anti-platelet agent. Laparoscopic surgery was completed in two cases of HPC uneventfully.

CONCLUSIONS:
Adrenal HPC may have radiographic characteristics similar to those of pheochromocytoma. Adrenal HPC should be considered as a differential diagnosis of pheochromocytoma.

PMID: 23563219 http://dx.doi.org/10.3275/8928

11. Am Surg. 2013 Nov;79(11):1196-202. **IF:0.98**

Role of preoperative adrenergic blockade with doxazosin on hemodynamic control during the surgical treatment of pheochromocytoma: a retrospective study of 48 cases.

Conzo G, Musella M, Corcione F, Depalma M, Stanzione F, Della-Pietra C, Palazzo A, Napolitano S, Pasquali D, Milone M, Agostino-Sinisi A, Ferraro F, Santini L.
Author information

Abstract

Authors evaluated the effects of selective adrenergic blockade by means of doxazosin on blood pressure in 48 patients operated on forpheochromocytoma by a multicenter retrospective study. Age, tumor size, surgical approach, and operative time were analyzed as predictive factors of intraoperative hypertensive crises. Forty-eight patients underwent adrenalectomy--four open surgery and 44 laparoscopic surgery--forpheochromocytoma of adrenal glands from 1998 to 2008 after preoperative administration of doxazosin. Perioperative cardiovascular status modifications and surgical medium- and long-term outcomes were analyzed. There was no mortality, conversion rate was 4.5 per cent, and morbidity rate was 8.3 per cent. Intraoperative hypertensive crises (180/90 mmHg or higher) were observed in 14.5 per cent (seven of 48) of patients and were treated pharmacologically with no aftermath. None of the examined variables influenced the occurrence of intraoperative hypertensive episodes. Postoperative hypotension (lower than 90/60 mmHg) was observed in four of 48 patients (8.3%) and was treated by crystalloids and hydrocortisone. In the surgical treatment of pheochromocytoma, the preoperative adrenergic blockade by doxazosin does not prevent intraoperative hypertensive crises. Nevertheless, in our series, they were of short duration and were not associated with major cardiovascular complications. Perioperative hemodynamic instability was managed by preoperative pharmacological treatment, allowing low morbidity.

PMID: 24165257

12. Clin Imaging. 2013 Nov-Dec;37(6):1084-8. doi: 10.1016/j.clinimag.2013.07.011. Epub 2013 Sep 12. **IF:0.85**

FDG PET in the evaluation of phaeochromocytoma: a correlative study with MIBG scintigraphy and Ki-67 proliferative index.

Lin M, Wong V, Yap J, Jin R, Leong P, Campbell P.
Author information

Abstract

To compare 123I-metaiodobenzylguanidine (MIBG) and [Fluorine-18]-2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) in 22 patients with phaeochromocytomas and paragangliomas (PGL) retrospectively and to evaluate the correlation between FDG uptake and Ki-67 proliferative index. Fourteen of 17 (82%) patients at initial diagnosis had positive FDG uptake, more intensely in PGL. Eleven of 12 (92%) patients had positive MIBG uptake. PET and MIBG scintigraphy were concordant in 10 patients, discordant in 6. Combined results yielded no false negative findings and are complementary. Neither maximum standardised uptake value nor visual scores on MIBG correlated with Ki-67.

KEYWORDS:

FDG, Ki-67 index, PET, Paraganglioma, Phaeochromocytoma

PMID: 24035263 http://dx.doi.org/10.1016/j.clinimag.2013.07.011

ADRENAL

VAKA SUNUMU

1. BMC Res Notes. 2013 Oct 8;6:405. doi: 10.1186/1756-0500-6-405. **IF:1.45**

Adrenocortical carcinoma initially presenting with hypokalemia and hypertension mimickinghyperaldosteronism: a case report.

Huang CJ, Wang TH, Lo YH, Hou KT, Won JG, Jap TS, Kuo CS.
Author information

Abstract

BACKGROUND:
Adrenocortical carcinoma is a rare malignancy and rare cause of Cushing's syndrome.

CASE PRESENTATION:
A 65-year-old seemingly well male patient was referred to our clinic under the suspicion of hyperaldosteronism due to hypertension combined with hypokalemia. However, his serum aldosterone and plasma renin activity were within normal limits. Instead, Cushing'ssyndrome was diagnosed by elevated urine free cortisol and a non-suppressible dexamethasone test. Abdominal computed tomography showed a 7.8 × 4.8 cm mass lesion at the right adrenal gland with liver invasion. Etomidate infusion was performed to reduce his cortisol level before the patient received a right adrenalectomy and liver wedge resection. The pathology report showed adrenocortical carcinoma with liver and lymph node metastasis. According to the European Network for the Study of Adrenal Tumors (ENSAT) staging system, the tumor was classified as T4N1M1, stage IV. Recurrent hypercortisolism was found shortly after surgery. The patient died of Fournier's gangrene with septic shock on the 59th day after diagnosis.

CONCLUSIONS:
We report a case of rapidly progressive stage IV adrenocortical carcinoma with initial presentations of hypokaelmia and hypertension, mimicking hyperaldosteronism.

PMID: 24103295 http://dx.doi.org/10.1186/1756-0500-6-405

2. Case Rep Anesthesiol. 2013;2013:514714. doi: 10.1155/2013/514714. Epub 2013 Oct 28. **IF:0.18**

Phaeochromocytoma crisis: two cases of undiagnosed phaeochromocytoma presenting after elective nonrelated surgical procedures.

Johnston PC, Silversides JA, Wallace H, Farling PA, Hutchinson A, Hunter SJ, Eatock F, Mullan KR.
Author information

Abstract

Phaeochromocytoma is a catecholamine producing tumour and an uncommon cause of hypertension. We present two cases of relatively asymptomatic individuals, in which

previously undiagnosed phaeochromocytoma was unmasked by elective nonadrenal surgical procedures, manifesting as postoperative hypertensive crisis and subsequent cardiogenic shock. The initial management in intensive care is discussed, in addition to the clinical and biochemical diagnostic challenges present. Successful adrenalectomy was performed in each case.

PMID: 24288628 http://dx.doi.org/10.1155/2013/514714

NET

DERLEME

1. Cancer Metastasis Rev. 2013 Dec 28. [Epub ahead of print] **IF:8.61**

Systemic therapeutic strategies for GEP-NETS: what can we expect in the future?

Raymond E, García-Carbonero R, Wiedenmann B, Grande E, Pavel M.
Author information

Abstract

Over the last few years, there have been important advances in the understanding of the molecular biology of neuroendocrine tumors (NETs) that have already translated into relevant advances in the clinic. Several studies have extensively assessed the mutational profile of NETs, and have shown the key roles that angiogenesis and the PI3K-AKT-mTOR pathway play in the pathogenesis of these tumors. Recent data has also revealed the potential relevance of transcription factors such as death domain-associated protein, x-linked mental retardation, and α-thalassemia syndrome protein or ataxia telangiectasia-mutated in NETs of pancreatic origin. This fast progress is leading to a rapidly increasing number of new agents being explored in the field of NETs. However, and despite some unquestionable success, objective remission rates remain low, and evidence of a substantial survival impact is lacking. Thus, there is an important need to improve our ability to identify patients most likely to benefit from specific therapies, and to incorporate biomarkers in the management of NETs. In addition, further efforts to understand mechanisms of escape and acquired resistance to the different available agents is of utmost importance, and will likely require performing paired tumor biopsies (prior and after treatment) or sequential sampling of surrogate tissues. Combinations of approved agents with new agents, either in a rational or biomarker-driven manner, are certainly warranted in this field. Likewise, sequential strategies to modulate and compensate for escape phenomenons are also of great interest. It should also be noted, however, that targeted agents are not innocuous and frequently yield toxicities that need to be adequately addressed by experienced specialists, particularly when drug combinations are considered. This review summarizes the salient data on biomarker and new agent development for the treatment of NETs.

PMID: 24375390

2. Endocr Relat Cancer. 2013 Dec 9. [Epub ahead of print] **IF:5.67**

Incidence of gastroenteropancreatic neuroendocrine tumours: a systematic review of the literature.

Fraenkel M, Kim MK, Faggiano A, de Herder WW, Valk GD.
Author information

Abstract

Based on the current medical literature, the worldwide incidence of neuroendocrine tumours (NETs) has seemed to increase; however, a systematic literature overview is lacking. This review aimed to collect all available data on the incidence of gastroenteropancreatic (GEP) NETs and population characteristics in order to establish their epidemiology. A sensitive MEDLINE search was performed. The papers were selected via a cascade process which restricted the initial pool of 7,991 articles to 31, using predefined inclusion and exclusion criteria. Original articles evaluating the incidence of sporadic GEP-NETs in regional, institutional and national registries were considered. The majority of data originates from the USA

National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) database and from national cancer registries in Western Europe minimising selection bias. Age-adjusted incidence of GEP-NETs has steadily increased over the past four decades (1973-2007), increasing 3.65-fold in the USA and 3.8-4.8-fold in the UK. Incidence has changed variably from one anatomic site to another. The greatest increase in incidence occurred for stomach and rectum NETs, while the smallest increase was for NETs of the small intestine. There were gender and racial differences, which differed site by site and, in some cases, changed over time. Incidence rates of GEP-NETs have significantly increased in the last 40 years. Data are only available from North America, Western Europe and Japan. A site-by-site analysis revealed that for some NETs the incidence rate increased more than others.

PMID: 24322304

3. Endocr Relat Cancer. 2013 Dec 18. [Epub ahead of print] **IF:5.67**

Evaluating neuroendocrine tumors progression and therapeutic response: state of the art.

de Mestier L, Dromain C, d'Assignies G, Scoazec JY, Lassau N, Lebtahi R, Brixi H, Mitry E, Guimbaud R, Courbon F, D'herbomez M, Cadiot G.
Author information

Abstract

Well-differentiated neuroendocrine tumors (NETs) are a heterogeneous group of rare tumors. They are often slow-growing and patients can have very long survival, even at the metastatic stage. The evaluation of tumor progression and therapeutic responses is currently based on Response Evaluation Criteria In Solid Tumors v1.1 (RECIST) criteria. As for other malignancies, RECIST criteria warrant being revisited in the era of targeted therapies, because tumor response to targeted therapies is rarely associated with shrinkage, as opposed to prolonged progression-free survival. Therefore, size-based criteria no longer seem suited to the assessment of NET progression and therapeutic responses, especially considering targeted therapies. New imaging criteria, combining morphological and functional techniques have proven relevant for other malignancies treated with targeted therapies. To date, such studies have rarely been conducted on NETs. Moreover, optimizing the management of NET patients also requires considering clinical, biological and pathological aspects of tumor evolution. Our objectives herein were to comprehensively review current knowledge on the assessment of tumor progression and early prediction of therapeutic responses, and to broaden the outlook on well-differentiated NETs, in the era of targeted therapies.

PMID: 24351682 h

4. Eur J Nucl Med Mol Imaging. 2013 Oct;40(11):1770-80. doi: 10.1007/s00259-013-2482-z. Epub 2013 Jul 20. **IF:4.82**

Somatostatin receptor PET/CT in neuroendocrine tumours: update on systematic review and meta-analysis.

Geijer H, Breimer LH.
Author information

Abstract

PURPOSE:
Neuroendocrine tumours (NET) are uncommon and may be localized in many different places in the body. Traditional imaging has mainly been performed with CT and somatostatin receptor scintigraphy (SRS). Recently, it has become possible to use somatostatin receptor PET/CT (SMSR PET) instead, which might

improve diagnostic quality. To evaluate the diagnostic quality of SMSR PET we performed a meta-analysis as an update of a previous study published in 2012.

METHODS:
A literature search was performed searching MEDLINE, Embase and five other databases with a combination of the expressions "PET", "positron emission tomography", "neuroendocrine" and "NET". The search was updated to 31 December 2012. Studies were selected which evaluated the sensitivity and specificity of SMSR PET for NET in the thorax or abdomen with a study size of at least eight patients. The methodological quality of the included studies was evaluated with QUADAS-2.

RESULTS:
Eight studies fulfilled the inclusion criteria and were selected for final analysis, and 14 articles from a previous meta-analysis were added for a total of 22 articles. A total of 2,105 patients were included in the studies, an increase from 567 in the previous meta-analysis. The pooled sensitivity was 93 % (95 % CI 91 - 94 %) and specificity 96 % (95 % CI 95 - 98 %). The area under the summary ROC curve was 0.98 (95 % CI 0.95 - 1.0). In the previous meta-analysis the pooled sensitivity was 93 % (95 % CI 91 - 95 %) and specificity 91 % (95 % CI 82 - 97 %).

CONCLUSION:
SMSR PET has good diagnostic performance for evaluation of NET in the thorax and abdomen, better than SRS which has been the previous standard method. This meta-analysis gives further support for switching to SMSR PET.

PMID: 23873003 http://dx.doi.org/10.1007/s00259-013-2482-z

5. J Am Coll Surg. 2013 Nov 6. pii: S1072-7515(13)01184-8. doi: 10.1016/j.jamcollsurg.2013.11.001. [Epub ahead of print] **IF:4.11**

Reassessment of the Current American Joint Committee on Cancer Staging System for PancreaticNeuroendocrine Tumors.

Qadan M, Ma Y, Visser BC, Kunz PL, Fisher GA, Norton JA, Poultsides GA.
Author information

Abstract

BACKGROUND:
Adopting a unified staging system for pancreatic neuroendocrine tumors (PNETs) has been challenging. Currently, the American Joint Committee on Cancer (AJCC) recommends use of the pancreatic adenocarcinoma staging system for PNETs. We sought to explore the prognostic usefulness of the pancreatic adenocarcinoma staging system for PNETs.

STUDY DESIGN:
The Surveillance, Epidemiology, and End Results program data were used to identify patients with PNETs who underwent curative-intent surgical resection from 1983 to 2008. The discriminatory ability of the AJCC system was examined and a new TNM system was devised using extent of disease variables.

RESULTS:
In 1,202 patients identified, lymph node metastasis was associated with worse 10-year overall survival after resection (51% vs 63%; $p < 0.0001$), as was the presence of distant metastatic disease (35% vs 62%; $p < 0.0001$). The current AJCC system (recorded by the Surveillance, Epidemiology, and End Results program in 412 patients since 2004) distinguished 5-year overall survival only between stages I and II ($p = 0.01$), but not between stages II and III ($p = 0.97$), or stages III and IV ($p = 0.36$). By modifying the T stage to be based on size alone (0.1 to 1.0 cm, 1.1 to 2.0 cm, 2.1 to 4.0 cm, and >4.0 cm) and revising the TNM subgroups, we propose a novel TNM system with improved discriminatory ability between disease stages (stages I vs II; $p = 0.16$; II vs III; $p < 0.0001$; and III vs IV; $p = 0.008$).

CONCLUSIONS:
In this study evaluating the current AJCC staging system for PNETs, there were no significant differences detected between stages II and III or stages III and IV. We propose a novel TNM system that might better discriminate between outcomes after surgical resection of PNETs.

PMID: 24321190 http://dx.doi.org/10.1016/j.jamcollsurg.2013.11.001

NET

RETROSPEKTİF

1. JAMA Surg. 2013 Oct;148(10):932-9. doi: 10.1001/jamasurg.2013.3376. **IF:13.51**

Pattern and clinical predictors of lymph node involvement in nonfunctioning pancreatic neuroendocrine tumors(NF-PanNETs).

Partelli S, Gaujoux S, Boninsegna L, Cherif R, Crippa S, Couvelard A, Scarpa A, Ruszniewski P, Sauvanet A, Falconi M.
Author information

Abstract

IMPORTANCE:
Nonfunctioning pancreatic neuroendocrine tumors (NF-PanNETs) are often indolent neoplasms without lymph node (LN) metastasis at diagnosis. Therefore, in patients with low risk of LN metastasis, the extent of surgery and lymphadenectomy could be limited and follow-up adjusted to the very low risk of relapse.

OBJECTIVE:
To construct a predicting model to assess the risk of pN+ prior to surgical resection for NF-PanNETs using preoperative retrievable variables.

DESIGN:
Retrospective review using multiple logistic regression analysis to construct predictive model of pN+ based on preoperatively available data.

SETTING:
The combined prospective databases of the Surgical Departments of the University of Verona, Verona, Italy, and Beaujon Hospital, Clichy, France, were queried for clinical and pathological data.

PARTICIPANTS:
All patients with resected (R0 or R1), pathologically confirmed NF-PanNETs between January 1, 1993 and December 31, 2009.

MAIN OUTCOME AND MEASURE:
Risk of lymph node metastases in patients with pancreatic neuroendocrine tumors.

RESULTS:
Among 181 patients, nodal metastases were reported in 55 patients (30%) and were associated with decreased 5-year disease-free survival (70% vs 97%, P < .001). Multivariable analysis showed that independent factors associated with nodal metastasis were radiological nodal status (rN) (odds ratio [OR], 5.58; P < .001) and tumor grade (NET-G2 vs NET-G1: OR, 4.87; P < .001) (first model). When the tumor grade was excluded, rN (OR, 4.73; P = .001) and radiological tumor size larger than 4 cm (OR, 2.67; P = .03) were independent predictors of nodal metastasis (second model). The area under the receiver operating characteristic curve for the first and second models were 80% and 74%, respectively.

CONCLUSIONS AND RELEVANCE:
Patients with NF-PanNET-G1 have a very low risk of pN+ in the absence of radiological signs of node involvement. When preoperative grading assessment is not achieved, the radiological size of the lesion is a powerful alternative predictor of pN+. The risk of pathological nodal involvement in patients with NF-PanNETs can be accurately estimated by a clinical predictive model.

PMID: 23986355 http://dx.doi.org/10.1001/jamasurg.2013.3376

2. Int J Cancer. 2013 Dec 18. doi: 10.1002/ijc.28675. [Epub ahead of print] **IF:6.15**

Analysis of 320 gastroenteropancreatic neuroendocrine tumors identifies TS expression as independent biomarker for survival.

Lee HS, Chen M, Kim JH, Kim WH, Ahn S, Maeng K, Allegra CJ, Kaye FJ, Hochwald SN, Zajac-Kaye M.
Author information

Abstract
Thymidylate synthase (TS), a critical enzyme for DNA synthesis and repair, is both a potential tumor prognostic biomarker as well as a tumorigenic oncogene in animal models. We have now studied the clinical implications of TS expression in gastroenteropancreatic (GEP) neuroendocrine tumors(NETs) and compared these results to other cell cycle biomarker genes. Protein tissue arrays were used to study TS, Ki-67, Rb, pRb, E2F1, p18, p21, p27 and menin expression in 320 human GEP-NETs samples. Immunohistochemical expression was correlated with univariate and multivariate predictors of survival utilizing Kaplan Meier and Cox proportional hazards models. Real time RT-PCR was used to validate these findings. We found that 78 of 320 GEP-NETs (24.4%) expressed TS. NETs arising in the colon, stomach and pancreas showed the highest expression of TS (47.4%, 42.6% and 37.3%, respectively), whereas NETs of the appendix, rectum and duodenum displayed low TS expression (3.3%, 12.9% and 15.4%, respectively). TS expression in GEP-NETs was associated with poorly differentiated endocrine carcinoma, angiolymphatic invasion, lymph node metastasis and distant metastasis ($p < 0.05$). Patients with TS-positive NETs had markedly worse outcomes than TS-negative NETs as shown by univariate ($p < 0.001$) and multivariate ($p = 0.01$) survival analyses. Expression of p18 predicted survival in TS-positive patients that received chemotherapy ($p = 0.015$). In conclusion, TS protein expression was an independent prognostic biomarker for GEP-NETs. The strong association of increased TS expression with aggressive disease and early death supports the role of TS as a cancer promoting agent in these tumors.

KEYWORDS:

gastroenteropancreatic neuroendocrine tumor, immunohistochemistry, survival analysis, thymidylate synthase

PMID: 24347111

3. Am J Surg Pathol. 2013 Nov;37(11):1671-7. doi: 10.1097/PAS.0000000000000089. **IF:5.53**

Grading of well-differentiated pancreatic neuroendocrine tumors is improved by the inclusion of both Ki67 proliferative index and mitotic rate.

McCall CM, Shi C, Cornish TC, Klimstra DS, Tang LH, Basturk O, Mun LJ, Ellison TA, Wolfgang CL, Choti MA, Schulick RD, Edil BH, Hruban RH.
Author information

Abstract
The grading system for pancreatic neuroendocrine tumors (PanNETs) adopted in 2010 by the World Health Organization (WHO) mandates the use of both mitotic rate and Ki67/MIB-1 index in defining the proliferative rate and assigning the grade. In cases when these measures are not concordant for grade, it is recommended to assign the higher grade, but specific data justifying this approach do not exist. Thus, we counted mitotic figures and immunolabeled, using the Ki67 antibody, 297 WHO mitotic grade 1 and 2 PanNETs surgically resected at a single institution. We quantified the Ki67 proliferative index by marking at least 500 cells in "hot spots" and by using digital image analysis software to count each marked

positive/negative cell and then compared the results with histologic features and overall survival. Of 264 WHO mitotic grade 1 PanNETs, 33% were WHO grade 2 by Ki67 proliferative index. Compared with concordant grade 1 tumors, grade-discordant tumors were more likely to have metastases to lymph node (56% vs. 34%) (P<0.01) and to distant sites (46% vs. 12%) (P<0.01). Discordant mitotic grade 1 PanNETs also showed statistically significantly more infiltrative growth patterns, perineural invasion, and small vessel invasion. Overall survival was significantly different (P<0.01), with discordant mitotic grade 1 tumors showing a median survival of 12 years compared with 16.7 years for concordant grade 1 tumors. Conversely, mitotic grade 1/Ki67 grade 2 PanNETs showed few significant differences from tumors that were mitotic grade 2 and either Ki67 grade 1 or 2. Our data demonstrate that mitotic rate and Ki67-based grades of PanNETs are often discordant, and when the Ki67 grade is greater than the mitotic grade, clinical outcomes and histopathologic features are significantly worse than concordant grade 1 tumors. Patients with discordant mitotic grade 1/Ki67 grade 2 tumorshave shorter overall survival and larger tumors with more metastases and more aggressive histologic features. These data strongly suggest that Ki67 labeling be performed on all PanNETs in addition to mitotic rate determination to define more accurately tumor grade and prognosis.

PMID: 24121170 http://dx.doi.org/10.1097/PAS.0000000000000089

4. Neuroendocrinology. 2013 Dec 17. [Epub ahead of print] **IF:3.86**

Enucleation and Limited Pancreatic Resection Provide Longterm Cure for Insulinoma in Multiple Endocrine Neoplasia Type 1?

Bartsch DK, Albers M, Knoop R, Kann PH, Fendrich V, Waldmann J.
Author information

Abstract

Aim: To assess the characteristics and longterm outcome after surgery in patients with multiple endocrine neoplasia type 1 (MEN1) associated insulinoma. Methods: Retrospective analysis of prospectively collected data of MEN1 patients with organic hyperinsulinism at a tertiary referral center. Results: Thirteen (17%) of 74 patients with MEN1 had organic hyperinsulinism. The median age at diagnosis was 27 (range 9 to 48) years. In 7 patients insulinoma was the first manifestation of the syndrome. All patients had at least one pancreatic neuroendocrine neoplasm (pNEN) upon imaging, including CT, MRI or endoscopic ultrasonography. Seven patients had solitary lesions upon imaging, 4 patients had one dominant tumor with coexisting multiple small pNENs and 2 patients had multiple lesions without dominance. Eight patients had limited resections (1 segmental resection, 7 enucleations), 4 subtotal distal pancreatectomies and 1 patient a partial duodenopancreatectomy. There was no postoperative mortality. Six patients experienced complications, including pancreatic fistula in 5 patients. Pathological examination revealed median three (range 1-14) macro-pNENs sized between 6 to 40 mm, and a total of 14 potentially benign insulinomas were detected in the 13 patients. After median follow-up of 156 months only one patient developed recurrent hyperinsulinism after initial enucleation. Twelve patients developed new pNENs in the pancreatic remnant and 4 patients underwent reoperations (3 for metastatic ZES, 1 for recurrent hyperinsulinism). One of 5 patients with an initial extended pancreatic resection developed insulin-dependent diabetes mellitus. Conclusion: Enucleation and limited resection provide longterm cure for MEN1 insulinoma in patients with solitary or dominant tumors. Subtotal distal pancreatectomy should thus be preserved for patients with multiple pNENs without dominance given the risk of exocrine and endocrine pancreas insufficiency in the mostly young patients.

PMID: 24356648

5. J Clin Gastroenterol. 2013 Dec 18. [Epub ahead of print] **IF:3.75**

Long-term Follow-up of Asymptomatic Pancreatic Neuroendocrine Tumors in Multiple Endocrine Neoplasia Type I Syndrome.

D'souza SL, Elmunzer BJ, Scheiman JM.
Author information

Abstract

BACKGROUND AND AIMS::
Pancreatic neuroendocrine tumors (PNETs) in asymptomatic patients may contribute to mortality. Endoscopic ultrasound (EUS) is the most accurate test to identify and monitor tumor size. The aim of this study was to examine the rate of growth and development of new tumors in multiple endocrine neoplasia type I (MEN 1).

MATERIALS AND METHODS::
A retrospective cohort study in a tertiary academic center. Patients identified in endoscopic databases were included if they had 2 or more EUS examinations with untreated asymptomatic tumors identified. The growth rate and incidence of new lesions was analyzed.

RESULTS::
A total of 11 patients were studied (7 female, 4 male). Initially, 18 lesions with an average size of 10.3 mm (range, 5 to 24 mm) were found. Mean surveillance was 79 months (range, 18 to 134 mo). The growth rate of index lesions was 1.32 mm/y; 11 lesions exhibited stability or a decrease in size. Twelve new lesions were identified in 7 patients during the surveillance period with an average growth rate of 3.0 mm/y. The earliest new lesion was identified at 12 months and the latest at 70 months after index EUS. New lesions had a faster growth rate than those seen on initial EUS (P=0.01).

CONCLUSIONS::
Multiple endocrine neoplasia type I patients exhibit an overall low rate of growth of pancreatic neuroendocrine tumors. Growth rate of newly diagnosed lesions was significantly faster, suggesting a variation in phenotypic expression of the disease. Therapy should be individualized based upon the tumor size and location, symptoms, overall clinical status, and operative risk.

PMID: 24356459

6. PLoS One. 2013 Dec 31;8(12):e86414. doi: 10.1371/journal.pone.0086414. **IF:3.67**

Second cancers in patients with neuroendocrine tumors.

Tsai HJ[1], Wu CC[2], Tsai CR[3], Lin SF[4], Chen LT[5], Chang JS[3].
Author information

Abstract

BACKGROUND:
Second cancers have been reported to occur in 10-20% of patients with neuroendocrine tumors (NETs). However, most published studies used data from a single institution or focused only on specific sites of NETs. In addition, most of these studies included second cancers diagnosed concurrently with NETs, making it difficult to assess the temporality and determine the exact incidence of second cancers. In this nationwide population-based study, we used data recorded by the Taiwan Cancer Registry (TCR) to analyze the incidence and distribution of second cancers after the diagnosis of NETs.

METHODS:
NET cases diagnosed from January 1, 1996 to December 31, 2006 were identified from the TCR. The data on the occurrence of second cancers were ascertained up to December 31, 2008. Standardized incidence ratios (SIRs) of second cancers were calculated based on the cancer incidence rates of the general population. Cox-proportional hazards regression analysis was performed to estimate the hazard ratio (HR)

and 95% confidence interval (CI) for the risk of second cancers associated with sex, age, and primary NET sites.

RESULTS:
A total of 1,350 newly diagnosed NET cases were identified according to the selection criteria. Among the 1,350 NET patients, 49 (3.63%) developed a second cancer >3 months after the diagnosis of NET. The risk of second cancer following NETs was increased compared to the general population (SIR = 1.48, 95% CI: 1.09-1.96), especially among those diagnosed at age 70 or older (HR = 5.08, 95% CI = 1.69-15.22). There appeared to be no preference of second cancer type according to the primary sites of NETs.

CONCLUSIONS:
Our study showed that the risk of second cancer following NETs is increased, especially among those diagnosed at age 70 or older. Close monitoring for the occurrence of second cancers after the diagnosis of NETs is warranted.

PMID:24392036 http://dx.doi.org/10.1371/journal.pone.0086414

7. Surgery. 2013 Nov 12. pii: S0039-6060(13)00465-0. doi: 10.1016/j.surg.2013.08.007. [Epub ahead of print] **IF:3.19**

Sporadic nonfunctioning pancreatic neuroendocrine tumors: Prognostic significance of incidental diagnosis.

Birnbaum DJ, Gaujoux S, Cherif R, Dokmak S, Fuks D, Couvelard A, Vullierme MP, Ronot M, Ruszniewski P, Belghiti J, Sauvanet A.
Author information

Abstract

BACKGROUND:
Sporadic nonfunctioning pancreatic neuroendocrine tumors (NF-PNETs) are increasingly diagnosed as incidentalomas, and their resection is usually recommended. The prognostic significance of this diagnosis feature is poorly studied, and management of these tumors remains controversial. Clinical, pathologic characteristics and outcome of resected incidentally diagnosed NF-PNET (Inc) were compared with resected symptomatic NF-PNET (Symp) to better assess their biologic behavior and tailor their management.

METHODS:
From 1994 to 2010, 108 patients underwent resection for sporadic nonmetastatic NF-PNET. Diagnosis was considered as incidental in patients with no abdominal symptoms or symptoms unlikely to be related to tumor mass. Patients with Inc were compared with patients with Symp, regarding demographics, postoperative course, pathology, and disease-free survival (DFS).

RESULTS:
Of the 108 patients, 65 (61%) had incidentally diagnosed tumors. Pancreas-sparing pancreatectomies (enucleation/central pancreatectomy) were performed more frequently in Inc (62% vs 30%, P = .001). Inc tumors were more frequently <20 mm (65% vs 42%, P = .019), staged T1 (62% vs 33%, P = .0001), node negative (85% vs 60%; P = .005), and grade 1 (66% vs 33%, P = .0001). One postoperative death occurred in the Inc group, and postoperative morbidity was similar between the two groups (60% vs 65%, P = .59). DFS was substantially better in the Inc group (5-year DFS = 92% vs 82%, P = .0016).

CONCLUSION:
Incidentally diagnosed NF-PNETs are associated with less aggressive features compared with symptomatic lesions but cannot always be considered to be benign. Operative resection remains recommended for most. Incidentally diagnosed NF-PNET may be good candidates for pancreas-sparing pancreatectomies.

PMID: 24238123 http://dx.doi.org/10.1016/j.surg.2013.08.007

8. Surgery. 2013 Oct;154(4):785-91; discussion 791-3. doi: 10.1016/j.surg.2013.07.004. **IF:3.19**

Predicting aggressive behavior in nonfunctioning pancreatic neuroendocrine tumors.

Cherenfant J, Stocker SJ, Gage MK, Du H, Thurow TA, Odeleye M, Schimpke SW, Kaul KL, Hall CR, Lamzabi I, Gattuso P, Winchester DJ, Marsh RW, Roggin KK, Bentrem DJ, Baker MS, Prinz RA, Talamonti MS.
Author information

Abstract

PURPOSE:
The biologic potential of nonfunctioning pancreatic neuroendocrine tumors (PNETs) is highly variable and difficult to predict before resection. This study was conducted to identify clinical and pathologic factors associated with malignant behavior and death in patients diagnosed with PNETs.

METHODS:
We used International Classification of Diseases 9th edition codes to identify patients who underwent pancreatectomy for PNETs from 1998 to 2011 in the databases of 4 institutions. Functioning PNETs were excluded. Multivariate regression Cox proportional models were constructed to identify clinical and pathologic factors associated with distant metastasis and survival.

RESULTS:
The study included 128 patients-57 females and 71 males. The age (mean ± standard deviation) was 55 ± 14 years. The body mass index was 28 ± 5 kg/m(2). Eighty-nine (70%) patients presented with symptoms, and 39 (30%) had tumors discovered incidentally. The tumor size was 3.3 ± 2 cm with 56 (44%) of the tumors measuring ≤2 cm. Seventy-three (57%) patients had grade 1 histology tumors, 37 (29%) had grade 2, and 18 (14%) had grade 3. Peripancreatic lymph node involvement was present in 31 patients (24%), absent in 75 (59%), and unknown in 22 (17%). Distant metastasis occurred in 18 patients (14%). There were 12 deaths, including 1 perioperative, 8 disease related, and 3 of unknown cause. With a median follow-up of 33 months, the overall 5-year survival was 75%. Multivariate Cox regression analysis identified age >55 (hazard ratio [HR], 5.89; 95% confidence interval [CI], 1.64-20.58), grade 3 histology (HR, 6.08; 95% CI, 1.32-30.2), and distant metastasis (HR, 8.79; 95% CI, 2.67-28.9) as risk factors associated with death ($P < .05$). Gender, race, body mass index, clinical symptoms, lymphovascular and perineural invasion, and tumor size were not related to metastasis or survival ($P > .05$). Three patients with tumors ≤2 cm developed distant metastasis resulting in 2 disease-related deaths.

CONCLUSION:
Age >55 years, grade 3 histology, and distant metastasis predict a greater risk of death from nonfunctioning PNETs. Resection or short-term surveillance should be considered regardless of tumor size.

PMID: 24074416 http://dx.doi.org/10.1016/j.surg.2013.07.004

9. World J Gastroenterol. 2013 Dec 21;19(47):9043-8. doi: 10.3748/wjg.v19.i47.9043. **IF:2.95**

Small bowel tumors detected and missed during capsule endoscopy: Single center experience.

Zagorowicz ES, Pietrzak AM, Wronska E, Pachlewski J, Rutkowski P, Kraszewska E, Regula J.
Author information

Abstract

AIM:

To characterize small bowel (SB) tumors detected by capsule endoscopy (CE), and identify missed tumors.

METHODS:

The study included 145 consecutive patients in whom 150 CEs were performed. Following CE, the medical records of the study population were reviewed. Results of double- or single-balloon enteroscopy performed after CE and the results of surgery in all patients operated on were retrieved. The patients were contacted through telephone interviews or postal mail. In addition, the national cancer registry and the polish clinical gastrointestinal stromal tumor (GIST) Registry were searched to identify missed neoplasms.

RESULTS:

Indications for CE included overt and occult obscure gastrointestinal bleeding (n = 81, 53.7%), anemia (n = 19, 12.7%), malabsorption (n = 18, 12%), abnormal CB follow through (n = 9, 6%), abdominal pain (n = 7, 5%), celiac disease (n = 5, 3%), neuroendocrine tumor (n = 3, 2%), Crohn's disease (n = 2, < 2%), Peutz-Jeghers syndrome (n = 2, < 2%), other polyposes (n = 2, < 2%), and diarrhea (n = 2, < 2%). The capsule reached the colon in 115 (76.6%) examinations. In 150 investigations, CE identified 15 SB tumors (10%), 14 of which were operated on or treated endoscopically. Malignancies included metastatic melanoma (n = 1), adenocarcinoma (n = 2), and GIST (n = 3). Benign neoplasms included dysplastic Peutz-Jeghers polyps (n = 4). Non-neoplastic masses included venous malformation (n = 1), inflammatory tumors (n = 2), and a mass of unknown histology (n = 1). During the follow-up period, three additional SB tumors were found (2 GISTs and one mesenteric tumor of undefined nature). The National Cancer Registry and Polish Clinical GIST Registry revealed no additional SB neoplasms in the post-examination period (follow-up: range 4.2-102.5 mo, median 39 mo). The sensitivity of CE for tumor detection was 83.3%, and the negative predictive value was 97.6%. The specificity and positive predictive value were both 100%.

CONCLUSION:

Neoplasms may be missed by CE, especially in the proximal SB. In overt obscure gastrointestinal bleeding, complementary endoscopic and/or radiologic diagnostic tests are indicated.

KEYWORDS:

Capsule endoscopy, Gastrointestinal bleeding, Gastrointestinal stromal tumor, Small bowel tumor, Tumor miss rate

PMID: 24379629 http://dx.doi.org/10.3748/wjg.v19.i47.9043

10. World J Gastroenterol. 2013 Dec 21;19(47):9012-9. doi: 10.3748/wjg.v19.i47.9012. **IF:2.95**

Clinically detected gastroenteropancreatic neuroendocrine tumors are on the rise: Epidemiological changes in Germany.

Scherübl H, Streller B, Stabenow R, Herbst H, Höpfner M, Schwertner C, Steinberg J, Eick J, Ring W, Tiwari K, Zappe SM.
Author information

Abstract

AIM:

To study the epidemiologic changes of gastroenteropancreatic neuroendocrine tumors (GEP-NET) in Germany, we analyzed two time periods 1976-1988 and 1998-2006.

METHODS:
We evaluated epidemiological data of GEP-NET from the former East German National Cancer Registry (DDR Krebsregister, 1976-1988) and its successor, the Joint Cancer Registry (GKR, 1998-2006), which was founded after German reunification. Due to a particularly substantial database the epidemiological data from the federal states of Mecklenburg-Western Pomerania, Saxony, Brandenburg and Thuringia, covering a population of more than 10.8 million people, were analyzed. Survival probabilities were calculated using life table analysis. In addition, GEP-NET patients were evaluated for one or more second (non-GEP-NET) primary malignancies.

RESULTS:
A total of 2821 GEP neuroendocrine neoplasms were identified in the two registries. The overall incidence increased significantly between 1976 and 2006 from 0.31 (per 100.000 inhabitants per year) to 2.27 for men and from 0.57 to 2.38 for women. In the later period studied (2004-2006), the small intestine was the most common site. Neuroendocrine (NE) neoplasms of the small intestine showed the largest absolute increase in incidence, while rectal NE neoplasms exhibited the greatest relative increase. Only the incidence of appendiceal NET in women showed little change between 1976 and 2006. Overall survival of patients varied for sex, tumor site and the two periods studied but improved significantly over time. Interestingly, about 20% of the GEP-NET patients developed one or more second malignancies. Their most common location was the gastrointestinal tract. GEP-NET patients without second malignancies fared better than those with one or more of them.

CONCLUSION:
The number of detected GEP-NET increased about 5-fold in Germany between 1976 and 2006. At the same time, their anatomic distribution changed, and the survival of GEP-NET patients improved significantly. Second malignancies are common and influence the overall survival of GEP-NET patients. Thus, GEP-NET warrant our attention as well as intensive research on their tumorigenesis.

KEYWORDS:

Endoscopy, Epidemiology, Gastrinoma, German history, Insulinoma, Neuroendocrine, Reunification, Second malignancy, Tumor

PMID: 24379626 http://dx.doi.org/10.3748/wjg.v19.i47.9012

11. World J Gastroenterol. 2013 Dec 14;19(46):8703-8. doi: 10.3748/wjg.v19.i46.8703. **IF:2.95**

Long-term follow up of endoscopic resection for type 3 gastric NET.

Kwon YH, Jeon SW, Kim GH, Kim JI, Chung IK, Jee SR, Kim HU, Seo GS, Baik GH, Choi KD, Moon JS.
Author information

Abstract

AIM:
To clarify the short and long-term results and to prove the usefulness of endoscopic resection in type 3 gastric neuroendocrine tumors (NETs).

METHODS:
Of the 119 type 3 gastric NETs diagnosed from January 1996 to September 2011, 50 patients treated with endoscopic resection were enrolled in this study. For endoscopic resection, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) was used. Therapeutic efficacy, complications, and follow-up results were evaluated retrospectively.

RESULTS:
EMR was performed in 41 cases and ESD in 9 cases. Pathologically complete resection was performed in 40 cases (80.0%) and incomplete resection specimens were observed in 10 cases (7 vs 3 patients in the EMR vs ESD group, P = 0.249). Upon analysis of the incomplete resection group, lateral or vertical margin

invasion was found in six cases (14.6%) in the EMR group and in one case in the ESD group (11.1%). Lymphovascular invasions were observed in two cases (22.2%) in the ESD group and in one case (2.4%) in the EMR group (P = 0.080). During the follow-up period (43.73; 13-60 mo), there was no evidence of tumor recurrence in either the pathologically complete resection group or the incomplete resection group. No recurrence was reported during follow-up. In addition, no mortality was reported in either the complete resection group or the incomplete resection group for the duration of the follow-up period.

CONCLUSION:
Less than 2 cm sized confined submucosal layer type 3 gastric NET with no evidence of lymphovascular invasion, endoscopic treatment could be considered at initial treatment.

KEYWORDS:

Carcinoid, Endoscopic resection, Neuroendocrine tumor, Stomach, Treatment

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12. Dig Dis Sci. 2013 Dec 10. [Epub ahead of print] **IF:2.65**

Surveillance Strategy for Rectal Neuroendocrine Tumors According to Recurrence Risk Stratification.

Kim DH, Lee JH, Cha YJ, Park SJ, Cheon JH, Kim TI, Kim H, Kim WH, Hong SP.
Author information

Abstract

BACKGROUND/AIM:
Rectal neuroendocrine tumors (NETs) have been increasing in incidence. However, the recommendations for disease surveillance after tumor resection have not been well established. We evaluated the long-term outcomes of rectal NETs and surveillance strategies according to recurrence risk stratification.

METHODS:
From January 2000 to July 2011, 188 patients diagnosed with rectal NETs were included in this study. Patient characteristics, treatment methods, recurrence rates, risk factors of recurrence, and surveillance schedules were analyzed.

RESULTS:
The male-to-female ratio was 1.29:1 and the mean age at diagnosis was 50.6 years. The mean tumor size was 6.5 (range 1-30) mm. A total of 144 patients (76.6 %) were treated with endoscopic resection, and 44 patients (23.4 %) were treated with surgical resection as the initial treatment. During the follow-up period, ten patients (5.3 %) had disease recurrence, including one case of local recurrence and nine cases of recurrence at a distant site. Tumor size of >10 mm, invasion of the muscularis propria, increased mitotic index, lymphovascular invasion, and regional lymph node metastases were statistically significant predictors of recurrence by univariate analysis. Among the 152 patients without risk factors of recurrence, only one patient who underwent transanal resection had a local recurrence at 15 months after surgery.

CONCLUSION:
Our patients with rectal NETs showed favorable clinical outcomes and had a low rate of recurrence. Intensive surveillance with endoscopy or imaging study may not be required in patients without risk factors for recurrence.

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13. J Hepatobiliary Pancreat Sci. 2013 Oct 20. doi: 10.1002/jhbp.47. [Epub ahead of print] **IF:2.44**

Analysis of risk factors for recurrence after curative resection of well-differentiated pancreatic neuroendocrine tumors based on the new grading classification.

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Author information

Abstract

BACKGROUND:
It is difficult to predict the malignant potential of pancreatic neuroendocrine tumors (PNETs) precisely. This study investigated the validity of a new grading system adopted by the World Health Organization 2010 classification to determine risk factors for recurrence of PNETs.

METHODS:
Data of 70 patients with PNETs who underwent curative resection were retrospectively examined by uni- and multivariate analyses. Histopathological findings were re-reviewed by experienced pathologists. NET G1 was defined as mitotic count <2 per 10 high power fields (HPF) and/or ≤2% Ki67 index, and NET G2 as 2-20 mitosis per 10 HPF and/or 3-20% Ki67 index.

RESULTS:
There were 58 patients with NET G1 and 12 with NET G2. Incidence of recurrence was 11.4%. Univariate analysis demonstrated significant risk factors for recurrence including NET G2 of histological grade (P = 0.0089), male gender (P = 0.0333), tumor size ≥ 20 mm (P = 0.0117), lymph node metastasis (P = 0.0004), liver metastasis (P < 0.0001), lymphatic invasion (P = 0.046), and neural invasion (P = 0.0002). By multivariate analysis, histological grade (hazard ratio; 59.76, P = 0.0022) and neural invasion (hazard ratio; 147.49, P = 0.0016) were significantly associated with recurrence of PNETs.

CONCLUSIONS:
This study confirmed the prognostic relevance of the new grading classification and that evaluation of perineural invasion and histological grade should be considered as prognostic predictors in well-differentiated PNETs (NET G1 and G2).

KEYWORDS:

Grading classification, Neural invasion, Pancreatic neuroendocrine tumor, Predictors of recurrence, WHO 2010 classification

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14. Pathol Int. 2013 Nov;63(11):532-8. doi: 10.1111/pin.12108. **IF:2.07**

Elevated Ki-67 labeling index in 'synchronous liver metastases' of well differentiated enteropancreaticneuroendocrine tumor.

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Author information

Abstract

There is no consensus as to whether or not metastatic nodules in the liver should be biopsied for tumor grading in cases of neuroendocrine tumorswith 'synchronous liver metastasis'. In this study, we compared the Ki-67 labeling index between the primary tumor and synchronous liver metastasis in 30 patients, who had received simultaneous resections. Examined tumors were of the small bowel (n = 18) or pancreas (n = 12), and G1 or G2 in primary histologic grade. In 20 patients (67%), the Ki-67 index was similar between

the primary tumor and liver metastasis, but 10 (33%) showed an elevation of 3.4-14.4% in the liver, which increased the tumor grade in 4 cases. The Ki-67 elevation in the liver was more common in G2 than G1 neoplasms (P = 0.002). The size, but not number, of liver metastases was significantly larger in patients with an elevated Ki-67 index (P = 0.006). Using 40 mm as a provisional cutoff for the greatest diameter of liver metastases, the positive predictive value of this discriminator for elevated Ki-67 was 56%, and the negative predictive value was 93%. In conclusion, synchronous liver metastases can yield a higher Ki-67 labeling index than primary neuroendocrine tumours, particularly when the secondary is greater than 40 mm.

KEYWORDS:

Ki-67, biopsy, grade, liver, neuroendocrine tumor, pancreas, small intestine

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15. Acta Cytol. 2013 Dec 10. [Epub ahead of print] **IF:0.93**

Fine Needle Aspiration of Oncocytic Variants of Pancreatic Neuroendocrine Tumor: A Report of Three Misdiagnosed Cases.

Chen S, Wang X, Lin J.
Author information

Abstract

Objectives: An oncocytic variant of pancreatic neuroendocrine tumors (PanNET) is exceedingly rare. Here we report cytomorphological features of the oncocytic variant of PanNET and discuss how to avoid diagnostic pitfalls. Study Design: A computerized search of our laboratory information system was performed over an 18-year period to identify all cytology and surgical pathology cases where a diagnosis of PanNET was made or considered in the differential diagnosis. Three cases of the oncocytic variant of PanNET were identified. Results: Endoscopic ultrasound-guided fine needle aspiration (FNA) smears showed cohesive clusters of large atypical cells with abundant eosinophilic granular cytoplasm, anisonucleosis, nuclear enlargement and overlapping, prominent nucleoli, and a relatively smooth nuclear membrane. Nuclei were round to oval with finely granular chromatin. Additional features included rare isolated cells and glandular formation. Some of these morphological features, such as anisonucleosis, nuclear enlargement, and overlapping, prominent nucleoli, are also commonly seen in the pancreatic adenocarcinoma. All these cases were misclassified by FNA as adenocarcinoma (2 cases) or suspicious for carcinoma (1 case) and were histologically confirmed to be oncocytic variants of PanNET. Conclusions: Useful salient features of the oncocytic variant of PanNET include abundant eosinophilic granular cytoplasm, finely granular chromatin, and relatively smooth nuclear membrane. The awareness of this variant will help to avoid misdiagnosis. © 2013 S. Karger AG, Basel.

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NET

VAKA SUNUMU

1. Pancreas. 2013 Nov;42(8):1323-32. doi: 10.1097/MPA.0b013e318292006a. **IF:3.49**

Giant insulinoma: a report of 3 cases and review of the literature.

Callacondo D, Arenas JL, Ganoza AJ, Rojas-Camayo J, Quesada-Olarte J, Robledo H.
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Abstract

Insulinoma is a rare pancreatic neuroendocrine tumor that is usually described as benign, sporadic, and very small (<2 cm). However, there have been rare case reports of insulinoma presenting as a giant tumor. We describe 3 cases of giant insulinomas, all of which developed liver metastases. The patients were aged 38, 63, and 67 years. Clinically, all patients presented with Whipple's triad associated with a large mass located in the pancreatic tail. The tumors ranged in size from 10 to 15 cm. On microscopic examination, the tumors were well differentiated with amyloid deposition ranging between 20% and 30%. Immunohistochemically, all 3 tumors showed strong diffuse expression of chromogranin and synaptophysin, whereas they were only focally positive for insulin. One patient developed liver recurrence 3 years after resection of the primary tumor yet remained asymptomatic without treatment. Another patient with liver recurrence underwent right hepatectomy and has been free of disease for 2 years. The third patient died of metastatic disease 13 years after initial surgery. Giant insulinomas are characterized by focal expression of insulin and high rates of liver metastases. Long-term follow-up is mandatory in these patients, as recurrence is expected after primary surgery.

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2. Case Rep Oncol Med. 2013;2013:930359. doi: 10.1155/2013/930359. Epub 2013 Dec 3. **IF:0.58**

Synchronous appearance of a high-grade neuroendocrine carcinoma of the ampulla vater and sigmoid colon adenocarcinoma.

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Abstract

Neuroendocrine carcinoma is a relatively rare tumor and its coexistence with other primary cancers is very exceptional. We present a case of a 63-year-old woman with biliary obstruction due to a high-grade neuroendocrine carcinoma located in ampulla of Vater who was found to have a synchronous sigmoid colon adenocarcinoma while undergoing staging laparotomy and pancreas head resection. Medical history was significant only for basal cell skin cancer. Immunohistochemical examination revealed the concurrence of histologically proved neuroendocrine carcinoma (chromogranin A, synaptophysin, and CD56 were positive) and Stage II (T3, N0, and M0) according to the TNM staging classification of colorectal cancer. The coexistence of neuroendocrine tumors with either synchronous or metachronous unrelated cancer is increasingly recognized. The patients with neuroendocrine carcinoma should be evaluated for secondary primary malignancies.

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