Nisan-Mayıs- Haziran 2013 Seçilmiş Yayın Taraması

Pubmed taramasında son 3 ayda Endokrin cerrahisi ile ilgili makaleler gözden geçirilmiş ve seçilmiş bazı yayınların özetleri verilmiştir. Yayınlar aşağıdaki tabloda yayın türlerine göre ayrılmıştır. Tablodaki yayın sayılarının, Word formatında Ctrl ile, Pdf formatında üzerine tıklanarak ilgili yayınların sayfasına ulaşılabilir. Makale özetlerinde Pubmed Id üzerine tıklanarak makalenin pubmed sayfasına, Doi linki üzerine tıklanarak ise (aboneliğiniz varsa) yayının dergi sayfasına ulaşabilirsiniz.

	Derlemeler	Retrospektif makaleler	Prospektif makaleler	Meta-analiz	Vaka sunumu/vaka kontrol
Tiroid	6	17	6	1	1
Paratiroid		2			
Adrenal	1		2		
NET	3	2			2

Tiroid: Derleme Makaleler

Lancet. 2013 Mar 23;381(9871):1046-57. doi: 10.1016/S0140-6736(12)62205-3. Epub 2013 Mar 22.

Controversies in primary treatment of low-risk papillary thyroid cancer.

McLeod DS, Sawka AM, Cooper DS.

Source

Department of Internal Medicine and Aged Care, Royal Brisbane and Women's Hospital, Herston, QLD, Australia.

Abstract

In many parts of the world, incidence of papillary thyroid cancer is increasing faster than any other malignancy. Most papillary thyroid cancers that are diagnosed are small and are generally regarded as being low risk, with little or no effect on mortality. Papillary thyroid cancer is a clinical challenge because it is difficult to prove benefit from the traditional therapeutic triad for this disorder (ie, total thyroidectomy with or without prophylactic central neck dissection, radioiodine remnant ablation, and suppression of serum thyroid-stimulating hormone with levothyroxine). However, risk of disease recurrence might be reduced by these therapies in a subset of patients with more aggressive disease. In the past decade, professional societies and other groups have established evidence-based clinical practice guidelines for management of papillary thyroid cancer, but these efforts have been made difficult by a paucity of randomised controlled trials. In this review, we summarise epidemiological data for disease incidence, discuss some controversies in disease management, and outline a therapeutic framework founded in the best available medical evidence and existing recommendations from clinical practice guidelines.

PMID: 23668555

http://dx.doi.org/10.1016/S0140-6736(12)62205-3

Lancet. 2013 Mar 23;381(9871):1058-69. doi: 10.1016/S0140-6736(13)60109-9. Epub 2013 Mar 22.

Progress in molecular-based management of differentiated thyroid cancer.

Xing M, Haugen BR, Schlumberger M.

Source

Laboratory for Cellular and Molecular Thyroid Research, Division of Endocrinology and Metabolism, Johns Hopkins University School of Medicine, Baltimore, MD, USA. mxing1@jhmi.edu

Abstract

Substantial developments have occurred in the past 5-10 years in clinical translational research of thyroid cancer. Diagnostic molecular markers, such as RET-PTC, RAS, and BRAF(V600E) mutations; galectin 3; and a new gene expression classifier, are outstanding examples that have improved diagnosis of thyroid nodules. BRAF mutation is a prognostic genetic marker that has improved risk stratification and hence tailored management of patients with thyroid cancer, including those with conventionally low risks. Novel molecular-targeted treatments hold great promise for radioiodine-refractory and surgically inoperable thyroid cancers as shown in clinical trials; such treatments are likely to become a component of the standard treatment regimen for patients with thyroid cancer in the near future. These novel molecular-based management strategies for thyroid nodules and thyroid cancer are the most exciting developments in this unprecedented era of molecular thyroid-cancer medicine.

PMID: 23668556

http://dx.doi.org/10.1016/S0140-6736(13)60109-9

Curr Opin Oncol. 2013 May;25(3):224-8. doi: 10.1097/CCO.0b013e32835ff44b.

Therapeutic strategies in the management of patients with metastatic anaplastic thyroid cancer: review of the current literature.

Granata R, Locati L, Licitra L.

Source

Head and Neck Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy.

Abstract

PURPOSE OF REVIEW:

Anaplastic thyroid cancer (ATC) is a rare and deadly malignancy. There is a need to speed up and support clinical research. This review article focuses on the new molecules that have been developed for the treatment of this aggressive tumor.

RECENT FINDINGS:

Improvement in the knowledge of pathogenesis and genetics of ATC led to the development of a variety of new molecules that may be used to treat this disease. In summary, these molecules are proteasome inhibitors, Aurora kinase inhibitors, vascular targeting agents, and gene therapies. All these molecules demonstrated a potentially therapeutic activity in metastatic ATC. To date, the largest prospective randomized multicenter, open-label, trial was conducted with combretastatin-A4.

SUMMARY:

More efficient drugs need to be developed through multinational efforts.

PMID: 23493194

http://dx.doi.org/10.1097/CCO.0b013e32835ff44b

J Clin Endocrinol Metab. 2013 Apr;98(4):1343-52. doi: 10.1210/jc.2012-4172. Epub 2013 Feb 28.

Clinical review: improving the measurement of serum thyroglobulin with mass spectrometry.

Hoofnagle AN, Roth MY.

Source

Departments of Laboratory Medicine, University of Washington, Seattle, WA 98195-7110, USA. ahoof@u.washington.edu

Abstract

CONTEXT:

Serum thyroglobulin (Tg) measurements are central to the management of patients treated for differentiated thyroid carcinoma. For decades, Tg measurements have relied on methods that are subject to interference by commonly found substances in human serum and plasma, such as Tg autoantibodies. As a result, many patients need additional imaging studies to rule out cancer persistence or recurrence that could be avoided with more sensitive and specific testing methods.

OBJECTIVES:

The aims of this review are to: 1) briefly review the interferences common to Tg immunoassays; 2) introduce readers to liquid chromatography-tandem mass spectrometry as a method for quantifying proteins in human serum/plasma; and 3) discuss the potential benefits and limitations of the method in the quantification of serum Tg.

RESULTS:

Mass spectrometric methods have traditionally lacked the sensitivity, robustness, and throughput to be useful clinical assays. These methods failed to meet the necessary clinical benchmarks due to the nature of the mass spectrometry workflow and instrumentation. Over the past few years, there have been major advances in reagents, automation, and instrumentation for the quantification of proteins using mass spectrometry. More recently, methods using mass spectrometry to detect and quantify Tg have been developed and are of sufficient quality to be used in the management of patients.

CONCLUSIONS:
Novel serum Tg assays that use mass spectrometry may avoid the issue of autoantibody interference and other problems with currently available immunoassays for Tg. Prospective studies are needed to fully understand the potential benefits of novel Tg assays to patients and care providers.

PMID: 23450057

http://dx.doi.org/10.1210/jc.2012-4172

Laryngoscope. 2013 Apr;123(4):1059-64. doi: 10.1002/lary.23838. Epub 2013 Feb 12.

Diagnosis and management of differentiated thyroid cancer using molecular biology.

Witt RL, Ferris RL, Pribitkin EA, Sherman SI, Steward DL, Nikiforov YE.

Source

Department of Surgery, Helen F. Graham Cancer Center, Christiana Care, Newark, Delaware and Department of Otolaryngology-Head & Neck Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania, USA. robertlwitt@gmail.com

Abstract

OBJECTIVES/HYPOTHESIS:
To define molecular biology in clinical practice for diagnosis, surgical management, and prognostication of differentiated thyroid cancer.

DATA SOURCES:
Ovid Medline 2006-2012

REVIEW METHODS:
Manuscripts with clinical correlates.

RESULTS:
Papillary thyroid carcinomas harbor point mutations of the BRAF and RAS genes or RET/PTC rearrangements, all of which activate the mitogen-activated protein kinase pathway. These mutually exclusive mutations are found in 70% of PTC. BRAF mutation is found in 45% of papillary thyroid cancer and is highly specific. Follicular carcinomas are known to harbor RAS mutation or PAX8/PPARγ rearrangement. These mutations are also mutually exclusive and identified in 70% of follicular carcinomas. Molecular classifiers measure the expression of a large number of genes on a microarray chip providing a substantial negative predictive value pending further validation.

CONCLUSIONS:
1) 20% to 30% of cytologically classified Follicular Neoplasms and Follicular Lesion of Undetermined Significance collectively are malignant on final pathology. Approximately 70% to 80% of thyroid lobectomies performed solely for diagnostic purposes are benign. Molecular alteration testing may reduce the number of unnecessary thyroid procedures, 2) may reduce the number of completion thyroidectomies, and 3) may lead to more individualized operative and postoperative management. Molecular testing for BRAF, RAS, RET/PTC, and PAX8/PPARγ for follicular lesion of undetermined significance and follicular neoplasm improve specificity, whereas molecular classifiers may add negative predictive value to fine needle aspiration diagnosis.

PMID: 23404751

http://dx.doi.org/10.1002/lary.23838

J Surg Oncol. 2013 May;107(6):665-72. doi: 10.1002/jso.23295. Epub 2012 Nov 28.

Well-differentiated thyroid carcinoma: the role of post-operative radioactive iodine administration.

Patel SS, Goldfarb M.

Source

Division of Breast/Soft Tissue and Endocrine Surgery, University of Southern California Keck School of Medicine, Los Angeles, CA, USA.

Abstract

Post-operative management of differentiated thyroid cancer (DTC) often involves administration of radioactive iodine (RAI) for remnant ablation or adjuvant therapy. However, given the favorable prognosis associated with DTC, the risk versus benefit ratio of RAI remains unclear. RAI is associated with substantial, albeit rare side effects, including a possible increased risk of secondary malignancy and altered fertility, which must be balanced against the magnitude of benefit for decreasing recurrence and improving survival.

PMID: 23192391

http://dx.doi.org/10.1002/jso.23295

Tiroid: Retrospektif makaleler

JAMA. 2013 Apr 10;309(14):1493-501. doi: 10.1001/jama.2013.3190.

Association between BRAF V600E mutation and mortality in patients with papillary thyroid cancer.

Xing M, Alzahrani AS, Carson KA, Viola D, Elisei R, Bendlova B, Yip L, Mian C, Vianello F, Tuttle RM, Robenshtok E, Fagin JA, Puxeddu E, Fugazzola L,Czarniecka A, Jarzab B, O'Neill CJ, Sywak MS, Lam AK, Riesco-Eizaguirre G, Santisteban P, Nakayama H, Tufano RP, Pai SI, Zeiger MA, Westra WH, Clark DP,Clifton-Bligh R, Sidransky D, Ladenson PW, Sykorova V.

Source

Laboratory for Cellular and Molecular Thyroid Research, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. mxing1@jhmi.edu

Abstract

IMPORTANCE:
BRAF V600E is a prominent oncogene in papillary thyroid cancer (PTC), but its role in PTC-related patient mortality has not been established.

OBJECTIVE:
To investigate the relationship between BRAF V600E mutation and PTC-related mortality.

DESIGN, SETTING, AND PARTICIPANTS:
Retrospective study of 1849 patients (1411 women and 438 men) with a median age of 46 years (interquartile range, 34-58 years) and an overall median follow-up time of 33 months (interquartile range, 13-67 months) after initial treatment at 13 centers in 7 countries between 1978 and 2011.

MAIN OUTCOMES AND MEASURES:
Patient deaths specifically caused by PTC.

RESULTS:
Overall, mortality was 5.3% (45/845; 95% CI, 3.9%-7.1%) vs 1.1% (11/1004; 95% CI, 0.5%-2.0%) (P < .001) in BRAF V600E-positive vs mutation-negative patients. Deaths per 1000 person-years in the analysis of all PTC were 12.87 (95% CI, 9.61-17.24) vs 2.52 (95% CI, 1.40-4.55) in BRAF V600E-positive vs mutation-negative patients; the hazard ratio (HR) was 2.66 (95% CI, 1.30-5.43) after adjustment for age at diagnosis, sex, and medical center. Deaths per 1000 person-years in the analysis of the conventional variant of PTC were 11.80 (95% CI, 8.39-16.60) vs 2.25 (95% CI, 1.01-5.00) in BRAF V600E-positive vs mutation-negative patients; the adjusted HR was 3.53 (95% CI, 1.25-9.98). When lymph node metastasis, extrathyroidal invasion, and distant metastasis were also included in the model, the association of BRAF V600E with mortality for all PTC was no longer significant (HR, 1.21; 95% CI, 0.53-2.76). A higher BRAF V600E-associated patient mortality was also observed in several clinicopathological subcategories, but statistical significance was lost with adjustment for patient age, sex, and medical center. For example, in patients with lymph node metastasis, the deaths per 1000 person-years were 26.26 (95% CI, 19.18-35.94) vs 5.93 (95% CI, 2.96-11.86) in BRAF V600E-positive vs mutation-negative patients (unadjusted HR, 4.43 [95% CI, 2.06-9.51]; adjusted HR, 1.46 [95% CI, 0.62-3.47]). In patients with distant tumor metastasis, deaths per 1000 person-years were 87.72 (95% CI, 62.68-122.77) vs 32.28 (95% CI, 16.14-64.55) in BRAF V600E-positive vs mutation-negative patients (unadjusted HR, 2.63 [95% CI, 1.21-5.72]; adjusted HR, 0.84 [95% CI, 0.27-2.62]).

CONCLUSIONS AND RELEVANCE:
In this retrospective multicenter study, the presence of the BRAF V600E mutation was significantly associated with increased cancer-related mortality among patients with PTC. Because overall mortality in PTC is low and the association was not independent of tumor features, how to use BRAF V600E to manage mortality risk in patients with PTC is unclear. These findings support further investigation of the prognostic and therapeutic implications of BRAF V600E status in PTC.

PMID: 23571588

http://dx.doi.org/10.1001/jama.2013.3190

J Clin Endocrinol Metab. 2013 Apr;98(4):1427-34. doi: 10.1210/jc.2012-3728. Epub 2013 Mar 12.

Papillary thyroid microcarcinomas: a comparative study of the characteristics and risk factors at presentation in two cancer registries.

Malandrino P, Pellegriti G, Attard M, Violi MA, Giordano C, Sciacca L, Regalbuto C, Squatrito S, Vigneri R.

Source

Endocrinology, Department of Clinical and Molecular Biomedicine, University of Catania, Garibaldi-Nesima Medical Center, Catania, Italy. p.malandrino@unict.it

Abstract

CONTEXT:

Papillary thyroid microcarcinoma (PTMC) is an indolent neoplasia, often asymptomatic and discovered incidentally. Some PTMCs, however, exhibit a more aggressive behavior, frequently recur, and can even cause cancer-related death.

OBJECTIVE:

The aim of this study was to evaluate the prevalence of PTMCs and the associated risk factors at presentation in 2 thyroid cancer registries from areas with different genetic and environmental characteristics.

DESIGN AND PATIENTS:

We conducted a retrospective, observational study of all incident cases of PTMCs recorded over a 5-year period in the Sicilian Regional Registry for Thyroid Cancer (SRRTC) and in the Surveillance Epidemiology and End Results (SEER) US registry.

SETTING:

The study took place at an academic hospital.

RESULTS:

The incidence of PTMCs was much higher in Sicily (1777 PTMC diagnosed in 2002-2006; age-standardized incidence rate for the world population [ASRw] = 5.8 per 100 000) than in the United States (14 423 PTMC in the period 2004-2008; ASRw = 2.9 per 100 000). Within the SRRTC, a significantly higher incidence was observed in the volcanic area (ASRw = 10.4 vs 4.6 in the rest of Sicily). In Sicily, the female to male ratio was higher, and PTMC patients were younger. In both registries, a significant inverse correlation was observed between age and tumor size. Young patients (≤45 y) exhibited a higher frequency of nodal metastases.

CONCLUSIONS:

PTMC incidence is twice as high in Sicily compared with the United States, and within Sicily, the incidence is twice as high in the volcanic area. In young patients, PTMCs are larger at presentation and exhibit more risk factors. In both registries, more than 35% of PTMCs exhibited 2 or more risk factors, suggesting that they may require surgery and follow-up similar to that of larger carcinomas.

PMID: 23482606

http://dx.doi.org/10.1210/jc.2012-3728

Br J Radiol. 2013 May;86(1025):20130007. doi: 10.1259/bjr.20130007.

Ultrasonography-guided core needle biopsy for the thyroid nodule: does the procedure hold any benefit for the diagnosis when fine-needle aspiration cytology analysis shows inconclusive results?

Hahn SY, Shin JH, Han BK, Ko EY, Ko ES.

Source

Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Gangnam-gu, Seoul, Republic of Korea.

Abstract

OBJECTIVE:

We evaluated the diagnostic role of ultrasonography-guided core needle biopsy (CNB) according to ultrasonography features of thyroid nodules that had inconclusive ultrasonography-guided fine-needle aspiration (FNA) results.

METHODS:

A total of 88 thyroid nodules in 88 patients who underwent ultrasonography-guided CNB because of previous inconclusive FNA results were evaluated. The patients were classified into three groups based on ultrasonography findings: Group A, which was suspicious for papillary thyroid carcinoma (PTC); Group B, which was suspicious for follicular (Hurthle cell) neoplasm; and Group C, which was suspicious for lymphoma. The final diagnoses of the thyroid nodules were determined by surgical confirmation or follow-up after ultrasonography-guided CNB.

RESULTS:

Of the 88 nodules, the malignant rate was 49.1% in Group A, 12.0% in Group B and 90.0% in Group C. The rates of conclusive ultrasonography-guided CNB results after previous incomplete ultrasonography-guided FNA results were 96.2% in Group A, 64.0% in Group B and 90.0% in Group C (p=0.001). 12 cases with inconclusive ultrasonography-guided CNB results were finally diagnosed as 8 benign lesions, 3 PTCs and 1 lymphoma. The number of previous ultrasonography-guided FNA biopsies was not significantly different between the conclusive and the inconclusive result groups of ultrasonography-guided CNB (p=0.205).

CONCLUSION:

Ultrasonography-guided CNB has benefit for the diagnosis of thyroid nodules with inconclusive ultrasonography-guided FNA results. However, it is still not helpful for the differential diagnosis in 36% of nodules that are suspicious for follicular neoplasm seen on ultrasonography. Advances in knowledge: This study shows the diagnostic contribution of ultrasonography-guided CNB as an alternative to repeat ultrasonography-guided FNA or surgery.

PMID: 23564885

http://dx.doi.org/10.1259/bjr.20130007

Eur J Endocrinol. 2013 May 2;168(6):853-9. doi: 10.1530/EJE-13-0023. Print 2013 Jun.

Diagnostic and prognostic value of immunocytochemistry and BRAF mutation analysis on liquid-based biopsies of thyroid neoplasms suspicious for carcinoma.

Rossi ED, Martini M, Capodimonti S, Straccia P, Cenci T, Lombardi CP, Pontecorvi A, Larocca LM, Fadda G.

Source

Division of Anatomic Pathology and Histology, Agostino Gemelli School of Medicine, Università Cattolica del Sacro Cuore, Rome, Italy. esther.rossi@rm.unicatt.it

Abstract

OBJECTIVE:

In the field of fine-needle aspiration cytology, the category of suspicious for malignancy (SM) thyroid lesions, that bears 55-85% risk of malignant histology, is a challenging topic in which morphology alone is not always able to make a correct diagnosis. Recently, immunocytochemistry (ICC) has been referred to as helpful in differentiating low- and high-malignant risk lesions and BRAF activating mutations have been identified in a significant amount of papillary thyroid carcinomas (PTC). The introduction of the liquid-based cytology (LBC) may simplify the application of these techniques to thyroid cytology.

DESIGN:

Our aim is to evaluate the diagnostic and prognostic role of both ICC and BRAF mutation for the SM category on LBC.

METHODS:

From October 2010 through June 2011, 113 LBC cytological cases (including 37 SM and 76 PTC) underwent surgery. All cases were studied for BRAF mutation and ICC.

RESULTS:

ICC resulted positive in 26 (86.6%) histologically malignant SM with 15 of which (40.5%) expressing a BRAF mutation. Overall, 63 cases showed a BRAF mutation resulting in PTC. Concerning the prognostic role of BRAF mutation for the two categories, we reported a significant correlation with multifocality, nodal involvement and extra-capsular invasion ($P<0.0001$).

CONCLUSIONS:

Special techniques such as ICC and molecular markers might be successfully carried out on LBC-processed material. For both categories, ICC is more sensitive whereas BRAF analysis is an interesting support due to its high specificity adding a prognostic value in both SM and PTCs.

PMID: 23513230

http://dx.doi.org/: 10.1530/EJE-13-0023

J Clin Endocrinol Metab. 2013 Apr;98(4):E761-8. doi: 10.1210/jc.2012-3762. Epub 2013 Mar 8.

Does addition of BRAF V600E mutation testing modify sensitivity or specificity of the Afirma Gene Expression Classifier in cytologically indeterminate thyroid nodules?

Kloos RT, Reynolds JD, Walsh PS, Wilde JI, Tom EY, Pagan M, Barbacioru C, Chudova DI, Wong M, Friedman L, LiVolsi VA, Rosai J, Lanman RB, Kennedy GC.

Source

Veracyte, Inc, South San Francisco, CA 94080, USA.

Abstract

OBJECTIVE:

The purpose of this study was to determine the frequency of BRAF mutation in cytologically indeterminate thyroid nodules and to investigate whether adding the BRAF test improves diagnostic accuracy of the Afirma Gene Expression Classifier (GEC).

DESIGN:

BRAF V600E mutational status was determined for DNA extracted from cytologically benign (n = 40), indeterminate (n = 208), and malignant (n = 48) fine-needle aspiration specimens previously categorized by GEC as molecularly Benign or Suspicious. Analytical performance of the BRAF assay was assessed to establish reproducibility and limits of detection. Molecular testing results were correlated with blinded expert histopathological diagnoses.

RESULTS:

The BRAF assay detected mutations reproducibly to 2.5% mutant allele frequency. The prevalence of BRAF mutations in cytologically benign specimens was 2 of 40 (5.0%, 95% confidence interval [CI], 0-16) and in cytologically malignant specimens was 36 of 48 (75.0%, 95% CI, 60-86). In the cytologically indeterminate category, 10.1% of specimens were BRAF+: 2 of 95 were subcategorized as atypia of undetermined significance or follicular lesion of undetermined significance (2.1%, 95% CI, 0-7); 1 of 70 as follicular neoplasm or suspicious for follicular neoplasm (1.4%, 95% CI, 0-9); and 18 of 43 as suspicious for malignancy (41.9%, 95% CI, 27-58). All BRAF+ specimens were classified as Suspicious by the GEC.

CONCLUSIONS:

BRAF mutations are uncommon in nodules with atypia of undetermined significance or follicular lesion of undetermined significance or follicular neoplasm or suspicious for follicular neoplasm cytology. Most cytologically indeterminate nodules that proved to be malignant were also BRAF-, and all nodules that were false-negative by GEC were also BRAF-. Similarly, all BRAF+ specimens were also GEC Suspicious. Neither GEC test sensitivity nor specificity was improved by addition of BRAF mutation testing.

PMID: 23476074

http://dx.doi.org/10.1210/jc.2012-3762

J Clin Endocrinol Metab. 2013 Apr;98(4):1476-82. doi: 10.1210/jc.2012-4072. Epub 2013 Mar 5.

Preoperative ultrasonographic features of papillary thyroid carcinoma predict biological behavior.

Nam SY, Shin JH, Han BK, Ko EY, Ko ES, Hahn SY, Chung JH.

Source

Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 135-710, Korea.

Abstract

BACKGROUND:

Although ultrasound (US) features of papillary thyroid carcinoma (PTC) are well established, little is known regarding biological behavior according US features. We investigated whether there was a difference in biological behavior between PTCs that did and did not meet malignant US criteria.

PATIENTS AND METHODS:

We retrospectively reviewed clinical records and histological and US findings of the index tumors in 488 patients who underwent surgery for PTC. Benign-looking PTC (B-PTC) was defined as showing none of the accepted US criteria for malignancy. Malignant-looking PTCs (M-PTCs) and B-PTCs were compared in terms of patients' age, sex, tumor size, histological subtype, multifocality, lymph node (LN) metastasis, extrathyroidal extension, stage, recurrence, and distant metastasis.

RESULTS:

B-PTCs accounted for 74 (15%) of all 488 PTCs. Mean tumor size was not significantly different between the groups, with 1.10 cm for M-PTC and 1.11 cm for B-PTC (P = .947). Univariate and multivariate analysis indicated that M-PTC more frequently had LN metastasis, extrathyroidal extension, and a higher stage than B-PTC (all P < .05). The results were significant in tumors ≥1.0 cm, whereas there were no significant differences in tumors <1 cm. As the number of malignant US features increased, multifocality, extrathyroidal extension, LN metastasis, and a higher stage were more likely.

CONCLUSION:

PTCs that did not meet malignant US criteria had better prognostic indicators than PTCs that met US criteria. Therefore, US features at the time of diagnosis can serve as a useful tool for predicting biological behavior in PTC.

PMID: 23463652

http://dx.doi.org/10.1210/jc.2012-4072

Eur J Endocrinol. 2013 Apr 15;168(5):779-86. doi: 10.1530/EJE-12-0943. Print 2013 May.

Radioactive iodine in the treatment of medullary thyroid carcinoma: a controlled multicenter study.

Meijer JA, Bakker LE, Valk GD, de Herder WW, de Wilt JH, Netea-Maier RT, Schaper N, Fliers E, Lips P, Plukker JT, Links TP, Smit JA.

Source

Department of Internal Medicine, Albert Schweitzer Hospital, Dordrecht, The Netherlands. jaa.meijer@asz.nl

Abstract

OBJECTIVE:

Radioactive iodine (RAI) therapy in medullary thyroid carcinoma (MTC) is applied in some centers, based on the assumption that cross-irradiation from thyroid follicular cells may be beneficial. However, no systematic studies on

the effect of RAI treatment in MTC have been performed. The aim of this study was to analyze the effect of RAI treatment on survival in MTC patients.

DESIGN:
Retrospective multicenter study in eight University Medical Centers in The Netherlands.

METHODS:
Two hundred and ninety three MTC patients without distant metastases who had undergone a total thyroidectomy were included between 1980 and 2007. Patients were stratified by clinical appearance, hereditary stage, screening status, and localization. All patients underwent regular surgical treatment with additional RAI treatment in 61 patients. Main outcome measures were disease-free survival (DFS) and disease-specific survival (DSS). Cure was defined as biochemical and radiological absence of disease.

RESULTS:
In multivariate analysis, stratification according to clinical appearance (P=0.72), hereditary stage (P=0.96), localization (P=0.69), and screening status (P=0.31) revealed no significant effects of RAI treatment on DFS. Multivariate analysis showed no significant difference in DSS for the two groups stratified according to clinical appearance (P=0.14). Owing to limited number of events, multivariate analysis was not possible for DSS in the other groups of stratification.

CONCLUSIONS:
Based on the results of the present analysis, we conclude that RAI has no place in the treatment of MTC.

PMID: 23462866

http://dx.doi.org/10.1530/EJE-12-0943

Otolaryngol Head Neck Surg. 2013 May;148(5):746-52. doi: 10.1177/0194599813479777. Epub 2013 Mar 5.

Salivary morbidity and quality of life following radioactive iodine for well-differentiated thyroid cancer.

Dingle IF, Mishoe AE, Nguyen SA, Overton LJ, Gillespie MB.

Source

Department of Otolaryngology-Head and Neck Surgery, University of California, San Diego, California 92130, USA. idingle@ucsd.edu

Abstract

OBJECTIVE:
Determine the prevalence of sialadenitis in a group of patients treated with radioactive iodine (RAI) for well-differentiated thyroid cancer and assess whether RAI treatment is associated with a reduction in swallowing-related or global head and neck quality of life.

STUDY DESIGN:
Retrospective self-administered questionnaire study.

SETTING:
Academic, tertiary care, National Cancer Institute-designated cancer center.

SUBJECTS AND METHODS:
Surviving patients seen for well-differentiated thyroid cancer were identified by review of the cancer center registry. Patients were mailed a baseline questionnaire, the M. D. Anderson Dysphagia Inventory (MDADI), the University of Washington Quality of Life Questionnaire (UW-QOL), and the Xerostomia-Related Quality of Life Scale (XeQOLS).

RESULTS:
The study included 121 women and 24 men, with a mean age of 52 years. Radioactive iodine exposure was correlated with an increase in sialadenitis and was dose dependent ($R(2) = 0.335$, $P < .001$). Sialadenitis was 2.47 times more likely to occur in patients who received greater than 150 mCi when compared with those who

received less than 150 mCi (P = .04). Radioactive iodine exposure of over 150 mCi was also associated with a reduction in the recreation domain of the UW-QOL (P = .04), the daily swallowing domain of the MDADI (P = .02), and the psychological/personal, pain, and social domains of the XeQOLS (P = .03, .03, and .04, respectively).

CONCLUSION:
Patients treated with RAI exhibited an increased risk for sialadenitis as well as a reduction in swallowing-related and global head and neck quality of life. Our findings suggest these patients should be screened for salivary morbidity and may benefit from both pre-RAI prophylaxis and post-RAI intervention.

PMID: 23462656

http://dx.doi.org/10.1177/0194599813479777

J Surg Res. 2013 May 1;181(1):6-10. doi: 10.1016/j.jss.2012.06.030. Epub 2012 Jul 6.

Reliability of fine-needle aspiration for thyroid nodules greater than or equal to 4 cm.

Albuja-Cruz MB, Goldfarb M, Gondek SS, Allan BJ, Lew JI.

Source

Division of Endocrine Surgery, University of Miami Leonard M. Miller School of Medicine, Miami, FL 33136, USA. maria.albuja-cruz@ucdenver.edu

Abstract

BACKGROUND:
Fine-needle aspiration (FNA) is considered the diagnostic test of choice in the evaluation of thyroid nodules. Some practice recommendations, however, suggest surgical resection of larger thyroid nodules due to concerns of FNA unreliability in the diagnosis of thyroid malignancy. The purpose of this study was to determine the reliability of FNA in thyroid nodules ≥4 cm.

METHODS:
Retrospective review of prospectively collected data of 1068 consecutive patients who underwent FNA and thyroidectomy at a single tertiary medical center from 2003 to 2010 was performed. Patients were divided into two groups: those patients with a dominant thyroid nodule ≥4 cm (n = 212) and those patients with a dominant thyroid nodule <4 cm (n = 856). Sensitivity, specificity, and negative and positive predictive values were calculated for FNA results and final histopathology after thyroidectomy.

RESULTS:
Of 212 patients with lesions ≥4 cm, 35% had thyroid malignancy on final pathology. Conversely, 54% of 856 patients with dominant thyroid nodules <4 cm had a final diagnosis of thyroid cancer after thyroidectomy. FNA demonstrated similar test characteristics among patients with lesions ≥4 cm and <4 cm, with a specificity of 99% (CI: 96%-100%) and 98% (CI: 96%-99.0%), respectively, and a sensitivity of 35% (CI: 23%-49%) and 42% (CI: 37%-46%), respectively. The positive predictive value of FNA was 82% (CI: 75%-100%) for nodules ≥4 cm and 96% (CI: 92%-98%) for nodules <4 cm. Negative predictive value was significantly different, with a value of 82% (CI: 75%-87%) for lesions ≥4 cm and only 59% (CI: 55%-63%) for lesions <4 cm.

CONCLUSIONS:
The reliability of FNA as a diagnostic test is not affected by the size of thyroid nodules. Routine surgical resection for all thyroid nodules ≥4 cm should not be used as the only independent factor in determining need for surgical resection.

PMID: 23428179

http://dx.doi.org/10.1016/j.jss.2012.06.030

J Am Coll Surg. 2013 Apr;216(4):571-7; discussion 577-9. doi: 10.1016/j.jamcollsurg.2012.12.022. Epub 2013 Feb 8.

Cancer after thyroidectomy: a multi-institutional experience with 1,523 patients.

Smith JJ, Chen X, Schneider DF, Broome JT, Sippel RS, Chen H, Solórzano CC.

Source

Department of Surgery, Vanderbilt University Medical Center, Nashville, TN 37232-6860, USA.

Abstract

BACKGROUND:
The incidence of thyroid cancer in patients treated operatively for thyroid disease has been historically low (<5%). Previous series have not specifically addressed cancer rates in both euthyroid and hyperthyroid patients. This study examined cancer frequency in patients referred for removal of benign thyroid disease in a multi-institutional series.

STUDY DESIGN:
A total of 2,551 patients underwent thyroidectomy at 3 high-volume institutions. Indeterminate/malignant fine-needle aspiration diagnosis was excluded (n = 1,028). Cancer cases were compared among 1,523 patients with Graves' disease (n = 264), nodular goiter (n = 1,095), and toxic nodular goiter (n = 164). Fisher's exact test, chi-square test, Wilcoxon rank sum, Kruskal-Wallis nonparametric t-tests, and multivariable logistic regression were used.

RESULTS:
Overall, 238 (15.6%) cancers were recorded: Graves' disease (6.1%), nodular goiter (17.5%), and toxic nodular goiter (18.3%). Cancer rates were significantly different among these groups ($p < 0.01$) and significantly higher in nodular goiter and toxic nodular goiter vs Graves' disease ($p < 0.01$); no significant differences in cancer rates were noted among institutions. Overall, 275 patients had thyroiditis (18%). There was a significant association with younger age, male sex, nodular thyroids, and cancer ($p < 0.05$). Presence of thyroiditis or performance of preoperative fine-needle aspiration was not associated with cancer. Mean cancer size was 1.1 cm (46% >0.5 cm; 39% >1 cm). Most patients underwent total thyroidectomy (80%).

CONCLUSIONS:
These data confirm higher than expected incidental thyroid cancer rates (15.6%) in the largest multi-institutional surgical series to date. Nodular thyroids, males, and young patients were more likely to harbor incidental carcinoma. These data support consideration of initial total thyroidectomy as the preferred approach for patients referred to the surgeon with bilateral nodular disease.

PMID: 23403140

http://dx.doi.org/10.1016/j.jamcollsurg.2012.12.022

Otolaryngol Head Neck Surg. 2013 Apr;148(4):564-71. doi: 10.1177/0194599813477364. Epub 2013 Feb 8.

Aggressive surgical resection of anaplastic thyroid carcinoma may provide long-term survival in selected patients.

Brown RF, Ducic Y.

Source

Department of Head and Neck Surgery, Kaiser Permanente, Denver, Colorado, USA.

Abstract

OBJECTIVE:

In this study, we present our experience with aggressive surgical treatment in selected patients with anaplastic thyroid cancer with extrathyroidal extension.

STUDY DESIGN:
Case series with chart review.

SETTING:
Tertiary care referral center.

SUBJECTS AND METHODS:
Retrospective chart review of all patients with anaplastic thyroid cancer surgically treated by the senior author from January 1998 to July 2012.

RESULTS:
A total of 38 cases of anaplastic thyroid cancer were treated (21 male and 17 female). The mean age was 64.5 years. Twenty-two patients were considered surgically unresectable (18 had distant metastases and 4 had extrathyroidal extension of cancer lateral to carotid arteries) and underwent biopsy with or without tracheostomy. The remaining 16 patients underwent surgical resection with curative intent. Fourteen of these patients underwent postoperative radiation therapy. None of these 16 patients developed local recurrence. Six developed distant metastasis at an average follow-up of 3.2 months, 1 died of an unrelated myocardial infarction at 3 months, 2 were lost to follow-up, and 7 remain disease free with an average follow-up of 4.8 years (range, 9 months to 8 years). Of those patients who underwent complete surgical resection followed by postoperative radiation, 7 of 14 (50%) are still alive, with a mean follow-up of 4.8 years.

CONCLUSION:
Selected patients with anaplastic thyroid cancer with extrathyroidal extension (stage IVB) who show no distant metastases by computed tomography or positron emission tomography scans and who do not have tumor extending lateral to the carotid arteries are candidates for complete surgical resection.

PMID: 23396588

http://dx.doi.org/10.1177/0194599813477364

Eur J Endocrinol. 2013 Mar 18;168(4):621-30. doi: 10.1530/EJE-12-0993. Print 2013 Apr.

Low malignancy risk of thyroid follicular lesion of undetermined significance in patients from post-endemic areas.

Słowińska-Klencka D, Woźniak E, Wojtaszek M, Popowicz B, Sporny S, Klencki M.

Source

Chair of Endocrinology, Department of Morphometry of Endocrine Glands, Medical University of Lodz, Lodz, Poland. dsk@tyreo.umed.lodz.pl

Abstract

OBJECTIVE:
New classification of the thyroid fine-needle aspiration biopsy (FNAB) results tries to stratify the risk of malignancy of thyroid follicular lesions using 'follicular lesion of undetermined significance' (FLUS) subcategory. Clinical significance of this category in the endemic (or post-endemic) areas has not been clearly established.

DESIGN:
The aim of the study was to determine the risk of malignancy for FLUS as well as to evaluate ultrasound (US) malignancy risk features (MRF) in such nodules in comparison with 'suspicious for neoplasm' (SFN) and 'benign lesions' (BL).

METHODS:
The US images and cytological diagnoses of 589 thyroid follicular lesions were analysed from January 2010 to July 2012. Cytological follow-up was assessed in 110 cases and surgical one in 100 cases.

RESULTS:
FLUS was diagnosed in 340 cases (3.8% of all cytological diagnoses and 57% of thyroid follicular lesions). Altogether, clinical and/or surgical follow-up revealed thyroid cancer in 3.2% patients with FLUS nodules. Repeat FNAB led to more specific diagnosis in 74.4% of FLUS (3.5%, papillary cancers or their suspicion; 2.3%, SFN; 68.6%, BL). The histopathological examination showed thyroid cancer in 6.4% cases of FLUS and 7.0% of SFN and follicular adenoma in 8.5% of FLUS and 11.6% of SFN (NS, FLUS vs SFN). FLUS showed MRF of intermediate values between BL and SFN; SFN more often than FLUS showed at least two MRF (53 vs 30%, P<0.0001).

CONCLUSIONS:
The risk of cancer in FLUS in areas with recently corrected iodine supply is low. In such areas, repeated biopsy leads to more precise cytological diagnosis in about 3/4 cases.

PMID: 23341072

http://dx.doi.org/10.1530/EJE-12-0993

Eur J Endocrinol. 2013 Mar 15;168(4):549-56. doi: 10.1530/EJE-12-0848. Print 2013 Apr.

Recurrence of differentiated thyroid cancer in the elderly.

Hollenbeak CS, Boltz MM, Schaefer EW, Saunders BD, Goldenberg D.

Source

Division of Outcomes Research and Quality, Department of Surgery, College of Medicine, The Pennsylvania State University, Hershey, Pennsylvania 17033, USA. chollenbeak@psu.edu

Abstract

OBJECTIVE:
Data from the Surveillance Epidemiology and End Results Medicare-linked database were used to estimate the incidence of and risk factors associated with recurrent thyroid cancer, and to assess the impact of recurrence on mortality following diagnosis, controlling for mortality as a competing risk.

DESIGN:
We identified 2883 patients over 65 years of age diagnosed with a single, primary well-differentiated thyroid cancer between 1995 and 2007. A recurrence was considered if the patient had evidence of I-131 therapy, imaging for metastatic thyroid carcinoma, or complete thyroidectomy beyond 6 months of diagnosis. Competing risk regressions were performed using Cox proportional hazards models with 1- and 2-year landmarks.

RESULTS:
Recurrence was observed in 1117 (39%) of the 2883 patients in the cohort. Age, stage, and treatment status were significant risk factors for developing recurrent disease (P<0.0001). Patients with recurrent disease had a higher risk of all-cause mortality within 10 years of diagnosis than patients with no recurrence at 1- and 2-year landmarks. Patients with follicular histology and a recurrence were less likely to die from cancer (hazard ratio 0.54; P=0.03) than patients with no recurrence.

CONCLUSIONS:
The rate of recurrence of well-differentiated thyroid carcinomas in this sample of elderly patients was 39%. Extent of disease and older age negatively impacted the risk of recurrence from differentiated thyroid cancer. In these data, patients with follicular histology and a recurrence were less likely to die, suggesting that mortality and recurrence are competing risks. These data should be taken into account with individualized treatment strategies for elderly patients with recurrent malignant thyroid disease.

PMID: 23337385

http://dx.doi.org/10.1530/EJE-12-0848

Laryngoscope. 2013 May;123(5):1305-9. doi: 10.1002/lary.23861. Epub 2013 Jan 4.

False negatives in thyroid cytology: impact of large nodule size and follicular variant of papillary carcinoma.

Mehanna R, Murphy M, McCarthy J, O'Leary G, Tuthill A, Murphy MS, Sheahan P.

Source

Department of Otolaryngology-Head and Neck Surgery, South Infirmary Victoria University Hospital, Cork, Ireland.

Abstract

OBJECTIVES/HYPOTHESIS:
Fine-needle aspiration (FNA) cytology is well established in the diagnosis of thyroid nodules. However, false-negative rates for malignancy of 3% to 10% are reported. The purpose of the present study was to investigate the impact of nodule size and follicular variant of papillary carcinoma (FVPTC) on false-negative FNA rates in thyroid nodules and on malignancy rates in nodules with indeterminate cytology.

STUDY DESIGN:
Retrospective study.

METHODS:
A total of 765 consecutive ultrasound-guided FNAs were reviewed. Histological correlation was available in 262 cases.

RESULTS:
The overall sensitivity of FNA for malignancy was 84%, and the false-negative rate 9.1%. Nodules ≥ 3 cm were significantly more likely to ultimately be diagnosed as cancer by histology than nodules <3 cm (14% vs. 6.8%, P = .006); however, they were also significantly more likely to undergo surgery than smaller nodules (P < .0001). Among the surgical series, the false-negative rate was 10.9% in nodules ≥ 3 cm and 6.1% in nodules <3 cm (P = .71). Most false negatives were due to FVPTC. FVPTC was significantly more likely to be missed by preoperative cytology than conventional or other variants of papillary carcinoma (P < .001). Among cases with indeterminate cytology, nodule size and Thy-3f versus Thy-3a subclassification did not have any significant impact on likelihood of malignancy.

CONCLUSIONS:
The sensitivity of FNA for detection of FVPTC is reduced compared to conventional papillary carcinoma. The impact of nodule size is not significant.

PMID: 23293053

http://dx.doi.org/10.1002/lary.23861

Surgery. 2013 May;153(5):711-7. doi: 10.1016/j.surg.2012.11.009. Epub 2012 Dec 4.

Significance of MDM2 and P14 ARF polymorphisms in susceptibility to differentiated thyroid carcinoma.

Zhang F, Xu L, Wei Q, Song X, Sturgis EM, Li G.

Source

Department of Head and Neck Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA.

Abstract

BACKGROUND:
Murine double minute 2 (MDM2) oncoprotein and p14(ARF) tumor suppressor play pivotal roles in regulating p53 and function in the MAPK pathway, which is mutated frequently in differentiated thyroid carcinoma (DTC). We

hypothesized that functional polymorphisms in the promoters of MDM2 and p14(ARF) contribute to the interindividual difference in predisposition to DTC.

METHODS:
MDM2-rs2279744, MDM2-rs937283, p14(ARF)-rs3731217, and p14(ARF)-rs3088440 were genotyped in 303 patients with DTC and 511 cancer-free healthy controls. Multivariate logistic regression analysis was performed to calculate odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS:
MDM2-rs2279744 and p14(ARF)-rs3731217 were associated with a significantly increased risk of DTC (MDM2-rs2279744: TT versus TG/GG; OR, 1.5; 95% CI, 1.1-2.0; p14(ARF)-rs3731217: TG/GG versus TT; OR, 1.7; 95% CI, 1.2-2.3). No association was found for MDM2-rs937283 or p14(ARF)-rs3088440. Individuals carrying 3-4 risk genotypes of MDM2 and p14(ARF) had 2.2 times (95% CI, 1.4-3.5) the risk for DTC of individuals carrying 0-1 risk genotypes (P trend = .021). The combined effect of MDM2 and p14(ARF) on risk of DTC was confined to young subjects (≤ 45 years), nonsmokers, nondrinkers, and subjects with a first-degree family history of cancer. These associations were quite similar in strength when cases were restricted to those with papillary thyroid cancer.

CONCLUSION:
Our results suggest that polymorphisms of MDM2 and p14(ARF) contribute to the interindividual difference in susceptibility to DTC, either alone or more likely jointly. The observed associations warrant further confirmation in independent studies.

PMID: 23218882

http://dx.doi.org/10.1016/j.surg.2012.11.009

Ann Surg. 2013 Apr;257(4):751-7. doi: 10.1097/SLA.0b013e31826bc239.

Benefit-risk balance of reoperation for persistent medullary thyroid cancer.

Machens A, Dralle H.

Source

Department of General, Visceral and Vascular Surgery, Martin Luther University Halle-Wittenberg, Ernst-Grube-Str. 40, D-06097 Halle (Saale), Germany. AndreasMachens@aol.com

Abstract

OBJECTIVE:
This investigation aimed at exploring the prospects of a cure for persistent medullary thyroid cancer (MTC) stratified by basal calcitonin levels before reoperation and the number of lymph node metastases previously removed at outside facilities.

BACKGROUND:
There is no evidence-based information supporting the balance of surgical benefit and risk in persistent MTC.

METHODS:
This retrospective study of 334 patients with persistent MTC referred to a tertiary surgical center, who were compared with 367 patients with previously untreated MTC referred to that institution during the same time period, evaluated biochemical cure rates after systematic lymph node dissection.

RESULTS:
The relationship between the incremental serum calcitonin level before reoperation and the number of lymph node metastases at reoperation and biochemical cure was strong after previous removal of 0 (r = 0.74 and 77%-0%) and 1 to 5 lymph node metastases (r = 0.61 and 60%-0%) elsewhere. It disappeared once more than 5 lymph node metastases had been cleared at other hospitals (nonsignificant and 5%). When serum calcitonin levels were 1000 pg/mL or lower before reoperation, biochemical cure rates were 44% (59 of 133 patients) and 18% (12 of 65 patients) after previous removal of 0 and 1 to 5 lymph node metastases, respectively. These rates

plummeted to 5% (2 of 43 patients) after a previous clearance of more than 5 lymph node metastases. When serum calcitonin levels exceeded 1000 pg/mL before reoperation, a biochemical cure was exceptional (1%; 1 of 76 patients).

CONCLUSIONS:
With serum calcitonin levels of 1000 pg/mL or lower before reoperation and the previous removal of 5 or fewer lymph node metastases, systematic lymph node dissection seems worthwhile for persistent MTC. These findings will need to be validated in independent series before being adopted more widely as a new standard of care.

PMID: 23023200

http://dx.doi.org/10.1097/SLA.0b013e31826bc239

Cancer Cytopathol. 2013 Apr;121(4):197-205. doi: 10.1002/cncy.21229. Epub 2012 Aug 7.

BRAF mutation detection in indeterminate thyroid cytology specimens: underlying cytologic, molecular, and pathologic characteristics of papillary thyroid carcinoma.

Ohori NP, Singhal R, Nikiforova MN, Yip L, Schoedel KE, Coyne C, McCoy KL, LeBeau SO, Hodak SP, Carty SE, Nikiforov YE.

Source

Department of Pathology, University of Pittsburgh Medical Center-Presbyterian, Pittsburgh, Pennsylvania 15213, USA. ohorinp@upmc.edu

Abstract

BACKGROUND:
BRAF mutations are highly specific for papillary thyroid carcinoma (PTC) and many cytology specimens with BRAF mutations are expected to demonstrate cytologic features typical of PTC. However, indeterminate thyroid cytology cases are inevitable and understanding the significance of the BRAF mutation within the context of the Bethesda System for Reporting Thyroid Cytopathology would be valuable.

METHODS:
Thyroid cytology cases submitted for conventional cytomorphologic evaluation and BRAF mutational analyses were selected from the authors' cytopathology files from April 2007 to October 2011. From this group, the diagnostic usefulness of BRAF mutations in indeterminate and malignant cases was assessed and analyses of cytologic and histopathologic features associated with the mutations in this gene were performed.

RESULTS:
A total of 131 cases with a BRAF mutation were identified. Of these, 119 underwent surgical pathology resection follow-up and demonstrated PTC. Approximately 75% of the cases were cytologically diagnosed as being positive for malignancy and these cases were associated with both the classic and tall cell variants of PTC at the time of resection, a greater likelihood of extrathyroidal extension, and the V600E type of BRAF mutation. In contrast, BRAF-mutated cases with diagnoses of atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) and follicular neoplasm/suspicious for follicular neoplasm were found to be more strongly associated with the follicular variant of PTC, a K601E BRAF mutation, and a lower likelihood of extrathyroidal extension. However, a subset of AUS/FLUS cases with the V600E BRAF mutation appeared to represent sampling variability of the classic or tall cell variants of PTC.

CONCLUSIONS:
Bethesda thyroid diagnoses in the setting of a BRAF mutation reflect differences in PTC subtypes, the nature of cytology specimens, and molecular characteristics.

PMID: 22887810

http://dx.doi.org/10.1002/cncy.21229

Tiroid: Prospektif makaleler

Am J Epidemiol. 2013 Apr 15;177(8):800-9. doi: 10.1093/aje/kws315. Epub 2013 Mar 25.

A prospective study of medical diagnostic radiography and risk of thyroid cancer.

Neta G, Rajaraman P, Berrington de Gonzalez A, Doody MM, Alexander BH, Preston D, Simon SL, Melo D, Miller J, Freedman DM, Linet MS, Sigurdson AJ.

Source

Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Rockville, MD, USA. netagil@mail.nih.gov

Abstract

Although diagnostic x-ray procedures provide important medical benefits, cancer risks associated with their exposure are also possible, but not well characterized. The US Radiologic Technologists Study (1983-2006) is a nationwide, prospective cohort study with extensive questionnaire data on history of personal diagnostic imaging procedures collected prior to cancer diagnosis. We used Cox proportional hazard regressions to estimate thyroid cancer risks related to the number and type of selected procedures. We assessed potential modifying effects of age and calendar year of the first x-ray procedure in each category of procedures. Incident thyroid cancers (n = 251) were diagnosed among 75,494 technologists (1.3 million person-years; mean follow-up = 17 years). Overall, there was no clear evidence of thyroid cancer risk associated with diagnostic x-rays except for dental x-rays. We observed a 13% increase in thyroid cancer risk for every 10 reported dental radiographs (hazard ratio = 1.13, 95% confidence interval: 1.01, 1.26), which was driven by dental x-rays first received before 1970, but we found no evidence that the relationship between dental x-rays and thyroid cancer was associated with childhood or adolescent exposures as would have been anticipated. The lack of association of thyroid cancer with x-ray procedures that expose the thyroid to higher radiation doses than do dental x-rays underscores the need to conduct a detailed radiation exposure assessment to enable quantitative evaluation of risk.

PMID: 23529772

http://dx.doi.org/10.1093/aje/kws315

Eur J Endocrinol. 2013 Apr 15;168(5):649-55. doi: 10.1530/EJE-12-0936. Print 2013 May.

Prospective evaluation of thyroid imaging reporting and data system on 4550 nodules with and without elastography.

Russ G, Royer B, Bigorgne C, Rouxel A, Bienvenu-Perrard M, Leenhardt L.

Source

Centre of Pathology and Radiology, 14 Avenue René Coty, 75014 Paris, France. gilles.russ@wanadoo.fr

Abstract

OBJECTIVE:

To evaluate prospectively the diagnostic accuracy of the thyroid imaging reporting and data system (TI-RADS) and its interobserver agreement and to estimate the reduction of indications of fine-needle aspiration biopsies (FNABs).

DESIGN:

A prospective comparative study was designed.

METHODS:

In 2 years, 4550 nodules in 3543 patients were prospectively scored using a flowchart and a six-point scale and then submitted to US-FNAB. Results were read according to the Bethesda system. Histopathological results were available for 263 cases after surgery. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value, and accuracy were calculated for the gray-scale score, elastography, and a combination of both methods. Interobserver agreement was calculated using the kappa statistic. The reduction in the number of FNABs was estimated.

RESULTS:
When compared with cytopathological results, sensitivity, specificity, NPV, and accuracy were 95.7, 61, 99.7, and 62% for the TI-RADS gray-scale score; 74.2, 91.1, 98, and 90% for elastography; and 98.5, 44.7, 99.8, and 48.3% for a combination of both methods respectively. When compared with histopathological results, the sensitivity of the gray-scale score, elastography, and a combination of both methods were 93.2, 41.9, and 96.7% respectively. Interobserver agreement for the six-point scale and the recommendation for biopsy were substantial (κ value=0.72 and 0.76 respectively). The reduction in the number of FNABs was estimated to be 33.8%.

CONCLUSION:
The TI-RADS score has high sensitivity and NPV for the diagnosis of thyroid carcinoma. A hard nodule should always be considered as suspicious for malignancy but elastography cannot be used alone. Combination of elastography with gray-scale can be used to improve sensitivity or specificity. Interobserver agreement and decrease in unnecessary biopsies are significant.

PMID: 23416955

http://dx.doi.org/10.1530/EJE-12-0936

Eur J Endocrinol. 2013 Apr 15;168(5):675-81. doi: 10.1530/EJE-12-1029. Print 2013 May.

Expressions of miRNAs in papillary thyroid carcinoma and their associations with the BRAFV600E mutation.

Huang Y, Liao D, Pan L, Ye R, Li X, Wang S, Ye C, Chen L.

Source

Department of Vascular and Thyroid Surgery, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, Guangdong 510080, China.

Abstract

OBJECTIVE:
Alterations in microRNA (miRNA) expression have been described in thyroid tumors, suggesting a role for miRNAs in thyroid carcinogenesis. BRAF(V600E) is the most frequently identified genetic alteration in papillary thyroid carcinoma (PTC). We investigated the link between BRAF(V600E) status and the expression of miRNAs in PTC and analyzed the associations of these factors with clinicopathological characteristics.

DESIGN AND METHODS:
Prospective study of patients who underwent thyroid surgery between October 8, 2008 and November 1, 2010. BRAF(V600E) status was determined by mutant allele-specific amplification PCR and direct sequencing of exon 15 of the BRAF gene in 69 PTC tissues and 69 respective paracancerous normal thyroid tissues. Initially, miRNA expression was analyzed in 12 PTC tissues and three associated paracancerous tissues using a miRNA microarray. miRNAs differentially expressed between BRAF(V600E)-positive and -negative PTC tissues were then validated by real-time quantitative PCR on 69 PTC tissues and 69 paracancerous tissues. We also explored the associations between BRAF(V600E) status or differential miRNA expression and clinicopathological characteristics.

RESULTS:
The mutation rate of BRAF(V600E) in PTC was 47.8%. Twelve miRNAs were upregulated and six were downregulated in PTC tissues, among which miR-15a, 15a*, 34a*, 34b*, 551b, 873, 876-3p, and 1274a were first

identified. miR-21* and 203 were significantly dysregulated (P<0.05) in PTC tissues with BRAF(V600E). Additionally, there were significant associations (P<0.05) between BRAF(V600E) and a higher tumor-node-metastasis staging (III/IV), and between miR-21* over-expression and lymph node metastasis.

CONCLUSIONS:
We identified two miRNAs that are differentially expressed in PTC tissues with BRAF(V600E) and revealed their associations with clinicopathological features. These findings may lead to the development of a potential diagnostic biomarker or prognostic indicator of PTC.

PMID: 23416953

http://dx.doi.org/10.1530/EJE-12-1029

Br J Surg. 2013 Apr;100(5):662-6; discussion 666-7. doi: 10.1002/bjs.9044. Epub 2013 Jan 23.

Prospective study on loss of signal on the first side during neuromonitoring of the recurrent laryngeal nerve in total thyroidectomy.

Sitges-Serra A, Fontané J, Dueñas JP, Duque CS, Lorente L, Trillo L, Sancho JJ.

Source

Endocrine Surgery Unit, Hospital del Mar, Barcelona, Spain. asitges@hospitaldelmar.cat

Abstract

BACKGROUND:
Staged thyroidectomy has been recommended when loss of the signal from intraoperative nerve monitoring is observed after first-side dissection of the recurrent laryngeal nerve. There is no high-quality evidence supporting this recommendation. In addition, it is not clear whether signal loss predicts postoperative vocal cord paralysis.

METHODS:
This was a prospective observational study of consecutive adult patients undergoing neuromonitored total thyroidectomy for either malignancy or multinodular goitre. The prevalence of first-side loss of signal was recorded. Surgery was completed, and vagus and laryngeal nerves on the first side were rechecked at the end of the procedure.

RESULTS:
Two-hundred and ninety patients were included. Loss of signal on the first side was noted in 16 procedures (5.5 per cent). Thyroidectomy was completed and, at retesting, 15 of 16 initially silent nerves recovered an electromyographic signal with a mean(s.d.) amplitude of 132(26) mcV. Mean time to recovery was 20.2 (range 10-35) min. In no patient was the signal lost on the opposite side. Only three of 15 nerves with a recovered signal were associated with transient vocal cord dysfunction.

CONCLUSION:
After loss of signal of the recurrent laryngeal nerve dissected initially, there was a 90 per cent chance of intraoperative signal recovery. In this setting, judicious bilateral thyroidectomy can be performed without risk of bilateral recurrent nerve paresis.

PMID: 23341266

http://dx.doi.org/10.1002/bjs.9044

Surgery. 2013 May;153(5):705-10. doi: 10.1016/j.surg.2012.10.013. Epub 2013 Jan 4.

Robotic transaxillary total thyroidectomy through a single axillary incision.

Aliyev S, Taskin HE, Agcaoglu O, Aksoy E, Milas M, Siperstein A, Berber E.

Source

Department of General Surgery, Cleveland Clinic, Cleveland, OH, USA.

Abstract

BACKGROUND:

There is controversy in the literature about whether robotic total thyroidectomy should be performed through unilateral or bilateral axillary incisions. The aim of this study was to perform a detailed critical analysis of the single-incision technique with a focus on postoperative pain, morbidity, and oncologic outcomes.

METHODS:

Between June 2009 and May 2012, 30 patients underwent robotic neck surgery through a single axillary incision. The perioperative outcomes of 16 patients who underwent robotic total thyroidectomy were compared with 30 consecutive patients undergoing conventional total thyroidectomy. Data were collected from a prospectively maintained, institutional review board-approved database. All data are presented as mean values ± standard error of the mean.

RESULTS:

Both groups were similar regarding age, gender, body mass index, tumor size, and tumor type. For all patients, skin-to-skin operative time (OT) was less in the conventional group (139 ± 8 vs 183 ± 11 minutes, respectively; P = .002). In the robotic group, a significant improvement of the OT occurred after the 6th case: 245 ± 12 minutes for the first 6 cases versus 153 ± 10 minutes for the last 10 cases (P < .001). Estimated blood loss was similar between groups. The median hospital stay was 1 day for both groups. The morbidity was 13% in the conventional and 19% in the robotic group (P = .631).

CONCLUSION:

Our results show that robotic total thyroidectomy through a single axillary incision is feasible, with similar short-term oncologic results. However, owing to the extent of dissection, the 2-week operative site discomfort is greater after robotic versus conventional total thyroidectomy.

PMID: 23294877

http://dx.doi.org/10.1016/j.surg.2012.10.013

J Surg Res. 2013 Apr;180(2):216-21. doi: 10.1016/j.jss.2012.04.051. Epub 2012 May 14.

Differentiating benign from malignant thyroid nodules using micro ribonucleic acid amplification in residual cells obtained by fine needle aspiration biopsy.

Mazeh H, Levy Y, Mizrahi I, Appelbaum L, Ilyayev N, Halle D, Freund HR, Nissan A.

Source

The Surgical Oncology Laboratory, Department of Surgery, Hadassah-Hebrew University Medical Center, Mount Scopus, Jerusalem, Israel.

Abstract

BACKGROUND:

Fine needle aspiration biopsy (FNAB) is the most commonly used diagnostic tool to differentiate benign from malignant thyroid nodules. Nevertheless, some FNAB cytology results are not definite. In such cases diagnostic thyroid lobectomy is performed with malignancy rate on final histopathology ranging at 15%-75%. The aim of this study was to improve on the accuracy of FNAB-based cytology by amplification of microRNAs (micro ribonucleic acids [miRs]) from the residual cells left in the FNAB needle after submission for cytology.

METHODS:
Residual cells were collected from the needle cup after FNAB cytology of 77 consecutive patients with thyroid nodules. miR-enriched RNA was extracted for all patients with cytology showing either follicular lesion or suspicion for malignancy (n=11). The expression of miR-21, -31, -146b, -187, -221, and -222 was determined using real-time polymerase chain reaction. Results were compared with final surgical histopathology.

RESULTS:
RNA was successfully extracted from all FNAB specimens. Five patients had FNAB cytology suspicious for malignancy. The miR panel was positive in all five (100%). Six patients had follicular lesions on FNAB. The miR panel was positive in three of four patients (75%) with confirmed malignancy and was negative in two of two (0%) patients with benign pathology results. This corresponded to a specificity of 100%, sensitivity of 88%, and accuracy of 90%.

CONCLUSIONS:
RNA extraction from FNAB residual cells is feasible, and a miR panel amplified from the extracted RNA seems like a promising diagnostic tool in this limited number of patients.

PMID: 22626557

http://dx.doi.org/10.1016/j.jss.2012.04.051

Tiroid: Meta analiz

J Clin Endocrinol Metab. 2013 Apr;98(4):1353-60. doi: 10.1210/jc.2012-3682. Epub 2013 Feb 22.

Low- or high-dose radioiodine remnant ablation for differentiated thyroid carcinoma: a meta-analysis.

Cheng W, Ma C, Fu H, Li J, Chen S, Wu S, Wang H.

Source

Department of Nuclear Medicine, Xin Hua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China.

Abstract

CONTEXT:
There is uncertainty over the dose of (131)I required for thyroid remnant ablation. Most previous studies have been inadequately powered to establish the best fixed dose of (131)I for effective ablation.

OBJECTIVE:
The aim of the study was to assess the effects of low- vs high-dose regimens of radioiodine in thyroid remnant ablation for patients with differentiated thyroid carcinoma.

DATA SOURCES:
Sources included the Cochrane Library, MEDLINE, EMBASE, and SCOPUS (all until September 2012).

STUDY SELECTION:
Randomized controlled trials that assess the efficacy of low- or high-dose of radioiodine ablation of thyroid remnants were collected.

DATA EXTRACTION:
Two authors performed the data extraction independently.

DATA SYNTHESIS:
Nine randomized controlled trials involving 2569 patients were included. The 1100-MBq vs the 3700-MBq radioiodine showed no statistically significant difference in successful thyroid remnant ablation (risk ratio [RR], 0.91 [0.79 to 1.04]; P = .15), both the 1100 vs the 1850 MBq (RR, 0.95 [0.83 to 1.10]; P = .52) and the 1850 vs the 3700 MBq (RR, 1.00 [0.85 to 1.17]; P = .98) also showed no significant differences (95% confidence intervals were calculated for each estimate). Also, no significant differences existed in quality-of-life scores on the SF-36 between different (131)I-dose groups both on the day of ablation (RR, 0.15 [-0.65 to 0.96], P = .71; I(2) = 29%, P = .24) and 3 months after ablation (RR, -1.1 [-2.37 to 0.17], P = .09; I(2) = 22%, P = .26). A low dose of 1100 MBq radioiodine showed significant benefits in reducing adverse effects (total RR, 0.65 [0.55 to 0.77], P < .1; I(2) = 31%, P =.14) and shorter hospital isolation (RR, 0.4 [0.32 to 0.50]; P < .05).

CONCLUSIONS:
The low dose of 1100 MBq radioiodine activity is sufficient for thyroid remnant ablation as compared to 3700 MBq radioiodine activity with similar quality of life, less common adverse effects, and a shorter hospital stay.

PMID: 23436920

http://dx.doi.org/10.1210/jc.2012-3682

Tiroid: Vaka sunumu

Hum Pathol. 2013 Apr;44(4):556-65. doi: 10.1016/j.humpath.2012.06.019. Epub 2012 Oct 15.

Papillary thyroid microcarcinoma with fatal outcome: evidence of tumor progression in lymph node metastases: report of 3 cases, with morphological and molecular analysis.

Piana S, Ragazzi M, Tallini G, de Biase D, Ciarrocchi A, Frasoldati A, Rosai J.

Source

Pathology Unit, IRCCS-Arcispedale Santa Maria Nuova, 42123 Reggio Emilia, Italy. Simonetta.Piana@asmn.re.it

Abstract

Papillary thyroid microcarcinoma generally carries an excellent prognosis, and fatal cases are becoming increasingly rare. Their pathologic and molecular features, however, remain largely unknown. We describe 3 cases of papillary thyroid microcarcinoma that, despite surgical and radioiodine treatment, recurred, metastasized, and eventually caused the death of the patients. In addition to morphology, immunohistochemical (cyclin D1 and p53) and molecular analyses (BRAF [v-raf Murine sarcoma viral oncogene homolog B1], KRAS [V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog], HRAS [v-Ha-ras Harvey rat sarcoma viral oncogene homolog], NRAS [neuroblastoma RAS viral oncogene homolog], and PIK3CA [phosphoinositide-3-kinase, catalytic, alpha polypeptide]) were performed. Interestingly, all 3 cases presented with massive lymph node metastases that showed morphological evidence of "tumor progression" (tall cell features, poorly differentiated areas, and high-grade cytologic features). Cyclin D1 was consistently immunoreactive in both primary and metastatic site, whereas p53 was negative. BRAF V600E was absent in both sites, and KRAS, HRAS, NRAS, and PIK3CA were consistently wild type. These data suggest that, in cases of metastatic papillary thyroid microcarcinoma, an accurate morphologic analysis of the metastatic deposits could contribute to a more accurate prediction of tumor behavior.

PMID: 23079204

http://dx.doi.org/10.1016/j.humpath.2012.06.019

Paratiroid: Retrospektif makaleler

Laryngoscope. 2013 May;123(5):1310-3. doi: 10.1002/lary.23863. Epub 2013 Apr 2.

The diagnostic value of parathyroid hormone washout after fine-needle aspiration of suspicious cervical lesions in patients with hyperparathyroidism.

Abdelghani R, Noureldine S, Abbas A, Moroz K, Kandil E.

Source

Division of Endocrine and Oncologic Surgery, Department of Surgery, and Section of Surgical Pathology and Cytopathology, Tulane University School of Medicine New Orleans, Louisiana 70124, USA.

Abstract

OBJECTIVES/HYPOTHESIS:
We aimed to study the diagnostic value of parathyroid hormone (PTH) concentration in the needle washout of fine-needle aspiration (FNA) compared to cytology of suspicious lesions suggestive of culprit parathyroid glands in patients with recurrent or persistent primary hyperparathyroidism (PHPT).

STUDY DESIGN:
Retrospective review.

METHODS:
Patients with recurrent or persistent PHPT, who were referred to one surgeon and underwent FNA of the culprit parathyroid lesion preoperatively, were included in this study. All patients underwent comprehensive neck ultrasound, and suspicious lesions underwent ultrasound-guided FNA by the same surgeon. The aspiration cytology was read by a single dedicated cytopathologist blinded to the PTH washout results. A positive cutoff value for PTH washout concentration was defined as superior to serum PTH level obtained at the same time. The final diagnosis after reoperative surgery was confirmed by the same cytopathologist.

RESULTS:
Twenty-four consecutive patients were included. The mean serum PTH and calcium were 111.5 ± 106.25 pg/mL (normal: 15-65 pg/mL) and 10.8 ± 0.5 mg/dL (normal: 8.6-10.2 pg/mL), respectively. Twenty-two patients (91.6%) had elevated PTH washout concentrations with a positive predictive value (PPV) of 100%. Cytopathology was successful in confirming parathyroid tissue only in seven patients (29%). An adenoma was identified in 19 patients (79.1%); however, five patients (20.8%) were found to have multiglandular disease.

CONCLUSIONS:
An elevated PTH washout concentration can help identify culprit parathyroid gland lesions with a high PPV in patients requiring reoperative parathyroid surgery. This diagnostic technique allows for targeted surgical approach in reoperative settings, especially in patients with negative preoperative

PMID:23553068

http://dx.doi.org/10.1002/lary.23863

Eur J Endocrinol. 2013 Apr 29;168(6):811-9. doi: 10.1530/EJE-12-0947. Print 2013 Jun.

Histology and immunohistochemistry of the parathyroid glands in renal secondary hyperparathyroidism refractory to vitamin D or cinacalcet therapy.

Vulpio C, Bossola M, Di Stasio E, Tazza L, Silvestri P, Fadda G.

Source

Istituto di Clinica Chirurgica, Università Cattolica del Sacro Cuore, Largo A. Gemelli, 8, Rome 00168, Italy. c.vulpio@alice.it

Abstract

BACKGROUND:
Cinacalcet is a new effective treatment of secondary hyperparathyroidism (SHPT) in hemodialysis patients (HP), but the alterations of parathyroid gland (PTG) hyperplasia determined by cinacalcet and vitamin D have not been extensively investigated in humans.

METHODS:
We performed histological analyses of 94 PTGs removed from 25 HP who underwent parathyroidectomy (PTx) because of SHPT refractory to therapy with vitamin D alone (group A=13 HP and 46 PTGs) or associated with cinacalcet (group B=12 HP and 48 PTGs). The number, weight, the macroscopic cystic/hemorrhagic changes, and type of hyperplasia of PTG (nodular=NH, diffuse=DH) were assessed. In randomly selected HP of group A (4 HP and 14 PTGs) and group B (4 HP and 15 PTGs), the labeling index of cells positive to Ki-67 and TUNEL and the semiquantitative score of immunohistochemistry staining of vitamin D receptor, calcium-sensing receptor, and vascular endothelial growth factor-α (VEGF-α) were measured in the entire PTGs and in the areas with DH or NH.

RESULTS:
The number and weight of single and total PTG of each HP were similar in the two groups as well as the number of PTG with macroscopic cystic/hemorrhagic areas. TUNEL, Ki-67, and VEGF-α scores were higher in NH than in DH areas.

CONCLUSION:
This observational study of a highly selected population of HP, submitted to PTx because SHPT refractory to therapy, shows that the macroscopic, microscopic, and immunochemistry characteristics of PTG in HP who received or did not receive cinacalcet before PTx did not differ significantly.

PMID: 23520248

http://dx.doi.org/10.1530/EJE-12-0947

Adrenal: Derlemeler

Adv Clin Exp Med. 2012 Nov-Dec;21(6):821-9.

Genetic aspects of pheochromocytoma.

Kolačkov K, Tupikowski K, Bednarek-Tupikowska G.

Source

Department of Endocrinology, Diabetology and Isotope Therapy, Wroclaw Medical University, Wroclaw, Poland. katarzyna.kolackov@gmail.com

Abstract

Pheochromocytomas are derived from chromaffin cells of the adrenal medulla which synthesize and secrete catecholamines, thus affecting the cardiovascular system and metabolic processes. Pheochromocytoma is a tumor of the following multicarcinoma hereditary syndromes: type 2 multiple endocrine neoplasia, von Hippel-Lindau disease, type 1 neurofibromatosis and the pheochromocytomas/paragangliomas syndrome. Pheochromocytomas are relatively rare, and because of non-specific manifestation of these tumors and the possible lack of signs and symptoms for extended periods of time, the diagnosis may be delayed, which may, in turn, lead to death. Pheochromocytomas may occur sporadically. However, due to the frequent incidence of hereditary forms of these cancers, the presymptomatic genetic testing of family members with a positive family history is indicated, thus allowing for selecting people with higher risk of cancer. Early detection of the syndrome and the coexisting tumors (which may be malignant) may lead to a correct diagnosis, regular surveillance, preventive examinations and implementation of appropriate early treatment. Recent examinations have shown significant involvement of RET, VHL, NF1, SDHB and SDHD as well as the newly discovered KIF1Bβ, TMEM127 and MAX genes in pathogenesis of these tumors. The microarray-gene expression studies, based on the analysis of cellular pathways, have revealed two distinct clusters indicating two different routes of tumorgenesis. The genotype-phenotype correlations are still being studied and future research can give us clearer information about the function of these genes, which may prove crucial from the clinical point of view.

PMID: 23457139

Adrenal: Prospektif makaleler

J Clin Endocrinol Metab. 2013 Apr;98(4):1651-8. doi: 10.1210/jc.2012-3625. Epub 2013 Feb 22.

Changes in energy metabolism in pheochromocytoma.

Petrák O, Haluzíková D, Kaválková P, Štrauch B, Rosa J, Holaj R, Brabcová Vránková A, Michalsky D, Haluzík M, Zelinka T, Widimsky J Jr.

Source

Third Department of Medicine, General University Hospital, Prague 2, Czech Republic. Ondrej.Petrak@vfn.cz

Abstract

CONTEXT:
Catecholamine overproduction in pheochromocytoma affects basal metabolism, resulting in weight loss despite normal food intake.

OBJECTIVE:
The objective of the study was to evaluate changes in energy metabolism expressed as resting energy expenditure (REE) in patients with pheochromocytoma before and after adrenalectomy and the possible relationship with circulating inflammatory markers.

DESIGN:
We measured REE in 17 patients (8 women) with pheochromocytoma by indirect calorimetry (Vmax-Encore 29N system) before and 1 year after adrenalectomy. Body fat percentage was measured with a Bodystat device. Inflammatory markers (leukocytes count and C-reactive protein) and cytokines (TNF-α, IL-6, and IL-8) were analyzed with a Luminex 200.

RESULTS:
REE measured in the pheochromocytoma group was 10.4% higher than the predicted value (1731 ± 314 vs 1581 ± 271 kcal/d; P = .004). Adrenalectomy significantly increased body mass index (P =0.004) and the percentage of body fat (P = .01), with a proportional increase in fat distribution (waist circumference, P = .045; hip circumference, P = .001). REE significantly decreased after adrenalectomy (1731 ± 314 vs 1539 ± 215 kcal/d; P = .002), even after adjustments in body surface and body weight (P < .001). After adrenalectomy, we found a significant decrease in leukocyte counts (P = .014) and in the levels of TNF-α (P < .001), IL-6 (P = .048), and IL-8 (P = .007) but not C-reactive protein (P = .09). No significant correlations among calorimetry parameters, hormones, and proinflammatory markers were detected.

CONCLUSIONS:
Chronic catecholamine overproduction in pheochromocytoma may lead to a proinflammatory and hypermetabolic state characterized by increased REE. Adrenalectomy leads to the normalization of energy metabolism followed by an increase in body mass index and body fat content and decreases in inflammatory markers and cytokines.

PMID: 23436923

http://dx.doi.org/10.1210/jc.2012-3625

Eur J Endocrinol. 2013 Apr 15;168(5):683-7. doi: 10.1530/EJE-12-1106. Print 2013 May.

High penetrance of pheochromocytoma in multiple endocrine neoplasia 2 caused by germ line RET codon 634 mutation in Japanese patients.

Imai T, Uchino S, Okamoto T, Suzuki S, Kosugi S, Kikumori T, Sakurai A; MEN Consortium of Japan.

Source

Division of Breast and Endocrine Surgery, Department of Surgery, Aichi Medical University, Nagakute, Aichi, Japan. timai@med.nagoya-u.ac.jp

Abstract

OBJECTIVE:

The precise penetrance of pheochromocytoma (PHEO) in multiple endocrine neoplasia type 2 (MEN2) has not been reported in a large cohort. In this study, we aimed to clarify the codon-specific penetrance of PHEO in MEN2.

DESIGN:

We established a study group designated the 'MEN Consortium of Japan' in 2008 and asked physicians and surgeons to provide clinical and genetic information on patients they had treated up to 2011.

METHODS:

Data were collected on patients identified as carriers of the RET mutation or diagnosed with medullary thyroid carcinoma (MTC) and/or PHEO with family history from 52 institutions all over Japan.

RESULTS:

Of 493 registered MEN2 patients, RET mutation data were available for 390. Of these, 144 developed PHEOs, while 246 did not. The penetrance of PHEO was 25% by age 30 years, 52% by age 50 years, and 88% by age 77 years in RET mutation carriers with a codon 634 mutation. All patients with a codon 918 mutation (MEN2B) developed PHEO by age 56 years. Less than 32%penetrance of PHEO was seen in patients with mutations at codons other than 634 and 918.

CONCLUSIONS:

Most patients with a codon 634 mutation develop PHEOs as well as MTC during their lifetime.

PMID: 23416954

http://dx.doi.org/10.1530/EJE-12-1106

NET: Vaka sunumu

Anticancer Res. 2013 May;33(5):2175-7.

Radiotherapy in the management of pancreatic neuroendocrine tumors (PNET): experience at three institutions.

Saif MW, Ove R, Ng J, Russo S.

Source

Tufts University School of Medicine, Division of Hematology/Oncology, Department of Medicine, Director, GI Oncology Program 800 Washington Street, Box 245, Boston, MA 02111, USA. wsaif@tuftsmedicalcenter.org

Abstract

AIM:

Advanced pancreatic neuroendocrine tumor (PNET) presents a therapeutic challenge as many are unresectable and relatively resistant to systemic therapy with a high malignant potential. We share our experience using concurrent capecitabine or infusional 5-fluorouracil with radiation for patients with resected and locally advanced PNET.

PATIENTS AND METHODS:

Six patients (two females, four males) with PNET were treated with capecitabine or infusional 5-FU and concurrent radiation.

RESULTS:

The median age was 52 years (range: 38 to 63 years), with ECOG Performance Status (PS) 0-1, grade 0-1 weight loss, and grade 0-1 pain. One patient underwent resection with negative margins, two with positive margins, and three had unresectable locally advanced disease. All six patients demonstrated partial radiographic response and sustained local control. The treatment was tolerable with only grade 2 hand-foot syndrome and grade 1 mucositis observed.

CONCLUSION:

Prospective studies to further investigate the role of chemoradiation in this setting are warranted.

KEYWORDS:

5-FU, PNET, capecitabine, chemoradiation

PMID: 23645772

NET: Vaka Kontrol

Eur J Endocrinol. 2013 Apr 15;168(5):689-97. doi: 10.1530/EJE-12-0968. Print 2013 May.

Quality of life is decreased in patients with paragangliomas.

van Hulsteijn LT, Louisse A, Havekes B, Kaptein AA, Jansen JC, Hes FJ, Smit JW, Corssmit EP.

Source

Department of Endocrinology and Metabolic Diseases, Leiden University Medical Center, Leiden, The Netherlands.

Abstract

CONTEXT:

Germline mutations in succinate dehydrogenase (SDH) genes predispose carriers for developing paragangliomas, and studies on their quality of life (QoL) are scarce.

OBJECTIVES:
The objectives of this study were to assess QoL in patients with paragangliomas (PGL), to evaluate long-term QoL, and to explore potential differences in QoL between SDH mutation carriers and paraganglioma patients without an SDH mutation.

DESIGN:
Cross-sectional, case-control study.

SETTING:
Tertiary referral center.

SUBJECTS:
ONE HUNDRED AND SEVENTY FOUR PARAGANGLIOMA PATIENTS WERE INCLUDED: 25 SDHB, two SDHC, and 122 SDHD mutation carriers and 25 patients without an SDH mutation. They provided 100 peers as control persons. Furthermore, patients were compared with age-adjusted reference populations.

MAIN OUTCOME MEASURES:
QOL WAS ASSESSED USING THREE VALIDATED HEALTH-RELATED QOL QUESTIONNAIRES: the Hospital Anxiety and Depression Scale, the Multidimensional Fatigue Index 20, and the Short Form 36.

RESULTS:
Patients reported a significantly impaired QoL compared with their own controls, mainly on fatigue and physical condition subscales. Compared with age-adjusted literature values, patients had significantly impaired scores on physical, psychological, and social subscales. A decreased QoL was mainly related to paraganglioma-associated complaints. There was no difference in QoL between the various SDH mutation carriers or paraganglioma patients without an SDH mutation. QoL in asymptomatic mutation carriers, i.e. without manifest disease, did not differ from QoL of the general population. Long-term results in 41 patients showed no alteration in QoL besides a reduced level of activity.

CONCLUSION:
QoL is decreased in paraganglioma patients but stable when measured over time.

PMID: 23392211

http://dx.doi.org/10.1530/EJE-12-0968

NET: Derlemeler

Surg Clin North Am. 2013 Jun;93(3):675-91. doi: 10.1016/j.suc.2013.02.001. Epub 2013 Apr 3.

Management of pancreatic neuroendocrine tumors.

Dickson PV, Behrman SW.

Source

Division of Surgical Oncology, Department of Surgery, University of Tennessee Health Science Center, 910 Madison Avenue, Suite 208, Memphis, TN 38163, USA.

Abstract

Pancreatic neuroendocrine tumors account for 1% to 2% of pancreatic neoplasms and may occur sporadically or as part of a hereditary syndrome. Patients may present with symptoms related to hormone secretion by functional tumors or to locally advanced or metastatic nonfunctional tumors. Asymptomatic pancreatic neuroendocrine tumors are increasingly detected incidentally during abdominal imaging performed for other reasons. The management of localized pancreatic neuroendocrine tumors is surgical resection. Hepatic metastases are common and their management involves a variety of liver-directed therapies, which should be tailored according to extent of disease, symptoms, presence of extrahepatic metastases, and patient performance status.

PMID: 23632152

http://dx.doi.org/10.1016/j.suc.2013.02.001

Eur J Endocrinol. 2013 Mar 15;168(4):R77-83. doi: 10.1530/EJE-12-0418. Print 2013 Apr.

Endocrine tumours: epidemiology of malignant digestive neuroendocrine tumours.

Lepage C, Bouvier AM, Faivre J.

Source

Registre Bourguignon des Cancers Digestifs, INSERM CRI 866, Université de Bourgogne, CHU de Dijon, Dijon, France. come.lepage@u-bourgogne.fr

Abstract

Little is known about patients with malignant digestive neuroendocrine tumours (MD-NETs). Although their incidence is increasing, MD-NETs remain a rare cancer, representing 1% of digestive cancers. Most MD-NETs are well-differentiated. MD-NET poorly differentiated carcinomas account for 20% of cases on average. Anatomical localisation of MD-NETs varied according to geographic region. Stage at diagnosis and prognosis for patients with MD-NETs in the general population are considerably worse than often reported from small hospital case series. Prognosis varies with tumour differentiation, anatomic site and histological subtype. There are significant differences in survival from MD-NETs among European countries, independent of other prognostic factors. Early diagnosis is difficult; new therapeutic options appear to represent the best approach to improving prognosis.

PMID: 2334933

http://dx.doi.org/10.1530/EJE-12-0418

Cancer Treat Rev. 2013 May;39(3):270-4. doi: 10.1016/j.ctrv.2012.06.009. Epub 2012 Jul 20.

Chemotherapy in gastroenteropancreatic (GEP) neuroendocrine carcinomas (NEC): a critical view.

Fazio N, Spada F, Giovannini M.

Source

Unit of Upper Gastrointestinal and Neuroendocrine Tumors, Department of Medicine, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy. nicola.fazio@ieo.it

Abstract

Neuroendocrine tumors (NET) are classified according to the Ki67 in low-intermediate grade (Ki67<20%) and high grade (Ki67>20%). The NET of the latter group are also known as neuroendocrine carcinoma (NEC), and their prognosis is dismail. While in the former group biotherapy and radionuclide therapy can be proposed, chemotherapy represents the only treatment usually proposed for NEC. Cisplatin/etoposide combination is usually chosen based on the rationale that NEC are clinically similar to small cell lung cancer. However, evidence for cisplatin/etoposide in NEC is poor and controversial, and different schedules and response rate have been published so far. These aspects, combined with the heterogeneous characteristics of NEC, prompt us to have some doubt in considering cisplatin/etoposide as the gold standard. Some evidence exists that carboplatin can be used instead of cisplatin and irinotecan instead of etoposide without reducing efficacy. Furthermore other drugs, as gemcitabine, oxaliplatin or temozolomide can be evaluated in NEC with non-neuroendocrine component or in mixed adenoneuroendocrine carcinomas. NEC are a category of NET that should be deeply studied to verify if the response to cisplatin/etoposide is homogeneous related to the different Ki67, different morphology and/or different primary site.

PMID: 22819619

http://dx.doi.org/10.1016/j.ctrv.2012.06.009

NET: Retrospektif makaleler

Am J Surg Pathol. 2013 Apr;37(4):606-12. doi: 10.1097/PAS.0b013e318275d1d7.

Tumor staging but not grading is associated with adverse clinical outcome in neuroendocrine tumors of the appendix: a retrospective clinical pathologic analysis of 138 cases.

Volante M, Daniele L, Asioli S, Cassoni P, Comino A, Coverlizza S, De Giuli P, Fava C, Manini C, Berruti A, Papotti M.

Source

Department of Clinical & Biological Sciences, University of Turin at San Luigi Hospital, Orbassano, Turin, Italy. marco.volante@unito.it

Abstract

Appendiceal neuroendocrine neoplasms (NENs) are rare and usually incidentally discovered. Most cases are clinically indolent, although the rare aggressive ones are poorly predictable. The aim of this study was to test the applicability and prognostic significance of the new World Health Organization (WHO) classification and to test the several pathologic features and TNM staging systems (American Joint Committee on Cancer and European Neuroendocrine Tumor Society) in these tumors. A multi-institutional retrospective series of 138 appendiceal NENs was selected on the basis of the availability of both pathologic material and clinical information, including follow-up data. All cases were reviewed to record pathologic features and to apply year 2000 and 2010 WHO classifications, as well as European Neuroendocrine Tumor Society and American Joint Committee on Cancer TNM stages. Clinical and pathologic characteristics were compared with disease outcome by contingency, univariate, and multivariate survival analyses. Although up to one third of cases presented several malignancy-associated pathologic features, only 4 patients died of the disease. Adverse outcome was significantly associated with extramural extension (including mesoappendix), well-differentiated carcinoma diagnosis (2000 WHO classification), pT3-4 stage, older age, and presence of positive resection margins, but not with tumor size, mitotic or proliferative indexes, and, consequently, 2010 WHO grading. In the appendix, at variance with midgut/hindgut NENs, the 2000 WHO classification performs better than the grading-based 2010 WHO scheme and, together with tumor stage, is the most relevant parameter associated with clinical aggressiveness.

PMID: 23426123

http://dx.doi.org/10.1097/PAS.0b013e318275d1d7

J Surg Oncol. 2013 May;107(6):659-64. doi: 10.1002/jso.23297. Epub 2012 Dec 11.

Malignant pheochromocytoma and paraganglioma: a population level analysis of long-term survival over two decades.

Goffredo P, Sosa JA, Roman SA.

Source

Department of Surgery, Milano-Bicocca University, Monza, Italy.

Abstract

BACKGROUND AND OBJECTIVES:

Pheochromocytoma (PHEO) and paraganglioma (PGL) are rare tumors. Aims of this study were to describe and to compare demographic, clinical, pathologic, and survival characteristics of malignant PHEO and PGL.

METHODS:

Patients were identified in SEER, 1988-2009. Analyses included chi-square, ANOVA, Kaplan-Meier, and Cox proportional hazard regression.

RESULTS:
Gender distribution and mean age were similar for PHEO and PGL. Surgery was performed in 74.3% of PHEO and 78.9% of PGL; external beam radiation was administered in 8.0% of PHEO and 28.1% of PGL ($P < 0.001$). Compared to PGL, PHEO were larger (mean size 7.7 vs. 4.5 cm PGL, $P = 0.001$) and more were SEER-staged as localized (17.3% vs. 49.6%, respectively, $P < 0.001$). PGLs were more often located in the trunk than in the head/neck (53.8% vs. 38.0%, $P < 0.001$). PHEO had lower overall and disease-specific survival than PGL (54.0% and 73.5% vs. 73.3% and 80.5% for PGL, respectively, $P < 0.001$ and $P = 0.118$). Independent factors associated with mortality for PHEO included not undergoing surgery and metastases at diagnosis; for PGL, these were age 61-75 years, size ≥5 cm, and presenting with metastases.

CONCLUSIONS:
Malignant PHEO has a more aggressive course than malignant PGL; long-term survival has not improved over the last two decades. Multi-institutional efforts should be pursued to seek novel treatments.

PMID: 23233320

http://dx.doi.org/10.1002/jso.23297