1. Eur J Surg Oncol. 2017 Jun 22. pii: S0748-7983(17)30544-9. doi: 10.1016/j.ejso.2017.06.004. [Epub ahead of print]

Management of the lateral neck in well differentiated thyroid cancer.

Cracchiolo JR[1], Wong RJ[2].

Abstract

Lateral neck lymph node metastases in well differentiated thyroid cancer are common, ranging from 30% to 60%, with the majority of these foci identifiable only as microscopic deposits. A skilled ultrasound evaluation of the lymph nodes in the lateral neck is recommended for all patients presenting with newly diagnosed thyroid cancer undergoing surgical management. Ultrasound guided fine needle aspiration biopsy may be used to cytologically confirm suspected lateral neck nodal metastases prior to surgery. For patients with large volume nodal disease, extranodal extension, or multiple nodal metastases, computed tomography (CT) scan of the neck with contrast is an important additional imaging modality to accurately localize disease prior to surgery. Primary surgical management for lateral neck disease typically includes lateral neck dissection in conjunction with total thyroidectomy. Postoperative adjuvant radioactive iodine is typically recommended for patients with clinically evident nodal metastases, or for those with over 5 micrometastatic nodes. In the recurrent or persisting disease setting, complete surgical resection of local and regional disease remains the main treatment approach. However, sub-centimeter nodal disease may take an indolent course, and active surveillance may be a reasonable approach in selected clinical circumstances. Conversely, external beam radiation therapy (EBRT) may be considered for scenarios with unresectable disease, or microscopic residual disease following surgery in a clinically unfavorable setting. Two multi-kinase inhibitors (sorafenib and lenvatinib) are now FDA approved for treatment of RAI refractory thyroid cancer and now play an important role in the management of progressive, metastatic and surgically incurable disease.

2. Clin Oncol (R Coll Radiol). 2017 May;29(5):283-289. doi: 10.1016/j.clon.2017.01.001. Epub 2017 Jan 13.

Differentiated and Medullary Thyroid Cancer: Surgical Management of Cervical Lymph Nodes.

Asimakopoulos P[1], Nixon IJ[2], Shaha AR[3].

Abstract

Thyroid cancer metastasises to the central and lateral compartments of the neck frequently and early. The impact of nodal metastases on outcome is affected by the histological subtype of the primary tumour and the patient's age, as well as the size, number and location of those metastases. The impact of extranodal extension has recently been highlighted as an important prognosticating factor.

Although clinically evident nodal disease in the lateral neck compartments has a significant impact on both survival and recurrence, microscopic metastases to the central or the lateral neck in well-differentiated thyroid cancer do not significantly affect outcome. Here we discuss the surgical management of neck metastases in well-differentiated and medullary thyroid carcinoma.

3. World J Surg Oncol. 2016 May 17;14:149. doi: 10.1186/s12957-016-0879-4.

Role of prophylactic central compartment lymph node dissection in clinically N0 differentiated thyroid cancer patients: analysis of risk factors and review of modern trends.

Conzo G[1], Tartaglia E[2], Avenia N[3], Calò PG[4], de Bellis A[5], Esposito K[5], Gambardella C[1], Iorio S[5], Pasquali D[5], Santini L[1], Sinisi MA[6], Sinisi AA[6], Testini M[7], Polistena A[3], Bellastella G[5].

Abstract

In the last years, especially thanks to a large diffusion of ultrasound-guided FNBs, a surprising increased incidence of differentiated thyroid cancer (DTC), "small" tumors and microcarcinomas have been reported in the international series. This led endocrinologists and surgeons to search for "tailored" and "less aggressive" therapeutic protocols avoiding risky morbidity and useless "overtreatment". Considering the most recent guidelines of referral endocrine societies, we analyzed the role of routine or so-called prophylactic central compartment lymph node dissection (RCLD), also considering its benefits and risks. Literature data showed that the debate is still open and the surgeons are divided between proponents and opponents of its use. Even if lymph node metastases are commonly observed, and in up to 90% of DTC cases micrometastases are reported, the impact of lymphatic involvement on long-term survival is subject to intensive research and the best indications of lymph node dissection are still controversial. Identification of prognostic factors for central compartment metastases could assist surgeons in determining whether to perform RLCD. Considering available evidence, a general agreement to definitely reserve RCLD to "high-risk" cases was observed. More clinical researches, in order to identify risk factors of meaningful predictive power and prospective long-term randomized trials, should be useful to validate this selective approach.

4. Front Oncol. 2017 Jun 19;7:122. doi: 10.3389/fonc.2017.00122. eCollection 2017.

The Role of Central Neck Lymph Node Dissection in the Management of Papillary Thyroid Cancer.

Shirley LA[1], Jones NB[2], Phay JE[1].

Abstract

Papillary thyroid cancer (PTC) is the most common thyroid malignancy, and cervical nodal metastases are frequent at presentation. The most common site for nodal metastases from PTC is the central compartment of the ipsilateral neck in the paratracheal and pretracheal regions. The decision to resect these lymph nodes at the time of thyroidectomy often depends on if nodes with suspected malignancy can be identified preoperatively. If nodal spread to the central neck nodes is known, then the consensus is to remove all nodes in this area. However, there remains significant controversy regarding the utility of removing central neck lymph nodes for prophylactic reasons. Herein, we review the potential utility of central neck lymph node dissection as well as the risks of performing this procedure. As well, we review the potential of molecular testing to stratify patients who would most benefit from this procedure. We advocate a selective approach in which patients undergo clinical neck examination coupled with ultrasound to detect any concerning lymph nodes that warrant additional evaluation with either fine needle aspiration or excisional biopsy in the operating room. In lieu of clinical lymphadenopathy, we suggest the use of patient and disease characteristics as identified by multiple groups, such as the American Thyroid Association and European Society of Endocrine Surgeons, which include extremes of ages, large primary tumor size, and male gender, when deciding to perform central neck lymph node dissection. Patients should be educated on the potential long-terms risks versus the lack of known long-term benefits.

5. Langenbecks Arch Surg. 2014 Feb;399(2):141-54. doi: 10.1007/s00423-013-1145-7. Epub 2013 Nov 22.

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

Iacobone M[1], Jansson S, Barczyński M, Goretzki P.

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.

6. Langenbecks Arch Surg. 2014 Feb;399(2):165-84.

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.

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.

7. Thyroid. 2016 Jan;26(1):1-133. doi: 10.1089/thy.2015.0020.

2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer.

Haugen BR[1], Alexander EK[2], Bible KC[3], Doherty GM[4], Mandel SJ[5], Nikiforov YE[6], Pacini F[7], Randolph GW[8], Sawka AM[9], Schlumberger M[10], Schuff KG[11], Sherman SI[12], Sosa JA[13], Steward DL[14], Tuttle RM[15], Wartofsky L[16].

Abstract

BACKGROUND:

Thyroid nodules are a common clinical problem, and differentiated thyroid cancer is becoming increasingly prevalent. Since the American Thyroid Association's (ATA's) guidelines for the management of these disorders were revised in 2009, significant scientific advances have occurred in the field. The aim of these guidelines is to inform clinicians, patients, researchers, and health policy makers on published evidence relating to the diagnosis and management of thyroid nodules and differentiated thyroid cancer.

METHODS:

The specific clinical questions addressed in these guidelines were based on prior versions of the guidelines, stakeholder input, and input of task force members. Task force panel members were educated on knowledge synthesis methods, including electronic database searching, review and selection of relevant citations, and critical appraisal of selected studies. Published English language articles on adults were eligible for inclusion. The American College of Physicians Guideline Grading System was used for critical appraisal of evidence and grading strength of recommendations for therapeutic interventions. We developed a similarly formatted system to appraise the quality of such studies and resultant recommendations. The guideline panel had complete editorial independence from the ATA. Competing interests of guideline task force members were regularly updated, managed, and communicated to the ATA and task force members.

RESULTS:

The revised guidelines for the management of thyroid nodules include recommendations regarding initial evaluation, clinical and ultrasound criteria for fine-needle aspiration biopsy, interpretation of fine-needle aspiration biopsy results, use of molecular markers, and management of benign thyroid nodules. Recommendations regarding the initial management of thyroid cancer include those relating to screening for thyroid cancer, staging and risk assessment, surgical management, radioiodine remnant ablation and therapy, and thyrotropin suppression therapy using levothyroxine. Recommendations related to long-term management of differentiated thyroid cancer include those related to surveillance for recurrent disease using imaging and serum thyroglobulin, thyroid hormone therapy, management of recurrent and metastatic disease, consideration for clinical trials and targeted therapy, as well as directions for future research.

CONCLUSIONS:

We have developed evidence-based recommendations to inform clinical decision-making in the management of thyroid nodules and differentiated thyroid cancer. They represent, in our opinion, contemporary optimal care for patients with these disorders.

8. Eur Thyroid J. 2012 Apr;1(1):5-14. doi: 10.1159/000336977. Epub 2012 Mar 28.

2012 European thyroid association guidelines for metastatic medullary thyroid cancer.

Schlumberger M[1], Bastholt L[2], Dralle H[3], Jarzab B[4], Pacini F[5], Smit JW[6]; European Thyroid Association Task Force.

Abstract

Distant metastases are the main cause of death in patients with medullary thyroid cancer (MTC). These 21 recommendations focus on MTC patients with distant metastases and a detailed follow-up protocol of patients with biochemical or imaging evidence of disease, selection criteria for treatment, and treatment modalities, including local and systemic treatments based on the results of recent trials. Asymptomatic patients with low tumor burden and stable disease may benefit from local treatment modalities and can be followed up at regular intervals of time. Imaging is usually performed every 6-12 months, or at longer intervals of time depending on the doubling times of serum calcitonin and carcinoembryonic antigen levels. Patients with symptoms, large tumor burden and progression on imaging should receive systemic treatment. Indeed, major progress has recently been achieved with novel targeted therapies using kinase inhibitors directed against RET and VEGFR, but further research is needed to improve the outcome of these patients.

9. Langenbecks Arch Surg. 2014 Feb;399(2):185-97. doi: 10.1007/s00423-013-1139-5. Epub 2013 Dec 3.

Timing and extent of thyroid surgery for gene carriers of hereditary C cell disease--a consensus statement of the European Society of Endocrine Surgeons (ESES).

Niederle B[1], Sebag F, Brauckhoff M.

Abstract

PURPOSE:

This "consensus statement" aims to summarise the current evidence-based knowledge as to "timing" and planning the "extent" of thyroid surgery in terms of an optimal balance between the prevention of thyroid malignancy (involving metastasis) and the risks associated with more extended surgery (permanent hypoparathyroidism, permanent paralysis of the recurrent laryngeal nerve). Surgery "in time" is influenced by genetic findings and age. Basal (and stimulated) calcitonin levels may individualise the timing and extent of surgery.

MATERIALS AND METHODS:

The review of English-language studies addressing the management of REarranged during Transfection proto-oncogene mutation carriers including the time, extent of thyroid surgery and results. Evidence is mostly obtained from well-designed, non-experimental descriptive investigations, such as comparative, correlation and case-control studies (level III) with a grading of recommendation B, or from expert committee reports or opinions and/or the clinical experience of respected authorities (level IV) with a grading of recommendation C, respectively.

RESULTS:

"Risk level D" includes multiple endocrine neoplasia 2B cases. Thyroidectomy is recommended within the first year of life, preferably as soon as possible, due to the very early transformation of C cell hyperplasia to more aggressive tumours. Calcitonin levels may be less helpful. In patients with codon 634 mutations (risk level C), thyroidectomy between ages 2 and 4 years has been proposed based upon evidence of age-dependent and codon-specific progression of early medullary thyroid cancer. In "risk level B" (codons 609, 611, 618, 620, 630 and 804), tandem mutation (804-778) patients should undergo thyroidectomy before the age of 6 years. "Risk level A" includes patients with mutations in codons 321, 515, 533, 600, 603, 606, 635, 649, 666, 768, 776, 790, 791, 804 (single mutation), 833, 844, 861, 891 or 912. Surgery may be postponed until the age of 10 years. However, postponing surgery and avoiding central (level VI) neck dissection in patients with risk levels A to C are only justified in families with a less aggressive MTC history and in combination with the results of basal (and calcium- or pentagastrin-stimulated) serum calcitonin levels. The moment of transition from C cell hyperplasia to MTC seems to occur when calcitonin levels rise. In patients with normal basal and stimulated calcitonin levels, the chance of micro-MTC increases significantly.

CONCLUSIONS:

Hereditary C cell disease acts as a model to apply the results of bedside genetic testing, age and calcitonin levels (genotype-age-calcitonin-concept) for the individual timing of thyroid surgery and its extent.

10. Clin Endocrinol (Oxf). 2014 Jul;81 Suppl 1:1-122. doi: 10.1111/cen.12515.

    Guidelines for the management of thyroid cancer.

    Perros P[1], Boelaert K, Colley S, Evans C, Evans RM, Gerrard Ba G, Gilbert J, Harrison B, Johnson SJ, Giles TE, Moss L, Lewington V, Newbold K, Taylor J, Thakker RV, Watkinson J, Williams GR; British Thyroid Association.

11. Eur J Surg Oncol. 2017 May 3. pii: S0748-7983(17)30444-4. doi: 10.1016/j.ejso.2017.04.002. [Epub ahead of print]

    Selective use of radioactive iodine (RAI) in thyroid cancer: No longer "one size fits all".

Marti JL1, Morris LGT2, Ho AS3.

Abstract

A remarkable, evidence-based trend toward de-escalation has reformed the practice of radioactive iodine (RAI) administration for thyroid cancer patients. Updated guidelines have supported both decreased RAI doses for select populations, as well as expanded definitions of low-risk and intermediate-risk patients that may not require RAI. Correspondingly, there is now increased flexibility for hemithyroidectomy without need for RAI, and relaxed TSH suppression targets for low-risk thyroidectomy patients. Clinical judgment remains indispensable where multiple risk factors co-exist that individually are not indications for RAI. This is especially salient in intermediate-risk patients with a less than excellent response to therapy, determined through thyroglobulin and ultrasound surveillance. Such judgment, however, may lead to patterns of inappropriate RAI practices or overuse with little benefit to the patient and unnecessary harm. A multidisciplinary, risk-adapted approach is ever more important and obliges the surgeon to understand the likelihood that their patients will receive RAI. The risks and benefits of RAI, its evolved role in contemporary guidelines, and current patterns of use among endocrinologists are reviewed, as well as the practical implications for thyroid surgeons.

12. Updates Surg. 2017 Jun;69(2):145-150. doi: 10.1007/s13304-017-0449-5. Epub 2017 Apr 12.

Surgical management of papillary thyroid carcinoma: an overview.

Miccoli P[1], Bakkar S[2,3].

Abstract

The surgical management of papillary thyroid carcinoma remains contentious and the optimal surgical strategy has not been yet established. The extent of thyroid resection has been the nub of this debate. Literature lacks prospective randomized controlled trials that could help put this debate to rest, and these have been labeled as being impractical. Consequently, large retrospective studies and expert opinion have constituted the basis of clinical practice guidelines. Recent American Thyroid Association and National Comprehensive Cancer Network guidelines consider a conservative approach in the form of a thyroid lobectomy sufficient for low-risk disease and that total thyroidectomy remains the standard of care in the presence of high-risk features. Nevertheless, many authorities still advocate more aggressive therapy for low-risk disease. The challenge in standardizing the surgical strategy to papillary thyroid carcinoma is mainly related to a major tumor characteristic: the high frequency of occult cancerous foci whether within the thyroid gland itself or within loco-regional lymph nodes as this tumor characteristic has been incriminated for a higher risk of recurrent disease and its adverse sequelae. The purpose of this article is to provide an overview of the surgical management of papillary thyroid carcinoma

and the main arguments surrounding this hotly debated topic. All evidences for this review article were drawn from PubMed articles in English language mostly cross-referenced with international guideline statements.

13. Surg Oncol Clin N Am. 2016 Jan;25(1):41-59. doi: 10.1016/j.soc.2015.08.002.

Current Guidelines for Postoperative Treatment and Follow-Up of Well-Differentiated Thyroid Cancer.

Yoo JY[1], Stang MT[2].

Abstract

Well-differentiated thyroid cancer is increasing in incidence but the disease-specific mortality remains very low. The only effective adjuvant treatment is radioactive iodine ablation. Guidelines regarding the use and dosage of radioactive iodine depend on pathologic features of the primary and metastatic tumor that define risk. Long-term treatment includes thyroid-stimulating hormone suppression and surveillance with serum thyroglobulin and radiologic assessment for nodal recurrence.