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Overview

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

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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. Crown Copyright © 2017 Published by Elsevier Ltd on behalf of The Royal College of Radiologists. All rights reserved.

Key words: Lymphatic metastasis; surgery; thyroid gland; thyroid neoplasms

Statement of Search Strategies Used and Sources of Information

All evidence for this review article was drawn from PUBMED articles cross-referenced with international guideline statements.

Introduction

Thyroid cancer often metastasises to the central and lateral compartments of the neck. Papillary thyroid cancer (PTC) metastasises early, and in some series rates are as high as 80% after prophylactic neck surgery [1,2]. Features of the primary tumours associated with increased rates of nodal metastases include young patient age, increasing tumour size, histological type and specific genotypes (e.g. BRAF

(Table 1). Advancements in the resolution of imaging modalities and improvements in biochemical testing (e.g. calcitonin) have led to an increased rate of detection of previously occult nodal metastases. Appropriate recognition of the preoperative disease burden is critical to decision making and appropriate surgical planning.

Surgical excision of gross, clinically evident nodal disease in well-differentiated thyroid cancer (WDTC) is widely accepted to be associated with improved outcomes both in terms of recurrence and survival. The role of surgery in occult metastatic nodal disease is, however, controversial as there is no clear benefit in patients who undergo prophylactic neck dissection compared with patients who are managed conservatively with observation of their neck. Medullary thyroid carcinoma (MTC) is a more aggressive disease and therefore prophylactic surgical management of the neck is recommended. However, once lateral neck node metastases are detected, irrespective of the extent of node dissection carried out, biochemical cure is rarely achieved.

Here we review the lymphatic drainage of the thyroid gland and the frequency and clinical impact of regional metastases. We consider both prophylactic and therapeutic indications for neck surgery in DTC and MTC.

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Table 1
Factors associated with nodal spread in well-differentiated thyroid carcinoma

Tumour/patient factors	Impact on nodal metastases
Patient age	More common in younger patients
Primary tumour size	More common in larger tumours
Histology	More common in papillary > medullary > follicular carcinoma
Genotype	More common in papillary thyroid cancer with BRAF mutations

Discussion

Lymphatic Drainage of the Thyroid Gland

The first echelon lymph nodes of the thyroid gland are in the central compartment (level VI) of the neck with subsequent drainage to the lower jugular chain (level IV) and the upper mediastinum (level VII). The most commonly involved central compartment lymph nodes are the pre-aryngeal (Delphian), pretracheal and the right and left paratracheal nodes. The only exception to this rule is the upper pole lesion, which can metastasise to the lateral neck in some cases without evidence of central neck disease [3]. Rates of metastasis to the regional nodes are related to the histological type of tumour, with papillary and medullary carcinoma being associated with high rates of metastasis in contrast to follicular and Hurthle cell carcinoma, which infrequently spread to lymph nodes.

Incidence and Clinical Significance of Lymph Node Metastases: Differentiated Thyroid Carcinoma

The clinical impact of lymph node metastases on overall survival of patients with WDTC is small [4]. Early cohorts, such as those reported by the Lahey clinic in the 1970s, suggested that nodal metastases might even exert a positive prognostic effect [5]. However, a matched-pair analysis from Memorial Sloan-Kettering Cancer Center subsequently showed that nodal involvement in patients older than 45 years of age was associated with a poor outcome [6]. It remains clear, however, that the impact of nodal metastases on outcome for younger patients is less significant. A recent analysis of the National Cancer Data Base and the Surveillance, Epidemiology and End Results (SEER) database showed that patients younger than 45 years with lymph node metastases have a significantly increased risk of death compared with younger patients without involved lymph nodes, and that having incrementally more metastatic lymph nodes (up to six involved nodes) confers additional mortality. However, it took a cohort size of almost 50 000 patients to show this clinical effect [7]. The number of involved metastatic lymph nodes has recently been suggested as a more accurate prognostic factor than nodal traditional TNM staging alone [8]. The size of lymph nodes, particularly larger than 3 cm, has also been shown to negatively affect outcomes [9–12].

In a large series of patients with PTC, Yamashita *et al.* [13] showed that extranodal extension is associated with a higher recurrence rate and a poor overall prognosis. In 2012, the American Thyroid Association (ATA)'s Surgical Affairs Committee's Taskforce on Thyroid Cancer Nodal Surgery reported that the presence of extranodal extension was associated with a 24% median risk of recurrence [14]. Extranodal extension as a prognosticating factor has been recently examined in a review by Urken *et al.* [15]. In this paper, the authors were critical of using clinical evidence of metastatic nodes as a prognosticating factor as accuracy of preoperative ultrasound, clinical examination and perioperative assessment all lack sufficient diagnostic accuracy. They also criticised the number of involved lymph nodes as a prognosticating factor due to a potential lack of completeness in comprehensive compartmental dissection, inexperience of pathology residents processing specimens and errors in identifying micrometastatic foci during sectioning before staining. Urken *et al.* [15] supported the finding that extranodal extension confers a negative prognosis and should be incorporated into staging and risk stratification systems. The size of lymph nodes (in contrast to the size of the metastasis confined within) should not confer prognosticating value as a small focus of thyroid cancer does not need to fill the entire node before it breaks out into the surrounding soft tissues. However, the authors highlighted the wide variation in pathological criteria currently used to report extranodal extension, calling for a more standardised approach.

Although it is now well accepted that macroscopic nodal metastases affects prognosis, the effect of occult regional disease is far more limited. Such low volume disease has no impact on survival and, at most, a limited impact on rates of recurrence [14,16]. It is critical when appraising the literature that the reader confirms the surgical approach of the clinical team reporting their results. Those groups who favour prophylactic neck dissection report high rates of nodal disease (cN0pN1) with generally favourable outcomes in contrast to those groups who practice only therapeutic neck dissection. Such groups have lower rates of nodal disease (cN1pN1) and those patients with metastases tend to have poorer outcomes.

In relation to the neck, the current staging model relies solely on the presence or absence of metastatic disease in the central (N1a) or lateral (N1b) compartment. This system will probably be superseded by a system that takes into consideration not only the presence of disease but the size, position, number of nodes and presence of extracapsular extension.

Incidence and Clinical Significance of Lymph Node Metastases: Medullary Thyroid Carcinoma

Patients with MTC have relatively high rates of nodal metastases and once disease has escaped the thyroid gland, 'cure' rates drop considerably. This is particularly true if disease is present in the lateral compartment. In fact if there is contralateral lateral neck disease, patients are considered incurable irrespective of treatment approach. Therefore, a

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