

HEAD AND NECK

Central neck dissection in differentiated thyroid cancer: technical notes

Dissezione centrale del collo nei carcinomi differenziati della tiroide: note tecniche

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SUMMARY

Differentiated thyroid cancers may be associated with regional lymph node metastases in 20-50% of cases. The central compartment (VI-upper VII levels) is considered to be the first echelon of nodal metastases in all differentiated thyroid carcinomas. The indication for central neck dissection is still debated especially in patients with cN0 disease. For some authors, central neck dissection is recommended for lymph nodes that are suspect preoperatively (either clinically or with ultrasound) and/or for lymph node metastases detected intra-operatively with a positive frozen section. In need of a better definition, we divided the dissection in four different areas to map localization of metastases. In this study, we present the rationale for central neck dissection in the management of differentiated thyroid carcinoma, providing some anatomical reflections on surgical technique, oncological considerations and analysis of complications. Central neck dissection may be limited to the compartments that describe a predictable territory of regional recurrences in order to reduce associated morbidities.

KEY WORDS: Thyroid cancer • Central neck dissection

RIASSUNTO

I tumori differenziati della tiroide possono essere associati a metastasi linfonodali regionali nel 20-50% dei casi. Il compartimento centrale (VI livello – VII livello superiore) è considerato la prima sede di metastasi linfonodali in tutti i carcinomi tiroidei differenziati. L'indicazione per la dissezione del centrale (CND) è ancora in discussione soprattutto in pazienti cN0. Per alcuni autori, la dissezione centrale è raccomandata solo in pazienti sospetti preoperatoriamente (clinicamente o alla ecografia) e/o per metastasi linfonodali rilevate intra-operativamente. Per una migliore definizione abbiamo diviso la dissezione in quattro diverse aree per mappare la localizzazione delle metastasi. In questo studio presentiamo il razionale per la dissezione centrale del collo in pazienti affetti da carcinoma differenziato della tiroide, fornendo alcune considerazioni anatomiche sulla tecnica chirurgica, considerazione oncologiche e l'analisi delle complicanze. La dissezione centrale del collo potrebbe essere limitata ai compartimenti che descrivono un'area prevedibile di recidive locali, al fine di ridurre la morbilità.

PAROLE CHIAVE: Carcinoma della tiroide • Svuotamento centrale del collo

Acta Otorhinolaryngol Ital 2014;34:9-14

Introduction

Differentiated thyroid cancers generally have a very good prognosis, with a 10-year survival rate greater than 90%¹. However, lymph node metastases are frequent (20-50%)², and up to 15% of patients will develop a regional recurrence after total thyroidectomy³. The prognostic value of nodal metastases is controversial: some Authors consider their presence predictive of local disease recurrence⁴⁻¹¹, but overall disease-specific survival does not seem to be adversely affected. Loco-regional metastasis to the cervical lymph node network can take place in one or more of the levels originally described by Robbins¹². Cervical lymph node levels VI and the upper part of VII, most commonly known as the central compartment, are often

involved in thyroid malignancy. This anatomical district is considered to be the first echelon of nodal metastases in all thyroid carcinomas¹³.

The most important morbidities associated with central neck dissection (CND) consist of recurrent laryngeal nerve damage and hypocalcaemia related to parathyroid hypo-function or to accidental parathyroidectomy. The incidence of surgical complications is variable, surgeon- and centre-dependent, and correlates with pathological features of the tumour. It is important to keep in mind the data available in the most current scientific literature: transient hypocalcaemia has been reported with an incidence of up to 30%¹⁴, while recurrent laryngeal nerve injury has been observed with an incidence of in 1-3%^{15,16}.

Complications are an unpleasant, and sometimes unavoidable, which are a reality of intense surgical activity. Minimization of their incidence can only come from accurate knowledge of the relevant surgical anatomy, standardized and careful surgical techniques and clear therapeutic indications.

In the latest guidelines published by the European Thyroid Association (ETA)¹⁷, compartment-oriented microdissection (CND) of lymph nodes is recommended for lymph nodes that are suspect preoperatively and/or lymph node metastases detected intra-operatively with a positive pathologic examination¹⁸. The rationale for this recommendation is based on the evidence that radical primary surgery has a favorable impact on survival in high-risk patients, and on the recurrence rate in low-risk patients¹⁹⁻²¹. The American Thyroid Association (ATA) Surgery Working Group in collaboration with the AAES, AAO-HNS and the AHNS recently published a consensus statement on the Terminology and Classification of central neck dissection for thyroid cancer²². These guidelines were formulated in response to inconsistencies in the terminology pertaining to central neck dissection in the current scientific literature. While the terminology may now be standardized, controversy remains surrounding treatment indications for CND in papillary thyroid carcinoma. With a view to maximizing disease-free survival and minimizing morbidity, in this paper the Authors provide some technical considerations for CND, as this is often a site of persistent disease or subclinical node involvement.

Materials and methods

Anatomical considerations

The central compartment is composed of level VI and the upper part of level VII (Fig. 1). The VI level (or the anterior neck compartment) is defined as the anatomical area between the hyoid bone, supra-sternal notch and carotid arteries (bilaterally); it includes the peri-thyroidal paralaryngeal, paratracheal (in the tracheo-esophageal groove), pretracheal and prelaryngeal (or Delphian) nodes. The VII level contains the upper anterior mediastinal lymph nodes found above the innominate (brachiocephalic) artery²³.

The peri-glandular lymphatic network and tracheal plexus provide drainage of the thyroid gland to the pre-laryngeal, pre- and para-tracheal lymph nodes. Laterally, lymphatic vessels along the superior thyroid vessels drain to the deep cervical nodes, and additional drainage is provided by the brachiocephalic nodes in the superior mediastinum towards the tracheo-bronchial nodes and ultimately to the thoracic duct.

Most studies show that metastatic lymph nodes are situated in the lateral neck (II III IV levels), and central neck nodes (VI VII levels); I and V levels are of less frequent localization²⁴⁻²⁷. Lateral neck nodes are usually identified

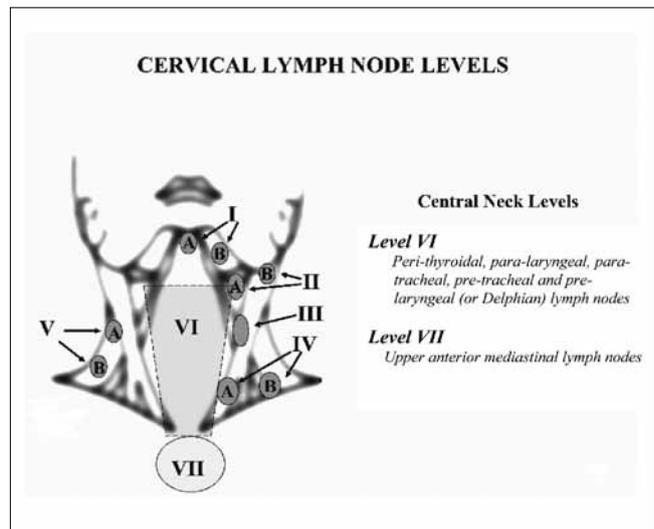


Fig. 1. Standard classification for neck node levels.

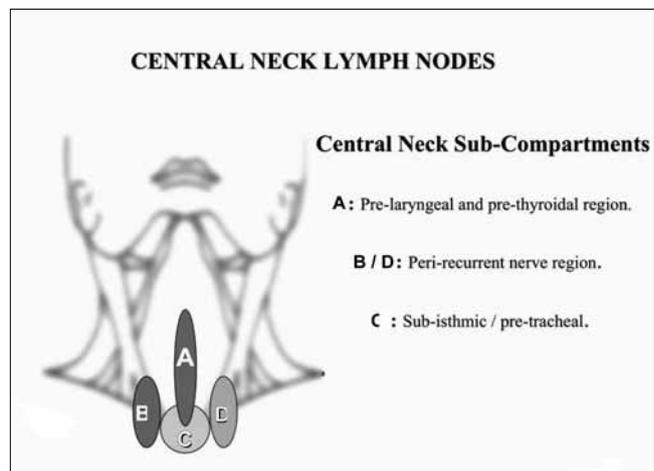


Fig. 2. Central neck sub-compartment. The author's classification.

both with clinical evaluation and/or ultrasound scan, while central neck nodes often bear subclinical metastasis. For this reason, adequate removal of central neck lymph nodes should include: 1) lymph nodes along the midline (linea alba) between the strap muscles; 2) lymph nodes present between the major neurovascular bundles of the neck. It is possible to delineate four areas (or sub-compartments) where the clinically most important lymph nodes are usually found, starting from the classification recently described by Orloff²⁸ (Figs. 2, 3). These sub-compartments may be described in detail as containing the following structures:

Area A: the delphian and pre-thyroidal lymph nodes included in the adipose tissue present in a medial sub-platysmal space that develops from the median fascial folds. This area corresponds to the region of the neck commonly defined as the muscular linea-alba and is superficial to the thyroid capsule and cartilage.

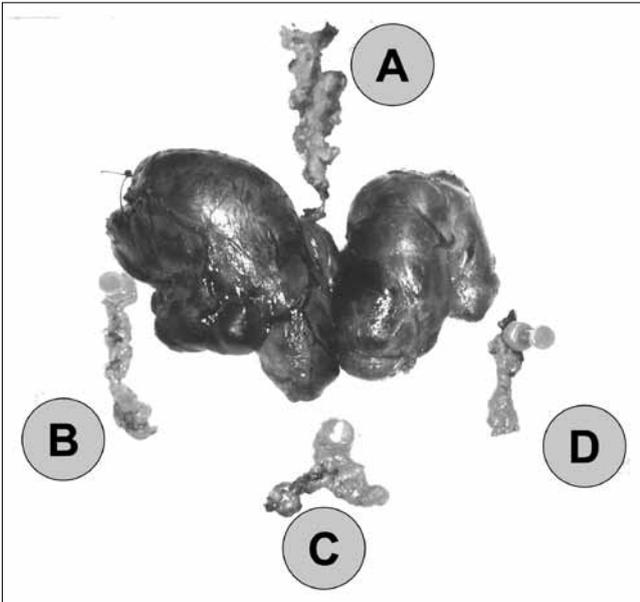


Fig. 3. View of surgical specimen: thyroid gland and central compartment nodes.

Areas B/D: deep lymph nodes contained in the adipose tissue on the right (B) and left side (D) respectively; they are bound laterally by the neuro-vascular bundle of the neck, medially by the trachea, posteriorly by the oesophagus, anteriorly by each lobe of the thyroid, cranially by the horizontal line delimited by the entrance point of the recurrent laryngeal nerves into the cryco-thyroid membrane and inferiorly by the brachiocephalic (innominate) trunk.

Area C: deep pre-tracheal nodes present in the adipose tissues bound superficially by the strap muscles, the pre-tracheal fascia at its deepest point, cranially by the thyroid isthmus and caudally by the brachiocephalic (innominate) trunk.

Oncological considerations

There is a general consensus with regards to the treatment of clinically-evident neck metastases in PTC patients². In contrast, the benefits of prophylactic, *en-bloc*, CND are still controversial²⁹⁻⁴⁰.

Factors supporting prophylactic CND are: 1) accurate staging of disease to plan the best treatment and follow-up; 2) changing radioiodine treatment indication or dosing; 3) decreased rates of local recurrence and the potential morbidity of reoperation^{5 8 9 26}; and 4) possible improvement in overall survival^{30 31}.

Factors against CND are: possible side-effects of dissection, primarily transient or permanent hypocalcaemia related to parathyroid gland damage and recurrent laryngeal nerve injury and overtreatment in N0 patients.

The literature offers no definitive evidence that CND improves both overall survival and disease-free survival. Indeed, most studies are limited to retrospective analysis of

case series. A common bias is the insufficient stratification of nodal involvement according to primary tumour size and overall stage. The indolent course of disease progression⁴¹ is an important obstacle to the evaluation of treatment efficacy and recurrence. Finally, most practitioners do not perform a true CND: sometimes lymphadenectomy is limited to the peri-glandular, pre-tracheal, pre-laryngeal and delphian nodes *without* dissection above the thyroid cartilage all the way to the hyoid bone²³. For all these reasons, the need and the extent of prophylactic CND according to the tumour size and localization are still a matter of debate.

Surgical technique

A recent report in the literature provides one of the first attempts to give a standard and rational description of the surgical technique for central neck (or central compartment) dissection⁴². Lymphadenectomy can be performed either unilaterally (A-B-C/A-D-C areas), or bilaterally (A-B-C-D), (Figs. 2, 3).

We perform a standard Kocher incision. The skin flaps are raised and the strap muscles are dissected and separated to maximize lateral retraction. Visualization of the median inter-muscular line allows identification of area A (the delphian and pre-laryngeal lymph nodes anterior to the cryco-thyroid membrane.) leaving the loose fibro-fatty glandulo-stromal tissue adhering to the thyroid capsule.

After isolation and dissection of the strap muscles on the right side and thus removing the A area, the homolateral hemi-thyroid is visualized, the middle thyroid vein is ligated and the carotid fascia is isolated. Progressing cranially, the superior pole vasculature is ligated preserving the superior parathyroid gland in situ along with its primary blood supply from the superior branch of the inferior thyroid artery. The inferior thyroid artery is identified and ligated terminally after it branches to the parathyroid gland. The inferior thyroid artery allows identification of the recurrent laryngeal nerve in its medial and lateral branches which are visualized and preserved (the nerve may follow a different path, above, below or in between the arterial branches). Superior retraction of the thyroid gland allows removal of compartment B from the medial aspect of the common carotid artery to its origin at the branching point of the innominate trunk. The dissection proceeds in its deepest portion from lateral to medial, detaching the glandulo-stromal tissue from the oesophageal musculature and the lateral aspect of the trachea, taking great care to preserve the branches of the sympathetic cervical plexus and the recurrent laryngeal nerve. The most caudal portion of the compartment (Area C) from the thymus gland and the innominate trunk is dissected after ligation of the inferior thyroid veins and eventually IMA by the innominate trunk, until the left tracheal margin is reached. The right hemi-thyroidectomy is completed *en-bloc* with lymph node compartments B and C after sec-

tioning Berry's ligament and releasing the isthmus from the pre-tracheal fascia.

The B area and the D area differ in some anatomical asymmetries and thus can lead to changes in the surgical approach, but procedures are the same: after left hemithyroidectomy, compartment D is dissected and removed with preservation of the left parathyroid glands, ligation of the inferior thyroid arteries, and identification and preservation of the left recurrent laryngeal nerve in the tracheo-oesophageal recess as described for the right side. It

Table I. Clinical, pathological and follow-up characteristics of patients who received total thyroidectomy and central neck dissection for differentiated thyroid cancer (n = 65).

Characteristics	Value (%)
Age (years)	
Median (range)	51 (26-82)
Sex	
Male	16 (24.6)
Female	49 (75.4)
Tyr	
4	19 (29.2)
5	46 (70.8)
Lateral Neck Dissection	
No	48 (73.9)
Monolateral	16 (24.6)
Bilateral	1 (1.5)
Histology	
Papillary	65 (100)
Multifocality/multicentricity	
Yes	28 (43.1)
Pathological tumour stage	
T1a	15 (23.1)
T1b	15 (23.1)
T2	3 (4.6)
T3	26 (40.0)
T4a	6 (9.2)
Pathological neck stage	
No	29 (44.6)
N1a	20 (30.8)
N1b	16 (24.6)
Post surgery complications	
Yes	37 (56.9)
Transient hypocalcaemia	26 (40.0)
Permanent hypocalcaemia	6 (9.2)
Transient recurrent nerve paresis	8 (12.3)
Permanent recurrent nerve paresis	0 (-)
Local infection	1 (1.5)
Other	2 (3.1)
Follow-up (months)	
Median (range)	16 (1-31)
Status at last clinical visit	
Alive with no evidence of disease	65 (100)
Type of relapsed	
Lateral neck	1 (1.5)

^{*}Dysphagia, lymphorrhoea.

is important to remember the virtual line extending from the brachio-cephalic trunk on the right side to the carotid artery on the left, which delineates the inferior boundary of the central compartment to be dissected and removed.

Results

Between April 2010 and December 2011, 65 patients, 16 (24.6%) males and 49 (75.4%) females with a median age 51 years old (26-82 years), underwent total thyroidectomy and CND with the new technique of 4 areas (A, B, C, D) for papillary thyroid cancer, according to the guidelines currently used at IEO, and were included in this preliminary study.

CND was performed simultaneously during total thyroidectomy. Written informed consent was obtained for surgical options from all patients. The clinical, pathological and follow-up characteristics of patients are shown in Table I.

A total of 601 lymph nodes from central compartment (A, B, C, D areas) were removed in the first 65 patients. Of these, 44 lymph nodes were from A area, 218 from B, 145 from C and 194 from D. The number of metastases were 11 in A, 42 in B, 42 in C and 34 in D. The mean of removed lymph nodes was 9 with a range between 1 and 22. Before using the new technique in IEO we previously had a mean of 4 lymph nodes from each patient.

In 64 (98.5%) patients, the analysis of nodal spreading showed an homolateral nodal diffusion (B if right, D if left) and/or central (A and C) lymph nodal diffusion when T disease arises within each lobe. Lesions from isthmus had wide diffusion, involving both sides and indifferently any areas. One (1.5%) patient had a contralateral nodal spread.

A more recent update of our data showed that from April 2010 to March 2012 167 patients underwent CND of the four areas. Of these, 122 (73%) were total thyroidectomy (TT), of which 101 (83%) were carcinomas. In 122 patients undergoing total thyroidectomy, only 2 patients (3.1%) had metastases in a contralateral side.

Discussion

CND is currently performed for patients with pathological nodes that are clinically apparent at diagnosis. It is clear from the available scientific literature and from the approach taken in multiple major clinical centres worldwide that CND and the central compartment of the neck are not one and the same. As recently pointed out^{23 43 44}, CND should be limited, in an effort to reduce the associated morbidity, to the compartments that describe a predictable territory of regional disease presentation. Our clinical experience is congruent with the consensus recommendation to remove all four areas of the central neck in patients with cN1 disease. The decision to perform a prophylactic CND in patients with cN0 disease should be

taken into account not only for T3 and T4 tumours, but also for all lesions above 1 cm in diameter, because complete pathological examination of central neck nodes can change both the tumour stage and therapeutic approach, especially for small tumours. In fact, pT1 tumours with central node metastasis (pT1pN1) are usually submitted to radioiodine treatment, while larger tumours such as pT2 without nodal involvement can avoid it^{43,44}.

For patients with DTC, neck ultrasound is the most important imaging technique for pre-operative assessment of non-palpable lymph node metastasis, but diagnostic accuracy in central neck disease is lower than that for lateral node disease, even in skilled hands²⁴. CND can overcome the shortcomings of diagnostic techniques. For early stage non-multifocal tumours (T1-T2), we advocate hemi-thyroidectomy plus selective lymphadenectomy of the ipsilateral compartments (A+B+C or A+D+C, Fig. 3), because we found contralateral nodal metastasis only in more advanced or multifocal diseases. In the first 20 months of our experience, the approach seems to be very promising to obtain up a lymphatic drainage map from each tumour localization, and to assess the genuine prognostic value of nodal metastases and micrometastases. These very preliminary data must be validated by further ongoing studies, and currently represent an active area of prospective clinical research in our Institute.

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Received: December 3, 2012 - Accepted: March, 18, 2013

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