metodi, tecniche, farmaci

Neck node dissection in thyroid cancer. A review

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SUMMARY: **Neck node dissection in thyroid cancer. A review.**

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Introduction: *thyroid cancer recurs most commonly in one or more cervical lymph nodes. Surgical treatment for differentiated or medullary thyroid carcinoma consists of total thyroidectomy (TT). The aim is to elucidate the potential benefits and drawbacks of neck dissection TT related.*

Materials and methods: *differences between therapeutic and prophylactic neck dissection were analysed to prevent post-operative morbidity, neck recurrences and improve survival.*

Discussion: *there is considerable controversy regarding the treatment of patients with cervical node metastases specially in differentiated thyroid cancer. Considering that a neck dissection might help to reduce local recurrence, especially in medullary carcinoma, controversial remains regarding the modality and extension of cervical dissection. There are several surgical strategies to cervical lymphadenectomy as a prophylactic node dissection or a dissection only in symptomatic patients or the "node-picking" technique for selective lymphadenectomy or sentinel node biopsy. So it is possible to employ several kind of neck-node compartment related dissection. The risk of iatrogenic lesion during neck dissection is relatively high specially for nerve structures (i.e.: recurrent laryngeal nerve or spinal accessory nerve), so an experienced surgeon must mind the risk is higher during a re-operation in an anatomical subverted region.*

Conclusions: *the extent of dissection and the experience of the surgeon both play important roles in determining the risk of surgical complications and recurrence. The decision to add neck dissection to total thyroidectomy weighed against documented benefits and risks. Injuries may also occur as a result of inadequate technique or as a result of poor expertise of the surgeon. We believe that deep knowledge of the thyroid region's surgical anatomy is necessary to realize a skilled and careful surgery of the neck.*

RIASSUNTO: **La dissezione laterocervicale nei carcinomi della tiroide. Revisione della letteratura.**

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Introduzione. *I carcinomi della tiroide metastatizzano frequentemente ai linfonodi cervicali e poichè il trattamento chirurgico standard prevede la tiroidectomia totale con linfoadenectomia secondo l'istotipo del tumore, scopo della nostra revisione della letteratura è valutare i potenziali rischi e benefici della linfoadenectomia associata alla tiroidectomia totale.*

Pazienti e metodi. *Sono state valutate le differenze tra la linfoadenectomia profilattica e terapeutica in termini di morbidità post-operatoria, recidiva e sopravvivenza.*

Discussione. *Ad oggi non c'è concordanza sul trattamento dei pazienti con metastasi ai linfonodi cervicali, specialmente in quelli con neoplasie tiroidee differenziate. Considerando che la dissezione linfonodale del collo può aiutare a ridurre la recidiva locale, specialmente davanti a carcinomi midollari della tiroide, controversie rimangono comunque sul tipo di linfoadenectomia da eseguire. Sono descritte linfoadenectomie profilattiche e dissezioni solo nei pazienti sintomatici, la tecnica "node-picking" e quella del linfonodo sentinella, che possono essere utilizzate in sinergia. Va ricordato però il rischio di danno iatrogenico alle strutture nervose (nervo laringeo inferiore e nervo accessorio spinale) specie nei reinterventi.*

Conclusioni. *L'estensione della linfoadenectomia laterocervicale e l'esperienza del chirurgo sono fondamentali nel determinismo del rischio chirurgico stesso e nella incidenza di recidive e la decisione di eseguire una linfoadenectomia deve considerare i potenziali vantaggi e svantaggi, poiché lesioni nervose sono spesso causate da tecnica inadeguata o da poca esperienza dell'équipe chirurgica. Siamo certi che una profonda conoscenza anatomo-chirurgica delle regioni del collo sia fondamentale per potere eseguire in sicurezza la dissezione dei linfonodi del collo, indipendendentemente dall'istotipo della neoplasia.*

KEY WORDS: Thyroid cancer - Neck node metastasis - Node dissection - Neck dissection.
Carcinoma tiroideo - Metastasi linfonodali laterocervicali - Dissezione del collo - Dissezione linfonodale.

Introduction

Regional lymph node metastases are present at the time of diagnosis in 20-90% of patients with papillary thyroid carcinoma (PTC) and a lesser proportion of patients with other histotypes. In many cases, these lymph

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nodes do not appear abnormal to inspection (1-7). The role of neck dissection in differentiated thyroid cancer remains controversial (3). Surgical treatment for differentiated (papillary and follicular) or medullary thyroid carcinoma consists of TT (2). An additional central or lateral modified-radical neck dissection might help to reduce local recurrence, especially in medullary thyroid carcinoma (MTC), but still does not influence significantly the survival rates (4). The prophylactic lymph node dissection is not indicated for patients with PTC or follicular thyroid cancer (FTC) because the nodal metastases can be removed when they become symptomatic, and the overall survival is comparable to that of patients treated therapeutically. It was also reported that nodal metastases is a significant risk factor for a poor outcome in particularly patients and that prophylactic neck dissection improves the prognosis (1). Today there isn't any controversy regarding the treatment of choice for patients with cervical metastases from differentiated thyroid cancer: disease in the central compartment requires a TT and central compartment neck dissection. Suspected or proven lateral compartment metastases should be treated by selective neck dissection (1). The role of "node-picking" is still controversy. In our opinion there is no role for node-picking. Other Authors think that the node-picking is equally effective as more radical surgical procedures (8). Sentinel node biopsy plays no role and neither does elective lateral compartment surgery in patients with no clinical or radiological evidence of disease (5). However, the surgeon must considerate the re-operation risks of nerve injuries during neck dissection.

Lymph nodes in the neck and neck dissection classification

To describe the lymph nodes of the neck is necessary to subdivide anatomically the neck into 6 areas called levels. A further level VII to denote lymph node group in the superior mediastinum is no longer used (9) (Fig. 1).
• Level I: includes the submental and submandibular lymph nodes. The submental triangle (sublevel IA) is bounded by the anterior belly of the digastric muscles (laterally) and the hyoid (inferiorly). The submandibular triangle (sublevel IB) is bounded by the body of the mandible (superiorly), the stylohyoid muscle (posteriorly) and the anterior belly of the digastric (anteriorly).
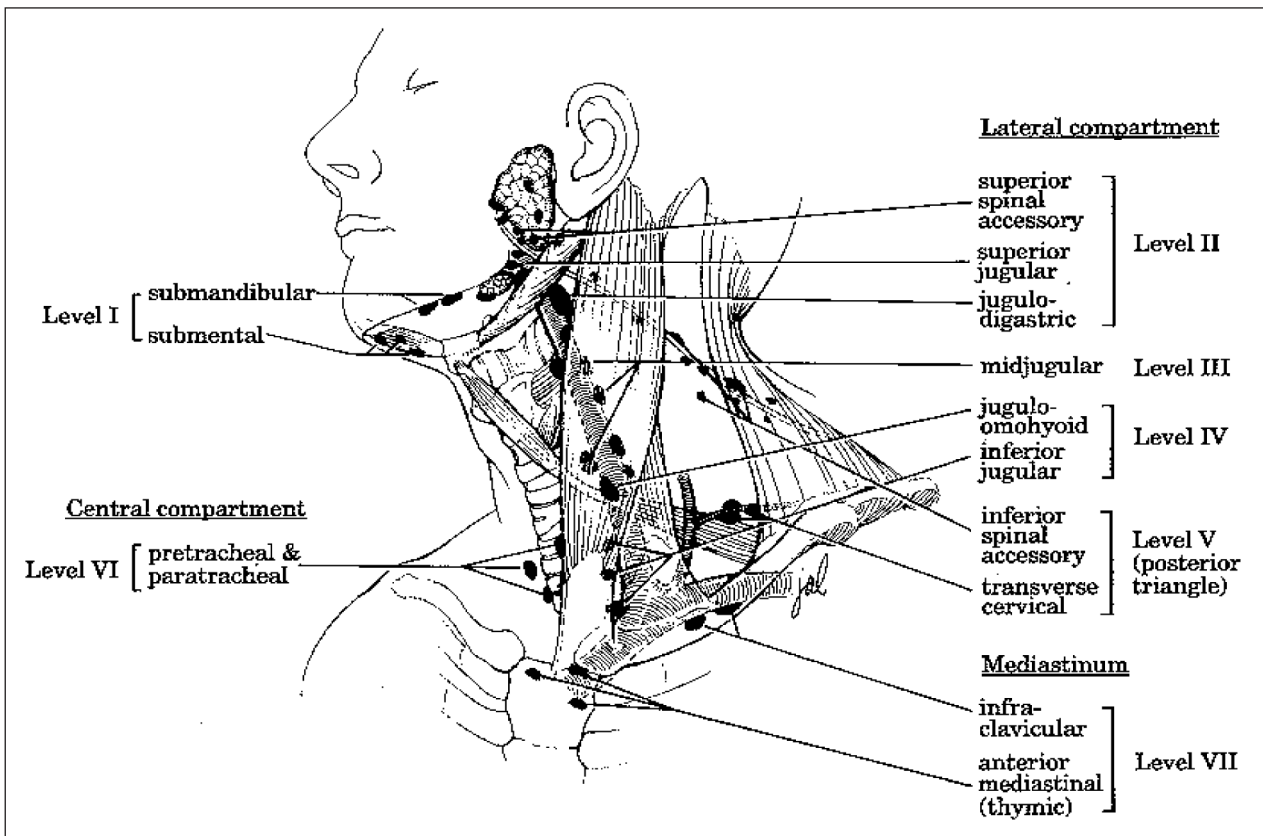

Fig. 1 - Musholt TJ, Moley JF. Management of recurrent medullary thyroid carcinoma after total thyroidectomy. Prob Gen Surg 1997; 14: 89-110.

• Level II: includes lymph nodes of the upper jugular group and is divided into sublevels IIA and IIB. Level II is bounded by the inferior border of the hyoid (inferiorly), the base of skull (superiorly), the stylohyoid muscle (anteriorly) and the posterior border of the sternocleidomastoid muscle (SCM) (posteriorly). Sublevel IIA nodes lie anterior to the Spinal Accessory Nerve (SAN). Sublevel IIB nodes lie posterior to the SAN.

• Level III: includes lymph nodes of the middle jugular group. This level is bounded by the inferior border of the hyoid (superiorly) and the inferior border of the cricoid (inferiorly), the posterior border of the sternohyoid muscle (anteriorly) and the posterior border of the SCM (posteriorly).

• Level IV: includes lymph nodes of the lower jugular group. This level is bounded by the inferior border of the cricoid (superiorly), the clavicle/sternal notch (inferiorly), the posterior border of the sternohyoid muscle (anteriorly) and the posterior border of the SCM (posteriorly).

• Level V: includes posterior compartment lymph nodes. This compartment is bounded by the clavicle (inferiorly), the anterior border of the trapezius (posteriorly), the posterior border of the SCM (anteriorly). It is divided into sublevels VA (lying above a transverse plane marking the inferior border of the anterior cricoid arch) and VB (below the aforementioned plane).

• Level VI: includes the anterior compartment lymph nodes. This compartment is bounded by the common carotid arteries (laterally), the hyoid (superiorly), the suprasternal notch (inferiorly).

• Level VII: includes lymph node of the anterior-superior mediastinum (infraclavicular and anterior mediastinal or thymic).

All these node stations are grouped in four compartments (10) and in agreement with the American Head and Neck Society (AHNS) and the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) the neck dissection is classified as follows (11) (Fig. 2):

Central Neck Dissection (CND) refers to removal only of the node group of level VI.

Radical Neck Dissection (RND) refers to removal of all ipsilateral cervical lymph node groups from levels I through V, together with SAN, sternocleidomastoid muscle (SCM) and internal jugular vein (IJV).

Modified Radical Neck Dissection (MRND) refers to removal of all lymph node groups routinely removed in a RND, but with preservation of one or more non-lymphatic structures (SAN, SCM and IJV) (Fig. 3).

Selective Neck Dissection (SND) (together with the use of parentheses to denote the levels or sublevels removed) refers to cervical lymphadenectomy with preservation of one or more lymph node groups that are routinely removed in a RND. Thus for oral cavity cancers, SND (I-III) is commonly performed. For oropharyngeal, hypopharyngeal and laryngeal cancers, SND (II-IV) is the procedure of choice.

Extended Neck Dissection refers to removal of one or more additional lymph node groups or non-lympha-
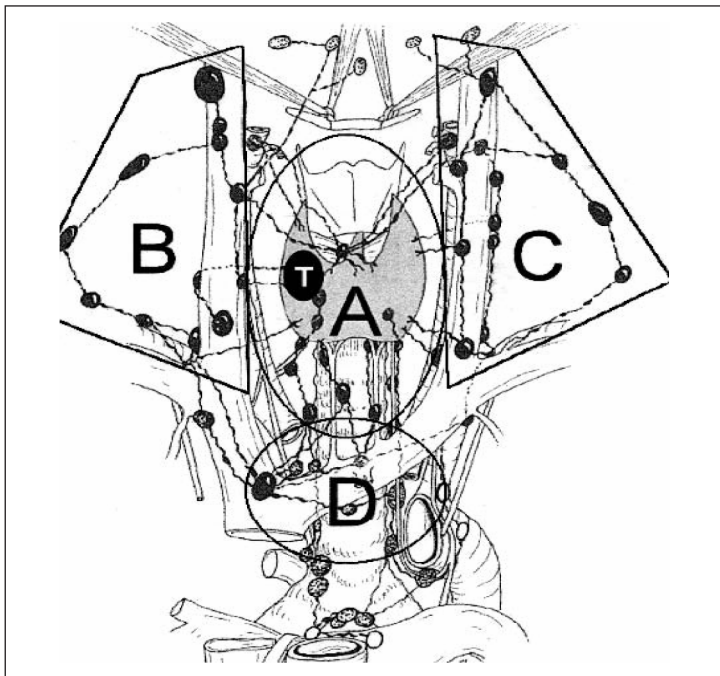

Fig. 2 - A (central compartment): flanked by the carotid sheaths, from the hyoid bone and superior thyroid vessels of each side down to the brachiocephalic vein. Including the pretracheal, paratracheal, and recurrent laryngeal lymphatic chain (level VI).
B (ipsilateral compartment) and C (contralateral compartment): comprise the triangular region flanked by the internal jugular vein in the midline (from the subclavian vein to the mastoid process), the trapezoid muscle and spinal accessory nerve lateral-posteriorly and the subclavian vein inferiorly, and include the lymph nodes of the jugular vein, those between the branches of the cervical plexus and those of the supraclavicular groove (levels II, III, IV, and V).
D (mediastinal compartment): represents the bilateral one of the trachea from the brachiocephalic vein down to the tracheal bifurcation and includes the anterior and posterior lymphatic chains (level VII).
T: tumor.
From: Goropoulos A, Karamoshos K, Christodoulou A, Ntitsias T, Paulou K, Samaras S, Xirou P, Efstratiou I. World J. Surg. 28, 1275–1281, 2004.
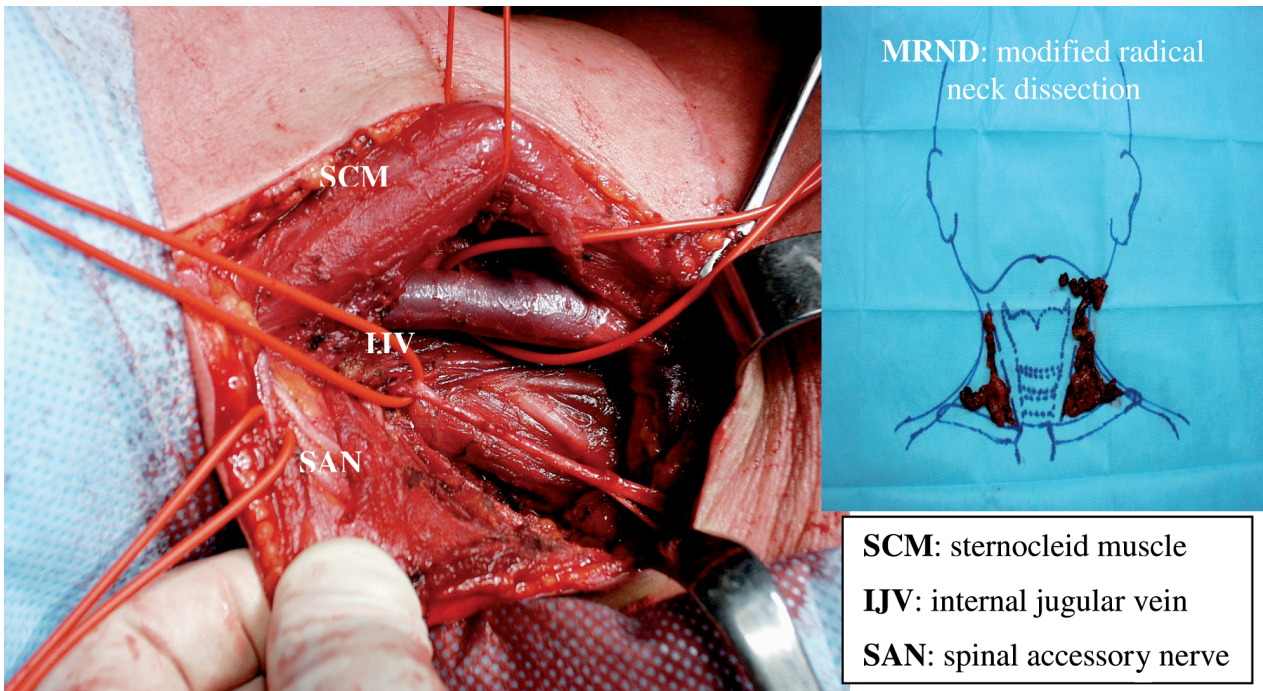
MRND: modified radical neck dissection

SCM: sternocleid muscle

IJV: internal jugular vein

SAN: spinal accessory nerve

Fig. 3 - Modified radical neck dissection.

tic structures, or both, not encompassed by the RND.

Discussion

Papillary and follicular thyroid carcinomas are the most common form of endocrine carcinomas. Lymph node involvement seems to be a low risk factor for death, but it increases the risk for loco-regional recurrences and distant metastases. The central lymph node dissection (CND) is recommended for high-risk patients, as male, patients more than 45 or less than 21 years old, papillary carcinomas greater than 1 cm or follicular carcinoma more than 2 cm in diameter. Lateral lymph node dissection is performed when the nodes of the central compartment are involved, more than 3 cm in diameter, and bulked; prophylactic lymphadenectomy is useless.

When thyroid carcinoma is known postoperatively, re-operation depends on the cervical mass and of the results on the radioactive iodine treatment (12). In differentiated thyroid carcinoma extensive node dissection at presentation has been stated to offer no advantage versus selective lymphadenectomy, causing increased morbidity. However, experienced surgeons report a low incidence (less than 5%) of accessory spinal nerve and cervical plexus permanent sequelae after functional neck dissection. In our opinion, patients with cervical lymph node metastases require a complete loco-regional neck dissection. Systematic lymphadenectomy, performed by la-

TABLE 1 - RISK FACTORS FOR CONTRALATERAL NODE INVOLVMENT.

Male sex
Large primary tumor
Tumor extension over the isthmus
Extracapsular adhesion or invasion to surrounding tissues
Presence of gross nodal metastasis at initial surgery

teral neck plus upper anterior mediastinal dissection, can yield a high disease-free survival (6). The benefits of prophylactic central neck dissection (PCND) in patients with differentiated thyroid carcinoma (DTC) have not been clearly demonstrated so far and should be weighed against the potential risks of the procedure (i.e.: recurrent laryngeal nerve injuries and parathyroid ablation). After total thyroidectomy (TT) for DTC, PCND does not increase recurrent laryngeal nerve morbidity but it is responsible for a high rate of hypoparathyroidism, especially in the early postoperative course. Even taking into account the possible benefits, the results make it difficult to advocate PCND as a routine procedure in all patients presenting a DTC (13, 14). This approach could change in some conditions, specially for patients at high risk for contralateral nodal recurrence considering the nodal recurrence at the contralateral cervical side as a poor prognosis for patients with papillary thyroid cancer. The possibility to employ a bilateral modified radical neck dissection (MRND) during initial surgical management is thus considered to improve the prognosis of some pa-

pillary carcinoma patients at risk for recurrence in the contralateral cervical lymph nodes (15). The risk factors for contralateral nodal recurrence were male sex, large primary tumor, tumor extension over the isthmus, extracapsular adhesion or invasion to surrounding tissues, and the presence of gross nodal metastasis at initial surgery (16) (Tab. 1). Lateral neck compartmental lymph node dissection should be performed for patients with biopsy proven metastatic cervical lymphadenopathy detected clinically or by imaging, especially when they are likely to fail radioactive iodine treatment based on lymph node size, number, or other factors, such as aggressive histology of the primary tumor (7). Regarding the role of node-picking the functional compartmental en-bloc dissection is favoured over selective dissection (berry picking) with limited data suggesting improved mortality. Most surgeons endorse complete ipsilateral compartmental dissection of involved compartments with persistent/recurrent disease while sparing vital structures as opposed to berry picking or selective lymph node resection procedures, because microscopic lymph node metastases are commonly more extensive than would appear from imaging studies alone (7). Today the role of the sentinel lymph node has to be avoided considering the possibility of skip metastases in thyroid cancer (17). It is not clear that treatment of locoregional disease is beneficial in the setting of untreatable distant metastases, except for possible palliation of symptoms or prevention of airway or aero-digestive obstruction. Impalpable metastatic lymph nodes, visualized on ultrasound or other anatomic imaging modality, have survived initial 131I therapy and should be considered for resection (7).

Papillary thyroid carcinoma

Papillary thyroid carcinoma (PTC) is well known as a lymphotropic type of cancer. In more than 50 percent of all cases it metastasizes first and mainly in regional lymph nodes. In PTC lymphnode metastases at presentation do not seem to adversely affect survival, but do increase the risk of loco-regional tumor recurrence. The value of systematic versus selective lymphadenectomy is far less standardized, whereas the role of postoperative radioiodine in preventing either nodal recurrence or cancer death remains controversial. Total thyroidectomy (TT) is the treatment of choice in the management of PTC, while the efficacy and safety of neck dissection (e.g.: modified radical neck dissection, MRND) are still debate (6, 18). The benefits of prophylactic central neck dissection (PCND) in patients with PTC have not been clearly demonstrated so far and should be weighed against the potential risks of the procedure as laryngeal nerve palsy and permanent ipoparathyroidsm (5% and 4% respectively) (13, 19). After TT with MRND of the affected side, nodal recurrence at the contralateral cervical side indicates a poor prognosis for patients with PTC,

thus some surgeons made bilateral MRND to improve the prognosis in patients at risk for contralateral nodal recurrence (15) (Tab. 1). In PTC extensive lymphnode dissection at presentation has been stated to offer no advantage versus selective lymphadenectomy, causing increased morbidity. However, experienced surgeons report a low incidence (less than 5%) of nerve injuries after functional neck dissection. Patients with cervical lymph node metastases require a complete loco-regional neck dissection (6). The literature data revealed better survival rates and quality of life in patients who had undergone TT with MRND in comparison with those ones who had undergone TT with berry picking (BP). MRND is an effective and comparatively safe procedure for the treatment of patients with PTC and regional lymph nodes metastases. If adequately performed it ensures better quality of life, longer survival and improves further control on distant metastases (16). After TT for PTC, PCND does not increase recurrent laryngeal nerve morbidity but it is responsible for a high rate of hypoparathyroidism, especially in the early postoperative course. Even taking into account the possible benefits, the results make it difficult to advocate PCND as a routine procedure in all patients presenting a PTC. Bilateral MRND should be considered for patients with papillary carcinoma who show risk factors for contralateral nodal recurrence, as it could prevent a second operation and may improve their outcome.

Follicular thyroid carcinoma

Follicular thyroid carcinoma (FTC) is the next most common type of thyroid cancer. FTC is much less common than papillary thyroid cancer, making up about 5% to 10% of thyroid cancers. It is more common in countries where people don't get enough iodine in their diet. These cancers usually remain in the thyroid gland but can spread to other parts of the body, such as lungs and bone. Lymph node involvement is far less common than in papillary carcinoma (8-13%). The prognosis of follicular carcinoma is probably the same or slightly worse than that of papillary carcinoma, and is related to degree of vascular invasion and to the age (> 40) (20). The diagnosis of FTC cannot always be made at the time of initial surgery: usually are solid tumors within the thyroid and only 10% are multifocal or involve regional lymph nodes (21, 22). The optimal treatment of lymph node metastases has not yet been defined. Two trends are evident concerning lymphadenectomy: the first one suggests routine lymphadenectomy, the second supports lymphadenectomy by necessity. The lymphadenectomy is recommended only in the presence of clinical evidence of lymph node involvement (23).

Medullary thyroid carcinoma

Medullary thyroid carcinoma (MTC) is a tumor de-

TABLE 2 - LIMPH NODE METASTASIS IN MTC.

	Central compartment	Ipsilateral compartment	Contralateral compartment
Sporadic MTC	50%	57%	28%
Hereditary MTC	45%	36%	19%
(Reff. 19, 24)			

rived from the parafollicular C cells; it represents 3% to 10 % of thyroid gland malignancies, but it is responsible for up to 13.4% of deaths that are caused by thyroid cancer. MTC is usually considered an indolent disease, with prolonged survival, although it spreads early in its course to regional lymph nodes. Lymph node metastases were found in half of patients (Tab. 2). Contralateral lymph nodes were found in upper of 30% of metastatic patients with unilateral tumoral involvement of the thyroid gland. A strong association was observed between tumor size and lymph node involvement for both hereditary and sporadic MTC. MTC patients treated by TT and central and bilateral neck dissection, confirm that lymph node metastases are frequent, being found in 55% of MTC patients. Palpable MTC is reported to present with cervical lymph node metastases in 25-82% of cases (19, 24). Several studies have shown that survival in patients with MTC is dependent upon the adequacy of the initial surgical procedure. For several reasons TT and systematic CND is indicated for both the hereditary and sporadic forms (24). TT and CND is recommended for all MTC patients, but the indication for lateral neck dissection is still controversial. Some authors recommend inclusion of the lateral neck dissection only if central or lateral lymph node metastases are proved, or if the primary tumor is palpable. Others recommend systematic lateral modified neck lymph node dissection, based on

the notoriously high incidence of regional lymphatic involvement. Contralateral lymph node dissection may be omitted only in patients with an unilateral thyroid tumour and with no ipsilateral and central lymph node involvement (Tab. 3). If mediastinal lymph node metastases are proved, this compartment should be dissected systematically (19, 25, 26). Thus, there is considerable confusion regarding standard surgical treatment of MTC. Furthermore, the incidence of complications related to neck dissection, including hypoparathyroidism, recurrent laryngeal nerve palsy, injury of the trachea or oesophagus, has to be considered (27-30).

Conclusion

The extent of dissection and the experience of the surgeon both play important roles in determining the risk of surgical complications and recurrence. Completeness of surgical resection is an important determinant of outcome, while residual metastatic lymph nodes represent the most common site of disease recurrence. Several choices exist to prevent or to treat the neck node diffusion of thyroid tumor. Considering the differentiated thyroid cancers, the central compartment dissection can be achieved with low morbidity in experienced hands and should be considered for patients with papillary thyroid carcinoma. Total thyroidectomy without central node dissection may be appropriate for follicular cancer, and when followed by radioactive iodine therapy, may provide an alternative approach for papillary cancer. For those patients in whom nodal disease is evident clinically, on preoperative ultrasound or at the time of surgery, surgical resection may reduce the risk of recurrence and possibly mortality. Surgery is favoured for locoregional (i.e., cervical lymph nodes and/or soft tissue tumor in the neck) recurrences, when distant metastases are not present. Approximately one

TABLE 3 - LIMPH NODE METASTASIS IN MTC.

Neck dissection	Society Surgical Oncology*	National Comprehensive Cancer Network°	German guidelines^
Ipsilateral dissection	Sporadic MTC + palpable tumor Central compartment involvement	Sporadic MTC (diameter > 1 cm)	Sporadic MTC
Contralateral dissection	----	Bilateral disease	Sporadic MTC + Ipsilateral involvement
Central compartment	----	Sporadic MTC (diameter < 1 cm)	----
Bilateral routine dissection	----	----	Hereditary MTC
*(Reff.: * = 31, 32; ° = 33; ^ = 29, 34*			

third to one half of patients may become free of disease in short-term follow up. In consideration of the high incidence of lymph node metastases in the medullary thyroid cancer both in the central and lateral neck compartments, including in the contralateral neck compartment, we agree a standard approach to neck surgery is necessary, similar for sporadic and hereditary cancer patients. A central and bilateral neck dissection should be performed in all medullary thyroid cancer patients; however, contralateral node dissection may be avoided in patients with certain unilateral tumoral involvement of the thyroid gland without an ipsilateral and central neck compartments involvement. The decision to add neck dissection to total thyroidectomy weighed against documented benefits and risks. Injuries may also occur as a result of inadequate technique or as a result of poor expertise of the surgeon. We believe that deep knowledge of the thyroid region's surgical anatomy is necessary to realize a skilled and careful surgery of the neck.

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