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Differentiated thyroid cancer: role of the lymph node dissection

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SUMMARY: **Differentiated thyroid cancer: role of the lymph node dissection.**

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Thyroid cancer is the most common endocrine malignancy with the highest mortality, so it has generated considerable debate and voluminous literature by endocrinologists, surgeons, and nuclear physicians. If total thyroidectomy is the primary treatment for patients with differentiated thyroid cancers (DTC) and it has proven to be effective and safe, the extent of lymph nodes dissection remains controversial among experts in the field. This controversy persists largely due to the lack of a prospective randomized controlled trial to define whether the addition of central lymph node dissection (CLND) to total thyroidectomy for papillary thyroid cancer (PTC) confers an increased risk of permanent hypoparathyroidism and permanent nerve injury. According to the Consensus Conference of the UEC's Club therapeutic modified radical neck dissection (MRND) should be performed only in the patients with evidence of neoplastic multiple lymph node involvement. Although central lymph node dissection may increase the risk of hypoparathyroidism and nerve injury when compared with total thyroidectomy without CLND, it may decrease recurrence of PTC and likely improves disease specific survival and offers a sufficient alternative to routine prophylactic modified radical neck dissection. Selective central lymph node dissection should be performed, under the care of experienced surgeons, in high risk patients (50 years or older aged, large tumor expansion within the thyroid, or with extrathyroid extension), with the extension to the station II-III-IV in case of single lymph node involvement.

RIASSUNTO: **Carcinoma differenziato della tiroide: ruolo della linfoadenectomia.**

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Il cancro della tiroide è la più comune neplasia maligna endocrina con la più alta mortalità. La tiroidectomia totale è il trattamento primario per pazienti con cancro differenziato della tiroide (DTC) e si è dimostrata efficace e sicura. L'estensione della dissezione linfonodale rimane controversa tra esperti nel campo.Questa controversia persiste largamente anche per la mancanza di uno studio prospettico controllato randomizzato che riconosca come la dissezione linfonodale centrale (CLND) per cancro papillare della tiroide (PTC) conferisca alla tiroidectomia totale un aumentato rischio di ipoparatiroidismo e di lesione ricorrenziale permanente. Secondo la Consensus Conference del UEC's Club la dissezione radicale terapeutica modificata del collo (MRND) dovrebbe essere eseguita solo in pazienti con evidenza di coinvolgimento lonfonodale neoplastico multiplo. Sebbene la dissezione linfonodale centrale possa aumentare il rischio di ipoparatiroidismo e di lesione del ricorrente a confronto con la tiroidectomia totale senza CLND, essa può ridurre le metastasi da PTC e probabilmente migliorare la sopravvivenza specifica della malattia. Offre inoltre un'alternativa sufficiente alla dissezione radicale profilattica modificata del collo. La dissezione linfonodale centrale selettiva deve essere eseguita da mani esperte, in pazienti ad alto rischio (maggiori di 50 anni, larga diffusione del tumore intra o extratiroidea), con l'estensione alle stazioni II-III-IV in caso di coinvolgimento linfonodale singolo in esse.

KEY WORDS: Differentiated thyroid cancer - Lymph node dissection.
Cancro differenziato della tiroide - Dissezione linfonodale.

Introduction

Thyroid cancer, excluding ovarian cancer, is the most common endocrine malignancy with the highest mortality (1), so it has generated considerable debate and voluminous literature from endocrinologists, surgeons, and nuclear physicians. However, controversy continues regarding the optimal management of patients with differentiated thyroid cancer because no prospective ran-

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domized studies assess the merits of diagnostic evaluation, extent of surgery, postoperative adjuvant therapy and follow-up. If total thyroidectomy is the primary treatment for patients with differentiated thyroid cancers (DTC) and it has proven to be effective and safe, the extent of lymph nodes dissection remains controversial among experts in the field. This controversy persists largely due to the lack of a prospective randomized controlled trial to define whether the addition of central lymph node dissection (CLND) to total thyroidectomy for papillary thyroid cancer (PTC) confers an increased risk of permanent hypoparathyroidism and permanent nerve injury. Thyroid cancer is divided into differentiated and another group. The differentiated thyroid cancers derives from follicular epithelial cells and includes papillary, follicular, Hürthle cell and a mixed variety. The other group includes medullary carcinoma, lymphoma, anaplastic cancer and certain rare varieties such as sarcoma or metastatic tumours. Papillary and follicular carcinoma represent almost 90% of the thyroid malignancies, being responsible for 70% of the mortality generated by thyroid cancer (2). Papillary thyroid cancer is the most common endocrine malignancy (3); it is also one of the most curable human cancers, with a 5-year survival rate of 95%. While the follicular carcinoma has more of a propensity to metastasize hematogenously to the lungs and bones, papillary carcinoma usually shows mild characteristics, and it metastasizes and shows recurrence to the lymph node in high incidence. Cervical lymph node metastases are quite common in papillary thyroid cancer and are present in 20%–50% of patients (4).

Discussion

The surgical treatment of cervical lymph nodes in DTC remains controversial. It has been traditionally accepted that regional lymph node metastases in PTC may increase local recurrence rates but do not affect survival. This conventional wisdom has been challenged by recent reports indicating that regional lymph node metastases are the cause of increase mortality. Thus, there has been renewed interest in operative control of nodal disease for PTC (3). Although thyroid cancer is the only human cancer in which the presence of lymph node metastasis has no major implication on the overall prognosis (5), a worse prognosis was correlated with papillary carcinoma demonstrating two or more of the following four characteristics; male gender, age 55 years or older, maximal tumour diameter larger than 3 cm, and massive extrathyroid extension (6).

The management protocols in thyroid surgery have been reviewed and updated by Consensus Conference called on the topic by the Italian Association of Endocrine Surgery Units (UEC Club) which provides the rationale of the thyroid patient management (7). When neck dissection is recommended it can be performed as prophylactic or therapeutic lymph node dissection. The term "prophylactic" denotes removal of lymph nodes that are deemed normal pre-or intraoperatively by palpation or imaging studies (8). "Therapeutic" dissection denotes removal of lymph nodes that likely contain metastatic disease based on palpation, imaging studies or pathological data (9, 10).

According to the Academy's Committee for head and neck surgery and oncology, (11) the classification of neck dissection includes: radical neck dissection (RND) and extended radical neck dissection (ERND), modified radical neck dissection (MRND), selective neck dissection (SND). Radical neck dissection and extended radical neck dissection are the more extended dissection of the neck's lymphatic and nonlymphatic structures. Modified radical neck dissection preserves nonlymphatic structures of the neck. Selective neck dissection denotes removal of only one or more groups of lymph nodes. How widely accepted we consider the classification by the American Academy of Head and Neck Surgery in six levels and sublevels (12). Particularly, the level VI nodes lies in a central position in the neck. Nodes in level VI correspond to those in the central neck compartment and are, in a high percentage of cases, the elective localization of the metastases (8). Its superior border is the hyoid bone, the inferior border is the suprasternal notch, and the lateral borders are the common carotid arteries. Level VI lymph nodes include pretracheal and paratracheal nodes, the precricoid node, and the perithyroidal nodes, including nodes along the recurrent laryngeal nerves. One kind of selective neck dissection denotes removal of the VI level's nodes. Complications of total thyroidectomy include permanent hypoparathyroidism and permanent nerve injury. Exactly, total thyroidectomy without lymph node dissection, performed by experienced surgeons, results in permanent hypoparathyroidism in 1%–2% of patients and permanent nerve injury (recurrent laryngeal, external branch of the superior laryngeal) in 1%–2% of patients (13,14). Actually, there is no consensus about the risk of these complications after central lymph node dissection. Multiple case series attempted to address this topic (15-17), but the best available data are provided by two prospective and two retrospective cohort studies (18,19). No prospective, randomized studies exist to define whether the addition of CLND to total thyroidectomy for PTC confers an increased risk of permanent hypoparathyroidism and permanent nerve injury. However, Matthew L. et al. demonstrates, through a systematic review of the Literature using evidence based criteria, that there may be a higher rate of permanent hypoparathyroidism and unintentional permanent nerve injury when CLND is performed with total thyroidectomy than for total thyroidectomy alone (8).

Methods

In our experience we found that the optimal treatment of the differentiated thyroid cancer consists in the modulation of the extension of the lymph node dissection. This kind of treatment of a tumour "biologically indolent" makes possible eventually needing reoperations with a low morbidity if performed by experienced surgeons.

Then, we consider an important part of the therapeutical treatment the adjuvant radioactive iodine treatment. We finally think it is fundamental to obtain the optimal treatment to select patients with high risk of recurrent loco-regional tumour, expression of possible distant metastasis. We recommend prophylactic central neck node dissection only for high risk patients who present two or more of the following four characteristics: male gender, age 55 years or older, maximal tumour diameter more than 3 cm and massive extrathyroid extension. In case of multiple lymph node involvement we perform a functional MRND, recommending the selective central node dissection (station VI) and of the station II-III-IV (upper, medium and lower jugular) in case of single lymph node involvement.

Conclusion

According to the Consensus Conference of the UEC's Club (7, 20) therapeutic modified radical neck dissection (MRND) should be performed only in the patients with evidence of neoplastic multiple lymph node involvement. Although central lymph node dissection may increase the risk of hypoparathyroidism and nerve injury when compared with total thyroidectomy without CLND, it may decrease local recurrence of PTC and likely improves disease specific survival and offers a sufficient alternative to routine prophylactic modified radical neck dissection. Selective central lymph node dissection should be performed, under the care of experienced surgeons, in high risk patients (50 years or older aged, large tumor expansion within the thyroid, or with extrathyroid extension), with the extension to the station II-III-IV in case of single lymph node involvement.

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