

REVIEW

The Role of Lymphadenectomy in the Management of Papillary Carcinoma of the Thyroid

LORNE ROTSTEIN, MD, FRCSC, FACS*
University of Toronto, Toronto, Canada

Impact of nodal involvement in papillary thyroid cancer remains controversial. The incidence of nodal metastases is high and the presence of involved nodes has a negative impact on recurrence and possibly on survival as well, particularly in older patients. The risk of nodal disease increases with age, tumor size, and BRAF oncogene expression. Most thyroid surgeons sample the ipsilateral central nodes as a minimum and clear the central compartment if there is gross adenopathy present. Lateral compartment neck dissection is reserved for patients with known metastatic disease. This article attempts to review the literature on surgery of lymph nodes in papillary thyroid cancer.

J. Surg. Oncol. 2009;99:186–188. © 2009 Wiley-Liss, Inc.

KEY WORDS: papillary thyroid cancer; staging; lymph node metastases

INTRODUCTION

Papillary thyroid cancer (PTC) is by far the most common thyroid malignancy, with approximately 15,000 new cases diagnosed last year in the USA. PTC represents more than 90% of new thyroid malignancies overall [1]. Cervical nodal metastases are quite commonly seen in PTC, and when prophylactic neck dissections have been performed, micro metastases can be found in up to 90% of cases [2]. Nodal metastases are associated with an increase in recurrence rate and may impact negatively on survival as well [3]. Any discussion of lymph node metastases in PTC is confounded by the lack of any prospective clinical trials and by the usually indolent natural history of the disease.

PATTERNS OF SPREAD

The lymphatic drainage pattern of the thyroid is uniform and consistent, allowing patterns of metastatic spread to be relatively predictable.

Initial nodal spread from PTC almost always occurs in the central compartment of the ipsilateral neck in the paratracheal and pretracheal nodes in level VI. Cases of macroscopic skip metastases to the lateral compartment of the neck in the absence of central disease are exceedingly uncommon [4]. Machens et al. [5] have however demonstrated microscopic skipping of the central compartment in 19.7% of patients in their series with PTC. When there is gross tumor in the nodes of the lateral neck, levels II–V are predictably affected, usually with multiple areas of spread in more than one of these levels. Spread of PTC to nodes in the submental and submandibular nodes (level I) is so rare as to preclude routine dissection of this area [4].

PREDICTORS FOR NODAL METASTASES

Overall, the probability of nodal metastases in PTC has been reported in the range of 30–90% with an average of 60% [6].

Factors which may increase the probability of patients having lymph node metastases, include age, gender, size of the primary, and tumor oncogene expression. Pediatric PTC patients have an incidence of clinical lymph node metastases as high as 80% [7]. Similarly, in the

geriatric patient with PTC, nodal metastatic disease is more likely than in mid life. Histological features that seem to predict for lymph nodal spread are vascular invasion, and extracapsular involvement. Tumor size may not be an independent predictor of nodal spread as the data in the literature are contradictory, precluding any clear statement [7,8]. Several oncogenes are now being assessed histologically in PTC including p53 and BRAF. BRAF positivity predicts for poor prognosis as well as a higher probability of nodal spread [9].

DEFINITIONS

Prophylactic Versus Therapeutic Neck Dissection

“Prophylactic” denotes removal of lymph nodes that have been deemed to be normal on pre- and intraoperative assessment by palpation or imaging studies. Therapeutic implies removal of lymph nodes that are suspicious or proven to have metastatic disease based on pre- or intraoperative palpation, imaging, and/or cytological assessment.

Central Versus Lateral Compartment

There is a standardized classification system describing cervical nodal groups and neck dissections developed by the American Head and Neck Society and the American Academy of Otolaryngology in 1991 and modified by Robbins in 2002 [10].

“Central” dissection refers to removal of those nodes in the central neck bounded superiorly by the Hyoid Bone, inferiorly by the Innominate Vein, medially by the Trachea, and laterally by the Carotid

*Correspondence to: Dr. Lorne Rotstein, MD, FRCSC, FACS, Professor of Surgery, Toronto General Hospital, University Health Network, E N 10 220, 200 Elizabeth Street, Toronto, ON, Canada M2G 2C4. Fax: 416-340-3808. E-mail: lorne.rotstein@uhn.on.ca

Received 11 November 2008; Accepted 10 December 2008

DOI 10.1002/jso.21234

Published online 23 January 2009 in Wiley InterScience (www.interscience.wiley.com).

Artery. Nodal groups encompassed in this compartment include pretracheal, paratracheal, precricoid, and perithyroidal. Some authors suggest that the jugular chain nodes from levels IV and III can and should be excised as part of a central neck dissection but it seems that it is difficult, if not impossible to remove these in a comprehensive manner as part of a central dissection through a conventional thyroidectomy incision [11].

“Lateral” dissection is a poor term and it is more appropriate to describe the formal removal of nodes in the lateral neck for PTC as a selective functional neck dissection, which consists of removal of those nodes around the internal jugular vein from the level of the skull base superiorly to the subclavian vein inferiorly, as well as the nodes in the posterior triangle, posteriorly to the level of the anterior border of the Trapezius muscle, that is, the nodes in levels II, IIa, III, IV, V, sparing the internal jugular vein, accessory nerve, submandibular contents, greater auricular nerve, omohyoid, and sternomastoid muscles [10]. This procedure was originally described by Bocca in 1980 [12], and defined clearly by Robbins et al. in 2002. Structures at risk in a selective functional neck dissection include the accessory nerve and on the left side, the thoracic duct.

IMPACT OF METASTATIC DISEASE ON SURVIVAL

The prognostic implication of nodal involvement in PTC on survival is open to debate in that most early studies suggested that the presence of involved nodes did not have an adverse effect on either recurrence or ultimate survival [13,14]. More recent articles, however, show that lymph nodal metastases are indeed associated with an increase in recurrence rates and impact negatively on survival. Harwood et al. [15] looking at this question retrospectively, matching patients by age, have demonstrated that in individuals over the age of 45 years, nodal disease was associated with a decrease in survival and higher neck recurrence rates than for same T stage No patients. Mazzaferri et al. [3], in a study of 1,300 patients with differentiated thyroid carcinoma followed for 30 years, showed that those who had lymph nodal metastases had an increase in disease specific mortality (10% vs. 6%) with the majority of those patients having events at greater than 20 years from initial treatment; suggesting that the conflicting data from the earlier reports may be erroneous due to limitations in follow-up duration as well as small patient numbers. The majority opinion in 2008 is that nodal metastases do increase the risk of both recurrence and mortality particularly if the patient is older, or the nodes are fixed, bilateral, or demonstrate extra capsular extension. This is reflected in the current AJCC staging system whereby presence of nodal disease in patients over 45 years of age upstages [16].

PROPHYLACTIC NODE DISSECTION

There is no prospective randomized controlled trial data looking at the effect on outcome of prophylactic central neck node dissection in PTC. One Swedish prospective non-randomized study with comparison to a contemporaneous cohort suggests a decrease in disease specific mortality at 13 years from 8.4% to 1.6% [17]. Other data show similar but more modest benefits in survival [18]. On the opposite side of the equation, there are numerous reports that show that thyroidectomy with prophylactic central neck node dissection is associated with higher rates of permanent hypocalcemia (0% vs. 4%) and recurrent laryngeal nerve injury (0% vs. 1.5%) than thyroidectomy performed alone [18].

Despite the limited data on efficacy and the documented increased risk, prophylactic central neck node dissection is being performed routinely on a large proportion of patients with PTC with the rationale that the potential morbidity of a central node recurrence is reduced,

reoperation avoided, staging made more accurately, and conditions optimized for postoperative radioiodine administration. Many surgeons will opt to perform a prophylactic central neck node dissection based on tumor risk factors including age, primary size, evidence of extra glandular extension of disease. Similarly, in the finding of unsuspected significant adenopathy in the central neck at the time of thyroidectomy, most thyroid surgeons would opt to clear the nodes from the central compartment if this had not been part of their initial operative plan [18].

Prophylactic lateral neck dissection, on the other hand, is not generally felt to be indicated, as this procedure requires extension of the incision, is technically demanding [19], and has significant potential associated morbidities. There is data from Sweden and Japan demonstrating recurrence and survival benefits associated with elective functional neck dissection in PTC [17,18,20]. A number of other authors have shown that despite the high incidence of micrometastases found after prophylactic lateral neck dissection, the recurrence rate in this part of the neck in those individuals who have not undergone dissections is only in the range of 5–15%, therefore they feel that postponement of lateral neck dissection until metastases become clinically apparent does not negatively impact prognosis [18,21].

THERAPEUTIC LATERAL NECK NODE DISSECTION

In the past, many surgeons performed local node enucleations to remove grossly enlarged nodes. These so called “Berry Picking” operations have been demonstrated to be associated with unacceptably high local recurrence rates (100% vs. 9%), necessitating more radical reoperative procedures that have higher morbidity than if a selective functional neck dissection had been performed in the first place [22,23]. Similarly, limited modified neck dissections in which the dissection is confined to those areas below the level of the accessory nerve, has been shown to be associated with higher neck recurrence rates than for more comprehensive procedures [24]. If a therapeutic lateral selective neck dissection is performed for metastatic PTC, the nodes in the central compartment in level VI should be removed as well, if this had not been done at the time of initial surgery [18]. Although selective functional neck dissection is technically challenging, in experienced hands, it can be performed expeditiously and safely. Kupsterman et al. [25] have reported shoulder weakness in 27% and chyle leak in 4.5% of patients. Others report Phrenic paralysis, Horner’s syndrome, Cervical Plexus Neuropathic pain syndromes and other complications in up to 1% of cases [26]. Reported recurrence rates in the neck following selective functional neck dissection are in the range of 10% [22,27].

Radioiodine ablation and subsequent T4 suppression are known to be effective adjuvants to surgery in the patient with metastatic PTC after lymphadenectomy but are not a substitute. In a small study reported by Wilson et al. [28] of those patients with macroscopic nodal disease treated with I131 and no surgery, the recurrence rate was 47% with a 36% mortality rate.

DISCUSSION

Making recommendations for the management of the neck in PTC is difficult for several reasons. The overwhelming majority of reports are retrospective cohorts at best or case series. The disease is by and large slow growing and indolent so that detection of differences in outcome requires large numbers of cases followed for many years. The varying terminology used in the past to describe neck dissections makes comparison of outcomes confusing. It would seem that there is agreement in the role of therapeutic selective functional neck dissection in the management of known macroscopic nodal metastatic

disease and that prophylactic dissection in the lateral neck is not indicated. There is also general agreement that prophylactic removal of the nodes in the central compartment, at least on the ipsilateral side, is beneficial in the management of node negative PTC.

In summary, lymph node assessment in PTC has been increasingly recognized to be important in predicting prognosis as well as directing appropriate surgical therapy. Aggressive, comprehensive management of demonstrated metastatic adenopathy in the neck provides a therapeutic benefit in respect to local/regional recurrence and possible overall survival as well.

REFERENCES

- Estatia-Rutter CF, Corssmit EP, Nienke R, et al.: Survival and death causes in differentiated thyroid carcinoma. *J Clin Endocrinol Metab* 2006;91:313–319.
- Machens A, Hinze R, Thomusch O, et al.: Pattern of nodal metastasis for primary and preoperative thyroid cancer. *World J Surg* 2002;26: 22–28.
- Mazzaferrri EI, Thiang SM: Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 1994;97:418–428.
- Gimn O, Rath FW, Dralle H: Pattern of lymph node metastases in papillary thyroid carcinoma. *Br J Surg* 1998;85:252–254.
- Machens A, Holzhausen HJ, Drulle H: Skip metastases in thyroid cancer leaping the central lymph node compartment. *Arch Surg* 2004;139:43–45.
- De Groot LJ, Kaplan EI, McCormick M, et al.: National history, treatment, and course of papillary thyroid carcinoma. *J Clin Endocrinol Metab* 1990 71:414–424.
- Miraille E, Sagan C, Hamy A, et al.: Predictive factors for node involvement in papillary thyroid carcinoma. Univariate and multivariate analysis. *Eur J Cancer* 1999;35:420–423.
- McConahey WM, Hay ID, Woolner LB, et al.: Papillary thyroid cancer treated at the Mayo Clinic, 1946 through 1970: Initial manifestations, pathological findings, therapy and tomorrow. *Expert Rev Mol Diagn* 2005;5:573–584.
- Balogh LW, LiVolsi VA: Pathological diagnosis of papillary thyroid carcinoma: Today and tomorrow. *Expert Rev Mol Diagn* 2005;5:573–584.
- Robbins KI, Clayman G, Levine PA, et al.: Neck dissection classification update: Revisions proposed by the American Head and Neck Society and Academy of Otolaryngology Head and Neck surgery. *Arch Otolaryngol Head Neck Surg* 2002;128:751–758.
- White ML, Gauger PG, Doherty GM: Central lymph node dissection in differentiated thyroid cancer. *World J Surg* 2007;31: 895–904.
- Bocca E, Pignataro O, Oldini C, et al.: Functional neck dissection: An evaluation and review of 843 cases. *Laryngoscope* 1954;94: 942–945.
- Cady B: Lymph node metastases: Indicates but not governors of survival. *Arch Surg* 1984;119:1067–1072.
- Shah Jp, Loree TR, Dharker D, et al.: Prognostic factors in differentiated carcinoma of the thyroid gland. *Am J Surg* 1992; 164:658–661.
- Harwood J, Clark OH, Dunphy JE: Significance of lymph node metastases in differentiated thyroid cancer. *Am J Surg* 1978;136: 107–112.
- Green FL, Fritz AG, Balch CM, et al.: *AJCC Staging Manual American Joint. Committee on Cancer. USA: Lipincott Ravern Publishers; 2002.*
- Tissell LE: Role of lymphadenectomy in the treatment of differentiated thyroid carcinomas. *Br J Surg* 1998;85:1025–1026.
- Dionigi G, Diogini R, Bartalena L, et al.: Surgery of lymph nodes in papillary thyroid cancer. *Expert Rev Anticancer Ther* 2006;6: 1217–1229.
- Ito Y: Lateral and mediastinal lymph node dissection in differentiated thyroid carcinoma: Indications benefits and risks. *World J Surg* 2007;31:905–915.
- Noguchi S, Murakami N, Yomashita H, et al.: Papillary thyroid carcinoma: Modified radical neck dissection improves prognosis. *Arch Surg* 1998;133:276–280.
- Pillitteri P: Use and misuse of neck dissection in the management of thyroid cancer. *J Am Coll Surg* 2001;193:97–98.
- Musacchio MJ, Kim Aw, Vijungco JD, et al.: Greater local recurrence occurs with “berry picking” than neck dissection in thyroid cancer. *Am J Surg* 2003;69:191–196.
- McGregor Gj, Luoma A, Jackson SM: Lymph node metastases from well-differentiated thyroid cancer. A clinical review. *Am J Surg* 1985;149:610–612.
- Pingpark JF, Sasson AR, Hanlon AL, et al.: Tumor above the spinal accessory nerve in papillary thyroid cancer that involves lateral neck nodes: A common occurrence. *Arch Otolaryngol Head Neck Surg* 2002; 128:1275–1278.
- Kupsterman ME, Patterson DM, Mandel SJ, et al.: Safety of modified radical neck dissection for differentiated thyroid carcinoma. *Laryngoscope* 2004;114:403–406.
- Attie JN: Modified neck dissection in treatment of thyroid cancer: A safe procedure. *Euro J Cancer Clin Oncol* 1988;24:315–324.
- Shah MD, Hall FT, Eski IJ, et al.: Clinical course of thyroid carcinoma after neck dissection. *Laryngoscope* 2003;113:2102–2107.
- Wilson S, Block G: Carcinoma of the thyroid metastolic lymph nodes of the neck. *Arch Surg* 1971;102:285–289.