Metastatic papillary thyroid cancer with lateral neck disease: Pattern of spread by level

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ABSTRACT: *Background.* Currently, there is no clear consensus on the extent of this lateral neck dissection required in papillary thyroid cancer (PTC) with lateral neck metastasis. The purpose of this study was to review our experience with metastatic PTC, and identify the pattern of lymphatic spread to the lateral neck.

Methods. A retrospective medical chart review of PTC patients treated with lateral neck dissection (levels II–Vb) at our institution between January 2004 and 2011. A total of 185 patients underwent 248 selective lateral neck dissections.

Results. Levels II, III, IV, and Vb were respectively involved in 49.3%, 76.6%, 61.6%, and 29.2% of cases.

Conclusion. We advocate for a routine excision of levels II, III, IV, and Vb in PTC with metastasize to any lateral neck level. Although we have routinely dissected level IIb, it may be appropriate to omit its dissection, as well as level Va, when there are no clinical, radiologic, or intraoperative evidence of disease involving these sublevels. © 2012 Wiley Periodicals, Inc. *Head Neck* **00:** 000–000, 2012

KEY WORDS: thyroid, papillary cancer, metastasis, lateral, neck dissection, level

INTRODUCTION

Papillary thyroid cancer (PTC) commonly metastasizes via lymphatic spread to local and regional lymph nodes.[1] A high rate of clinical and occult metastases has been well documented in the literature with a range from 30% to 90%.[2–4] lymph node metastases in PTC has a significant impact on disease-free survival (DFS) and disease-specific survival (DSS).[5–10]

Because of the growing body of evidence on the effect of PTC metastasis on recurrence, survival, and possibly quality of life, the American Thyroid Association (ATA) advocates that a "therapeutic lateral neck compartmental lymph node dissection should be performed for patients with biopsy proven metastatic lateral cervical lymphadenopathy."[11] While patterns of PTC metastasis to lateral neck lymph nodes are relatively predictable, there is no clear consensus on the proper extent of the lateral neck dissection. Current practices include extensive modified radical neck dissection, selective neck dissection, and "berry picking" procedures focusing on an echelon of suspicious or involved nodes. Nonetheless, the most recent recommendations from the Triological Society and the ATA advocate a more comprehensive selective lateral neck dissection.[12,13]

The purpose of this study is to review our experience with lateral neck dissections in metastatic PTC, and identify the pattern of lateral neck metastasis related to PTC. With this study, we hope to contribute to the evidence and future recommendations on the optimal extent of lateral neck dissections required in this patient population.

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MATERIALS AND METHODS

After approval by the Mount Sinai Hospital research ethics review board, a retrospective medical chart review was conducted reviewing all patients with PTC treated between January 2004 and 2011.

Inclusion criteria included preoperative fine needle aspiration biopsy proven PTC of a lateral neck lymph node, undergoing selective lateral neck dissection including levels IIa and IIb, III, IV, and Vb (II–Vb), and postoperative pathology confirming the diagnosis of PTC in one or more lymph nodes in the lateral neck. Included were primary cases with total or completion thyroidectomy and recurrent cases presenting with lateral neck disease alone. Our series also included unilateral and bilateral neck dissections, which were performed at either the same time as the thyroidectomy or at a later date. Cases with less than a selective neck dissection of levels II to Vb, incomplete pathology report, pathology other than PTC, or a history of previous lateral neck dissection were excluded from the study. Clinical, demographic, and pathologic data, including lymph node level and number were collected for each patient.

All surgeries were performed by the senior author (J.F.) and his team (fellow and/or resident). The anterior triangle including level IIb was routinely approached from the medial aspect of the sternocleidomastoid muscle, whereas the posterior triangle was approached laterally, starting at the level of cranial nerve XI and dissecting caudally.

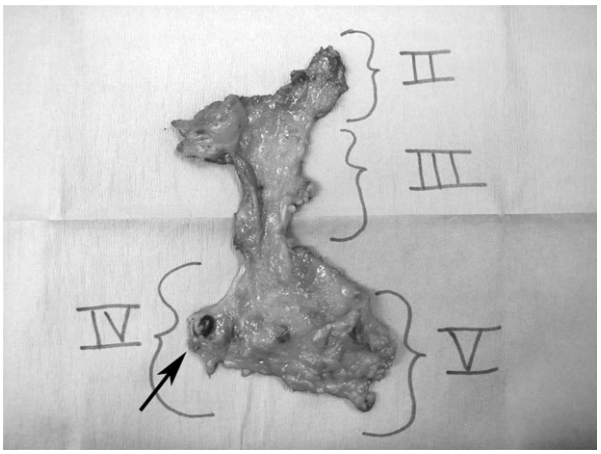

FIGURE 1. Picture of lateral neck dissection specimen labeled for pathology. Arrow pointing to a clinically positive lymph node in level IV.

Neck levels and sublevels were defined as previously published, with an exception of extending level Vb dissection to the level of the accessory nerve.[14]

Excised neck tissue were laid on a blue towel and marked before being sent to the pathology department (Figure 1). Central neck tissue (level VI) was not included with the lateral neck specimen. Level Va, above the accessory nerve, was not routinely excised unless there was clinical, radiological, or intraoperative evidence of involvement.

RESULTS

Demographics and pathological data are presented in Table 1. A total of 185 patients underwent 248 selective lateral neck dissections for metastatic PTC. Of these, 126 patients (68.1%) received unilateral selective neck dissections and 59 patients (31.9%) received bilateral selective neck dissections. Forty-four percent of our patients had selective neck dissections for recurrent disease in the lateral neck versus 56% who underwent selective neck dissection at the time of their total thyroidectomy. The distribution of primary tumor pathological subtypes are presented in Figure 2. Classical PTC was the most common pathological subtypes (64.9%) followed by the follicular variant (17.5%). Aggressive subtypes of PTC were present in 14% of our patients (tall cell 7.0%, insular 2.6%, and diffuse sclerosing 2.6%). Hürthle cells were predominantly present in an additional 4.4%.

Figure 3 illustrates the percentage of involvement for each lateral neck unit. Levels II, III, IV, and Vb were found to harbor metastasis in 122 (49%), 189 (76%), 152 (61%), and 72 (29%) of our patients, respectively. More than two thirds of our patients (73%) had 2 or more neck levels involved, and 11.4% had involvement at all 4 levels. Levels III and IV were both involved in 46% of cases (Figure 4). Skip metastasis, defined as positive nodes in level II or Vb without metastasis in levels III and IV, were detected in 9% of our patients.

DISCUSSION

In our series, levels II, III, IV, and Vb were respectively involved in 49%, 76%, 61%, and 29% of cases. To the best of our knowledge, this is the largest published series in the English literature describing the pattern of disease spread in PTC with lateral neck metastasis.

The extent of lateral neck dissection in metastatic PTC remains a debatable topic. In our series, we detected a relatively high rate of disease at all levels of the lateral neck. More than 73% of our cohort had involvement at multiple levels, and skip lesions were detected in an additional 9%. We therefore advocate for the routine excision of levels II, III, IV, and Vb in metastatic PTC with disease detected at any lateral neck levels.

Although previous recommendations regarding the management of the lateral neck in metastatic PTC vary widely, there seems to be some consensus in the most recent literature, with which our data and recommendations coincide. Recent studies from single-center high

TABLE 1. Demographics, tumor size, and number of lymph nodes.

	No. of patients (%)	Mean (SD)
Patients		
Total	185	
Selective neck dissections		
Total	248	
Unilateral	126 (68.1)	
Bilateral	59 (31.9)	
Primary (with TT)	104 (56)	
Age, in years		46 (14.8)
Sex		
Male	93 (50.2)	
Female	92 (49.8)	
Maximum tumor diameter, in cm		2.5 (1.8)
No. of lymph nodes/neck dissection		
Total		66 (30.7)
Positive		9.8 (10.9)

Abbreviation: TT, total thyroidectomy.

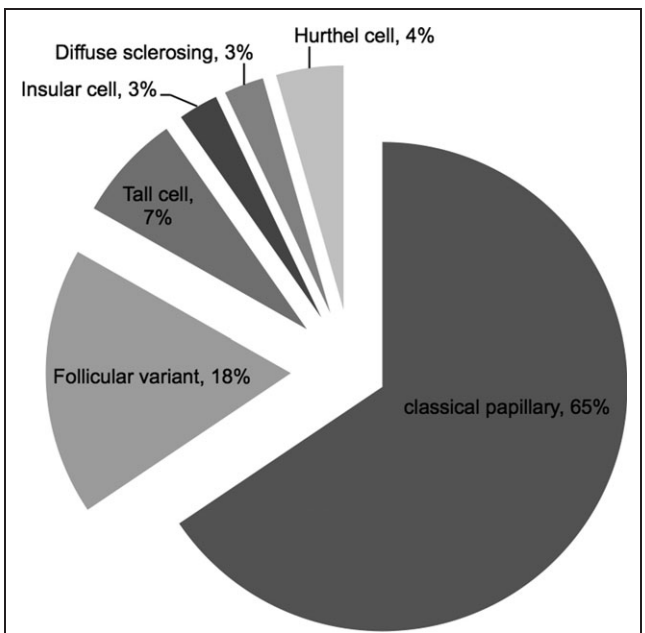

FIGURE 2. Distribution of pathological diagnosis of primary tumors (%) 2 changes.

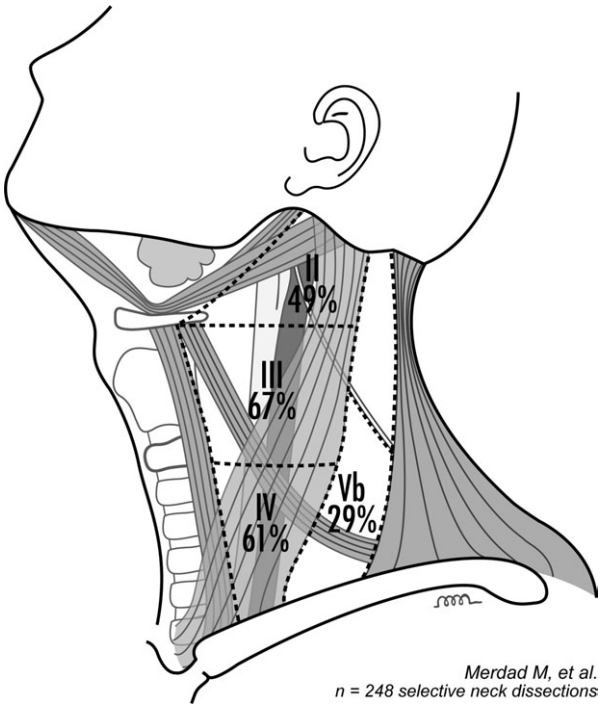

FIGURE 3. Incidence of neck level involvement in papillary thyroid cancer (PTC) with lateral neck metastasis.

volume institutions have advocated for routine excision of levels II to V.[15–17] The Triological Society Best Practice guidelines published in 2010 recommend a selective neck dissection with excision of levels IIa to Vb with or without the inclusion of levels IIb and Va.[12] Based on a nonsystematic review, the ATA's recent consensus review on lateral neck dissection in differentiated thyroid cancer similarly advocate for a comprehensive neck dissection of at least nodal levels IIa, III, IV, and Vb.[13]

Lymph node metastasis from PTC to level V ranges from 8% to 53%.[18] Much of this variation in level V lymph node involvement can be explained by differences in the timing of the dissection relative to the course of the disease, variations in treatment algorithms and cohort selection criteria. A recent nonsystematic review on level V involvement in metastatic PTC by Khafif et al,[18] recommended against the routine complete excision of level V. The authors favored limiting the dissection of sublevel Vb to cases with positive nodes in level IV, multiple positive nodes in levels II and III, and in cases with radiological or intraoperative evidence of nodal disease at that level. Based on these criteria, one might need to perform a second procedure addressing level Vb on a significant number of patients after reviewing the final neck dissection pathology report. In our opinion, level Vb involvement in 29% of our cohort justifies the routine dissection of this sublevel.

Close to one third of our cohort had disease involvement at level V and hence the controversy at this point no longer lies on whether or not it should be dissected but rather to what extent. Dissection of the accessory nerve is associated with a low but not insignificant level of postoperative morbidity. If a dissection of the nerve can be avoided in level V, this should be advocated. Level Vb positivity rate in our cohort is in keeping with others that addressed this level separately.[17–19] Interestingly, none of the studies found disease at level Va, when it was routinely dissected.[17–19] In our opinion, level Va (above the accessory nerve) does not require routine dissection except when there is radiological, biopsy, or intraoperative evidence of involvement.

Data on the utility of level IIb dissection remains controversial. When examined separately, level IIb was found to harbor metastasis in 4.5% to 21% and this was found to be mainly in cases where level IIa was involved with metastasis.[17,20] Although we routinely excise both levels IIa and IIb, our study does not address level IIb involvement separately. Avoiding dissection of level IIb may be appropriate in the absence of clinical, radiological, or intraoperative evidence of involvement, and in the absence of gross intraoperative involvement of level IIa. Our rationale for the routine excision of level IIb is largely based on the relatively high rate of occult disease and the subsequent increase in risk of recurrence. The few studies addressing level IIb separately, demonstrated a higher rate of metastasis than was previously thought. Roh et al,[19] Pingpank et al,[21] and Lee et al[22] detected disease at level IIb in 17%, 21%, and 22%, respectively. Caron et al[3] in 2006 demonstrated a 20% rate of recurrence at level II when it was not included in the initial neck dissection. This is a significant rate of recurrence especially for patients with regional disease whom are already at a higher risk of further recurrences. Furthermore, a distinct separation of levels IIa and IIb is somewhat arbitrary, surgeon-dependent, and in many instances not possible. This is especially true in cases in which IIa harbors clinically apparent disease. Finally, although the rates of accessory nerve injury in expert hands is low, the dissection around the nerve in recurrent cases might carry a higher risk for nerve injury.

Our study has a number of strengths. It is the largest series in the literature addressing this question. Excised neck dissection specimens were in each case oriented and marked by the senior surgeon (J.F.) before being sent to the pathology department, thereby facilitating the pathologists' synoptic report by level (Figure 1). All surgeries were performed by the senior author and his team who used a consistent treatment paradigm throughout the study period.

This study, like most studies addressing lateral neck disease in PTC, is a retrospective medical chart review. Our cohort had a single surgeon with consistency in specimen

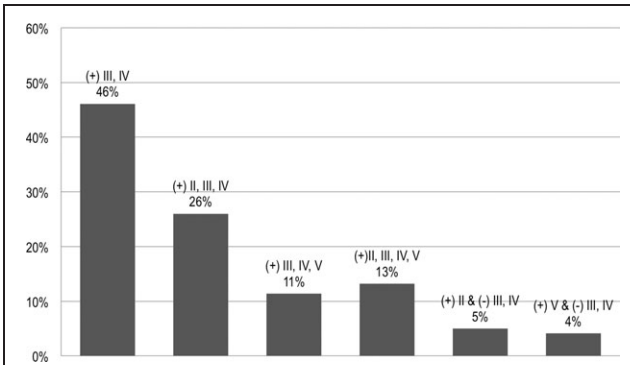

FIGURE 4. Concurrent level involvement in papillary thyroid cancer (PTC) with lateral neck metastasis. (+) positive lymph nodes, (-) negative lymph nodes.

labeling and we do not think that a change in our methodology to a prospective one would have influenced our results. It would have been ideal to have a single pathologist review all of our cases, to assure consistency in assessment of the number of positive lymph nodes, but this is, however, quite impractical and was not adopted by any of the other studies reviewed. In our series specimen marking did not separate levels IIa and IIb, prompting our pathologists to report both levels as a combined level II. Thus, our study is not equipped to answer specific questions about level IIb dissection in this population. Another limitation of our study relates to previous treatment with radioactive iodine (RAI). Forty-four percent of our cohort had surgery for disease in the lateral neck manifesting after the initial thyroid gland surgery. A large number of these patients may have received RAI treatment after their initial thyroid surgery, and this might have affected the sensitivity and specificity of radiological investigations and surgical pathology results. A subgroup analysis of this group of patients would have enriched our analysis, but the information is absent in our database given that large number of our patients' RAI treatment is administered and managed by endocrinologists at different medical centers.

The exact impact of PTC recurrence on survival is not yet well established. There are a few studies suggesting an increase in recurrence without an effect on survival, although these studies are flawed in design and power.[23–25] A more recent body of evidence with better long-term follow-up, larger sample sizes, and better methodology, including a study from our group, indicate that lymph node metastases in PTC is a statistically significant prognostic factor in DFS or DSS.[5–10] Two of these studies with large sample sizes used powerful population-based administrative and cancer databases which provide valid and reliable long-term data.[9,10] This falls in line with our recommendation for a more extensive neck dissection, including levels II to Vb, aiming to minimize the chance of recurrence and prolong the DFS and DSS.

CONCLUSION

Our data lead us to advocate for routine excision of levels II, III, IV, and Vb in PTC that has metastasized to any lateral neck level. Although we have routinely dissected level IIb, it may be appropriate to omit its dissection, as well as level Va, when there is no clinical, radiological, or intraoperative evidence of disease involving these sublevels.

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REFERENCES

1. Noguchi S, Noguchi A, Murakami N. Papillary carcinoma of the thyroid. I. Developing pattern of metastasis. *Cancer* 1970;26:1053–1060.
2. Shaha AR. Implications of prognostic factors and risk groups in the management of differentiated thyroid cancer. *Laryngoscope* 2004;114: 393–402.
3. Caron NR, Clark OH. Papillary thyroid cancer: surgical management of lymph node metastases. *Curr Treat Options Oncol* 2005;6: 311–322.
4. Davidson HC, Park BJ, Johnson JT. Papillary thyroid cancer: controversies in the management of neck metastasis. *Laryngoscope* 2008;118: 2161–2165.
5. Beasly NJ, Lee J, Eski S, Walfish P, Witterick I, Freeman JL. Impact of nodal metastases on prognosis in patients with well-differentiated thyroid cancer. *Arch Otolaryngol Head Neck Surg* 2002;128:825–828.
6. Noguchi S, Murakami N, Yamashita H, Toda M, Kawamoto H. Papillary thyroid carcinoma: modified radical neck dissection improves prognosis. *Arch Surg* 1998;133:276–280.
7. Shah MD, Hall FT, Eski SJ, Witterick IJ, Walfish PG, Freeman JL. Clinical course of thyroid carcinoma after neck dissection. *Laryngoscope* 2003; 113:2102–2107.
8. Tubiana M, Schlumberger M, Rougier P, et al. Long-term results and prognostic factors in patients with differentiated thyroid carcinoma. *Cancer* 1985;55:794–804.
9. Lundgren CI, Hall P, Dickman PW, Zedenius J. Clinically significant prognostic factors for differentiated thyroid carcinoma: a population-based, nested case-control study. *Cancer* 2006;106:524–531.
10. Podnos YD, Smith D, Wagman LD, Ellenhorn JD. The implication of lymph node metastasis on survival in patients with well-differentiated thyroid cancer. *Am Surg* 2005;71:731–734.
11. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1167–1214.
12. Hasney CP, Amedee RG. What is the appropriate extent of lateral neck dissection in the treatment of metastatic well-differentiated thyroid carcinoma? *Laryngoscope* 2010;120:1716–1717.
13. Stack BC Jr, Ferris RL, Goldenberg D, et al. American Thyroid Association consensus review and statement regarding the anatomy, terminology, and rationale for lateral neck dissection in differentiated thyroid cancer. *Thyroid* 2012 22:501–508.
14. Robbins KT, Clayman G, Levine PA, et al. Neck dissection classification update: revisions proposed by the American Head and Neck Society and the American Academy of Otolaryngology–Head and Neck Surgery. *Arch Otolaryngol Head Neck Surg* 2002;128:751–758.
15. Kupferman ME, Patterson M, Mandel SJ, LiVolsi V, Weber RS. Patterns of lateral neck metastasis in papillary thyroid cancer. *Arch Otolaryngol Head Neck Surg* 2004;130:857–860.
16. Ahmadi N, Grewal A, Davidson BJ. Patterns of cervical lymph node metastases in primary and recurrent papillary thyroid cancer. *J Oncol* 2011; 2011:735678.
17. Farrag T, Lin F, Brownlee N, Kim M, Sheth S, Tufano RP. Is routine dissection of level II–B and V-A necessary in patients with papillary thyroid cancer undergoing lateral neck dissection for FNA-confirmed metastases in other levels. *World J Surg* 2009;33:1680–1683.
18. Khafif A, Medina JE, Robbins KT, et al. Level V in therapeutic neck dissections for papillary thyroid carcinoma. *Head Neck* 2012 [Epub ahead of print].
19. Roh JL, Kim JM, Park CI. Lateral cervical lymph node metastases from papillary thyroid carcinoma: pattern of nodal metastases and optimal strategy for neck dissection. *Ann Surg Oncol* 2008;15:1177–1182.
20. Vayisoglu Y, Ozcan C, Turkmenoglu O, et al. Level IIb lymph node metastasis in thyroid papillary carcinoma. *Eur Arch Otorhinolaryngol* 2010; 267:1117–1121.
21. Pingpank JF Jr, Sasson AR, Hanlon AL, Friedman CD, Ridge JA. 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.
22. Lee BJ, Wang SG, Lee JC, Son SM, Kim IJ, Kim YK. Level IIb lymph node metastasis in neck dissection for papillary thyroid carcinoma. *Arch Otolaryngol Head Neck Surg* 2007;133:1028–1030.
23. Hugues CJ, Shaha AR, Shah JP, Loree TR. Impact of lymph node metastasis in differentiated carcinoma of the thyroid: a matched-pair analysis. *Head Neck* 1996;18:127–132.
24. McHenry CR, Rosen IB, Walfish PG. Prospective management of nodal metastases in differentiated thyroid cancer. *Am J Surg* 1991;162: 353–356.
25. Hubert JP Jr, Kiernan PB, Beahrs OH, McConahey WM, Woolner LB. Occult papillary carcinoma of the thyroid. *Arch Surg* 1980;115: 394–398.