Philosophy on Neck Dissection in Thyroid Cancer—Current Controversies and Consensus

Benzon M. Dy¹ · Ashok R. Shaha¹

Received: 31 October 2017 / Accepted: 14 December 2017 / Published online: 21 December 2017
© Indian Association of Surgical Oncology 2017

Abstract

Thyroid cancer commonly metastasizes to lymph nodes either in the central compartment or lateral neck in at least 50% of patients. Over the past several decades, our understanding of the natural progression of thyroid cancer has changed. Our current practice reflects our increasingly sophisticated understanding of the biology of thyroid cancer while taking into account the morbidity and mortality associated with aggressive variants of the disease.

Keywords Delphian lymph nodes · Thyroid cancer · Dissection

Introduction

The incidence of thyroid cancer is rapidly rising all around the world [1, 2]. Diagnosis has quadrupled in the USA over the past 20 years with many nodules discovered as an incidental finding during routine examination of the neck or during investigation for an unrelated pathology [3]. Differentiated thyroid cancer has risen exponentially in South Korea 6.4-fold from 1999 to 2008 where routine ultrasound of the neck was considered to be part of appropriate cancer screening [4]. Interestingly, the majority of these tumors are micro-carcinomas, and overall survival in this group approaches 99% in the long term [5]. The mortality from thyroid cancer has remained unchanged in the USA despite this meteoric rise in incidence and diagnosis [6]. The majority of patients dying of thyroid cancer will have an aggressive thyroid malignancy including poorly differentiated and anaplastic thyroid carcinoma or patients presenting initially with locally aggressive thyroid cancer or distant metastases [7].

The biology of thyroid cancer is quite unique, and it is vitally important to recognize the prognostic factors and risk group stratification in the management of thyroid cancer. The prognostic factors of thyroid cancer such as age, grade, size of the tumor, extrathyroidal extension, and distant metastasis are very well-described in the literature with criteria established from Lahey

clinic, Mayo Clinic, and Memorial Sloan Kettering Cancer Center among others [8–10]. Interestingly, none of these prognostic factors have included nodal metastasis as a cause of concern. Nodal metastasis in the majority of the human cancers is considered to be major factor in survival, and the favorable outcomes decrease considerably when present. Most of these patients would require additional treatment and would be considered advance stage tumors. However, in patients with well-differentiated thyroid carcinoma, the presence of nodal metastasis has very little prognostic implication, and in individuals below the age of 55, it does not change the staging or the survival outcome [11]. This clearly represents a unique biology in thyroid carcinoma; however, over the last two decades, several controversies have been raised in the evaluation, management, and follow-up of patients with nodal metastasis.

This article will discuss the current controversies and consensus in evaluation and management of patients with thyroid cancer with and without nodal involvement.

Initial Evaluation

The incidence of nodal metastasis in well-differentiated thyroid carcinoma is quite common. Approximately 40–60% of patients present with nodal metastasis that is either clinically apparent or microscopic and occult [12, 13]. The presence of microscopic nodal metastasis is unlikely to have any major impact on the long-term outcome in patients with well-differentiated thyroid carcinoma [14]. The most common sites of nodal metastasis are

✉ Benzon M. Dy
Dy.benzon@mayo.edu

¹ Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA

found in the central compartment and paratracheal area followed by the involvement of the jugular chain prior to distant disease [15]. The leveling system in the neck has been standardized and has been used for almost three quarters of a century, which initially started at Memorial Sloan Kettering Cancer Center. Level I is in the submandibular area, and levels II, III, and IV involve the jugular chain at high, mid, and low levels. Level V lymph nodes include lateral lymph nodes behind the sternomastoid muscle. This leveling system has been subclassified as levels IA and IB where the incidence of thyroid metastasis is quite low. Levels IIA and IIB are defined above and below and above the accessory nerve, and level V has been divided as Va and Vb. Level VI nodes are located in the paratracheal area and tracheoesophageal groove region, while level VII lymph nodes include lymph nodes between level of the sternum and innominate vessels [16]. Levels VI and VII nodes are fairly common in patients with larger tumors or locally aggressive thyroid cancers with extrathyroidal extension. These are also commonly involved in patients with medullary thyroid cancer, which may extend in the paratracheal area deep in the mediastinum. The distinction between levels VI and VII is quite vague and quite often many clinicians do not make a major distinction between levels VI and VII nodes [17].

All the patients with suspected or proven thyroid cancer should undergo a thorough preoperative evaluation of the neck including central and lateral compartments. The central compartment may be somewhat difficult to evaluate especially in presence with thyroid gland; however, the lateral compartment needs to be evaluated very carefully even when the lymph nodes are not clinically suspicious. The radiological findings of size of the lymph node, shape of the lymph node, irregularity, and punctate calcification are well-known indicators of metastatic disease [18]. If there are any suspicious lateral neck nodes, many surgeons will consider preoperative fine needle aspiration biopsy to confirm the presence of nodal metastasis.

Occasionally, the cytology may not yield a definitive diagnosis, and a thyroglobulin wash of the needle aspiration is generally quite helpful. If the thyroglobulin wash in the needle aspirant is high, it is both sensitive and specific for the diagnosis of metastatic thyroid carcinoma, and appropriate surgical extension may be considered in these patients [19]. If the lymph nodes are clinically palpable in the lateral neck, a thorough neck mapping CT scan with intravenous iodinated contrast should be considered. Our experience has shown this will better evaluate the extent of the disease and more specifically define the location of metastasis especially in areas not well visualized by ultrasonography such as the superior mediastinum, parapharyngeal space, and retropharyngeal area.

The CT scan is more critical in evaluation of patients with recurrent nodal disease. Obviously, the CT scan should be performed with contrast even though there has been some concern raised in the past about use of contrast, which would generally delay the radioactive iodine ablation by 6–8 weeks.

However, we need to recognize that the surgical procedure will be much more complete if the surgeon is aware about the extent of the disease and certain hidden areas are better evaluated including levels II and the superior mediastinal lymph nodes. These are the areas which require special attention during initial surgical procedure [20].

Surgical Management

The extent of surgery required during operative intervention is guided by our preoperative imaging as well as our experience with the pattern of metastasis in previously reported literature. In patients with gross central nodal disease, a thorough level VI dissection will be undertaken bilaterally taking care to preserve the recurrent laryngeal nerve and inferior parathyroid glands. If these glands require removal for a thorough dissection, they will be autoimplanted in the sternocleidomastoid muscle. Dissection of the central compartment involves clearance of the prelaryngeal, pretracheal, and paratracheal compartments from the thyroid cartilage down to the thoracic inlet to the level of the innominate artery and laterally to the carotid artery. Extra care must be taken around the Delphian lymph nodes and pyramidal lobe to ensure complete clearance in these areas especially for tumors present in the upper 1/3 of the thyroid lobe.

Patients with lateral neck metastasis will routinely undergo levels II, III, and IV dissections and possibly level V depending on the extent of disease. Although previous reports have shown that a cephalad dissection may not be required in patients with only levels III or IV metastasis, our experience has shown superior durability in recurrence free survival when a routine complete modified radical neck dissection is performed in patients with lateral neck metastasis. A thorough neck dissection of clinically apparent nodes has several important implications including a decline in overall thyroglobulin level, removes artifact from ultrasound-guided post-operative detection, and may decrease overall recurrence free survival even in patients with no overt clinical signs of metastasis during the initial operation.

Post-operative Follow-up

Post-operatively, our protocol for patients with thyroid carcinoma is similar in those with and without nodal metastasis. Every 6 months to 1 year, a thorough neck ultrasound is performed including the central and lateral neck [20]. If there are subcentimeter areas of recurrence, we generally will monitor these sites until they approach 1 cm in size especially if they do not harbor aggressive features or are not adjacent to vital structures such as the recurrent laryngeal nerve or trachea [21]. We monitor thyroglobulin levels and as long as these remain < 1, we are often encouraged that there is no clinically relevant disease present. If this rises, additional studies such as an I-123 scan or low dose I-131 scan may be undertaken to identify areas of persistent or recurrent disease.

In patients with recurrent nodal disease, if ultrasonography identifies recurrence greater than 1 cm, we recommend obtaining a CT scan with intravenous contrast to demonstrate the extent of disease as well as areas not evident on CT to decrease the chance of persistent disease post-operatively. Although this may delay radioactive iodine treatment by several weeks, a thorough and complete operation for recurrence is the mainstay of treatment for recurrent thyroid cancer. PET scan is rarely utilized in patients unless there is a thyroglobulin level that is markedly elevated with no clear source of disease. In addition, PET scan is utilized in patients with poorly differentiated carcinoma who may not produce thyroglobulin or uptake radioactive iodine.

Controversies in Neck Dissection

In patients without gross disease in compartment VI, the philosophy of a prophylactic neck dissection has been quite controversial over the past several decades. Routine dissection has often been performed electively with microscopic foci of metastasis present in 40–60% of patients. This has not had any significant implication in overall survival as lymph node metastasis [14]. There may be a benefit in rendering a patient's thyroglobulin level to near undetectable levels avoiding a nuclear scan or further imaging during follow-up. However, there are patients with differentiated thyroid cancer that do not produce thyroglobulin so that one may be encouraged by a low thyroglobulin level, but it does not obviate the necessity of regular imaging during follow-up.

There has also been a consideration that recurrence free survival and possibly overall survival may be improved with a prophylactic central compartment dissection [22]. This has been debunked over time with large prospectively maintained data from Memorial Sloan Kettering showing that clinically significant recurrence after surgery does not differ whether performed with or without neck dissection if lymph nodes are not clinically relevant prior to thyroidectomy [14].

As mentioned previously, patients with lateral neck disease should be managed with a neck dissection involving at least levels II, III, and IV. Level IIb above the accessory nerve may be avoided if there is no gross disease present prior to surgery in order to reduce the morbidity of accessory nerve dysfunction which can be present in up to 30% of patients after neck dissection.

Rarely, disease may manifest itself in compartments I and V, and if these are evident prior to surgery, these areas should be included in neck dissection. Although some have proposed less aggressive dissections when level II is not clinically involved preoperatively, clinically relevant recurrence can be decreased to as low as 3% when a thorough neck dissection is performed when appropriate [14].

Sentinel lymph node biopsy has been proposed as a diagnostic tool to aid in identifying lymph nodes that represent the

disease burden present within the central compartment. Using radioactive isotopes or dye for identification. Yeh et al. showed a high specificity of 100%, but the negative predictive value of SLNB was 0% which renders interpretation of the technique difficult in differentiated thyroid cancer and hence has not been widely adopted [23].

Recurrent Disease

During follow-up, Mazzaferri et al. had initially proposed that up to 30% of patients will experience a recurrence of thyroid cancer during their lifetime, with up to 2/3 of patients experiencing recurrence in the first 10 years [24]. Recent studies have lowered this expectation and have risk stratified recurrent disease based on multiple factors including tumor subtype, number of lymph nodes containing metastasis, extranodal extension, size of metastasis, and molecular profile. In patients stratified to low-risk categories, recurrence is estimated to be 5%, intermediate risk is 15%, and high risk up to 50% [20, 25].

It is of paramount importance to temper our aggressiveness in pursuing sites of recurrent disease until they become clinically relevant or a risk to the patient. Ultrasound identified recurrence of less than 1 cm should be monitored as fewer than 10% of these patients will have growth of suspicious lymph nodes greater than 5 mm during a median follow-up on 3–4 years [24]. Many patients will live with solitary micrometastatic recurrence without requiring an aggressive reoperation that places them at risk for recurrent laryngeal nerve injury, accessory nerve injury, and hypoparathyroidism to name a few of the morbid complications that may occur. We must make sure “the punishment fits the crime” so that we are not overtreating patients with small volume disease and placing them at risk with an unnecessary operation that has no bearing on their overall quality of life or disease free survival.

In patients with central or lateral neck recurrence, a compartment-oriented selective nodal dissection is preferred with accurate preoperative imaging [26]. Other options include ethanol ablation with the largest experience documented by the Mayo Clinic [27]. This should only be considered in experienced hands with patients with small volume disease.

Conclusion

Thyroid cancer has had an increasing prevalence over the past several decades, and we have learned many things while caring for patients with both well-localized disease as well as nodal disease. The unique pathophysiology of well-differentiated thyroid nodal disease has tempered our treatment to an increasingly conservative approach. However, it is important to risk stratify patients during every step of their treatment as to not become complacent in our treatment and

miss opportunities to help patients with truly aggressive disease who will benefit from aggressive nodal dissection and adjuvant treatment. We should recognize the importance of “primum non-nocere”—first do no harm. However, we must not miss the boat or miss the opportunity to cure patients with available modalities.

References

- Kilfoy BA, Zheng T, Holford TR, Han X, Ward MH, Sjodin A, Zhang Y, Bai Y, Zhu C, Guo GL, Rothman N, Zhang Y (2009) International patterns and trends in thyroid cancer incidence, 1973–2002. *Cancer Causes Control* 20(5):525–531. <https://doi.org/10.1007/s10552-008-9260-4>
- La Vecchia C, Malvezzi M, Bosetti C et al (2015) Thyroid cancer mortality and incidence: a global overview. *Int J Cancer* 136:2187–2195
- American Cancer Society (2017) *Cancer Facts & Figures 2017*. American Cancer Society, Atlanta
- Park S, Oh CM, Cho H, Lee JY, Jung KW, Jun JK, Won YJ, Kong HJ, Choi KS, Lee YJ, Lee JS (2016) Association between screening and the thyroid cancer “epidemic” in South Korea: evidence from a nationwide study. *BMJ* 355:i5745
- Davies L, Welch HG (2006) Increasing incidence of thyroid cancer in the United States, 1973–2002. *J Am Med Assoc* 295(18):2164–2167. <https://doi.org/10.1001/jama.295.18.2164>
- Howlander N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds) (2013) *SEER Cancer Statistics Review, 1975–2010*, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2010/, based on November 2012 SEER data submission, posted to the SEER web site
- Wang LY, Palmer FL, Nixon IJ, Thomas D, Patel SG, Shaha AR, Shah JP, Tuttle RM, Ganly I (2014) Multi-organ distant metastases confer worse disease-specific survival in differentiated thyroid cancer. *Thyroid* 24(11):1594–1599. <https://doi.org/10.1089/thy.2014.0173>
- Hay ID, Bergstralh EJ, Goellner JR, Ebersold JR, Grant CS (1993) Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. *Surgery* 114(6):1050–1057
- Cady B, Rossi R (1988) An expanded view of risk-group definition in differentiated thyroid carcinoma. *Surgery* 104(6):947–953
- Shaha AR, Loree TR, Shah JP (1994) Intermediate-risk group for differentiated carcinoma of the thyroid. *Surgery* 116:1036–1041
- Amin MB, Edge SB, Greene FL et al (eds) (2017) *AJCC cancer staging manual*, 8th edn. Springer, New York. <https://doi.org/10.1007/978-3-319-40618-3>
- Mazzaferri EL, Doherty GM, Steward DL (2009) The pros and cons of prophylactic central compartment lymph node dissection for papillary thyroid carcinoma. *Thyroid* 19(7):683–689. <https://doi.org/10.1089/thy.2009.1578>
- Alvarado R, Sywak MS, Delbridge L, Sidhu SB (2009) Central lymph node dissection as a secondary procedure for papillary thyroid cancer: is there added morbidity? *Surgery* 145(5):514–518
- Nixon IJ, Wang LY, Ganly I, Patel SG, Morris LG, Migliacci JC, Tuttle RM, Shah JP, Shaha AR (2016) Outcomes for patients with papillary thyroid cancer who do not undergo prophylactic central neck dissection. *Br J Surg* 103(3):218–225. <https://doi.org/10.1002/bjs.10036>
- Kim H, Kim TH, Choe JH, Kim JH, Kim JS, Oh YL, Hahn SY, Shin JH, Chi S, Jung SH, Kim YN, Kim HI, Kim SW, Chung JH (2017) Patterns of initial recurrence in completely resected papillary thyroid carcinoma. *Thyroid* 27(7):908–914. <https://doi.org/10.1089/thy.2016.0648>
- Robbins KT, Clayman G, Levine PA, Medina J, Sessions R, Shaha A, Som P, Wolf GT, the Committee for Head and Neck Surgery and Oncology, American Academy of Otolaryngology–Head and Neck Surgery (2002) 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* 128(7):751–758
- Wang LY, Palmer FL, Thomas D, Nixon IJ, Tuttle RM, Shah JP, Patel SG, Shaha AR, Ganly I (2015) Level 7 disease does not confer worse outcome than level 6 disease in differentiated thyroid cancer. *Ann Surg Oncol* 22(2):441–445
- Li Q, Lin X, Shao Y, Xiang F, Samir AE (2017) Imaging and Screening of Thyroid Cancer. *Radiol Clin North Am*
- Al-Hilli Z, Strajina V, McKenzie TJ, Thompson GB, Farley DR, Regina Castro M, Algeciras-Schimmich A, Richards ML (2017) Thyroglobulin measurement in fine-needle aspiration improves the diagnosis of cervical lymph node metastases in papillary thyroid carcinoma. *Ann Surg Oncol* 24(3):739–744. <https://doi.org/10.1245/s10434-016-5625-1>
- Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L (2016) 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 26(1):1–133. <https://doi.org/10.1089/thy.2015.0020>
- Wang LY, Migliacci JC, Tuttle RM, Shaha AR, Shah JP, Patel SG, Ganly I (2017) Management and outcome of clinically evident neck recurrence in patients with papillary thyroid cancer. *Clin Endocrinol* 87(5):566–571. <https://doi.org/10.1111/cen.13378>
- Zaydfudim V, Feuer ID, Griffin MR, Phay JE (2008) The impact of lymph node involvement on survival in patients with papillary and follicular thyroid carcinoma. *Surgery* 144(6):1070–1077. <https://doi.org/10.1016/j.surg.2008.08.034>
- Mazzaferri EL, Jhiang SM (1994) Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 97(5):418–428. [https://doi.org/10.1016/0002-9343\(94\)90321-2](https://doi.org/10.1016/0002-9343(94)90321-2)
- Yan X, Zeng R, Ma Z, Chen C, Chen E, Zhang X, Cao F (2015) The utility of sentinel lymph node biopsy in papillary thyroid carcinoma with occult lymph nodes. *PLoS One* 10(6):e0129304. <https://doi.org/10.1371/journal.pone.0129304>
- Tufano RP, Clayman G, Heller KS, Inabnet WB, Kebebew E, Shaha A, Steward DL, Tuttle RM, American Thyroid Association Surgical Affairs Committee Writing Task Force (2015) Management of recurrent/persistent nodal disease in patients with differentiated thyroid cancer: a critical review of the risks and benefits of surgical intervention versus active surveillance. *Thyroid* 25(1):15–27. <https://doi.org/10.1089/thy.2014.0098>
- Welch K, McHenry CR (2013) Selective lateral compartment neck dissection for thyroid cancer. *J Surg Res* 184(1):193–199. <https://doi.org/10.1016/j.jss.2013.04.084>
- Hay ID, Lee RA, Davidge-Pitts C, Reading CC, Charboneau JW (2013) Long-term outcome of ultrasound-guided percutaneous ethanol ablation of selected “recurrent” neck nodal metastases in 25 patients with TNM stages III or IVA papillary thyroid carcinoma previously treated by surgery and 131I therapy. *Surgery* 154(6):1448–1454