Surgical Management of Lymph Node Compartments in Papillary Thyroid Cancer

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KEYWORDS

• Papillary thyroid cancer • Lymph node dissection • Recurrent thyroid cancer
• Lymph node metastases • Central neck lymph node dissection

KEY POINTS

- When central or lateral compartment cervical lymph node metastases are clinically evident at the time of the index thyroid operation for PTC, formal surgical clearance of the affected nodal basin is the optimal management.
- Prophylactic central neck dissection for PTC is practiced by some high-volume surgeons with low complication rates, but is considered controversial because there appears to be a higher risk of complications with an uncertain clinical benefit.
- When a clinically significant recurrence is detected in a previously undissected central or lateral cervical compartment, a comprehensive surgical clearance of the lateral compartment is the preferred treatment.
- When a nodal recurrence is found in a previously dissected central or lateral neck field, the reoperation may focus on the areas where recurrence is demonstrated.

INTRODUCTION

In endocrine surgery, controversy abounds. It is difficult, in fact, to find a topic in surgical endocrinology for which there is little or no controversy. The management of cervical nodal metastases from papillary thyroid cancer (PTC) is no exception. Fortunately, there is widespread agreement regarding the management of clinically evident nodal metastases. It seems clear, based on the risks of persistent or recurrent disease, that the optimal management is formal surgical clearance of the affected nodal basin or basins when cervical nodal metastases are clinically evident at the

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time of the index thyroid operation. On the other hand, because of the high frequency and uncertain clinical significance of occult nodal metastases from PTC, considerable controversy surrounds the management of the clinically negative central compartment, and the performance of so-called prophylactic central neck dissection (CND). Likewise, there is uncertainty regarding the thresholds for recommending remedial CND, given the attendant risks of the procedure and uncertain benefits. Within this contribution to the *Surgical Oncology Clinics of North America*, the data relevant to the surgical management of the lymph nodes of the central and lateral compartments of the neck in PTC are reviewed and discussed.

NOMENCLATURE: PROPHYLACTIC VERSUS THERAPEUTIC

As defined in the American Thyroid Association (ATA) consensus statement on the terminology and classification of CND for thyroid cancer,[1] a therapeutic neck dissection is one that is performed for clinically apparent nodal metastases, whether they are recognized before or during an operation, and regardless of the methodology used to detect the nodal metastases (eg, imaging, physical examination, frozen section). A prophylactic neck dissection is one that is performed on a nodal basin for which there is no clinical or imaging study evidence of nodal metastases. Prophylactic neck dissection is also synonymous with elective neck dissection.

EPIDEMIOLOGY OF CENTRAL NECK METASTASES

Metastases from PTC are frequently found in the central compartment lymph nodes. Nodal metastases from PTC are found in the central compartment in 12% to 81% of cases, depending on the completeness of the nodal dissection by the surgeon and the level of scrutiny to identify lymph nodes by the pathologist.[2] In surgical series of patients with PTC treated with prophylactic CND, occult positive central compartment nodes are found in at least one-third, and up to two-thirds of cases.[2,3] Given the high frequency of nodal metastases in the central compartment, some experts routinely clear the central compartment in a prophylactic fashion.

CONTROVERSY REGARDING PROPHYLACTIC CENTRAL NECK DISSECTION

Routine prophylactic CND for patients with clinically node-negative PTC is controversial. The controversy is centered on the fact that there is risk associated with the performance of a prophylactic CND, and that it is unclear if there is any survival or quality-of-life benefit. Furthermore, the finding of occult nodal disease will upstage patients older than 45 and may influence the usage of radioiodine.

Given the high rate of occult nodal metastases, some experts recommend that a thyroidectomy for PTC be accompanied by at least an ipsilateral central compartment nodal dissection. Proponents of prophylactic CND argue that because of the high rate of occult central nodal metastasis, prophylactic CND should decrease the need for reoperative neck surgery by reducing locoregional recurrence and simplify follow-up by lowering postoperative serum thyroglobulin.[4–6] In a study of 134 patients with PTC wherein all patients underwent a CND, the authors found that 29% of patients undergoing primary surgery for PTC had ipsilateral central neck metastases and also 29% had ipsilateral lateral neck metastases.[3] These authors recommended routine central and ipsilateral lateral nodal compartment dissection for patients undergoing primary surgery for PTC with a T1b or larger primary tumor. Other experts cite the higher complication rate when thyroidectomy is combined with CND, with no apparent improvement in survival, as rationale against prophylactic CND.[4] They maintain that

prophylactic CND exposes patients to the additional risks of recurrent laryngeal nerve (RLN) injury and hypoparathyroidism without proven benefit.

Several recent retrospective analyses have compared outcomes of PTC patients who underwent total thyroidectomy with and without CND.[5,7–9] In one study, 20 prophylactic CNDs were required to prevent one central compartment reoperation.[5] A meta-analysis performed on studies that evaluated recurrence and complications associated with prophylactic CND found that the number needed to treat to prevent one recurrence was 31.[10] Two meta-analyses have demonstrated an increased rate of transient hypocalcemia following prophylactic CND without showing a difference in permanent hypoparathyroidism or RLN injury.[7,9] In most studies, prophylactic CND is associated with a higher rate of temporary hypocalcemia and parathyroid gland removal.[11] In most formal cost-effectiveness analysis studies, prophylactic CND has not been found to be cost-effective for PTC.[12,13]

The presence of nodal metastases may have a significant impact on the stage of disease based on the current American Joint Commission on Cancer (AJCC) TNM staging for thyroid cancer.[14] Patients 45 years of age or older are upstaged to stage III for any central neck nodal metastases regardless of the size and number of metastases found. Prophylactic neck dissection is therefore likely to upstage many patients to stage III for subclinical disease. Because the AJCC staging system for differentiated thyroid cancer was not derived or validated during an era of widespread CND, it is not clear if patients upstaged for subclinical metastases found during prophylactic dissection will have the same prognosis as patients with clinically evident central neck metastases.

It is also not certain how the practice of prophylactic nodal dissection might affect the likelihood to receive therapeutic doses of radioactive iodine (RAI). Some studies indicate that patients are more likely to receive RAI after total thyroidectomy with CND.[11] One hypothesis is that a greater frequency of detection of nodal metastases, and the associated upstaging of disease, leads to a greater utilization of RAI. Other studies show that prophylactic CND is associated with a lower probability of receiving RAI.[15] This finding, in turn, may be due to the fact that a more complete surgical clearance of the central compartment may lead to lower preablation thyroglobulin levels, and consequently, to a lower utilization of RAI. In a study by Lang and colleagues,[16] 51% of the patients who underwent prophylactic CND had undetectable preablative thyroglobulin.

A recent single-institution randomized controlled trial of total thyroidectomy with or without prophylactic CND in patients with PTC without evidence of preoperative or intraoperative lymph node metastases has been reported by Viola and colleagues[15] from Pisa, Italy. Their study of 181 patients with a median follow-up of 5 years found that clinically node-negative patients treated with prophylactic CND had a reduced necessity for repeat RAI treatments compared with those patients who did not undergo CND. However, the prophylactic CND patients also had a significantly higher prevalence of permanent postoperative hypoparathyroidism (19.4 vs 8.0%).

PREOPERATIVE ASSESSMENT OF THE CERVICAL NODAL COMPARTMENTS

The assessment of lymph node status before an operation for PTC is necessary because the presence and location of metastatic lymph nodes may not be clinically apparent, and the identification of nodal metastases will frequently alter the planned procedure. All patients should undergo a comprehensive history and physical examination focused on determining the extent of disease. Unfortunately, physical examination is notoriously unreliable for the exclusion of cervical nodal metastases.

Imaging studies, however, can detect abnormal lymph nodes in patients who have no palpable lymphadenopathy and may also yield information that alters the extent of the operation, even when overt nodal metastases are present.

Imaging Studies

Routine preoperative sonographic imaging of the cervical nodal basins changes the extent of surgery in as many as 41% of patients.[17,18] In a retrospective cohort study of 486 patients who underwent neck ultrasound before initial operation for PTC, ultrasound detected abnormal lymph nodes in 16% of patients who had nonpalpable lymph nodes on physical examination and changed the extent of surgery in 15 of 37 (41%) patients who had palpable lymph nodes on physical examination.[18] Similarly, in a retrospective study of 151 patients who underwent neck ultrasound before initial operation for differentiated thyroid cancer, ultrasound detected abnormal lymph nodes in 52 (34%) patients who had nonpalpable lymph nodes on physical examination.[17] Most patients with PTC who have lymph node metastases will have them in the inferior aspect of the neck. In a retrospective study of 578 lymph nodes that underwent fine needle aspiration (FNA) biopsy in 588 patients with differentiated thyroid cancer, 67% of malignant lymph nodes were found in the inferior third of the neck, whereas 46% of lymph nodes biopsied in the superior third of the neck were benign.[19]

Multiple imaging modalities have been studied for the preoperative staging of patients with PTC. Computed tomography (CT) is the preferred imaging modality for the preoperative staging of patients with head and neck squamous cell cancers, but is not used routinely for the staging of PTC. Nonetheless, CT can characterize the size, shape, appearance, and contrast enhancement pattern of lymph nodes and may be helpful in the prognostication of cervical lymph nodes in patients with PTC. CT features of malignant lymph nodes include size greater than 1.5 cm in levels I or II, greater than 0.8 in the retropharyngeal space, and greater than 1.0 cm in other locations; spherical shape; cystic change; presence of calcifications; and abnormal contrast enhancement.[20–22] In the setting of a known head and neck squamous cell cancer, CT has approximately 80% sensitivity and specificity for the detection of lymph node metastases.[20] There is no established size criterion for metastatic lymph nodes in PTC, however, and the sensitivity of CT may be lower in patients with PTC due to the higher rates of micrometastatic disease, which may not cause a change in the appearance of these lymph nodes on CT. In large retrospective studies evaluating the accuracy of CT in detecting metastatic lymphadenopathy in patients with PTC, CT has a sensitivity of 50% to 67% and specificity of 76% to 91% for detecting metastatic lymph nodes in the central compartment of the neck. Likewise, CT has a sensitivity of 59% to 82% and a specificity of 71% to 100% for detecting metastatic lymph nodes in the lateral compartment in PTC.[21,23,24]

The ATA guidelines on the management of thyroid cancer recommend against the routine use of preoperative imaging studies, such as CT, MRI, or PET, for the initial staging of PTC.[6] In some cases, however, these imaging modalities may play an important role in the preoperative evaluation of the patient. CT has been the most widely studied cross-sectional imaging modality, and its main advantages are that it is not operator dependent and that it generates high-resolution images with the ability to perform multiplanar image reconstructions. Its main limitation is that the iodine load associated with the intravenous contrast given during the scan may reduce RAI uptake for several weeks after administration.[25,26] CT can be particularly helpful in the evaluation and surgical planning for patients with advanced PTC, or those with large, fixed, or substernal cancers. In such cases, CT may accurately demonstrate extension of disease into the mediastinum, invasion into adjacent

structures such as the aerodigestive tract, or reveal lymph node metastases in areas that are poorly assessed by ultrasound (retropharyngeal/retrotracheal space, low-level VI/superior mediastinum).[21,23,27] MRI has not been found to be particularly helpful in the identification of cervical nodal metastases from thyroid cancer due to poor sensitivity and only moderate interobserver agreement.[28] PET scanning is useful for imaging patients with poorly differentiated thyroid cancers, but adds little to the imaging of well-differentiated thyroid cancers.

The ATA and National Comprehensive Cancer Network (NCCN) guidelines recommend comprehensive neck ultrasound for the preoperative staging of PTC.[6,27] High-resolution neck ultrasound has been reported to have sensitivity of 52% to 93% and specificity of 79% to 100% for the detection of abnormal lymph nodes in patients with PTC, in both index and reoperative settings.[17,18,29] Sensitivities vary widely between studies, while specificities are consistently high. Sensitivity is higher for the detection of abnormal lymph nodes in the lateral compartment of the neck compared with the central compartment of the neck, as the assessment of the central neck may be affected by surrounding structures, such as the tracheal air shadow, clavicle, and sternum.[17,29,30] Cervical sonography has several advantages over other imaging modalities. Compared with CT, ultrasound is less costly, does not expose the patient to radiation, can be performed repeatedly in children and pregnant women, is painless and noninvasive, does not require intravenous access, does not generally precipitate claustrophobic reactions, and does not have a maximum weight limit. Limitations of ultrasound include that it is operator dependent and that it may be limited in evaluating lymph nodes in patients with high body mass index or in certain locations, such as the retropharyngeal, paratracheal, or retrotracheal spaces, level VI, and the superior mediastinum.[21,23]

Ultrasound can help characterize a lymph node as benign or malignant based on size, shape, and appearance. Sonographic features of benign lymph nodes include flattened elongated shape, smooth border, and hyperechoic hilum.[19] Sonographic features of malignant lymph nodes include enlarged size, rounded shape, loss of hilar architecture, cystic change, hyperechoic punctate microcalcifications, and hypervascularity.[19,31,32] No single sonographic feature, however, has adequate sensitivity and specificity for the detection of metastatic disease. In a prospective study of 103 suspicious lymph nodes detected on ultrasound in 18 patients who underwent operation for recurrence of differentiated thyroid cancer, Leboulleux and colleagues[32] found that the criterion of long axis greater than 1 cm had only 68% sensitivity and 75% specificity for the detection of a lymph node metastasis. It should be noted that benign reactive lymphadenopathy is frequently encountered in the submental, submandibular, subdigastric, and high jugular regions; consequently, under normal conditions, lymph nodes in these areas may be considerably larger than lymph nodes in the remainder of the lateral neck. In Leboulleux's study as well as another similar prospective study of 350 lymph nodes evaluated in 112 patients with PTC by Rosario and colleagues,[31] loss of fatty hilum had 88% to 100% sensitivity and 29% to 90% specificity, and cystic appearance and hyperechoic punctate calcifications each had 100% specificity but only 11% to 20% and 46% to 50% sensitivity, respectively, for the detection of lymph node metastases.[32]

Image-Guided Needle Biopsy

A definitive diagnosis of malignancy in a cervical lymph node is best obtained by ultrasound-guided FNA biopsy. Cytology from FNA has high sensitivity (73%–86%) and specificity (100%) for the detection of metastatic PTC, but can be limited by nondiagnostic or inadequate samples.[33,34] Measurement of thyroglobulin in the FNA

biopsy aspirate fluid has been developed as an adjunct to the cytologic evaluation of suspicious-appearing cervical lymph nodes. This technique is semiquantitative in that it involves rinsing the needle used for the aspirate into 1 mL of saline and assaying the thyroglobulin level in that fluid by immunoradiometric or chemiluminescent assay.[33] Some reports describe rinsing the needle in thyroglobulin-free serum; however, a study by Frasoldati and colleagues[33] demonstrated that using normal saline as the washout fluid yielded equivalent results. The addition of the aspirate thyroglobulin level to the cytologic assessment can improve the diagnostic sensitivity of FNA to 86% to 100%, and can be diagnostic even when the number of cells is insufficient for standard cytologic analysis.[33,34] Several authors have proposed threshold values which, when exceeded, indicate metastatic thyroid cancer; however, universal agreement has not been achieved. Because it has been recognized that the aspirate thyroglobulin level is correlated to the serum TSH and serum thyroglobulin levels, it may be prudent to obtain all 3 samples in the same setting.[35,36] In one report, an aspirate thyroglobulin greater than 36 ng/mL in a patient with a thyroid gland and greater than 1.7 ng/mL in a patient without a thyroid gland was defined as being indicative of metastasis.[37] However, many studies suggest that much lower thresholds might be more sensitive. In one study, the threshold of 1.0 ng/mL was optimal for making the diagnosis of metastatic PTC with a sensitivity of 93.2% and a specificity of 95.9%.[35] Another investigator used the same thresholds of 1 ng/mL for patients with serum thyroglobulin less than 1 ng/mL and found that the sensitivity and specificity were 93% and 100%, respectively. The same study demonstrated that an aspirate to serum thyroglobulin ratio threshold of 0.5 for patients with a serum thyroglobulin greater than 1 ng/mL had a sensitivity of 98% and specificity of 98% for the detection of metastatic PTC.[36] In another study, an aspirate thyroglobulin threshold value of 0.2 ng/mL had a sensitivity of 100% and specificity of 87.5%.[38]

Although approximately 25% of patients with thyroid cancer have circulating antibodies that interfere with the assays used to detect thyroglobulin, these antithyroglobulin antibodies have not been found to interfere with the detection of thyroglobulin in FNA aspirate specimens.[37] Clearly, thyroglobulin only has utility as a tumor marker in patients with differentiated thyroid cancers of follicular cell origin. Consequently, an important limitation of this technique is in the evaluation of lymph node metastases from medullary thyroid cancer, or poorly differentiated or undifferentiated thyroid cancer. Thyroglobulin assay also has no role in the prognostication of thyroid nodules.

Implications for Surgical Planning

Systematic compartment-oriented dissection is indicated when cervical nodal metastases are identified. Formal clearance of the nodal basin has been shown to improve both recurrence rates and survival.[39] Selective lymph node removal ("berry picking") is not recommended, because this leaves behind lymph nodes that are at risk for developing recurrent disease, which would then be more difficult to remove in a reoperative field.

INTRAOPERATIVE ASSESSMENT OF LYMPH NODE STATUS

The role of prophylactic CND during thyroidectomy for PTC remains controversial. Some surgeons perform prophylactic CND routinely; some surgeons perform prophylactic CND only if there is metastatic disease in the lateral compartment, and some surgeons rely on intraoperative assessment of the lymph nodes in the central compartment and perform CND selectively. In this section, the methods of intraoperative assessment of the central and lateral compartments are described.

Intraoperative Inspection, Palpation, and Frozen Section

Many strategies exist for the intraoperative assessment of central compartment lymph nodes, including inspection and palpation and intraoperative frozen section. The accuracy of intraoperative inspection and palpation to assess the status of the central compartment lymph nodes was examined in a prospective study of 47 patients with PTC who underwent thyroidectomy with routine prophylactic CND. This study demonstrated poor sensitivity (49%–59%) and specificity (67%–83%) of inspection and palpation in identifying metastatic central neck lymph nodes regardless of level of surgeon experience (senior surgeon, fellow, or resident).[40] Some surgeons use the results of intraoperative frozen section of a central neck lymph node to decide on the necessity or extent of formal CND. The most common lymph nodes evaluated in this manner are the prelaryngeal, precricoid, or pretracheal nodes.

The Delphian lymph node is the eponymous term for a precricoid lymph node with potential for harboring metastatic PTC. The precricoid lymph nodes have been studied as predictors of advanced disease in thyroid cancer. Although the significance of a positive node is controversial, large, retrospective studies examining this issue have found that 20% to 25% of patients with PTC who had precricoid lymph nodes examined had a positive Delphian lymph node. Furthermore, a positive Delphian lymph node was associated with larger primary tumor size, multicentric PTC, extrathyroidal extension, lymphovascular invasion, and more nodal disease.[41–43] A positive Delphian node has also been found to predict additional central neck lymph node metastases with a sensitivity and specificity of 41% to 100% and 37% to 95%, respectively, and predicts lateral neck lymph node metastases with a sensitivity and specificity of 50% to 85% and 76% to 88%, respectively.[41–43] Because of the relationship between the Delphian lymph node and the status of the remainder of the central compartment, some surgeons will perform a CND whenever a Delphian node is identified. Caution must be exercised in interpreting these data, however, because not all studies examining this issue performed CND routinely, and therefore, the true negative predictive value of a benign precricoid lymph node is not known.

Intraoperative Assessment of the Lateral Compartments

Although the performance of routine prophylactic CND is controversial, there is little controversy regarding prophylactic lateral compartment lymph node dissection for PTC. Prophylactic dissection of the lateral compartments is not indicated for PTC. The sensitivity and specificity of high-resolution ultrasound for the evaluation of the lateral compartment of the neck are sufficient to rule out clinically significant nodal disease in the lateral compartment, and therefore, it is not necessary to explore the lateral compartment of the neck intraoperatively if the preoperative ultrasound is normal. Lateral compartment lymph node dissection is recommended only for therapeutic purposes, such as clinically apparent or biopsy-proven lymph node metastases.[6,27]

As an adjunct, some surgeons advocate intraoperative ultrasound after the completion of the lateral neck dissection to assess for residual disease. A prospective study of intraoperative ultrasound after lateral neck dissection in 25 patients with thyroid cancer (23 PTC, 2 medullary thyroid cancer) demonstrated that intraoperative ultrasound identified residual abnormal lymph nodes in 16% of patients.[44] Moreover, a retrospective study of 101 patients with PTC showed a statistically significant difference in the rate of residual/recurrent tumor in patients who underwent surgery with or without ultrasound guidance (2 vs 12%, $P<.05$).[45]

COMPARTMENTAL ANATOMY

Definition of the Central Neck Compartment

The first broadly accepted contemporary report to attempt to standardize CND terminology was by Robbins and colleagues[46] in 1991. In 2009, the ATA convened a multidisciplinary panel of experts and developed a consensus statement on the terminology and classification of CND for thyroid cancer.[1] The definitions from this consensus guideline are the most widely accepted standards and will thus be referenced in the following anatomic and procedural descriptions.

The nomenclature used to describe the neck nodal basins was originally developed by the Memorial Sloan-Kettering Head and Neck Surgery Service and modified and updated by the American Academy of Otolaryngology–Head and Neck Surgery.[47] The neck is divided into 7 node-bearing levels, and each is referred to by Roman numeral. Six sublevels have been described and are designated by the letters A or B. The central neck compartment (also known as the anterior compartment) is designated level VI. It is bounded by the hyoid bone superiorly, the suprasternal notch inferiorly, the common carotid artery (or lateral border of the sternohyoid muscle) laterally, the deep layer of the deep cervical fascia posteriorly, and the superficial layer of the deep cervical fascia anteriorly (**Fig. 1**, **Table 1**). Included in level VI are the precricoid

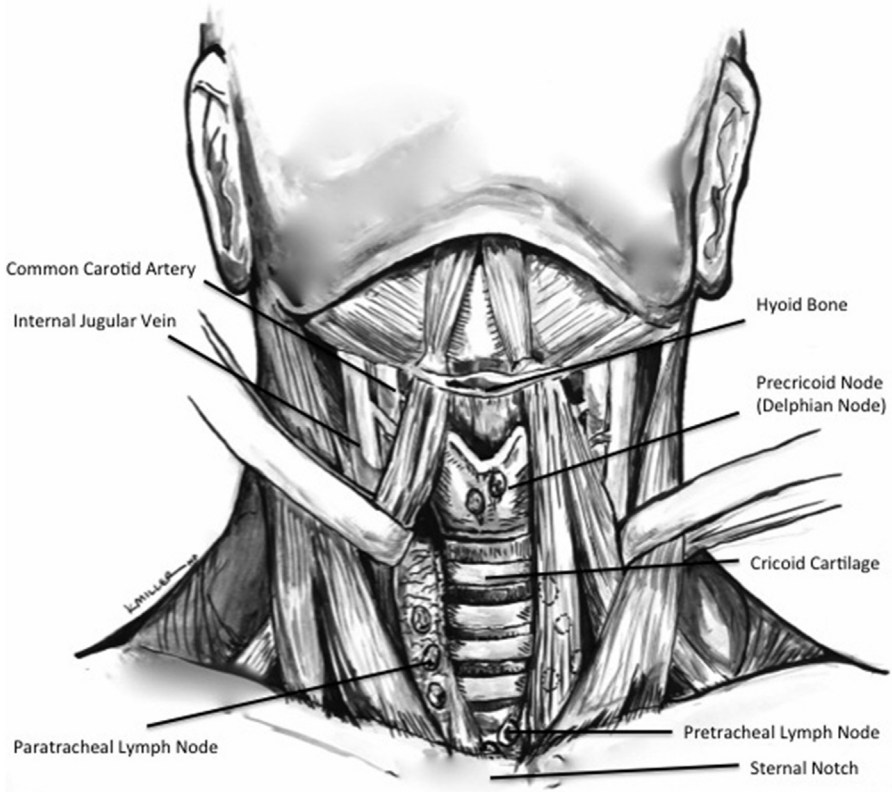

Fig. 1. The central neck compartment. It is bounded by the hyoid bone superiorly, the suprasternal notch inferiorly, the common carotid artery laterally, the deep layer of the deep cervical fascia posteriorly, and the superficial layer of the deep cervical fascia anteriorly. Lymph nodes in the precricoid and paratracheal areas are illustrated.

Table 1
Anatomic neck levels

Level	Anatomic Designation	Boundaries	Sublevel Designation/ Notable Contents
I	Submental (IA)	Triangular boundary from the anterior belly of the digastric muscles and hyoid bone	IA
	Submandibular (IB)	Anterior belly of digastric muscle to stylohyoid muscle to the body of the mandible. Includes: submandibular gland	IB Marginal mandibular nerve
II	Upper jugular	Upper third of the IJV and CN XI (superior) to the level of the hyoid bone (inferior), the stylohyoid muscle (anterior/ medial), and the posterior border of the SCM (posterior/lateral)	IIA: LN-bearing tissue anterior (medial) to CN XI IIB: LN-bearing tissue posterior (lateral) to CN XI Marginal mandibular nerve, IJV, CN XI, phrenic nerve, vagus nerve, cervical sympathetic trunk
III	Middle jugular	Middle third of IJV from inferior border of hyoid bone (superior) to inferior border of cricoid cartilage (inferior), lateral border of SHM (anterior/medial), and posterior border of SCM (posterior/lateral)	IJV, CN XI, phrenic nerve, vagus nerve, cervical sympathetic trunk, brachial plexus
IV	Lower jugular	Lower third of IJV from inferior border of cricoid cartilage (superior) to clavicle (inferior), lateral border of SHM (anterior/medial), and posterior border of SCM (posterior/lateral)	Virchow' node, IJV, CN XI, phrenic nerve, vagus nerve, cervical sympathetic trunk, brachial plexus, thoracic duct/right neck cervical lymphatic duct
V	Posterior triangle/ supraclavicular	Convergence of SCM and trapezius (superior) to clavicle (inferior), posterior border of SCM (anterior/ medial), anterior border of trapezius (posterior/lateral).	VA[a]: (superior) lymph nodes along CN XI VB[a]: (inferior) transverse cervical and supraclavicular lymph nodes
VI	Anterior (central) compartment	Hyoid bone (superior) to suprasternal notch (inferior) to common carotid arteries (lateral)	Delphian (precricoid) node, pretracheal, and paratracheal lymph nodes along the RLNs

Abbreviation: SHM, sternohyoid muscle.

[a] VA and VB are separated by a horizontal plane marking the inferior border of the anterior arch of the cricoid cartilage.

Adapted from 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(7):751–8; and Ferris R, Goldenberg D, Haymart MR, et al. American thyroid association consensus review of the anatomy, terminology and rationale for lateral neck dissection in differentiated thyroid cancer. Thyroid 2012;22(5):501–8.

lymph nodes, pretracheal lymph nodes, and the paratracheal lymph nodes both anterior and posterior to the RLNs; these 3 lymph node packets are the most commonly involved central compartment lymph nodes in PTC. The ATA consensus statement on CND includes level VII in the definition of the central neck compartment, which is bounded superiorly by the suprasternal notch, and inferiorly by the innominate artery, and contains lymph nodes and thymic tissue.[1]

Definition of the Lateral Neck Compartments

In 2012, the ATA published a consensus statement regarding the anatomy, terminology, and rationale for lateral neck dissection in differentiated thyroid cancer.[48] The important anatomic structures located within each level are enumerated in **Table 1** and are discussed in the section on technique of lateral neck dissection.

Roman numerals I through V are used to define the lateral neck lymph node levels and sublevels (**Fig. 2**; see **Table 1**). Level I includes the submandibular and submental lymph nodes. Level I is divided into sublevels IA and IB. Level IA (submental) nodes are located in the midline between the anterior bellies of the digastric muscles and the hyoid bone. Level IB (submandibular) nodes are located in a triangular field bounded

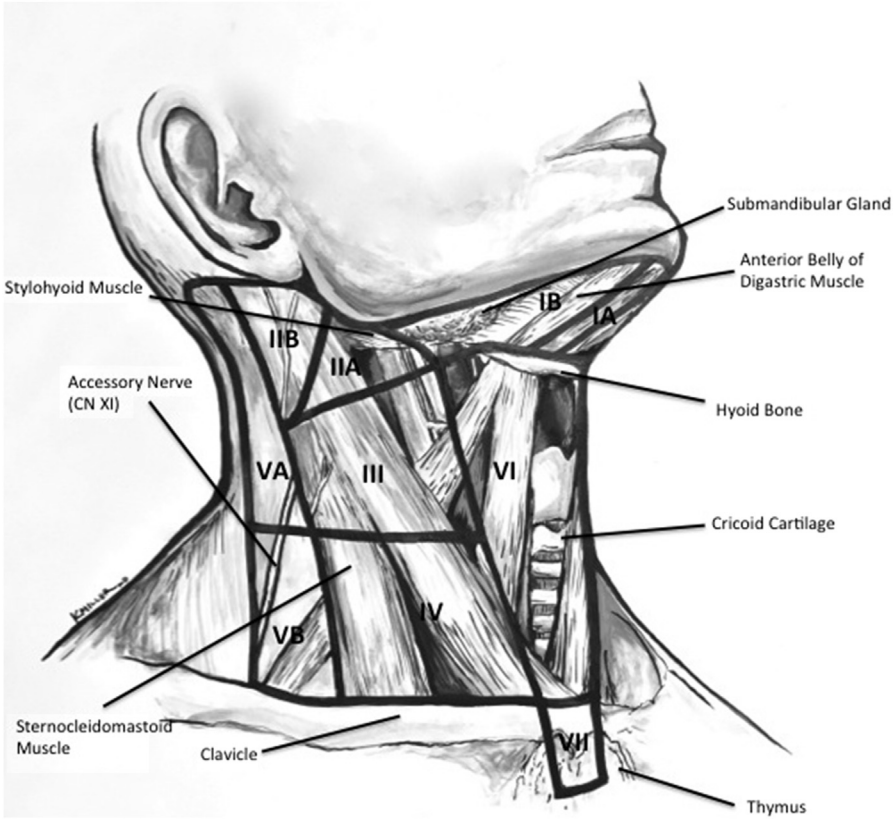

Fig. 2. The neck is divided into 7 node-bearing levels, and each is referred to by Roman numeral. Six sublevels have been described and are designated by the letters A or B. Levels I–V define the lateral neck. The central compartment is designated as level VI, and the region between the suprasternal notch and innominate is level VII.

superiorly by the body of the mandible, posteriorly by the stylohyoid muscle, and anteriorly by the anterior belly of the digastric muscle. Level IB contains the submandibular gland and associated lymph node–bearing tissue.

In aggregate, levels II, III, and IV describe the lymph node–bearing tissue in the quadrangle bounded superiorly by the skull base, inferiorly by the subclavian vein, anteromedially by the lateral border of the sternohyoid muscle, and laterally by the posterior border of the sternocleidomastoid muscle (SCM). Level II (upper jugular) lymph nodes are located along the superior third of the internal jugular vein (IJV) from the skull base superiorly to the hyoid bone inferiorly. Level II contains the jugulodigastric lymph nodes and the proximal portion of cranial nerve (CN) XI. The oblique course of this nerve divides this compartment into level IIA (anterior and inferior to CN XI) and level IIB (posterior and superior to CN XI). Level III (middle jugular) lymph nodes lie along the IJV extending from the lower body of the hyoid bone superiorly to the lower margin of the cricoid cartilage inferiorly. Level IV (lower jugular) lymph nodes are located in the region bordered by the lower margin of the cricoid cartilage superiorly to the level of the subclavian vein inferiorly.

Level V (posterior triangle) lymph nodes are found in a triangular-shaped compartment bounded by the posterior border of the SCM anteriorly, the anterior border of the trapezius muscle posteriorly, the subclavian vein inferiorly, and the apex of where the SCM and trapezius muscles meet superiorly. Level V is also divided into sublevel VA (superior) and VB (inferior) by a horizontal plane at the inferior border of the cricoid cartilage.

TECHNIQUE OF CENTRAL NECK DISSECTION

Timing and Indications for Central Neck Dissection

The efficacy of therapeutic CND is well established and is considered standard practice for patients with resectable lymph node metastases that are known at the time of the operation. The role of prophylactic CND is more controversial because there is a higher risk of complications and there are conflicting data on the impact of prophylactic CND on recurrence and survival.

It is well-established that a formal compartment-oriented dissection including the prelaryngeal, pretracheal, and paratracheal lymph nodes should be performed when nodal metastases from thyroid cancer are clinically evident at the index operation. The practice of “berry picking” only clinically apparent lymph node metastases is an oncologically inadequate operation and may be associated with higher recurrence rates and morbidity related to reoperation after recurrence.[1] The practice of “berry picking” central compartment lymph nodes is not synonymous with a selective, compartment-oriented dissection and is eschewed by most endocrine surgeons.

CND is most often performed at the time of the index thyroid operation. CND can be performed en bloc with the thyroidectomy specimen[49] or the nodal packet may be resected as a separate specimen. At the authors’ institution, they begin with resection of the precricoid (Delphian) lymph node packet as part of the exposure of the thyroid gland. Frozen section analysis is used in cases where the clinical information gained might alter the surgical approach. A standard extracapsular total or near-total thyroidectomy then proceeds in standard fashion without division of the isthmus.

Surgical Technique of Central Neck Dissection

Dissection of the central compartment begins with a careful inspection and palpation of the dissection field in order to determine the location and viability of the parathyroid glands, the anatomic relationship between the RLN and the inferior thyroid artery, and if there is clinical evidence of metastatic lymphadenopathy.

Before the compartmental dissection, any parathyroid gland that has been devascularized should be autotransplanted. Because inspection of the parathyroid gland is notoriously inaccurate in determining viability, many experts recommend piercing or cutting the capsule of the gland to determine if there is continued perfusion, as evidenced by the presence of brisk bleeding. The authors advocate liberal use of autotransplantation of any parathyroid gland in which ischemia is suspected, because this may prevent or significantly mitigate the risk of permanent postoperative hypoparathyroidism. Following the CND, parathyroid glands remaining in situ are again examined for evidence of ischemia and autotransplanted if necessary. The inferior glands are at highest risk for devascularization and are routinely autotransplanted by some experts.

The RLN must always be identified and traced from its insertion through its entire course as it passes caudally through the central neck compartment. Full visualization of the RLN is maintained throughout the dissection. Atraumatic technique with only gentle manipulation and minimal traction of the nearby tissues should be used during dissection along the RLN. When bulky lymphadenopathy exists, the position of the RLN may be displaced by the adenopathy; this is particularly true on the right side, where adenopathy may be located deep to the RLN.

The paratracheal lymph node packet is removed as one specimen. The dissection is usually performed in a cephalad to caudad manner, removing all the node-bearing fibrofatty tissue from the level of the hyoid bone superiorly down to the innominate artery inferiorly. The width of the dissection field extends from the carotid artery laterally to the anterior midpoint of the trachea medially. The pretracheal lymph nodes inferior to the thyroid gland should always be included within the dissection specimen. Thymectomy is not necessary during CND.[50] The dissection specimen should be clearly labeled and oriented to site and side. The operative note should clearly describe the levels included in the dissection and their borders, the disposition of the parathyroid glands, and if any anatomic variants were identified.

Some investigators have reported that very little node-bearing tissue is ever found above the level of the insertion of the RLN and have questioned the necessity of extending the paratracheal dissection field above the level RLN insertion. In one study of 31 paratracheal neck dissections for thyroid cancer in 27 patients, no lymph nodes, lymphatic tissue, or metastatic disease was identified in any upper paratracheal specimens retrieved above the level of the cricoid cartilage.[51] All benign and metastatic lymph nodes were located in the lower paratracheal specimens. Accordingly, it may be reasonable to use the level of the cricoid cartilage as the superior border of the CND in the absence of clinically apparent or biopsy-proven metastatic disease in the region between the cricoid and the hyoid bone. Furthermore, limiting the superior extent of the CND to the level of the cricoid might decrease the likelihood of devascularizing the superior parathyroid glands while not compromising the oncologic outcome of the operation.

Complications of Central Neck Dissection

Complications of CND are mainly related to injury to the RLN and external branch of the superior laryngeal nerve, and devascularization of the parathyroid glands. As described above, permanent postoperative hypoparathyroidism rates from CND can be as high as nearly 20%.[15] In experienced hands, the incidence of permanent RLN injury should be low, on the order of 1% to 6%.[52] Meticulous hemostatic dissection technique and operative experience are significant contributors to minimizing these complications.

TECHNIQUE OF LATERAL NECK DISSECTION

Timing and Indications for Lateral Neck Dissection

Dissection of the lateral cervical compartments is performed only for therapeutic purposes when there is evidence of nodal metastatic disease from PTC.[48] Unlike the central compartment, metastatic disease in the lateral compartment is usually demonstrable with standard sonographic imaging. Because it is possible to accurately survey the lateral neck for clinically significant nodal disease, prophylactic lateral neck dissection is not used for differentiated thyroid cancer. This more cautious approach to lateral neck dissection is due to the fact that the lateral neck is undisturbed during a thyroid operation, and there are significant risks to opening and dissecting the lateral compartment, including greater cosmetic deformity, chronic neck pain or numbness, chyle leak or fistula, and cranial nerve injury.

The controversial topic in lateral neck dissection for differentiated thyroid cancer is the extent of the dissection. The classic radical neck dissection described by Crile, which included sacrifice of the SCM, IJV, and CN XI, is rarely required for PTC and, instead, modified or selective neck dissections are performed wherein one or more of these structures are preserved (see **Table 1**). Because level I is rarely involved by metastatic thyroid cancer, this level is not usually included in the dissection. There is controversy regarding the inclusion or exclusion of levels IIB and VA. Dissection in levels II and V places CN XI at risk of injury. The ATA consensus statement on the rationale for lateral neck dissection leaves dissection of IIB and VA to the discretion of the surgeon and states that IIB dissection is not required unless there are suspicious lymph nodes in that region. Similarly, dissection of level VA should be reserved for cases where sonographic evaluation reveals metastatic disease in that sublevel. The ATA consensus statement recommends that selective lateral neck dissection for differentiated thyroid cancer metastases include levels IIA, III, IV, and VB. “Berry picking” is not recommended in the lateral neck, or any cervical compartment for metastatic thyroid cancer.[48]

General Principles of Incision and Exposure

Multiple incisions have been described for exposure of the lateral compartment. A long, low Kocher incision with a vertical extension along the posterior border of the SCM up to the mastoid process offers excellent exposure to all levels of the lateral neck. The lateral compartments can also be approached through just a long Kocher incision, which allows access to all but the highest level II lymph nodes. Another alternative approach is a parallel counterincision placed more cephalad and lateral to the Kocher incision.

Regardless of the incision used, subplatysmal flaps are raised with care taken to stay superficial to the external jugular vein. This site is the first point at which the great auricular nerve can be injured. The great auricular nerve arises from the second and third cervical nerve rami, curves around the posterior border of the SCM, and then ascends toward the ear on the anterior surface of the SCM, parallel to the external jugular vein. Injury to the great auricular nerve is one of the most common complications of lateral node dissection (LND), causing pain or numbness of the ear, which is often significantly bothersome to the patient. The marginal mandibular branch of the facial nerve (CN VII) can be injured during the dissection as well. The marginal mandibular branch runs along the inferior border of the mandible anterior to the facial artery and vein. Attention should be paid to retraction of the skin flaps in this area because compression of the marginal mandibular branch of the facial nerve can lead to palsy of the ipsilateral circumoral musculature and may be caused by retraction of the superior skin flap alone.

The SCM can almost always be preserved during a selective or modified radical neck dissection. The SCM is mobilized by sharply dissecting the muscle free of the underlying deep cervical fascia. If necessary, the SCM can be nearly circumferentially dissected, and encircled with a Penrose drain to aid with retraction and exposure. Branches of the transverse cervical cutaneous nerves are divided while mobilizing the SCM, which causes hypesthesia of the skin of the neck.

To complete the exposure of the lateral compartments, the omohyoid muscle is mobilized and may be divided, and the second layer of deep cervical fascia is incised in order to expose the lymph node–bearing fatty tissue packet.

The dissection of the lymph node packet can be performed by starting in level IV and continuing in a superomedial direction, or by starting in level II and then continuing in an inferolateral direction. For simplicity, the technique of caudad to cephalad dissection beginning in level IV is described.

Level IV Dissection

Level IV is the region bordered by a line at the level of the cricoid cartilage superiorly, the subclavian vein inferiorly, the sternohyoid muscle anteromedially, and the posterior edge of the SCM posterolaterally. The cervical lymphatics coursing between the level IV nodes and the thoracic duct should be identified at the junction of the IJV and the subclavian vein and ligated individually with a painstaking delicate technique. In the authors' experience, clips are not usually adequate to secure these lymphatics. The thoracic duct itself does not usually need to be ligated. The thoracic duct usually drains into the posterior left subclavian vein just proximal to its confluence with the left IJV. The right thoracic duct has a similar course in the neck, but is much smaller than the left. A Valsalva maneuver, or compression of the surrounding tissue, can distend the duct and lymphatic tributaries and aid with identification. If there is suspicion that the thoracic duct has been injured, it should be ligated to prevent a chylous leak or fistula, which can be difficult to manage and may lead to life-threatening complications, such as fluid and electrolyte disturbances, hypoalbuminemia, coagulopathy, immunoglobulin deficiency, wound infection, malnutrition, and chylothorax. When dissecting level IV, it should be kept in mind that lymph nodes lie in the soft tissue posterior to the IJV and retraction and possibly circumferential dissection of the IJV may be required in order to obtain an adequate dissection in this region. The deep border of the dissection of this lymph node packet should be superficial to the third layer of deep cervical fascia and will lessen the risk of injury to the phrenic nerve, which courses along the anterior surface of the anterior scalene muscle, and the brachial plexus, which emanates between the anterior and medial scalene muscles. Once the cervical lymphatics are ligated, the soft tissue packet should be sharply dissected off of the scalenes. The vagus nerve is quite large and should be easily identified and preserved along the medial margin of the dissection. Likewise, the phrenic nerve should be easily identified and preserved along the posterior margin of the dissection. The transverse cervical artery and vein are also preserved along the posterior border of the dissection field. The subclavian vein should be clearly visible at the inferior border of the dissection field, and care should be taken to avoid injury to the subclavian vessels or pleura in this region.

Level V Dissection

Level V is also known as the posterior triangle and is bounded by the posterior border of the SCM anteriorly, the trapezius muscle posteriorly, the subclavian vein inferiorly, and the apex of where the SCM and trapezius muscles meet superiorly. Level V is divided into sublevels VA (superior) and VB (inferior) by a horizontal plane extending

laterally from the cricoid cartilage. Level VA contains the lymph nodes along the distal portion of the spinal accessory nerve (CN XI). Level VB contains the transverse cervical vessels and associated lymph nodes as well as the supraclavicular lymph nodes.

If only level VB is to be dissected, then the lymph node–bearing fatty tissue along the transverse cervical vessels and in the supraclavicular region should be removed en bloc with the specimen. Care should be taken to identify CN XI and avoid injury to it even if the level VA lymph node packet is not included in the dissection.

If level VA is included, the anterior border of the trapezius muscle (the posterior-lateral border of level V) is identified and incised approximately 1 cm anterior to the border of the muscle. This incision will allow for easier and safer identification of CN XI as it inserts into the trapezius muscle. CN XI will be found coursing over the levator scapulae muscle and will be approximately parallel to the trapezius muscle itself. Much of the lymph node–bearing tissue in level VB (and level II) will be around CN XI, and thus, it must be clearly identified and carefully manipulated. As CN XI is dissected in a superomedial direction toward the upper posterior border of the SCM, a plexus of cervical nerve branches will be encountered at the posterior border of the SCM. The great auricular nerve can be found here just inferior to CN XI as it courses underneath the SCM. Often referred to as Erb point,[53] this plexus is a useful landmark to identify CN XI in a more superior and medial location.

Level III Dissection

Level III extends from the superior border of level IV to the hyoid bone. The medial and lateral borders are the same as level IV. Dissection of the node-bearing fibrofatty tissue packet should continue sharply over the scalene muscles and along the IJV through level III, with continued care taken to directly visualize and avoid injury to the phrenic and vagus nerves. Cervical sensory nerve fibers should be preserved if preservation will not compromise the oncologic outcome of the operation. The common trunk of the supraclavicular nerve can be identified beneath the SCM and should be preserved to avoid lateral neck, shoulder, and anterior chest numbness postoperatively. Staying superficial to the third layer of deep cervical fascia will lessen the likelihood of injury to all of the nerve structures except for the vagus nerve. The cervical sensory plexus can be used as a landmark that the superior portion of the dissection has almost been completed.

Level II Dissection

Level II extends from the superior border of level III to the skull base superiorly. The anteromedial border is the stylohyoid muscle and the lateral border is the posterior edge of the SCM. CN XI divides level II into level IIA and level IIB. If only level IIA is to be dissected, then identification of CN XI will represent the posterosuperior limit of the dissection, and the dissection specimen is sharply dissected from the IJV and CN XI and truncated at the apex of these 2 structures. If level IIB is to be included, the dissection should continue to the level of the posterior belly of the digastric muscle.

Once the dissection has been completed, the dissection specimen should be clearly labeled and oriented. The operative procedure note should clearly describe the levels included in the dissection and the borders. Drain placement is at the discretion of the surgeon.

Complications of Lateral Neck Dissection

The common and major complications of lateral neck dissection have been described above in relation to the steps of the procedure. In summary, the most common

complications are sensory deficits related to injury to the great auricular nerve or cervical sensory nerve fibers. Major, avoidable complications include chylous leak or chylothorax related to unrecognized injuries of the thoracic duct or other major lymphatic branches, shoulder weakness resulting from injury to CN XI, lip droop related to marginal mandibular nerve injury, and symptoms related to injuries to the other relevant nerves (phrenic, vagus, hypoglossal). Rough handling of major vascular structures such as the carotid artery and IJV can lead to vascular injuries, bleeding, embolic stroke (including air embolism), and carotid dissection. Clear visualization of the nervous, lymphatic, and vascular structures, delicate dissection technique, and meticulous hemostasis will minimize complications.

IMPACT OF NODAL CLEARANCE ON RECURRENCE AND SURVIVAL

Impact of Nodal Basin Clearance on Recurrence and Survival

Regional lymph node metastases at the time of presentation are relatively common in PTC.[17,54] There has been a long-standing controversy over the clinical significance of lymph node metastases in PTC in low-risk patients. However, the controversy over the significance of lymph node metastases in high-risk patients is less questioned. Multiple studies have shown that lymph node metastases are an independent predictor of poor outcome. Although the overall survival differences may be slight (82% for node-negative disease vs 79% for node-positive disease at 14 years), they are statistically significant,[1,55] and there is also an increased risk of recurrence in patients with lymph node metastases in PTC. Although there are fewer patients presenting with lateral neck metastases, there is evidence that lateral neck metastases are associated with a poorer outcome, namely increased risk of recurrence and possibly decreased survival.[17,56,57]

Clearance of the affected nodal basins of metastatic disease may offer other benefits beyond a small improvement in survival. First of all is the reduction in recurrence after CND or LND. Although there is a paucity of randomized controlled or other matched control studies in the literature, multiple studies have shown recurrence rates on the order of 10% after total thyroidectomy with CND in patients with or without known preoperative central neck lymph node metastases.[58,59] Multiple studies indicate that CND or LND can successfully control persistent or recurrent disease as reflected by meaningful decreases in serum thyroglobulin levels, with some studies finding that a substantial number of patients can have undetectable preablative thyroglobulin levels after surgery.[16,60] Recurrence after CND (and in patients who have not undergone CND) tends to occur in the lateral neck lymph node basins, particularly levels III and IV, rather than in the central neck compartment.[58,59] Prognostic factors for local recurrence include increasing number of metastatic lymph nodes and extracapsular lymph node extension on pathologic analysis.[1]

Prophylactic CND remains controversial because multiple studies indicate that the incidence of both temporary[61–63] and permanent[15,58] hypoparathyroidism is increased with CND. Furthermore, CND is associated with a higher incidence of RLN injury, most of which is temporary.[58,61,63] Multiple studies have shown that complication rates are lower in operations for thyroid cancer, including CND and LND, when the procedure is performed by a high-volume thyroid surgeon.[6] Therefore, the ATA consensus statements recommend that the surgeon's skill level be considered when making the decision whether a patient who requires CND or LND should remain in that surgeon's hands or be referred to a high-volume thyroid surgery center.[1,6,64]

RECURRENT NODAL METASTASES

A Comparison of Surveillance Strategies Recommended by the American Thyroid Association and National Comprehensive Cancer Network

Most patients who have been treated for PTC undergo long-term surveillance. The primary goals of long-term follow-up are the early and accurate detection of recurrent disease and the longitudinal monitoring of thyroxine replacement and TSH.[6] The ATA recommends that following total thyroidectomy, serum thyroglobulin and anti-thyroglobulin antibodies should be measured every 6 to 12 months in the same laboratory using the same assay. Rising thyroglobulin values over time are considered suspicious for recurrence. Periodic neck ultrasound is also recommended. In low-risk patients with no detectable tumor, the ATA recommends that a TSH-stimulated thyroglobulin be measured 12 months after radioiodine ablation to verify that there is no recurrent or persistent disease. For those patients who have no detectable stimulated thyroglobulin, the ATA recommends yearly clinical examination and unstimulated thyroglobulin.[6]

The NCCN guidelines recommend physical examination, TSH, thyroglobulin, and antithyroglobulin antibodies at 6 and 12 months and then annually thereafter if the patient is considered disease-free. Similar to the ATA recommendations, neck ultrasound is also recommended on a periodic basis by the NCCN.[27] The NCCN recommends that stimulated thyroglobulin be measured in patients who underwent radioiodine ablation and in those who have undetectable unstimulated thyroglobulin and no antithyroglobulin antibodies. Furthermore, TSH-stimulated radioiodine scanning should be considered for patients with detectable stimulated or unstimulated thyroglobulin, sonographic evidence of persistent or recurrent disease, rising antithyroglobulin antibody titer, or with radioiodine avid metastases, or in patients considered high risk. In patients with high-risk radioiodine avid tumors, especially those with detectable thyroglobulin, distant metastases, or extension into the soft tissues, the NCCN recommends radioiodine imaging every 1 to 2 years.

Ultrasound and Serum Thyroglobulin Measurement Are Highly Accurate at Detecting Recurrence

Sonographic cervical imaging has been found to be more accurate than radioiodine scanning for the detection of recurrent or persistent disease. In addition, the measurement of stimulated thyroglobulin has been found to be complementary to cervical sonography, increasing the accuracy of the surveillance strategy. In a series of 340 consecutive patients with differentiated thyroid cancer who underwent near-total thyroidectomy and radioiodine ablation, the combination of stimulated thyroglobulin and cervical sonography had the greatest accuracy at detecting persistent disease (sensitivity 96.3% and negative predictive value of 99.5%).[65] In a series of 80 consecutive patients with PTC microcarcinoma who underwent near-total thyroidectomy but did not undergo radioiodine ablation, cervical ultrasound was found to be more accurate than radioiodine scanning for the detection of persistent disease.[66] Although radioiodine scanning showed no pathologic uptake in any patient, cervical sonography identified nodal metastases in patients with or without detectable thyroglobulin. The authors concluded that in this low-risk population, ultrasound should be the primary screening modality, stimulated thyroglobulin was indicative of remnant normal thyroid tissue, and radioiodine scanning was not valuable for the detection of persistent disease. These findings support the recommendations from the ATA and NCCN that surveillance be conducted primarily via cervical sonography and measurement of serum thyroglobulin, and that radioiodine scanning be reserved for higher-risk patients with radioiodine avid disease.

Surveillance Frequently Reveals Recurrent or Persistent Disease

The ATA defines absence of disease using 3 criteria: no clinically detectable tumor recurrence, no evidence of recurrence on imaging, and undetectable stimulated and unstimulated thyroglobulin (when interfering antibodies are absent).[6] Unfortunately, because of the stringency of these criteria and the high sensitivity of current imaging modalities and methods for detection of thyroglobulin, many patients will not satisfy these criteria, especially if they have not undergone radioiodine ablation of the thyroid remnant.

The recurrence rate is relatively high in PTC and is related to the sensitivity of the tests used to conduct surveillance, the biology of PTC, and the initial treatment. Biologic variables that impact recurrence include the number of positive nodes, tumor burden, and the presence of extranodal extension.[2,67–70] Patients who are pathologically N0 are at lowest risk of recurrence. Patients with microscopic N1a disease are at an intermediate risk.[71] Patients with clinically positive or macroscopic N1 disease are at high risk. Patients with extranodal extension are at the highest risk. A recent meta-analysis stratified patients into risk groups based on the number of positive nodes. They found that the risk of recurrence was 4% with fewer than 5 positive nodes, 19% with more than 5 positive nodes, and 24% with clinically apparent nodes with extranodal extension.[2]

For patients with stable, low levels of detectable thyroglobulin whose disease cannot be detected on imaging, it is considered acceptable to continue active surveillance. For patients with recurrent or persistent disease that can be imaged, surgical resection is the preferred treatment.

Recommendations for Surveillance of the Lateral Neck

Metastases to the lateral compartment are common and are therefore one of the focal points of surveillance for patients with PTC. Ultrasound is the imaging modality of choice for the detection of lateral neck nodal metastases when performing surveillance. Sonographic surveillance of the lateral neck should be performed periodically depending on the likelihood of recurrent or persistent disease. The entire neck should be imaged (levels I through VII) by a sonographer experienced in surveillance of PTC. Special attention should be paid to the nodal basins ipsilateral to the primary tumor, because they are the most likely a location for recurrent or persistent disease.

Establishing the Diagnosis of Recurrent or Persistent Disease

The ATA published a consensus statement on the anatomy, terminology, and indications for lateral neck dissection in PTC.[64] They concluded that the initial modality should be ultrasound and that FNA of suspicious lymph nodes is the best way to establish the diagnosis of nodal metastases. In addition, the ATA Statement on Preoperative Imaging for Thyroid Cancer Surgery recommends that suspicious masses or lymph nodes be biopsied before a reoperation for persistent or recurrent disease.[72] Ultrasound has been shown to accurately detect the presence of central and lateral nodal metastases and has been found to alter the extent of surgery in up to 40% of index and reoperative cases.[18] Therefore, in the course of surveillance for PTC, sonographically suspicious lymph nodes should be interrogated with FNA biopsy. The aspirate may be assayed for thyroglobulin in order to increase the sensitivity and specificity for metastatic disease.

Is Positive Imaging Alone Ever Sufficient?

The 2009 ATA guidelines state that lateral neck dissection should not be performed prophylactically, but should be performed as a “therapeutic intervention for known

disease."[6] This statement raises the question of whether imaging alone would be sufficient to confirm the presence of metastatic disease. In some cases, the location of the lymph node may not be amenable to needle biopsy or patients may refuse needle biopsy. The ATA Subcommittee on Lateral Neck Dissection indicated in their recent review that lateral neck lymph nodes not amenable to FNA biopsy may be followed for growth by serial imaging. If the inaccessible node grows during follow-up, an open biopsy should be performed with conversion to formal lateral neck dissection if the frozen section is positive. The ATA Statement on Preoperative Imaging for Thyroid Cancer Surgery states that preoperative FNA may not be required under the following 2 conditions: "(a) abnormal lymph nodes are inaccessible or anatomically risky to biopsy, usually due to their location with respect to major vessels, and (b) unequivocally abnormal lymph nodes are found on imaging and surgery would be recommended regardless of FNA results."[72]

The Treatment of Recurrent or Persistent Nodal Disease

The management of low-volume recurrent or persistent nodal metastases is controversial. The 2 most reasonable treatment options are surgical resection and active surveillance.[73] The preferred treatment for locoregional recurrence, according to the NCCN, is surgical resection. Radioiodine therapy and external beam radiotherapy are alternative treatment options for tumors that either do or do not concentrate radioiodine, respectively. The NCCN recommends that clinically significant nodal metastases in a previously undissected nodal basin be treated with a formal compartmental clearance of the nodal basin involved. For recurrence in the central neck in a patient with no prior CND, a complete dissection of that ipsilateral central compartment is indicated. Likewise, recurrence discovered in a previously undissected lateral compartment should be treated with a formal modified radical neck dissection, including levels II, III, IV, and VB. Conversely, recurrence in a previously dissected central or lateral compartment should be adequately treated with a focused dissection of the region containing the nodal metastasis.[27]

The 2009 ATA guidelines for DTC state that the "preferred hierarchy of treatment for metastatic disease" is surgical resection for potentially curable patients with locoregional disease, radioiodine therapy for patients with iodine-avid disease, external beam radiation therapy, active surveillance in patients with stable or slowly progressive asymptomatic disease, and experimental trials.[6] They also indicate that more nontraditional management may also benefit selected patients, such as ethanol ablation, radiofrequency ablation, or chemoembolization. Furthermore, active surveillance is presented as a reasonable option for patients with stable asymptomatic disease that does not involve the central nervous system. Similar to NCCN, the ATA guidelines support a comprehensive dissection of previously unexplored cervical compartments harboring metastatic disease, and a more limited or focused dissection of previously operated compartments. Clinically significant nodal metastases are defined as those greater than 0.8 cm in size. The treatment of cervical nodal metastases in patients with untreatable distant metastases may be considered for palliation or avoidance of aerodigestive tract invasion.

SUMMARY

When central or lateral compartment cervical lymph node metastases are clinically evident at the time of the index thyroid operation for PTC, formal surgical clearance of the affected nodal basin is the optimal management. Prophylactic CND for PTC is practiced by some high-volume surgeons with low complication rates, but is considered

controversial because there appears to be higher risk of complications with an uncertain clinical benefit. Long-term surveillance strategies are performed for most PTC patients after their initial treatment, and due to the high sensitivity of both the imaging modalities used and thyroglobulin measurement, approximately 20% of patients will be found to have persistent or recurrent disease. It is unclear what exactly constitutes a clinically significant recurrence, but the most commonly used definition is a lymph node greater than 0.8 cm. Surgical resection and active surveillance strategies may both be used depending on the clinical context. When a clinically significant recurrence is detected in a previously undissected central or lateral cervical compartment, a comprehensive surgical clearance of the lateral compartment is the preferred treatment. When a nodal recurrence is found in a previously dissected central or lateral neck field, the reoperation should focus on the areas where recurrence is demonstrated.

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