

# Role of Lymph Node Dissection in Primary Surgery for Thyroid Cancer

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## Key Words

Thyroid carcinoma, lymph node dissection, preoperative ultrasonography

## Abstract

The preoperative evaluation of the clinically N0 neck and the operative management of cervical lymph nodes in patients with papillary and medullary thyroid cancer remains controversial. The appreciation that even patients with low-risk disease have a significant risk for recurrence has generated interest in a more comprehensive preoperative evaluation of the neck and has renewed debate on the extent of lymphadenectomy at the time of thyroidectomy. The authors recommend using preoperative ultrasound before thyroidectomy for all patients with thyroid cancer and before any subsequent surgeries for recurrent disease to identify the extent of lymph node metastases and thereby facilitate complete surgical removal of all gross disease in the neck. The optimal surgical procedure for removing cervical lymphadenopathy is compartment-oriented neck dissection based on the findings from preoperative ultrasound. (*JNCCN* 2007;5:623–630)

The extent of evaluation of the clinically N0 neck and the operative management of cervical lymph nodes in patients with papillary thyroid cancer (PTC) and medullary thyroid cancer (MTC) remain controversial among endocrinologists and endocrine surgeons. In patients with MTC, regional lymph node dissection is commonly performed because of the high incidence of lymph node metastases and the lack of response to thyroid stimulating hormone (TSH) suppression or adjuvant radioiodine (RAI) therapy. In addition, cervical lymph node metastases from MTC are

associated with an increased risk for disease-related death.<sup>1</sup> Patients with PTC also have a high incidence of cervical lymph node metastasis (30%–90%, depending on the method of diagnosis and disease extent)<sup>2–5</sup> but, unlike MTC, lymph node metastases do not impact overall survival in most patients with low- and intermediate-risk disease.<sup>6–8</sup> Some would argue that the excellent survival rate of most patients with PTC (10-year cancer-specific mortality rate of less than 10%<sup>9</sup>) cannot be improved, and therefore the debate over extent of lymph node dissection is misdirected. However, cervical recurrence, primarily in the form of regional lymph node metastases, is a significant clinical concern in PTC (and MTC) after initial treatment, occurring in 9% to 30% of patients depending on risk stratification.<sup>10,11</sup>

The appreciation that even patients with low-risk disease are at significant risk for recurrence has generated interest in a more comprehensive preoperative evaluation of the neck and has renewed debate on the extent of lymphadenectomy at the time of thyroidectomy.<sup>12</sup> This change in practice pattern is reflected in many of the published thyroid cancer guidelines, such as those from the National Comprehensive Cancer Network (NCCN) and the American Thyroid Association (ATA), and represents a rapid shift in patient care from a focus on overall survival to one on recurrence-free survival. Therefore, the operative strategy for addressing cervical lymph nodes in patients with PTC, the most common form of thyroid cancer, is at the forefront of controversy in endocrine surgery.

## Definitions

*Elective* or *prophylactic* lymph node dissection is the removal of lymph nodes that are normal on physical examination and radiographic imaging.<sup>13</sup> Dissection of clinically and radiographically normal lymph nodes is based on the theory that early detection and removal of microscopic disease in regional lymph nodes may prevent recurrence and improve survival. The decision to proceed with an

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Submitted May 15, 2007; accepted for publication May 25, 2007.

This work was supported by the Faith Fund for Endocrine Surgery Research and Treatment at The University of Texas M. D. Anderson Cancer Center.

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elective node dissection is based on assessment of the risks and benefits of the procedure. Morbidity of regional lymph node dissection varies with the anatomic region of the body and can include postoperative hemorrhage requiring reoperation, seroma, nerve injury, and the cosmetic complications of an unsightly scar. These complications must be balanced against the potential benefit of the procedure. This type of dissection is not based on visible disease in the targeted nodal basins, but on the potential for a radiographically occult tumor to exist. The pathologic results of an elective lymph node dissection may help predict the risk for future recurrence and, in some solid tumors, guide the delivery of adjuvant therapy.

*Therapeutic* lymph node dissection involves the removal of regional lymph nodes that are clinically or radiographically abnormal and therefore proven or suspected to harbor metastatic disease. Therapeutic dissection is based on the general belief that regional disease control is necessary to prevent morbidity from local tumor growth, maintain quality of life, and possibly maximize survival. The timing of a therapeutic dissection depends on when and how the lymph node metastases are discovered: either synchronous with the diagnosis of the primary thyroid cancer or after a period of latency before becoming clinically or radiographically evident (a metachronous recurrence).

Both elective and therapeutic lymph node dissections in the neck are based on defined, anatomic regional boundaries and may be referred to as *compartment-oriented dissections*. These procedures are in contrast to *node plucking* or *berry picking* where only individual lymph nodes are removed, rather than nodal tissue and associated soft tissue in anatomically defined compartments.

The practice of sentinel lymph node (SLN) biopsy, now widely accepted in determining the presence of nodal metastasis in breast cancer and melanoma, has also been used in patients with differentiated thyroid carcinoma. Several small studies have reported variable degrees of success in locating SLNs using intraoperative blue dye lymphatic mapping, lymphoscintigraphy, and intraoperative gamma probe detection.<sup>14-16</sup> The potential advantages of the SLN technique include improved selection of patients for compartment-oriented node dissection, avoiding unnecessary surgery and morbidity in those who have a negative sentinel node, and identification of lymph node metastasis outside the central neck compartment

allowing for a more limited dissection of the lateral neck compartment.<sup>17</sup> Because of the general favorable outcome for most patients with PTC, whether the improved detection of early lymph node metastases afforded by SLN biopsy will be viewed as clinical progress or simply increase the extent of neck dissection without a clinically meaningful impact on locoregional disease control or survival remains unknown.

### **Lymph Node Compartments and the Pattern of Nodal Metastasis**

A well-accepted level system composed of 6 major nodal regions (I–VI) is used to delineate the location of lymph nodes in the neck and defines a compartment-oriented neck dissection.<sup>18</sup> A central neck dissection involves removal of all level VI lymph nodes, which include the pretracheal and paratracheal, precricoid (Delphian), and perithyroidal lymph nodes, and those along the recurrent laryngeal nerves. Anatomically, the central compartment (level VI) is bound by the carotid sheaths laterally, the hyoid bone superiorly, and the thoracic inlet inferiorly. Access to the inferior extent of the central compartment depends on the ability of the surgeon to gain exposure to the thoracic inlet, which may vary based on surgeon experience and training. The lateral compartment dissection (modified radical neck dissection) involves removal of all soft tissue and lymph nodes in levels I to V, preserving the sternocleidomastoid muscle, jugular vein, carotid artery, vagus nerve, phrenic nerve, and spinal accessory nerve.<sup>19</sup> The lateral compartment extends laterally from the carotid sheath to the trapezius muscle and from the subclavian vein inferiorly to the hypoglossal nerve superiorly. The level I region, which includes submandibular lymph nodes, often is not dissected in patients with thyroid cancer in the absence of known disease because this level rarely contains metastatic lymph nodes.<sup>20</sup> Selective neck dissection is defined as a cervical lymphadenectomy in which there is preservation of one or more lymph node groups that are routinely removed in a radical neck dissection.<sup>18</sup> For thyroid cancer, most surgeons perform a selective lymph node dissection, confining the lateral neck dissection to levels IIA, III, IV, and V unless an obvious lymph node metastasis is present outside these regions.

The thyroid gland has extensive lymphatic drainage, which may flow in several directions. In a study examining the compartmental location of positive lymph nodes in 296 patients who underwent

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total thyroidectomy and neck dissection, Machens et al.<sup>21</sup> evaluated the pattern of cervical lymph node metastasis in both PTC and MTC. The 4 possible lymph node locations were the cervicocentral (central neck, level VI), ipsilateral and contralateral cervicolateral (lateral neck, levels II–V), and mediastinal compartments. The ipsilateral cervicolateral neck compartment was involved almost as often as the cervicocentral compartment in patients with both primary (lateral 29%, central 32%) and reoperative (lateral 21%, central 37%) PTC. In further dividing the cervicocentral compartment into ipsilateral and contralateral components, the ipsilateral central compartment harbored lymph node metastases almost twice as often as the contralateral central compartment (29% vs. 13%). The contralateral cervicolateral and mediastinal compartments were rarely affected in primary or recurrent PTC. In patients with MTC, the ipsilateral cervicolateral neck compartment was involved as often as the cervicocentral compartment (34% vs. 34%) and a trend was seen toward more involvement of the contralateral cervicolateral and mediastinal compartments. These findings suggest that the lymphatic flow from the thyroid is directed first toward the ipsilateral paratracheal and lower jugular lymph nodes. As the disease becomes more advanced, it appears to spread through the contralateral cervicocentral compartment to the contralateral cervicolateral compartment. Other studies have reported a similar direction of lymphatic tumor flow.<sup>20</sup>

## Rationale for Preoperative Ultrasound

### Pro

In patients with thyroid cancer, palpation of the cervical lymph node basins is an important part of the preoperative physical examination but will miss most lymph node metastases that are smaller than 2 cm, especially in large patients. In addition to a false-negative rate of at least 10% to 15%, a false-positive rate also exists for palpation alone in detecting lymph node metastasis.<sup>22</sup> In contrast, transcutaneous ultrasound of the neck is both sensitive and specific for diagnosing soft tissue and lymph node metastasis.<sup>23,24</sup> The 2006 NCCN Thyroid Cancer Clinical Practice Guidelines in Oncology recommended preoperative ultrasound for the routine management of patients with PTC, and also that preoperative ultrasound be considered in patients with follicular carcinoma and MTC.<sup>25</sup> In the same year, the ATA recommended preoperative neck

(central and bilateral) ultrasound for all patients undergoing thyroidectomy for malignant cytologic findings on fine-needle aspiration (FNA) biopsy.<sup>12</sup>

The authors previously reported the impact of preoperative ultrasonography on the operative management of a consecutive series of 212 patients with thyroid cancer.<sup>26</sup> Ultrasound-positive disease not detected on physical examination was found in 105 neck compartments of 82 patients (39%); 52 of 151 (34%) with differentiated thyroid carcinoma, and 26 of 61 (43%) with MTC. These radiographic findings prompted more extensive surgery in these patients. Cervical recurrence occurred in only 16 of 207 (8%) evaluable patients at a median follow-up of 36 months, and in only 6 patients (6%) who underwent their initial surgical procedure at the M. D. Anderson Cancer Center (after high-quality preoperative ultrasound staging of the neck).

An additional measure of the adequacy of surgical resection in patients with differentiated thyroid cancer is the uptake seen on the postoperative RAI scan. In patients who had the extent of their initial operation guided by preoperative ultrasound, 77% had cervical uptake of 1% or less of the ingested dose, which compared favorably with the 46% of patients reported by Hodgson et al.<sup>27</sup> who had a cervical uptake of 2% or less. Based on these findings, we recommended the use of preoperative ultrasound before the first neck operation for all patients with thyroid cancer and before any subsequent surgeries for recurrent disease to ensure complete surgical removal of all gross disease in the neck. This strategy may minimize cervical recurrence, with its negative impact on the physical and emotional state of the patient, and possibly reduce the indiscriminate use of RAI in patients with mild elevations in thyroglobulin levels.

### Con

Opposition to the preoperative use of ultrasound is based on the clinical observation that microscopic lymph node metastases are common whereas clinically evident lymph node recurrences are much less common. Therefore, many (most) microscopic lymph node metastases may never become clinically significant.<sup>28</sup> The United Kingdom guidelines for managing patients with thyroid cancer state that the routine use of preoperative ultrasonography is not indicated.<sup>29</sup> In a 2006 editorial, Franklyn<sup>30</sup> suggested the argument for this decision was a paucity of evidence that routine preoperative ultrasonography changed clinical outcome.

He further stated that even in the tertiary setting, the surgeon does not routinely have the skills or equipment to perform ultrasonography, necessitating referral to a radiologist. However, a radiology referral in the centrally funded, government-regulated National Health Services of the United Kingdom is believed to be too costly and time-consuming. Ultrasound is much more operator-dependent than other imaging modalities, which may be a detriment to its daily use in some institutions.

Importantly, ultrasonography is less sensitive for evaluating the central compartment when the thyroid gland is in situ. As a result, the authors' group routinely removes the ipsilateral paratracheal nodes in patients with PTC or Hürthle cell cancer.

## Pros and Cons for Lymph Node Plucking Versus Compartment-Oriented Dissection

### Lymph Node Plucking

For PTC, advocates of lymph node plucking base their practice on the observation that lymph node metastases do not influence survival in low- and intermediate-risk patients. Because compartment-oriented surgery of the lateral neck requires a large incision and is associated with complications such as injury to the spinal accessory nerve, a lesser dissection may decrease patient morbidity.<sup>31</sup> Bhattacharyya<sup>32</sup> examined 2187 patients with PTC from 1988 to 1999 who were extracted from the Surveillance, Epidemiology, and End Results (SEER) database. Cases were limited to patients who underwent total thyroidectomy and post-operative RAI therapy; they were divided into groups of those who had undergone lymph node plucking and those who had undergone a compartment-oriented dissection. No significant difference in 5- or 10-year survival rates was seen.

### Compartment-Oriented Dissection

Compartment-oriented anatomic lymph node dissections can decrease cancer recurrence rates by allowing removal of occult metastases that would be missed with node plucking.<sup>33</sup> In addition, minimizing the extent of disease may enhance the effect of RAI in the treatment of residual microscopic disease and the detection of distant metastases. A more complete resection of recurrent disease in the neck may improve the sensitivity of thyroglobulin in detecting recurrent disease. The technical difficulty in detecting small

(subcentimeter) lymph node metastases at surgery also argues for a standard compartment-oriented approach to neck dissection. From a technical perspective, lymph node plucking increases the potential for reoperation within a previously operated neck compartment. Complications tend to be more common with reoperative surgery, making a compartment-oriented approach potentially more attractive to the extent that it may prevent the need for reoperation within the dissected compartment.

## Current Recommendations

### PTC

In managing patients with FNA-proven PTC, the NCCN's most recent guidelines recommend ultrasound of the thyroid gland and entire neck for preoperative evaluation.<sup>25</sup> If positive lymph nodes are identified preoperatively or are found to be present at the initial surgery, the guidelines recommend a total thyroidectomy and a central or lateral neck dissection, based on the location of the positive nodes. Lateral neck dissections are usually accomplished with preservation of the spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle. The ATA, in its 2006 task force disclosure on thyroid cancer, recommended the routine use of central neck dissection (level VI) in patients with PTC and Hürthle cell cancer.<sup>12</sup> They suggest that bilateral central neck dissection may improve survival compared with historical controls, reduce the risk for nodal recurrence, and be achieved with low morbidity by experienced surgeons.<sup>5,34,35</sup>

For lymph node metastases in the lateral neck, the ATA recommended that a lateral neck compartmental lymph node dissection be performed for patients with biopsy-proven lymphadenopathy detected clinically or through imaging, especially when they are not likely to experience a response to radioactive iodine treatment based on lymph node size and number or other factors, such as aggressive histology of the primary tumor.

The authors' group's surgical approach to managing patients with PTC emphasizes complete surgical resection of clinically and radiographically evident disease within the neck. This group was the first to advocate comprehensive preoperative evaluation of the neck with high-quality ultrasound of the thyroid and soft tissues of the neck to determine the extent of disease.<sup>26</sup> For patients with suspicious or clearly

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abnormal clinical or ultrasound findings in the central or lateral neck, this group performs a compartment-oriented operation to include a central or lateral neck dissection. A central compartment dissection involves removal of all lymph nodes and soft tissues in level VI with preservation of the recurrent laryngeal nerves and at least the superior parathyroid glands; the inferior parathyroid glands are usually harvested from the surgical specimen and autografted into the sternocleidomastoid muscle. Performing an adequate paratracheal node dissection and preserving the inferior parathyroid glands in situ is difficult, and routine autografting will prevent permanent hypoparathyroidism. Lateral compartment dissection (modified selective radical neck dissection) is only performed if disease is seen on ultrasound or is palpable on physical examination, and involves removal of all lymph nodes and soft tissues in levels IIA, III, IV, and V with preservation of the jugular vein, carotid artery, vagus nerve, phrenic nerve, and spinal accessory nerve when possible. As the detection of lateral neck disease becomes more sensitive, patients may be found to have limited disease (e.g., only one abnormal lymph node) in level IV or VB, and the dissection may be limited to the lower neck (levels IV and VB). The approach to the ipsilateral neck in patients with known PTC and no known preoperative or intraoperative adenopathy includes an elective ipsilateral paratracheal lymph node dissection. Patients without a cytologic diagnosis of PTC before surgery (e.g., indeterminate thyroid nodule on FNA) and no evidence of adenopathy do not undergo any form of lymphadenectomy unless grossly abnormal paratracheal lymph nodes are seen at surgery. Extent of surgery for PTC depends upon the risk stratification of the patient and findings on preoperative studies. While ultrasound is always advocated, computed tomography of the cervical region is also recommended to higher risk patients (Table 1).

**MTC**

MTC arises from the parafollicular or C-cells of the thyroid and can occur as a sporadic event or as part of an inherited cancer syndrome caused by a germline mutation of the *RET* (rearranged in transfection) proto-oncogene. Familial MTC may occur as part of multiple endocrine neoplasia type 2 (MEN 2A and 2B) or familial (non-MEN) MTC. MTC typically spreads to the cervical lymph nodes early in its course. Therefore, central compartment lymph node dissection is standard care

for all patients with macroscopic MTC at initial surgery. Elective dissection of the lateral neck compartments remains controversial.<sup>36-38</sup> An elective neck dissection to include the lateral compartments is based on the hypothesis that MTC may metastasize to the regional lymph nodes in the absence of distant disease. A more extensive lymphadenectomy may prevent cervical recurrence and potentially result in a long-term clinical cure. In patients with sporadic MTC and no clinical or radiographic evidence of cervical lymph node involvement, the authors recommend total thyroidectomy with central compartment dissection; the addition of an ipsilateral, lateral neck dissection (levels IIA, III, IV, V) in these patients remains controversial. In patients with sporadic MTC and evidence of lymph node metastasis, all involved compartments are dissected.

Knowledge of the *RET* mutation status and disease extent is required to determine the appropriate surgical technique in patients with MTC.<sup>39</sup> All patients diagnosed with MTC should undergo *RET* analysis through DNA sequencing of exons 10, 11, and 13 to 16. This approach will diagnose most patients with hereditary MTC. In addition, *RET* testing is recommended for carrier screening of relatives from a MEN2 family to determine the appropriate timing for prophylactic thyroidectomy. The biologic behavior and age at presentation of inherited MTC are mutation-dependent and have allowed for stratification of risk (i.e., level 1, high risk; level 2, higher risk; level 3 highest risk).<sup>40</sup> Operative management of the neck, including extent of lymph node dissection and the management of devascularized parathyroid glands, is based on the presence or absence of a *RET* mutation and the specific mutation found, and was recently reviewed by the authors' group.<sup>39</sup>

**Technique****Central Compartment Dissection**

For the central compartment dissection, the neck is entered through a standard low-collar incision. The superior limit of dissection is the hyoid bone and the inferior limit is the suprasternal notch. The lateral limits are defined by the medial border of the carotid sheaths. The main focus of the level VI dissection is the paratracheal tissue, especially the nodes between the recurrent nerves and the trachea.<sup>28</sup> When grossly visible lymph node metastases are present in the paratracheal regions, a bilateral paratracheal dissection is

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**Table 1 Algorithm for the Preoperative Evaluation and Operative Management of Patients with Papillary Thyroid Cancer Based on Risk Stratification\***

Risk	Age (y)	Ultrasound		Preoperative Evaluation	Extent of Surgery
		T Stage	N Stage		
Low	< 45	1, 2	N0	US	TT, ipsilateral PT ND
	< 45	1, 2	N1a	US	TT, level VI ND
Intermediate	< 45	1–2	N1b	US/CT	TT, level VI ND, and involved lateral neck compartments
	> 45	1–2	N0	US	TT, ipsilateral PT ND
High	< 45	3, 4	Any N	US/CT	TT, level VI ND, and involved lateral neck compartments
	> 45	3, 4	Any N	US/CT	
		Any T	N1 (a or b)		TT, level VI ND, and involved lateral neck compartments

\*T and N stages are based on the 6th edition of the AJCC Cancer Staging Manual.

Abbreviations: CT, computed tomography of cervical region; PT ND, paratracheal lymph node dissection; TT, total thyroidectomy; US transcutaneous ultrasound of the neck.

very important to the long-term maintenance of locoregional disease control. Although an elective central compartment dissection is controversial in patients with PTC, it remains a recommended part of the initial thyroid surgery in patients with MTC. When dealing with an apparently localized PTC with no radiographic evidence of lymph node metastases, the authors commonly perform a paratracheal node dissection on the side of the primary tumor. The contralateral paratracheal lymph nodes may not be removed, or at least not to the extent of the ipsilateral side.<sup>18</sup> All tissue from the anterior surface of the trachea and tracheoesophageal groove are removed, including thymic tissue. The most important aspect of a therapeutic central compartment dissection is the removal of nodal tissue posterior to the recurrent laryngeal nerves in the paraesophageal space, especially on the right side where the nerve enters the central compartment at an angle and creates a potential space posterior to the recurrent nerve.

### Lateral Compartment Dissection

If dealing with a reoperative situation, the previous scar is excised and the incision extended laterally and cephalad. A standard subplatysmal flap is elevated and the sternocleidomastoid muscle completely mobilized. The limits of dissection are then defined as the posterior belly of the digastric muscle superiorly, the spinal accessory nerve posterolaterally, and the clavicle and thoracic inlet inferiorly. All fibro-fatty and lymphatic

tissues are elevated off of the precervical fascia and rotated lateral to medial anterior to the jugular vein, carotid artery, and vagus nerve as these structures are skeletonized. All soft tissue is elevated off the origin of the superior thyroid artery, which is divided, and the external branch of the superior laryngeal nerve is identified. As the dissection proceeds inferiorly, the omohyoid muscle is divided laterally and the transverse cervical artery and phrenic nerve are preserved. All lymphatic tissue is then removed from the thoracic inlet and the specimen is removed en bloc. After irrigation and hemostasis, and when ready to close the neck, the platysma is reapproximated with absorbable suture and the skin closed usually in 2 layers over a closed-suction drain.

### Complications

Potential complications from central neck dissection include hypoparathyroidism, recurrent laryngeal nerve palsy, external laryngeal nerve palsy, and injury to the trachea or esophagus.<sup>41</sup> When performed by trained endocrine surgeons, the addition of a central neck dissection (paratracheal dissection) at thyroidectomy poses no greater risk than thyroid surgery alone.<sup>31</sup> One would normally excise the ipsilateral inferior parathyroid gland with the operative specimen and then harvest it from the surgical specimen for autografting. In contrast, reoperative central neck dissection increases the risk for complications.<sup>42</sup> To avoid the complication of hypoparathyroidism, these authors recommend the

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routine autografting of any devascularized or removed parathyroid glands. In operations for cancer involving the central neck compartment, especially reoperations, preoperative direct laryngoscopy is performed to evaluate the status of the recurrent laryngeal nerves.

Potential complications from lateral neck dissection include injury to the internal jugular vein or carotid artery, thoracic duct (predominantly on the left), and the spinal accessory nerve, superficial cervical nerves, hypoglossal nerve, brachial plexus, phrenic nerve, and sympathetic cervical plexus. Knowledge of neck anatomy and an appropriate level of experience will minimize intraoperative complications.

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