



Review Article

Para-tracheal neck dissection – is dissection of the upper part of level VI necessary?

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Abstract Papillary thyroid carcinoma (PTC) has a high propensity for regional metastases, however, the impact of such metastases on the outcome of the patients is minimal. The central compartment of the neck is considered the first and the most common echelon of metastases from thyroid carcinoma. Physical examination along with ultrasonography are the gold standard pre-operative evaluation of patients with PTC. Ultrasonography is highly sensitive in evaluating lateral neck nodes, however, its value in evaluating the central compartment is limited, resulting in a relatively high rate of occult metastases in this compartment. The main potential complications of para-tracheal neck dissection (PTND) are recurrent laryngeal nerve paralysis and hypocalcemia and these may be higher in patients undergoing PTND compared to thyroidectomy alone. New histological data is available showing no evidence of lymph nodes in the central compartment above a level parallel to the inferior border of the cricoid cartilage. These findings support withholding dissection of the upper para-tracheal region routinely as a part of PTND in patients with well-differentiated thyroid cancer. By doing that, the complications may be lower and identical to thyroidectomy alone, thus may abolish arguments against more common use of elective PTND in patients with thyroid carcinoma.

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Introduction

Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy, accounting for approximately 80% of thyroid carcinoma.^{1,2} According to the SEER database, the incidence of PTC continues to increase.³

PTC has a high propensity for regional metastases⁴ via proliferation and invasion of new lymphatics into the tumor.⁵ Regardless, the impact of such metastases on the outcome of the patients is minimal.^{6–9}

The central compartment of the neck consists of the pre-laryngeal, pre-tracheal, para-tracheal and upper mediastinal lymph node groups, and is the first and the most common site of metastases from PTC.^{4,6,10,11} Consequently, the role of therapeutic para-tracheal neck dissection (PTND) is well established since the extraction of visible metastases only (Berry picking) was associated with high rates of regional recurrence (up to 100%). Moreover, the complication rates for salvage surgery were reported higher than with primary surgery.^{12,13} In contrary, the role of elective PTND for well differentiated thyroid carcinoma is debatable. The opponents of elective PTND argue that the complications of thyroidectomy alone are significantly lower compared to thyroidectomy in conjunction with central compartment dissection.^{14,15} One way to minimize complication rates is by performing a unilateral PTND, provided that there are no clinical evidence of metastases on both sides of the central compartment.^{14,15} Still, the rate of transient hypocalcemia is higher following thyroidectomy in conjunction with a unilateral PTND compared to thyroidectomy alone.^{16–18}

We hypothesized that the uppermost part of the para-tracheal (PT) region is devoid of lymph nodes and should not be part of a routine PTND. Therefore, neglecting this uppermost PT region may help minimize dissection of the upper parathyroid gland and to some extent-the dissection of the recurrent laryngeal nerve (RLN) and thus lowering the complication rates of PTND.

Another benefit of withholding dissection of the upper PT region is esthetic: in patients having lower PTND – the scar may be as small as a regular thyroidectomy scar (average 4 cm). In cases where the entire PTND is performed, a larger incision may be needed to enable dissection of the uppermost part of the paratracheal region.

In this review article, we will evaluate the existing data on the surgical upper limit of the central compartment and the need to dissect this compartment routinely as part of a PTND.

Central compartment anatomy

The American Head and Neck Society (AHNS) and American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) proposed standard classification and division of cervical lymph nodes into seven levels. The 2009 ATA consensus statement on the relevant anatomy and terminology of central neck dissection (CND) concluded that the central neck compartment includes levels VI and VII lymph nodes.¹⁹

The boundaries of the central compartment are defined superiorly by the hyoid bone, laterally by the carotid

arteries, anteriorly by the superficial layer of the deep cervical fascia, posteriorly by the deep layer of the deep cervical fascia, and inferiorly by the innominate artery on the right (at its point of tracheal crossing) and the corresponding axial plane on the left.^{6,19,20}

The lymph nodes of the central neck compartment are divided into discrete sub-compartments: pre-laryngeal (Delphian) lymph nodes, pre-tracheal lymph nodes, right para-tracheal lymph nodes and left para-tracheal lymph nodes.⁶

The pre-laryngeal lymph nodes are located around midline, between the lower half of the thyroid cartilage and the cricoid cartilage, usually in the V-shaped space bound by the cricothyroid muscles. Occasionally there is a node high at the level of the thyrohyoid membrane.

The pre-tracheal lymph nodes are located within the fibrofatty tissue anterior to the trachea, between the thyroid isthmus and the thymus or left innominate vein.

The para-tracheal lymph nodes are located along the recurrent laryngeal nerves and become sparser toward the upper end of the nerve.²¹

Main anatomic structures contained within the central compartment include vessels (inferior and superior thyroid arteries; inferior, middle, and superior thyroid veins), Laryngeal nerves (superior and recurrent), endocrine glands (thyroid and parathyroid), larynx, trachea and esophagus. The inferior and superior parathyroid glands are supplied mostly by the inferior thyroid artery via inferior and superior branches. Occasionally the superior parathyroid gland is supplied by the superior thyroid artery via the posterior branch.¹⁹

The external branch of the superior laryngeal nerve emerges from the vagus nerve coursing inferiorly together with the superior thyroid vasculature, then insert into the cricothyroid muscle.

The recurrent laryngeal nerve arises from the vagus nerve, coursing around the aortic arch on the left and around the subclavian artery on the right. From there it runs superiorly in the tracheoesophageal groove on the left and more lateral on the right. The superior parathyroid gland is most commonly situated 1 cm above the intersection between the RLN and the inferior thyroid artery, lateral to the curve of the RLN. The inferior parathyroid gland has more variable location but usually is anterior to the recurrent laryngeal nerve near the inferior pole of the thyroid gland.¹⁹

Patterns of spread

Lymphatic drainage of the thyroid runs along the blood vessels that drain the gland. Drainage of the lower part of the thyroid runs along the inferior thyroid artery, passing through the para-tracheal lymph node basin and continues toward the venous angle at the junction of the internal jugular and subclavian veins. The drainage courses help explain the high incidence of para-tracheal disease in patients with positive lateral neck nodes.²²

On the other hand, drainage of the upper pole of the gland follows the superior thyroid artery and vein toward the upper jugulodigastric lymph node basin and may bypass the central compartment lymph nodes.²² Evidence of skip

metastases was documented in up to 21.8% of patients presenting with lateral node metastasis^{6,23–26} and was associated with small tumors (<1 cm) and upper pole location.²³

Most commonly, however, the central compartment is considered the first location of drainage for most thyroid tumors. On lymphoscintigraphy, the sentinel node of thyroid tumors was located in the para-tracheal region in up to 75% of the patients.²⁷

Considering the limitations of physical examination and imaging studies in the clinical evaluation and staging of the central compartment of the neck, the rate of occult metastases in this compartment is relatively high. Only ~35% of patients with PTC present with cN1,⁶ although the rate of metastases in that region is higher. Among patients with positive lateral nodes and clinically negative central compartment undergoing selective neck dissection, the rate of occult metastasis in the central compartment was reported as high as 84%.^{6,28}

Central compartment metastases were associated with increased tumor size (above 1-1.5 cm),^{2,3,29} younger age (<35)² and extrathyroidal extension.²⁹

Pre-operative evaluation

Physical examination along with ultrasonography are the gold standard pre-operative evaluation of patients with PTC.

Ultrasonography is highly sensitive in detecting metastases to the jugular chain and posterior neck. However, its value in evaluating the central compartment is limited (sensitivity of approximately 35%), owing to the presence of the thyroid gland and small volume lymph nodes in the central compartment.^{7,8,28} Ultrasonography is known to be user-dependent and in experienced hands the sensitivity of this modality in detecting level VI metastases may be much higher and surpasses the sensitivity of intra-operative palpation. As a rule, however, imaging has a limited role in the surgical planning prior to central compartment dissection in most centers treating thyroid cancer. US guided FNA with onsite adequacy assessment may reduce the numbers of non-diagnostic aspirates, although this less significant when performed by experienced radiologists compared to less experienced radiologists.³⁰

Other radiological modalities are less accurate for staging of the paratracheal region; CT may be indicated in patients with multiple central compartment lymph node metastases in order to rule out metastases at level VII- low in the mediastinum. Computed Tomography (CT) with contrast is also helpful in assessing tracheal invasion by aggressive tumors. In most patients, however, CT is not superior to US for diagnosis of central compartment metastases from thyroid cancer. Magnetic Resonance Imaging (MRI) is less accurate for staging of the central compartment due to the clavicles that may obscure lymph nodes at that region. PET-CT is rarely indicated in the set-up of thyroid cancer and may be offered for patients that have a rising level of thyroglobulin following total thyroidectomy with no evidence of disease on sonography or on thyroid/post ablation scan.

Complications of PTND

The morbidity of para-tracheal neck dissection was reported as being low.³¹ The main complications are recurrent laryngeal nerve paralysis (transient: 3.7%–17%, permanent: 0–2%), Hypocalcemia (transient: 13%–31%, permanent: 0–2.7%), Superior laryngeal nerve injury and wound infection or seroma (8%).^{12,18,24,28,31–33}

The inferior parathyroid gland however, is more difficult to preserve during PTND due to the difficulty preserving its blood supply.²⁸ Nevertheless, comparing morbidity between thyroidectomy with concomitant PTND to thyroidectomy alone demonstrated a significant higher rate of transient complications (hypocalcemia and RLN paralysis) in the latter. No significant difference was found in long term morbidity.^{17,18,24,34} Bilateral PTND may harbor a potential elevated risk for transient or permanent hypocalcemia.^{14,34}

Prophylactic vs. therapeutic PTND

Therapeutic PTND is the standard of care in patients with proven (pre-operatively, intra-operatively or by imaging) metastases to the para-tracheal region.^{11,35} The management of patients with pre-operatively negative neck (cN0) is a constant source of controversy. Whether these patients should be treated with elective/prophylactic PTND was, and still is, a major debate in the literature with a paradigm shift in the past two decades.⁹

Overt positive lymph node status is known to increase local recurrence,^{3,17,36} while the influence of occult metastasis on local recurrence and survival remains unclear. Guidelines published by the American Thyroid Association In 2006 stated that routine central compartment lymph node dissection should be considered for papillary thyroid carcinoma more than 1 cm in diameter, however, this recommendation is rarely used.

Complete clearance of the disease by PTND concomitant to thyroidectomy was believed to reduce the chances of recurrence and the subsequent morbidity of re-operation.^{7,17,37} An additional role of PTND was in providing the pathological nodal status, effecting of the nodal staging and therefore influencing the adjuvant therapy.^{3,17,37} In cases of positive occult metastasis, there was an increase in both number of patients treated with iodine and the administrated dosage.^{3,17,26}

In recent years more studies support the prognostic impact of central compartment metastases on an increased risk of nodal recurrence, but not on survival.^{6–8} Moreover, the increased risk for nodal recurrence was observed almost exclusively in clinically apparent nodal disease rather than microscopically positive nodal disease.^{6,9,38} Despite the high incidence of occult lymph node micrometastasis in the central compartment, the median rate of recurrence for patients with cN0 disease is 2% whether a prophylactic PTND was performed or not.^{11,18}

The recent ATA guidelines published in 2015³⁹ as well as consensus statement by the American Head and Neck Society in 2017,⁶ Recommended prophylactic PTND in patients with PTC and clinically negative central neck lymph nodes (cN0) who have advanced primary tumors (T3/T4),

clinically involved lateral neck nodes (cN1b), or if the information will be used to plan further steps in therapy. Thyroidectomy without prophylactic PTND is appropriate for small (T1 or T2), noninvasive and clinically node-negative PTC (cN0).^{6,39}

Due to modern imaging, cytopathologic procedures and biochemical means in post-operative follow-up, the abandonment of routine prophylactic PTND in favor of performing the procedure only in selected cases was recommended.

Due to the high rate of cervical metastases in the central compartment, the complication rates of central compartment dissection are critical in the equation of watchful waiting (barring a risk of reoperation) vs. elective central compartment dissection (with its associated complications). If the morbidity of PTND was lower, then the recommendations in 2015, 2017 guidelines may have been different since these recommendations took into account a higher complication rate and thus precluded a more common use of PTND.

The superior extent of PTND – transforming common practice into standard of care

Unilateral CND involves removal of the pre-tracheal and pre-laryngeal lymph nodes, along with ipsilateral para-tracheal lymph nodes. Bilateral CND includes removal of the pre-tracheal, pre-laryngeal, and bilateral para-tracheal lymph nodes.^{6,19}

The formal superior border of the central compartment is the hyoid bone. Nevertheless, it is not clear whether this border extends laterally to the para-tracheal region, or perhaps it refers only the superior border of the pre-laryngeal sub-compartment to include the Delphian node. In the consensus statement published by the ATA surgery group in 2009,¹⁹ while the hyoid bone is defined as the superior border of the central compartment, they offer to perform PTND inferior to the cricoid cartilage.

The cricoid cartilage was defined as the superior border of the dissection in few more publications,^{25,40} while others use the thyroid cartilage as the superior border.³²

Shaha and Medina claimed that lymph nodes above the superior pole of the thyroid are rare and get sparser toward the upper part of the nerve.^{7,8,21} Surgeons felt comfortable not dissecting the uppermost part of the para-tracheal compartment, however, no evidence was available to support that practice.

The first prospective study addressing dissection of the upper para-tracheal region during routine PTND was published in 2014.³³ Twenty-seven patients with PTC were treated with PTND concomitant with thyroidectomy (21 patients) or PTND alone (6 patients with paratracheal recurrence after previous thyroidectomy). PTND was either unilateral or bilateral. The term “nerve curve line” was established, describing an imaginary line drawn between the curve of the RLN and the upper parathyroid gland inferiorly and the cricoid cartilage superiorly. Dissection of the region above this nerve curve line may increase the risk of jeopardizing the blood supply to the upper parathyroid gland and as well as increase the risk of RLN injury. In most patients, the nerve curve line corresponds to the level of

the lower edge of the cricoid cartilage. A total of 31 PTND specimens were sent for pathologic evaluation as separate specimens - upper (above the nerve curve line) and lower (below the nerve curve line). Lymph node metastases were detected in the specimens of 21 patients, 3 of them in the bilateral PTND group. All lymphatic structures were detected in the lower para-tracheal region and respectively all metastatic lymph nodes were also located in the lower PTND specimen. The upper specimens, above the nerve curve line, were devoid of lymphatic tissue or cancer-bearing lymph nodes and consisted of fibrofatty connective tissue only.³³

This study supports Shaha’s and Medina’s assumptions and supports the hypothesis that dissection of the upper PT region may not be needed routinely in PTND. Unfortunately, this study was not repeated but authors of this chapter as well other surgeons feel safe performing only dissection of the lower part of the para-tracheal region during a routine PTND preserving unless clinically involved.

Summary

PTND is an integral part of the treatment algorithm in patients with PTC. Taking into account the possible morbidity of this procedure along with its limited, if at all, effect on patients’ survival - recent guidelines suggest therapeutic PTND for clinically involved central nodes and prophylactic PTND only in T3/T4 patients or when lateral nodes are involved. The relation to the upper limit of the dissection varies significantly in the literature. Recent pathological data demonstrated the absence of lymphatic tissue in the upper paratracheal region, questioning the need to dissect this area routinely as a part of PTND in patients with well-differentiated thyroid cancer.

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Declaration of Competing Interest

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