Reoperation for Recurrent/Persistent Well-Differentiated Thyroid Cancer

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The incidence of thyroid cancer in the United States has been increasing over the past several decades. Some attribute this increase to improved detection rates of small papillary cancers with the widespread use of high-resolution ultrasonography in combination with fine-needle aspiration (FNA) biopsy of subcentimeter thyroid nodules.¹,² Most well-differentiated thyroid cancers (WDTC) have a favorable prognosis with excellent long-term overall survival. The American Thyroid Association has generated guidelines that help to clarify posttreatment surveillance strategies for patients diagnosed with WDTC.³ Similar to the observed trend of increased detection rates of smaller papillary cancers, sensitive assays including ultrasonography and monitoring of serum thyroglobulin levels have ushered in a new era in which clinicians are diagnosing small volume recurrent/persistent disease in lymph nodes of the neck. The effect of nodal recurrence/persistence on prognosis and survival is unclear, especially when it is in the form of small volume disease. Nonetheless, identification of recurrent/persistent disease requires critical thinking as to what, if any, intervention should be performed to control the disease while minimizing morbidity. This presentation discusses the preoperative and technical considerations in reoperative surgery for recurrent/persistent WDTC within the central and/or lateral necks.

PREOPERATIVE EVALUATION

When evaluating a patient in the reoperative setting for recurrent/persistent WDTC, a thorough preoperative evaluation is warranted to minimize the increased operative...
risks and, most importantly, the need for further revision surgeries. A detailed history and physical examination should be performed. It is imperative to review the previous operative reports to determine the extent of surgery performed at the initial operation. The pathology report and/or slides can provide further information regarding the extent of disease, status of the surgical margins, and integrity of the parathyroid glands. In addition, as part of the history and physical examination, it is important to ascertain if there were any associated complications with the previous surgeries. A detailed cranial nerve assessment should be performed including an analysis of vocal fold function before any reoperative surgery in the central neck.

Laboratory testing should include a serum calcium level and, if low or the patient is requiring calcium supplementation, obtaining an intact parathyroid hormone (PTH) level should be considered.

The cornerstone of postoperative surveillance for these patients is high-resolution ultrasonography of the thyroid bed and lateral neck. Ultrasound can help localize an area suspicious for recurrent/persistent disease and image-guided FNA biopsy can be used to confirm the presence of malignancy. It is important to have a clear understanding of where the disease is located as it relates to vital structures in the neck. The American Head and Neck Society has defined the compartments of the neck and this designation should be used by all practitioners so that disease localization can be clearly communicated (Fig. 1). In the setting of recurrent disease in a previously operated lateral neck, a computed tomography (CT) scan of the neck with intravenous contrast can often be useful in delineating compartments that were not addressed at the time of the initial lateral neck dissection. The presence of fatty tissue harboring lymph nodes can easily be visualized in axial cuts of the CT scan; whereas a lack of a plane between the great vessels and the sternocleidomastoid muscle can suggest previous dissection in that area (Fig. 2). However, before obtaining a CT scan, discussions with the endocrinologist are encouraged to ensure that this study would not delay postsurgical adjuvant radioactive iodine (RAI) treatment. An alternative study that can be used to delineate areas of previous dissection in the lateral neck but would not interfere with RAI therapy is a magnetic resonance imaging (MRI) scan with gadolinium. However, the costs associated with an MRI scan need to be considered in the context of whether the patient is a candidate for further RAI treatment.

**PATTERNS OF RECURRENCE IN THE NECK**

Metastasis to the cervical lymph nodes is common in the tumor progression of papillary thyroid cancer (PTC) and is reported to occur in 20% to 50% of patients. Micro-metastases occur at an even higher rate with a study reporting involvement in up to 90% of pathologically examined nodes. These high rates of nodal metastases may contribute to the observed persistence and recurrence rates of PTC. It has been reported that 5% to 20% of patients treated with total thyroidectomy develop palpable local recurrence within 10 years. Such recurrences have been reported to localize to the cervical lymph nodes in 60% to 75% of cases with the central compartment of the neck being the most frequently involved site. Cervical lymph node involvement has been associated with an increase in overall mortality in select patient populations. High-risk patient groups include patients older than 50 years of age with lymph node metastases greater than 3 cm in size. Patients with large nodal metastases have been shown to have increased incidence of local recurrence in the neck with involvement of the surrounding soft tissues of the neck including the carotid artery. At the time of primary surgery for WDTC, prophylactic node dissection is controversial; however, clinically positive lymph nodes should be systematically cleared to minimize the recurrence rates and need for reoperation. Reports in
Fig. 1. Compartment levels of the neck. The level Ia compartment of the neck consists of the submental triangle bound by the anterior belly of the digastric muscle and the mylohyoid muscle. Level Ib is the submandibular triangle and is defined by the anterior and posterior bellies of the digastric muscle and body of the mandible. Level II is bound by the lateral border of the sternohyoid muscle, posterior belly of digastric muscle, posterior border of the sternocleidomastoid muscle, skull base, and the level of the carotid bifurcation. Level IIa is anterior to XI and level IIb is posterior to XI. Level III is bound by the lateral border of the sternohyoid muscle, posterior border of the sternocleidomastoid muscle, carotid bifurcation, and omohyoid muscle. Level IV is bound by the lateral border of the sternohyoid muscle, posterior border of the sternocleidomastoid muscle, omohyoid muscle, and clavicle. Level V is bound by the posterior border of the sternocleidomastoid muscle, anterior border of the trapezius muscle, and clavicle. Level Va is defined by the lymphatic structures that follow the spinal accessory nerve. Level Vb is defined by the lymphatic structures that lie along the transverse cervical artery. (From Pai SI, Tufano RT. Central compartment neck dissection for thyroid cancer: technical considerations. ORL J Otorhinolaryngol Relat Spec 2008;70:292–97; with permission.)
the literature suggest that comprehensive compartmental resection of the central or lateral neck in the setting of clinically positive lymph nodes can result in better survival and lower recurrence rates. For recurrent/persistent WDTC cancer, an important element to achieving a successful surgical outcome is to have a systematic approach to the neck, both in surgical technique and extent of lymph node dissection within a defined compartment of the neck. Several studies have shown that for locally recurrent PTC a systematic neck dissection is recommended over simple local resection of recurrent tumors. Patients were reported to have a better prognosis after reoperation than those who underwent dissection of local lymph nodes or berry picking. In addition, several studies have demonstrated that patients who develop recurrent tumors within previously dissected areas have a worse outcome than those patients who develop recurrence outside the initial areas of dissection.

Although the pattern of cervical lymph node metastases at the time of the initial diagnosis of PTC has been described, little is known about the pattern of cervical nodal recurrence in the lateral neck and, subsequently, the extent of surgical intervention required.

Lee and colleagues reported that in the lateral neck, recurrences most frequently occurred in level IV (73.4%), followed by level III (13.3%), and level II (13.3%) and 80% of cases were found ipsilateral to the primary tumor.

Roh and colleagues evaluated the pattern of cervical nodal recurrence by performing a systematic nodal dissection of the ipsilateral central compartment as well as the lateral neck in 22 patients with recurrent/persistent PTC in the lateral neck. They reported that recurrences were common after incomplete resection of the thyroid gland with local recurrence in the remnant thyroid tissue and/or bed in patients who previously underwent partial resection of the gland. Pathologic examination of the removed lymph nodes demonstrated a high incidence (86%) of involved central nodes in patients with lateral nodal neck recurrence. Within the central compartment, the pretracheal and ipsilateral paratracheal sites were commonly involved, whereas, within the lateral compartment, the ipsilateral jugular nodes (levels II, III, and IV)
were commonly involved. In contrast, the posterior triangle (level V) and contralateral lateral neck were rarely involved, and skip lesions involving the lateral but not the central lymph nodes were also rare. Because this pattern of nodal recurrence is similar to the pattern of lymph node metastases reported for incidental PTCs, it has been suggested that the lesions may have been present at the time of the initial presentation rather than presenting through altered lymphatic drainage established after the initial surgery to remove the thyroid gland.

Farrag and colleagues evaluated 53 patients with PTC who had undergone therapeutic lateral neck dissection, and 43 of these patients had recurrent/persistent disease. They found that levels IIA, III, and IV were most commonly involved with recurrent/persistent disease. Level IIB was found to harbor disease in less than 10% of patients; however, if level IIA contained metastatic lymph nodes, 100% of patients also harbored disease in level IIB. Therefore, they recommended elective dissection of level IIB only when level IIA is involved based on FNA confirmation or gross involvement intraoperatively. Level VB lymph nodes along the course of the transverse cervical vessels or adjacent to the clavicle were involved in 16 of 40 neck dissection specimens whereas level VA was involved in 0% of specimens. Based on these findings, routine dissection of level VA was not warranted; however, dissection of Level VB should be strongly considered.

Therefore, we can conclude that a reoperative lateral neck dissection should attempt to clear levels II, III, IV, and VB if this was not addressed at a previous surgery. Resection of the recurrent nodal mass alone may be sufficient in those levels of the neck that have undergone previous extensive resection. It is our contention that this formal compartmental approach to clinically positive lymph nodes in the primary or reoperative setting will help to reduce the need for further surgeries.

REOPERATIVE CENTRAL COMPARTMENT DISSECTION

Reoperative surgery of the central compartment places the parathyroid glands and recurrent laryngeal nerves at increased risk for injury compared with primary surgery. Alvarado and colleagues performed a retrospective study and compared 170 patients who had undergone a central lymph node dissection (CLND) as part of their primary surgery with 23 patients who underwent a CLND as a secondary procedure. In this study, the investigators did not find any additional morbidity when the CLND was performed as a secondary procedure; however, other studies have reported an increased morbidity rate associated with reoperative surgery. Furthermore, the overall complication rate, including hypocalcemia and vocal cord paralysis, in patients undergoing bilateral central neck dissections (58%) was found to be significantly higher than those who underwent unilateral central compartment dissection (10%, \( P = .031 \)).

Technical surgical considerations for reoperative central compartment dissection include horizontal transection of the sternothyroid and, if necessary, the sternohyoid muscles. This allows for maximum visualization of the operative field. After the horizontal transection of the strap muscles, the muscle can be separated first medially from the trachea and the dissection carried laterally and superiorly or laterally and inferiorly over the fibrofatty tissue within the central compartment. When separating the superior and inferior limbs of the strap muscles from the paratracheal lymph nodes, the surgeon must be sure that all fibroadipose tissue that may lie immediately posterior to the strap muscle is included as part of the central compartment because metastatic lymph nodes can be adherent to the strap muscles and inadvertently left behind. The surgery can then proceed in a systematic approach to the central compartment. Because the right recurrent laryngeal nerve (RLN) loops around the subclavian artery
and ascends away from the tracheoesophageal groove, the right paratracheal lymph nodes can be divided into an anterior and posterior compartment that is separated by the nerve (Fig. 3). Recurrent/persistent disease is often localized to the posterior compartment on the right side. Therefore, it is important when performing a reoperation for recurrent/persistent disease in the right central compartment that the right RLN is mobilized and the posterior lymph node compartment removed as part of the dissection. Because the left RLN travels along the tracheoesophageal groove and the esophagus is present immediately posterior to the RLN, dissection of the lymph nodes along the prevertebral fascia and anterior to the left RLN is usually sufficient for the left side (Fig. 4).

**HYPOPARATHYROIDISM**

When performing a reoperation in the central compartment, the parathyroid glands are at increased risk for devascularization or inadvertent removal because of its residence in scar tissue and fibrosis within the thyroid bed. The incidence of temporary hypoparathyroidism following reoperative thyroid surgery ranges between 0.3% and 15%. The incidence of permanent hypoparathyroidism following reoperative thyroid surgery ranges between 0% and 3.5%. During reoperative surgeries,

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**Fig. 3.** Identification and dissection of right RLN in reoperative surgery. (A) After identification of the RLN low in the neck, typically inferior to the second tracheal ring, the operating surgeon can dissect carefully along the RLN inferiorly to the level of the clavicle with a Crile to allow for atraumatic mobilization from the surrounding lymph node bearing tissue. (B) To remove the anterior and posterior lymph node compartments, the right RLN needs to be transposed, which can be achieved without direct retraction of the nerve or without using a nerve hook. (C) The posterior compartment lymph nodes can then be mobilized anteriorly and transposed under the nerve. The anterior and posterior lymph node compartments can then be mobilized off the prevertebral fascia and esophagus, and the dissection carried inferiorly to the level of the innominate artery to incorporate the superior mediastinal lymph nodes as part of the central compartment dissection. (From Pai SI, Tufano RT. Central compartment lymph node dissection. Oper Tech Otolaryngol Head Neck Surg 2009;20(1):39–43; with permission.)
preservation of the inferior thyroid artery is recommended to prevent devascularization of the parathyroid glands. Furthermore, the authors recommend that the superior aspect of the central lymph node packet be defined by the inferior thyroid artery because metastatic lymph nodes are rarely found cephalad to the artery and this approach minimizes risk of injury to the superior parathyroid glands. If recurrent/persistent lymph nodes are present above the inferior thyroid artery, high-resolution ultrasonography is particularly helpful in the reoperative scenario in localizing the metastatic lymph node in the absence of a thyroid shadow. Fibrosis and multiple positive lymph nodes in the reoperative central compartment specimen can make identification and confirmation of parathyroid tissue difficult in situ. Therefore, after dissection of the central compartment packet, the specimen should be carefully examined for the presence of parathyroid tissue. If identified, a biopsy of the gland should be performed for histologic confirmation by frozen-section histopathologic analysis before reimplantation into muscle. Reimplantation of the parathyroid glands of questionable viability into the sternocleidomastoid muscle at the time of the revision surgery also diminishes the risk of long-term permanent hypoparathyroidism. In

Fig. 4. Dissection of the left RLN in reoperative surgery. (A) After identification of the left RLN, the lateral aspect of the paratracheal lymph nodes can be dissected away from the carotid sheath and the dissection extended inferiorly to the innominate artery or brachiocephalic vein. (B) Because the left RLN travels along the tracheoesophageal groove approximating the trachea and esophagus, there is a lack of lymph nodes deep to the left RLN and mobilization of the lymph nodes anterior and posterior to the left RLN without transposition of the nerve itself is usually sufficient for the left side. (Courtesy of Pai SI, Tufano RT. Central compartment lymph node dissection. Oper Tech Otolaryngol Head Neck Surg 2009;20(1):39–43; with permission.)
patients with extensive extracapsular lymph node spread and multiple involved lymph nodes, reimplantation must be performed with caution such that the surgeon does not inadvertently reimplant tumor with parathyroid tissue.

RECURRENT LARYNGEAL NERVE INJURY

The RLN is vulnerable to increased risk of injury in reoperative surgeries for thyroid cancer due to the displacement of the nerve from its normal position secondary to scar tissue as well as increased manipulation when performing a central compartment dissection. The incidence of permanent RLN injury in primary thyroid surgeries has been reported to range between 0 to 5.6%.

This risk increases to 1 to 12% in reoperative cases. Routine early identification of the RLN with subsequent visualization of the nerve during dissection in the central compartment has been found to considerably reduce the risk of injury and, therefore, is regarded as the gold standard of care in thyroid surgery. Recent studies have demonstrated that intraoperative nerve monitoring can assist in the identification of the RLN, particularly in the reoperative setting. However, the visual identification of the nerve remains the basis for protecting the integrity of the nerve and the nerve monitoring system serves only as an adjunct in its identification. Avoidance of nerve injury can be achieved by early identification during the surgery, dissection with the nerve in view, and the careful use of electro-cautery away from the nerve. Several strategies may be employed to identify the RLN. The RLN can be identified low in the neck typically distant from previous areas of dissection. On the right this usually can be accomplished at the level of the common carotid artery, innominate artery, and subclavian artery junction where the RLN courses deep to this intersection to enter the central neck. The left RLN will course in a more ventral position compared with the right and can be found inferiorly in the tracheoesophageal groove inferior to the second tracheal ring. Other potential approaches include a lateral approach which allows identification of the nerve in a previously undissected area. This method may be especially helpful when there have been multiple central neck reoperations.

SUMMARY

At the time of the initial thyroid surgery, a primary goal is to remove the thyroid gland and associated cervical metastatic disease when present. Therefore, any patient with a FNA-confirmed WDTC should undergo an ultrasound of the neck to evaluate for any suspicious lymph nodes that may need to be addressed at the time of the initial surgery. If nodal disease is present within the neck, a formal compartmental therapeutic nodal dissection should be performed. Removal of the primary thyroid cancer and involved regional lymph nodes in this way will likely lessen the need for reoperation. Currently, up to 20% of patients require reoperative surgery for recurrent/persistent disease. When performing a reoperation for WDTC, the algorithm that the authors have elucidated should be used to minimize any associated increased surgical risks and need for further revision surgery.

REFERENCES


