Central Neck Lymph Node Dissection for Papillary Thyroid Cancer

Comparison of Complication and Recurrence Rates in 295 Initial Dissections and Reoperations

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Background: The American Thyroid Association recently changed its management guidelines for papillary thyroid cancer (PTC) to include routine central neck lymph node dissection (CLND) during thyroidectomy. We currently perform CLND during thyroidectomy only if enlarged central nodes are detected by palpation or ultrasonography; we perform CLND in the reoperative setting for recurrence in previously normal-appearing or incompletely resected nodes. Critics of this approach argue that reoperative CLND has higher complication and recurrence rates than initial CLND. We sought to test this argument, using it as our hypothesis.

Design: Retrospective review.

Setting: University hospital.


Interventions: Thyroidectomy and CLND.

Main Outcome Measures: Complications (neck hematoma, recurrent laryngeal nerve injury, and hypoparathyroidism) and recurrence of PTC.

Results: Altogether, 295 CLNDs were performed: 189 were initial operations and 106 were reoperations. The rate of transient hypocalcemia (41.8% vs 23.6%) was significantly higher in patients undergoing initial CLND compared with those undergoing reoperative CLND. Rates of neck hematoma (1.1% vs 0.9%), transient hoarseness (4.8% vs 4.7%), permanent hoarseness (2.6% vs 1.9%), and permanent hypoparathyroidism (0.5% vs 0.9%) were not different between initial and reoperative CLND. In addition, recurrence rates in the central (11.6% vs 14.1%) and lateral (21.7% vs 17.0%) compartments were not different between the 2 groups.

Conclusions: Reoperative CLND for PTC has a lower rate of temporary hypocalcemia, the same rate of other complications, and the same rate of recurrence compared with initial CLND. Choosing to observe nonenlarged central neck lymph nodes for PTC does not result in increased complications or recurrence if reoperation is required.

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PAPILLARY THYROID CANCER (PTC) is the most common type of thyroid cancer and has the best overall prognosis. Most endocrine surgeons currently perform total thyroidectomy in patients with PTC because this operation eliminates multifocal disease, enables surveillance for recurrence using serum thyroglobulin and whole-body radioactive iodine scan, and allows for effective therapy for recurrence using radioactive iodine ablation. With this combination of treatment and surveillance modalities, the overall 10-year survival for patients with PTC is greater than 90%. Despite the excellent overall prognosis for patients with PTC, many of these patients will develop nodal metastases in the central neck (level VI) or lateral neck (levels II, III, and IV) at the time of presentation or during the course of follow-up. Most endocrine surgeons agree that compartment-based nodal dissection is appropriate and effective treatment for enlarged lymph nodes that are identified on preoperative imaging or physical examination or during intraoperative inspection and palpation. However, substantial controversy exists regarding the role of prophylactic neck dissection for patients with PTC. Few surgeons currently recommend prophylactic lateral neck lymph node dissection for nonenlarged nodes. The central neck, however, is the subject of considerable debate. The central neck lymph nodes (level VI) are located in the region bordered laterally by the carotid sheath, medially by the trachea, superiorly by the hyoid bone, and...
in inferiorly by the suprasternal notch. Some surgeons recommend routine prophylactic removal of the central neck lymph nodes at the same time as initial total thyroidectomy for PTC, with the goal of decreasing the risk of recurrence and “cleaning out” the central compartment so that future reoperation in a previously dissected field is not required. This practice has gained enough supporters to have prompted a significant change in the most recent practice guidelines of the American Thyroid Association; the guidelines now recommend consideration for central neck lymph node dissection (CLND) in all patients undergoing thyroidectomy for PTC, regardless of whether the nodes are enlarged.

Unfortunately, CLND carries a substantial risk of complications, even in experienced hands. The location of the central neck lymph nodes in the tracheoesophageal groove places the recurrent laryngeal nerves at risk for injury. In addition, enlarged lymph nodes may have an appearance similar to that of normal parathyroid tissue and share the same blood supply; CLND, therefore, has an increased associated rate of postoperative hypoparathyroidism. Central neck lymph node dissection also results in increased operating time.

Our practice has been to perform CLND for PTC only in patients who have enlarged central neck lymph nodes identified during preoperative ultrasonography or physical examination or during intraoperative inspection and palpation; we also perform ipsilateral CLND during initial thyroidectomy for PTC in patients who present with enlarged lateral lymph nodes because nodal metastases in PTC typically follow a stepwise progression from the thyroid gland to the central lymph nodes to the lateral lymph nodes. In patients with PTC and normal-appearing central and lateral lymph nodes, we perform total thyroidectomy only. During the course of follow-up for these patients, we may be required to perform reoperative neck dissection if enlarged nodes are detected, but this occurs in only 10% to 15% of patients. Opponents of this approach argue that reoperative dissection in the central neck has higher risks and recurrence rates than initial central neck dissection because of postoperative scarring and abnormal anatomy in the central neck after thyroidectomy. We therefore reviewed our experience with CLND for PTC over the past decade to compare the complication and recurrence rates of initial and reoperative CLND. We hypothesized that the technical difficulties associated with reoperative CLND would result in higher complication and recurrence rates when compared with initial CLND.

METHODS

We reviewed our cancer registry database to identify all patients with PTC who were operated on by our endocrine surgery practice within the past decade. All operations and reoperations were performed by one of 4 endocrine surgeons in our practice (W.T.S., E.K., Q.-Y.D., and O.H.C.). From this cohort we selected all patients who underwent CLND (either unilateral or bilateral). We included patients who had CLND at the same time as thyroidectomy, CLND in addition to lateral neck lymph node dissection, or CLND alone. We defined initial CLND as removal of central neck lymph nodes at the same time as initial total thyroidectomy, with or without additional lateral neck lymph node dissection. We defined reoperative CLND as removal of central neck lymph nodes from a central neck that had been operated on previously; this group included patients with growth of previously nonenlarged central neck lymph nodes or growth of central neck lymph nodes that were incompletely resected during a previous operation. All of the endocrine surgeons in our practice trained at our institution and use similar techniques for performing thyroidectomy and initial or reoperative lymph node dissection.

The main outcome measures derived from our cancer registry database and patient records included patient demographics; operation performed (including any lymphadenectomy in addition to CLND); postoperative complications, including neck hematoma, transient or permanent hypoparathyroidism, and transient hoarseness or permanent recurrent laryngeal nerve injury; and recurrence detected by postoperative surveillance and requiring reoperation. For the purposes of this study, transient hypoparathyroidism was defined as any serum calcium level less than 8.0 mg/dL within 24 hours after operation (to convert serum calcium to millimoles per liter, multiply by 0.25); permanent hypoparathyroidism was defined as a serum calcium level less than 8.0 mg/dL with associated low parathyroid hormone level requiring oral calcium carbonate and calcitriol supplementation beyond 6 months after the operation. Transient hoarseness was based on the surgeon’s assessment and the patients’ subjective report of symptoms during the immediate postoperative period, whereas permanent recurrent laryngeal nerve injury was defined by hoarseness persisting beyond 6 months after the operation and confirmed with direct laryngoscopy documenting ipsilateral vocal cord dysfunction.

Statistical significance was determined using the 2-tailed t test and Fisher exact test. P < .05 was considered significant. All data are presented as the mean (SEM), unless otherwise noted.

RESULTS

From January 1, 1998, to December 31, 2007, surgeons from our endocrine surgery practice performed 295 CLNDs for PTC. Of the 295 operations, 189 were initial operations consisting of total thyroidectomy with removal of central neck lymph nodes; the remaining 106 operations were reoperations for enlarged central neck lymph nodes in previously normal-appearing or incompletely resected central neck lymph nodes. We compared data from patients in the initial operation group with data from patients in the reoperation group. The demographic profiles of the 2 groups were similar, although patients undergoing reoperation were slightly older: patients undergoing CLND during initial thyroidectomy consisted of 54 men (28.6%) and 135 women (71.4%) with a mean age of 39.8 (16.0) years; the patients undergoing reoperative CLND consisted of 33 men (31.1%) and 73 women (68.9%) with a mean age of 46.5 (16.8) years.

Of the 189 initial CLNDs, 71 (37.6%) were unilateral and 118 (62.4%) were bilateral; in contrast, reoperative CLNDs were more likely to be unilateral (76 of 106 [71.7%]) unilateral vs 30 of 106 (28.3%) bilateral. Lateral neck lymph node dissection (levels IV, III, and, when involved, II) was performed in 81 of 189 initial CLNDs (42.9%) compared with 31 of 106 reoperative CLNDs (29.2%). Nerve monitoring using a nerve integrity monitoring system (Medtronic, Fridley, Minnesota) was used in 20 of the 189 initial operations (10.6%) and in 16 of the 106 reoperations (15.1%).

Complication rates for initial vs reoperative CLND were similar overall. Postoperative neck hematoma requiring reexploration occurred in 2 (1.1%) of the initial opera-
tions and 1 (0.9%) of the reoperations. Temporary postoperative hoarseness occurred in 9 (4.8%) of the initial operations and 5 (4.7%) of the reoperations. Permanent recurrent laryngeal nerve injury (persisting for >6 months after operation and confirmed with diagnostic laryngoscopy) occurred in 5 (2.6%) of the initial operations and 2 (1.9%) of the reoperations. The rates of transient postoperative hypocalcemia (serum calcium level <8.0 mg/dL ≤24 hours after operation) were significantly different between the 2 groups: 79 of 189 initial CLNDs (41.8%) compared with 25 of 106 reoperations (23.6%) (P = .0025). However, permanent hypoparathyroidism (hypocalcemia and low parathyroid hormone requiring calcium and cholecalciferol supplementation >6 months after operation) occurred in only 1 patient in each group (0.5% and 0.9%, respectively).

Injury to normal parathyroid glands is one of the major concerns when performing CLND. We perform autotransplantation of normal parathyroid tissue if there is any suspicion of injury to the parathyroid glands during the course of thyroidectomy or lymph node dissection. Of our 189 initial CLNDs, we performed 31 autotransplantations (16.4%); of our 106 reoperative CLNDs, we performed only 1 autotransplantation (0.9%) (P < .001). Despite careful intraoperative inspection by the surgeon, parathyroid glands may be identified by the pathologist in the final operative specimen; 62 (32.8%) of the initial CLND specimens contained normal parathyroid glands compared with 10 (9.4%) of the reoperative CLNDs (P < .001). Frozen section for parathyroid biopsy was used in 46 (24.3%) of the initial operations and 18 (17.0%) of the reoperations; these biopsy samples were not counted as parathyroid tissue in the final specimen.

The average nodal yield for CLND as documented by the pathologists was 8 nodes for the initial CLND and 5 nodes for the reoperations; the average number of positive central neck lymph nodes was 4 of 8 for the initial operations and 3 of 5 for the reoperations. The average total nodal yield (all central plus lateral neck lymph nodes removed during the operation) was 18 for the initial operations and 17 for the reoperations; the average total number of positive nodes was 7 of 18 for the initial operations and 6 of 17 for the reoperations.

Reurrence rates for PTC were similar between the 2 groups. Overall, of the 189 patients undergoing initial CLND, 49 (25.9%) developed locoregional or distant recurrence of their disease requiring reoperation or other further therapy. Of the 106 reoperative CLNDs, 31 (29.2%) developed recurrence. The location of recurrence was the central neck for 22 (11.6%) of the initial CLNDs and 15 (14.1%) of the reoperations; recurrence in the lateral neck was found in 41 (21.7%) of the initial CLNDs and 18 (17.0%) of the reoperations.

COMMENT

In this retrospective review of 295 CNLDs for PTC, we found that the rate of transient hypocalcemia was higher for initial CLND than for reoperative CLND, and the incidence of other complications and the recurrence rate were no different between the 2 groups. We had hypothesized that complication and recurrence rates would be higher in patients undergoing reoperative CLND because of the difficulties associated with scar tissue in the reoperative field and distorted anatomy in the central neck after thyroidectomy. Our data demonstrate, however, that initial CLND has a rate of complications that is similar to the rate for reoperative CLND and has a higher risk of transient postoperative hypocalcemia.

Injury to the parathyroid glands, especially the lower glands, is a well-known pitfall of CLND. The lower parathyroid glands are usually located anterior to the recurrent laryngeal nerve but have a more variable location than the upper parathyroid glands; in addition, the microscopic appearance of the parathyroid glands may be similar to that of the central neck lymph nodes. In this study, we found that initial CLND performed in conjunction with total thyroidectomy resulted in increased rates of transient hypoparathyroidism, autotransplantation, and parathyroid glands found in the final pathology specimen when compared with reoperative CLND; these findings may reflect the fact that total thyroidectomy is a bilateral procedure that places all 4 parathyroid glands at risk, whereas reoperative CLND is more frequently a unilateral procedure. However, our rates of transient hypocalcemia for total thyroidectomy alone in patients with PTC are significantly lower (approximately 10%) (W.T.S., unpublished data, December 2008) than the rates of transient hypocalcemia for patients undergoing total thyroidectomy plus CLND (41.8%), indicating that CLND does contribute significantly to the risk of injury to the parathyroid glands. Unfortunately, our rates of permanent hypoparathyroidism were considerably lower (0.5%-0.9%) for both initial and reoperative CLND, indicating return of function of the remaining parathyroid glands over time.

The rates of other postoperative complications (neck hematoma and recurrent laryngeal nerve injury) for both groups were lower than the rates of transient hypocalcemia; however, the rates of permanent recurrent laryngeal nerve injury (2.6% for the patients undergoing initial CLNDs and 1.9% for those undergoing reoperation) were still significantly higher than our usual rate of nerve injury for total thyroidectomy alone (<1%). This difference in nerve injury rates underscores the fact that CLND, whether initial or reoperative, contributes additional risk of postoperative complications and is one of the primary reasons we do not routinely perform prophylactic CLND and instead perform CLND only in patients with enlarged nodes.

The results of this study demonstrate that initial and reoperative CLND have similar rates of recurrence. Roughly one-quarter of patients in whom we performed CLND for PTC (25.9%) developed recurrence requiring reoperation; there was no difference between initial and reoperative CLND in terms of location of recurrence (central vs lateral). Despite the technical difficulties of operating in a reoperative field, there does not appear to be any decrease in the efficacy of CLND in the reoperative setting; the nodal yield for central nodes and total nodes was similar for both initial and reoperative CLND.

Although we conclude from this study that initial and reoperative CLND have similar complication and recur-
ence rates (except for the higher transient hypocalcemia rates after initial CLND), we do not intend to advocate leaving enlarged central neck lymph nodes behind during total thyroidectomy for PTC even though reoperation appears to be as safe and effective as an initial operation. Our standard practice is still to perform preoperative ultrasonography of the thyroid gland and the central and lateral lymph node compartments in all patients with PTC and to remove all enlarged central neck lymph nodes at the time of initial operation. After assessing the results of this study, we emphasize that all CLNDs, whether initial or reoperative, are associated with high rates of postoperative complications. There exist numerous proponents of routine prophylactic CLND for PTC even in patients with nonenlarged nodes. However, we prefer to take a “wait-and-see” approach to nonenlarged central neck lymph nodes; most patients who are observed will not develop nodal enlargement and, as demonstrated in this study, reoperation is as safe and effective as an initial operation. We believe that the increasing body of published data comparing the outcomes of prophylactic CLND against observation of nonenlarged central neck lymph nodes will continue to demonstrate that prophylactic CLND for nonenlarged nodes produces increased complications and minimal added benefit for the majority of patients with PTC.

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Author Contributions: Dr Shen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Shen, Ruan, Kebebew, Duh, and Clark. Acquisition of data: Shen, Ogawa, Ruan, and Suh. Analysis and interpretation of data: Shen, Suh, Kebebew, Duh, and Clark. Drafting of the manuscript: Shen. Critical revision of the manuscript for important intellectual content: Ogawa, Ruan, Suh, Kebebew, Duh, and Clark. Statistical analysis: Shen, Ruan, and Duh. Administrative, technical, and material support: Suh. Study supervision: Kebebew, Duh, and Clark.

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REFERENCES