Complications of Neck Dissections in Papillary Thyroid Carcinoma: A Modified Procedure to Reduce Parathyroid Morbidity

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Abstract. *Background/Aim: Hypoparathyroidism is the most significant morbidity after neck dissection for thyroid cancer. Addition of lateral neck dissection (ND) to central ND combined with total thyroidectomy (TT) increases the risk of postoperative hypoparathyroidism compared to TT plus central ND. The aim of this study was to verify if a modified procedure and different access to the neck for lateral ND may improve safety. Patients and Methods: In 62 patients with papillary thyroid cancer (PTC) undergoing TT plus central and lateral ND between 2010 and 2013, lateral ND was performed as first step approaching the neck via extrathyroideal space. Calcium in serum and parathormone (PTH) were determined preoperatively, intraoperatively and during the follow-up. Results: Twenty patients (32%) developed postoperative hypocalcemia. Calcium levels and PTH completely recovered for 58 out of 62 patients from 3 to 6 months after surgery. After a mean of 12 months' follow-up, only four patients (6.5%) had developed permanent hypoparathyroidism. The incidence of parathyroid complication after TT plus central ND and lateral ND did not differ from postoperative hypoparathyroidim after TT plus central ND. Conclusion: The presented surgical procedure may provide a better outcome in terms of parathyroid morbidity.*

Cervical lymph node metastases are a hallmark of papillary thyroid carcinoma (PTC). Cervical nodal involvement is very common in patients with PTC and, depending on the detection method employed, 20-80% of patients diagnosed

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with PTC harbor lymph node metastases, mostly in the central neck compartment (1, 2). Therefore, nodal disease represents the most important issue for surgeons managing patients with PTC attempting to optimize the surgical procedures balancing the risk and benefits of thyroidectomy combined with neck dissection.

The regions typically involved in papillary nodal disease include the cervicocentral compartment and the cervicolateral compartment. Nodal metastases predominate in the cervicocentral compartment and in the ipsilateral cervicolateral compartment in both primary and repeat surgery for PTC. There is a clear association between central neck involvement and the likelihood of lateral neck disease, as an increase in the number of positive central nodes is associated with a higher likelihood of lateral neck disease (3). The ipsilateral portion of the cervicocentral compartment is involved more frequently than the contralateral portion, and the caudal basins (level III and IV) of the cervicolateral compartments are involved more frequently than the cranial (level II) and posterior triangle (level V) (4). These findings imply that the cervical lymphatic flow is directed from the central compartment toward the ipsilateral lower jugular lymph nodes and the venous angle (caudal cervicolateral compartment). Lymphatic tumor cells spread through the contralateral cervicocentral compartment to the contralateral cervicolateral compartment and from the mediastinum compartment (level VII) to the hilar lymph nodes, and ultimately to the pulmonary lymphatic system (5).

Numerous national and international guidelines have been published specifying recommendations for the management of neck lymph nodes, both central and lateral. The American Thyroid Association (ATA) guidelines published in 2009 recommended that therapeutic lateral neck compartmental lymph node dissection should be performed for patients with clinical-positive lateral cervical lymphadenopathy (recommendation 28m, rating b) (6). Prophylactic central ND may be considered in

patients with high-risk thyroid cancer, such as advanced primary tumor (T3 or T4) or aggressive histology (Recommendation 27, rating C). Therapeutic CND for patients with clinically involved central or lateral neck lymph nodes should accompany total thyroidectomy (Recommendation 27, rating B).

Since the ATA revised the guidelines, therapeutic central ND and lateral ND, in addition to total thyroidectomy, are for most Institutions worldwide standard surgical management of patients with PTC complicated by neck nodal disease. While there is total agreement on the recommendation that prophylactic lateral ND should be never indicated, the use of routine or prophylactic central ND at the time of initial thyroid surgery remains a matter of debate. The decision-making regarding whether or not to perform central ND continues to rely on the judgment of the surgeon, based on preoperative and intraoperative evaluation of the central compartment along with evaluation of each patient's prognostic risk factors.

The current surgical procedure for treating the lateral compartment of the neck in PTC is modified ND with the removal of a selected group of lymph nodes. Selective dissection is based on knowledge of the distribution of nodal metastases from different primary sites and removes only the lymph node groups that are considered to be at high risk of containing metastases. For this reason, comprehensive neck dissection with the removal of nodal basins from level I to V may be considered an inappropriate procedure for patients with PTC (7). In PTC, the appropriate treatment of the lateral compartment, directed by the patterns of lymphatic drainage from the primary tumor, includes removal of the lymph nodes at levels IIa, III, IV and Vb, the most frequently involved nodal stations. The incidence of nodal involvement in PTC at level I (submandibular lymph nodes) is quite rare, and level I dissection is not routinely indicated. The incidence of nodal metastasis is quite low at level IIb and Va, and these basins may not need routine clearance, unless their involvement is proven (8).

In 1962, Suarez described the fascial compartments in the neck and the fascial envelope covering the cervical lymph nodes (9). On the basis of these anatomic concepts, he discussed "functional neck dissection". This surgical procedure removes all the connective tissue together with lymph nodes at level II, III, IV and V, as well as modified ND or radical ND, preserving the sternocleidomastoid muscle, accessory nerve and internal jugular vein, along with the cervical fascial envelope so that the integral anatomy of the muscles, vessels, and nerves of the neck remain. Given that the majority of patients with PTC present nodal disease in the neck without extranodal involvement (nodal cancer) functional ND may be the procedure of choice in the management of PTC with nodal disease. In patients with invasion of neck fascial planes or previously treated with radiotherapy or other types of neck surgery, functional ND is no longer possible.

The classical radial ND is indicated only in patients with extranodal disease (neck cancer).

Central ND includes removal of the nodal subgroups within the central compartment referred to as level VI of the neck, *i.e.* the pre-laryngeal, pre-tracheal and both the right and left paratracheal nodal basins (10). The superior mediastinal nodes (level VII), which are more of concern in patients with medullary thyroid carcinoma, should be included in cases with clinically metastatic disease at level VI.

Even though modified, as well as functional ND, are reliable and safe surgical procedures for metastatic thyroid carcinoma, due consideration must be given to certain complications. The more extensive dissection required for lateral neck lymph node metastases is associated with complications not associated with thyroidectomy alone with or without central ND. Complications such as injury to the accessory nerve, hypoglossal nerve, vagus nerve, brachial plexus, sympathetic trunk, cervical branches and chyle leakage are typical of lateral ND. Thyroidectomy alone or combined with central ND, including considerable dissection in the paratracheal area, has a direct implication in the higher incidence of injury to recurrent laryngeal nerves and parathyroid glands, structures both located in the central compartment.

Several studies of nodal dissection performed in patients with PTC reported that the major complication observed was injury to the parathyroid glands, leading to transient or permanent hypoparathyroidism (8, 11). Postoperative hypocalcemia occurred far more commonly when total thyroidectomy and central ND were combined with lateral ND (11, 12). The highest risk of postoperative hypocalcemia in those patients was believed to be related to increased vascular compromise (13).

The aim of the present study was to assess the possible role of vascular imbalance in increased risk of hypoparathyroidism during lateral neck surgery for PTC with nodal disease and to verify if a modified procedure in performing neck dissection may reduce hypocalcemic morbidity.

Patients and Methods

From January 2010 to December 2013, 62 patients with preoperative diagnosis of PTC and cervical nodal metastases underwent total thyroidectomy with central ND and functional ND (unilateral in 56 patients and bilateral in six patients). The only exclusion criterion was a previous history of thyroid or neck surgery.

Patient information regarding age, gender, pathology, surgical procedure, number of parathyroid glands preserved or autotransplanted, and symptoms of hypocalcemia were analyzed. All patients were preoperatively diagnosed as having PTC with cervical node involvement following fine-needle aspiration on thyroid/neck lymph nodes in 51 patients, and in 11 patients by perioperative nodal sampling.

A preoperative blood sample was drawn on the morning of surgery for baseline measurement of total calcium and intact

parathyroid hormone (PTH) levels. Serum calcium concentrations were obtained at 1, 24 and 72 hours after surgery. The normal range for total calcium in serum was 8.5 to 10.5 mg/dl. PTH levels were measured using a standard enzyme-linked immunoassay (Human/Mouse/Rat PTH Enzyme Immunoassay Kit; RayBio®, Norcross, GA, USA) at 1, and 72 hours after surgery. The minimum detectable concentrations of PTH declared by the manufacturer was 1.27 pg/ml, with detection range 1-1,000 pg/ml.

All patients were clinically evaluated for signs and symptoms of hypocalcemia. Hypocalcemia was considered in patients, both symptomatic or non-symptomatic, having a total serum calcium level less than 8.0 mg/dl during their hospital stay. Patients who developed hypocalcemia were administered oral calcium and vitamin D replacement, while intravenous calcium gluconate was administered for hypocalcemic crisis. Hypoparathyroidism was classified as either transient or permanent: transient hypoparathyroidism was defined as hypocalcemia that did not require prolonged calcium or calcitriol supplementation; permanent hypoparathyroidism was defined as hypocalcemia requiring calcium and calcitriol for longer than 12 months. The study protocol required hospitalization of all patients for a minimum of 3 days after surgery for blood tests. All patients were followed-up at 1 week and 1, 6 and 12 months after surgery, and total serum calcium and PTH levels were measured. Patient characteristics are summarized in Table I.

For the purpose of this study, a systematic surgical procedure was defined. All patients were managed according to our operative technique (14-16) and all underwent total thyroidectomy with lymphadenectomy of the cervicocentral compartment (level VI) and selective functional lateral ND (IIa, III, IV, and Vb levels).

Operative technique. In the surgical management of patients with PTC and neck involvement, we performed lateral ND as the first step of the procedure. Using a high cervical incision, we entered the lateral compartment *via* extrathyroideal space through the strap muscles and the sternocleidomastoid muscle, after the incision of the superficial fascia of the neck.

The anterior margin of the sternocleidomastoid muscle was freed, and the muscle retracted laterally. The neurovascular bundle was reached running along the superficial fascia of the neck, posteriorly to the sternocleidomastoid muscle, and finally was approached the cervicolateral lymph node system. The described access is, therefore, totally external to the thyroid space and provides a fully operative field, allowing dissection of the lateral compartment's nodes from the supraclavicular space (level IV) to the level of the carotid artery bifurcation (level II). The most important feature of the lateral compartment is that it is encased in fascia and can be dissected cleanly at the surface of the fascia without entering the central compartment. When the tumor was a nodal cancer, functional ND was performed by approaching the neck through the fascial planes, the nodal dissection was confined to the lateral compartment alone and complications were only those related to the lateral compartment. The central compartment and its content were not of interest during lateral ND but were protected from the dissected area by the pre-tracheal layer. After the lateral ND was completed, thyroidectomy with dissection of the cervicocentral nodal compartment was performed during the same surgical session approaching the thyroid space through the traditional middle line of the strap muscles.

Table I. *Patient demographics and clinical characteristics.*

Characteristic	Value
Gender (M/F), n	49/13
Mean age ± SD, years	54.2±13.9
Surgical procedure, n	
With MLND	56
With BLND	6
Parathyroid glands preserved	232
Parathyroid gland autotransplantation	7

M: Male; F: female; MLND: total thyroidectomy+central node dissection+monolateral node dissection; BLND: total thyroidectomy+central node dissection+bilateral node dissection.

Results

In all patients, the indication for surgery was PTC that had metastasized to the lateral compartment. From January 2010 to December 2013, a total of 62 patients, 49 women and 13 men (mean age=54.2±13.9 years) with preoperative diagnosis of PTC and cervical node metastases underwent total thyroidectomy with central plus lateral ND. Six patients required bilateral neck dissection.

Postoperatively, serum calcium concentrations were obtained at 1, 24 and 72 hours after surgery and serum intact PTH levels were measured at 1, and 72 hours after surgery. Preoperative levels of serum calcium and PTH were in the normal range for all patients.

Twenty of the 62 patients (32.5%) developed postoperative hypocalcemia (serum calcium level less than 8.0 mg/dl). Within the first 72 hours from surgery, five patients (8%), developed clinical symptoms of hypocalcemia and required intravenous calcium gluconate. Serum calcium and PTH levels decreased in both normocalcemic and hypocalcemic patients. From 1 hour to 7 days after surgery, serum calcium levels declined more rapidly than at later time points for both normocalcemic and hypocalcemic patients. For both groups, calcium levels slowly increased after 2 or 3 weeks, and had nearly completely recovered from 1 to 6 months after surgery (Figure 1). Serum PTH dropped in normocalcemic and hypocalcemic patients rapidly at 1 hour after surgery and remained low for 7 days to 1 month and then slowly recovered to preoperative levels from 3 to 6 months after surgery (Figure 2).

At a mean follow-up of 12.98±1.4 months, 58 patients (93.5%) out of 62 were normocalcemic, although 16 patients (25.8%) experienced transient hypoparathyroidism and four (6.5%) patients remained hypocalcemic and required oral administration of calcium and calcitriol. Total thyroidectomy plus combined central and lateral ND increased the risk of hypocalcemia compared with total thyroidectomy alone. However, the rate of hypoparathyroidism did not differ
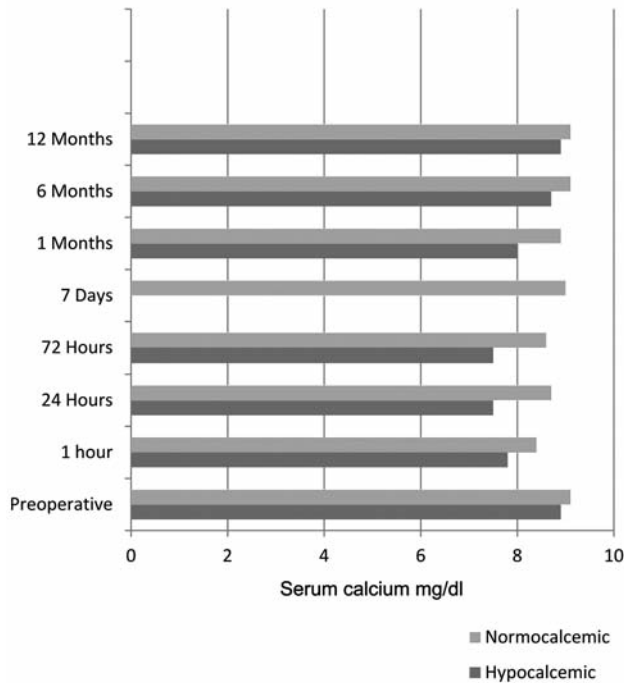
Figure 1. *Mean postoperative serum calcium level (normal range=8.5-10.5 mg/dl) in normocalcemic and hypocalcemic patients undergoing total thyroidectomy with central and lateral neck lymph node dissection.*

Figure 2. *Mean postoperative values of parathormone (PTH) (normal range=12-62 pg/ml) in normocalcemic and hypocalcemic patients undergoing total thyroidectomy with central and lateral neck lymph node dissection.*

between the group of 62 patients undergoing neck dissection with total thyroidectomy, according to the described surgical procedure, and other reported series undergoing central ND with total thyroidectomy, and was significantly lower when total thyroidectomy was traditionally performed with a neck dissection.

Discussion

The indication for performing a neck dissection in patients with PTC, as recommended by the ATA 2009 guidelines, is metastatic involvement of the cervical nodes. Complications related to the cervicocentral and cervicolateral compartment lymphadenectomy should be considered when making the decision regarding the extent of the nodal dissection. Potential complications from central ND include hypoparathyroidism, recurrent laryngeal nerve palsy, and injury to the trachea and esophagus. Potential complications from lateral ND include injury to the thoracic duct, internal jugular vein and carotid artery, and nerve injury, such as to the spinal accessory nerve, hypoglossal nerve, phrenic nerve, and to the sympathetic cervical plexus. The most significant morbidity following neck surgery for patients with PTC is hypoparathyroidism, both transient and permanent. The risk of injury t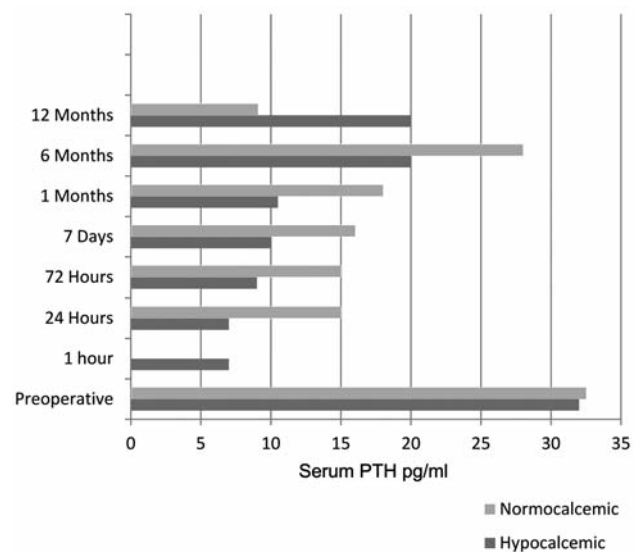o the parathyroid glands during thyroid surgery is very high, so that special attention must be given to the anatomic blood supply to the glands to prevent postoperative hypocalcemia.

Permanent hypocalcemia after total thyroidectomy has been reported to occur in 0.4-13.8% of cases (17-22). Transient hypocalcemia after total thyroidectomy is usually more commonly observed from 8.3-36.5% (13, 20, 22, 23). Recent multicenter cohort studies have shown that patients undergoing central ND experienced greater overall hypocalcemic morbidity compared with those who underwent total thyroidectomy alone. In patients undergoing nodal dissection, the incidence of postoperative transient hypocalcemia was from 23.2-51.9% (12, 13, 25, 26), while permanent hypoparathyroidism occurred in 0-16.2% of cases (12, 13, 25, 26). In their study, Roh *et al*., observed that hypocalcemia was also highest in patients who underwent combined central and lateral ND combined with total thyroidectomy (46.2%) (13). Addition of lateral to central ND resulted in an increased risk of postoperative hypocalcemia compared with total thyroidectomy plus central ND. In the above study, the increased hypoparathyroidism appeared not to be associated with incidental removal of the parathyroid glands or the number of the parathyroid glands preserved during surgery. They maintained that extending nodal dissection to include the both the central neck and the lateral compartment may increase the probability of compromising the vascularity of the dissected glands in the paratracheal area. A possible

explanation of why transient hypoparathyroidism occurs after performing lateral ND is that the nodal clearance between the internal jugular vein and the carotid artery may disturb the inferior thyroid artery at its origin, thereby interrupting its blood supply. The parathyroid vessels are tiny and terminal, and being preserved in the dissected area, respond to the injury by disrupting blood supply to the glands, prolonging the ischemic damage, with significant parathyroid morbidity. In addition, the dissection at level IV, in the supraclavicular space, very close to the inferior parathyroid glands, may compromise venous system drainage and favor postoperative venous congestion.

Taking into account these potential vascular implications, we modified our operative strategy in the management of patients with PTC and neck nodal involvement. As the first step of the surgical procedure, we perform lateral ND, which we approach *via* the extrathyroideal space, as described above. In this way, the lateral ND is performed in an area away from the parathyroid glands, which are protected from injury by the pre-tracheal layer. If we intraoperatively confirm the need for functional ND, based on anatomic concepts derived from fascial compartmentalization of the neck, and remove all the lymphatics, with conservation of non-lymphatic structures, we should be able to avoid complications related to central ND. The complications of the lateral compartment, approached separately from the central compartment, should only be those related to that area and should not include hypocalcemic morbidity. At final evaluation, the rates of transient and permanent hypoparathyroidism should not differ from those reported when total thyroidectomy is combined or not combined with central ND. Considering the data of the present study, we may comment that the result regarding the rate of postoperative hypoparathyroidism after total thyroidectomy combined with central plus lateral ND (32.5%) is similar to those reported in literature after total thyroidectomy and central ND (13, 25-26).

We believe that the results of the current study support our practice of performing lateral ND as first step of the surgical procedure in the management of PTC with nodal disease. Careful preservation of parathyroid vascularity and autotransplantation of de-vascularized parathyroid glands may reduce postoperative hypoparathyroidism, but we agree with the concern that extending nodal dissection to include the central neck compartment and the lateral cervical compartment may favor vascular dysfunction in the dissected central neck area, increasing the risk of ischemic injury to the glands.

The present study is limited by its retrospective nature and requires further evaluation in a prospective randomized trial, that would compare equivalent cohorts of patients stratified in two groups by the approach to the lateral compartment at the time of surgery. We have shown that neck dissection can be performed with no increase in parathyroid morbidity, but we are aware that our data should be verified by data from other high-volume centers.

Conclusion

Despite the small cohort of patients selected for the present study, our findings suggest that our modified approach in performing central ND combined with lateral ND in patients with PTC and nodal disease should be taken into consideration for providing a better outcome.

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