

Original Article

Thymectomy in central lymph node dissection for papillary thyroid cancer

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Abstract: Background: Central lymph node dissection (CND) has been proposed in the treatment of patients affected by papillary thyroid cancer (PTC) with clinically negative neck lymph nodes. The procedure allows pathologic staging of lymph nodes of the central compartment and treatment of the micrometastases. By comparing bilateral and unilateral thymectomy during total thyroidectomy with central lymph node dissection for postoperative complications in sonographically node-negative papillary thyroid carcinomas, we aimed to determine the optimal extent of prophylactic central lymph node dissection. Methods: Patients were divided into two study groups: Group 1, total thyroidectomy plus unilateral thymectomy during the CND; Group 2, total thyroidectomy associated with bilateral thymectomy (both upper poles) during the CND. Primary endpoints of the study were evaluated by comparing the postoperative complications between the two groups. Results: The only significant result found when comparing the two groups was the rate of transient hypocalcemia. (Group 1: 13.7%, Group 2: 52.4%, $p < 0.01$). A total of five cases of papillary thymic metastases were found in this study. And final pathology confirmed that all cases of thymic metastases were lymph node micrometastases of PTC, only situated in the ipsilateral thymus upper pole. Conclusions: Bilateral thymectomy during the CND did not provide a better carcinologic resection, as no contralateral thymic metastases were found. The unilateral thymectomy with total thyroidectomy during the CND may represent an effective strategy for reducing the rate of postoperative hypocalcemia.

Keywords: Thymectomy, papillary thyroid cancer, lymph node dissection

Introduction

Central lymph node dissection (CND) is a common adjunct to thyroidectomy in the treatment of papillary thyroid cancer (PTC) [1]. However, Postoperative hypocalcemia occurred commonly in this central dissection, which is related to the resection or devascularization of the inferior parathyroids together with thymectomy [2]. Because of the same embryologic origin of the thymus and the inferior parathyroids, they are in close proximity to each other and share blood supply [3, 4]. Both the thymus upper poles and the inferior parathyroid glands are located within the paratracheal area of the central compartment of the neck. This explains the increased postoperative hypocalcemia after a central lymph node dissection. Recent reports indicate thyroidectomy plus lymph node dissection resulted in 3% to 6% of PTC patients suffering postoperative hypocalcemia [5, 6]. In order

to minimize this complication, some surgeons perform unilateral thymectomy and preserve the thymus contralateral to the cancer [7]. However, few reports to date have closely analyzed postoperative hypocalcemia after thyroidectomy plus node dissection.

By comparing bilateral and unilateral thymectomy during total thyroidectomy with central compartment lymph node dissection for postoperative complications in sonographically node-negative papillary thyroid carcinomas, we aimed to determine the optimal extent of prophylactic central compartment lymph node dissection.

Materials and methods

From 2009 to 2012, a total of 155 consecutive patients, diagnosed as sonographically node-negative thyroid papillary carcinomas, were

Table 1. Patient Demographics and Clinical Characteristics

Variable	Group 1 (n=73)	Group 2 (n=82)	P*
Gender (M/F)	11/62	17/65	0.360
Age			
Mean±SD	48.1±10.7	48.7±10.4	0.770
Groups (<45/>45)	22/51	45/37	0.059
MACIS score			
Mean±SD	4.7±0.9	4.9±1.0	0.360
High vs low risk (<6/>6)	7/73	16/82	0.083
Tumor size (cm)			
Mean±SD	2.76±1.23	2.56±1.20	0.206

Group 1: Unilateral thymectomy group; Group 2: Bilateral thymectomy group. *test except for age, MACIS score, and tumor size (t test). MACIS indicates metastasis, age, completeness, invasiveness, size.

included in this study. All subjects underwent total thyroidectomy in conjunction with one of two types of central compartment lymph node dissection (lymph node level VI). Patients were excluded from the study if the patients who had undergone (1) previous thyroid or parathyroid surgery; (2) a unilateral lobectomy, subtotal, or completion thyroidectomy; (3) previous neck irradiation; and (4) concomitant surgery for hyperparathyroidism. The diagnosis of papillary thyroid carcinomas was reconfirmed by the surgical pathology in all patients.

The CND was carried out in a conventional manner and was well described and illustrated by Grodski et al [8], including all perithyroidal and paratracheal soft tissue and lymph nodes with borders extending superiorly to the hyoid bone, inferiorly to the innominate artery, and laterally to the common carotid arteries.

Patients were divided into two groups according to CND: One in whom patients had a total thyroidectomy plus unilateral thymectomy during the CND, leaving in situ the contralateral thymus upper pole. While the other group had a total thyroidectomy associated with bilateral thymectomy (both upper poles) during the CND. And the characteristics of the patients are presented in **Table 1**. Both groups' characteristics, including age, gender, MACIS score and tumor size, were comparable.

All patients were clinically evaluated for signs and symptoms of hypocalcemia. Transient hypocalcemia was defined as a symptomatic patient with an serum calcium level lower than

8.0 mg/dL at any time during the hospital stay [9]. While permanent hypocalcemia was defined as persistent symptomatic or biochemical (Ca level below 8.0 mg/dL) hypocalcemia at more than 6 months after surgery [9].

SPSS 12.0 for windows (SPSS Inc., Chicago, IL) was used for statistical analysis. Student t test was used when comparing continuous variables between groups; Statistical analysis of the differences in clinical variables between groups was conducted by the Chi-square test. A two-tailed P less than 0.05 was considered to be significant.

Results

As showed in **Table 2**, 73 patients had unilateral (ipsilateral) thymectomy (Group 1) and 82 patients had bilateral thymectomy (Group 2). There were no significant differences in the number of inferior parathyroid autotransplantation in the sternocleidomastoid muscle between the two groups ($P=0.657$). Transient hypocalcemia was documented in 10 patients (13.7%) in Group 1, in 43 patients (52.4%) in Group 2. Statistical analysis showed significant difference ($P<0.01$) in the rate of transient hypocalcemia between two groups. However, there were no significant differences in the rate of permanent hypocalcemia between two groups ($P=0.099$). Both Group 1 and Group 2 were found to have cases of thymic metastases (2.7%, 3.6% respectively), this difference did not reach statistical significance ($P=0.747$). Interestingly, final pathology examination confirmed that the five cases of thymic metastases were lymph node micrometastases of PTC, only situated in the ipsilateral thymus upper pole. No contralateral thymic metastases were found in either group.

Discussion

PTC is the most common thyroid malignancy and carries an excellent prognosis. While up to 20-90% patients with PTC may have lymph node metastasis detected during the initial surgery [10]. Lymph node metastases generally occur in a stepwise fashion and the central neck is the most common site of metastatic PTC [8, 11, 12]. In this study, pathologically confirmed central neck lymph nodes metasta-

Table 2. Comparative results between the two groups

Variable	Group 1 (n=73)	Group 2 (n=82)	P*
Parathyroid autotransplantation	5.1±1.5	5.2±1.3	0.657
Hypocalcemia			
Transient	10 (13.7%)	43 (52.4%)	<0.01
Permanent	0 (0%)	3 (3.6%)	0.099
Thymus metastases	2 (2.7%)	3 (3.6%)	0.747

Group 1: Unilateral thymectomy group; Group 2: Bilateral thymectomy group. *test except for Parathyroid autotransplantation (t test).

sis from PTC occurs commonly. In contrast to the preoperative assessment of the central compartment lymph nodes with ultrasound, our results are consistent with previously reported study [13]. Which indicating preoperative ultrasonography is an unreliable technique for detecting the central lymph node metastasis, this might be because the air-filled trachea as well as the fatty tissue containing the lymphatic tissue disturbed ultrasonography detection of lymph nodes that were small. Furthermore, suggesting prophylactic central neck dissection should be carried out for the management of cNO PTC.

The thymus is an important organ involved in cell-mediated immunological function. The parenchyma of the thymus has a blood-thymus barrier [14], which prevents the thymus from making direct contact with antigens or cancerous cells, thereby it has been considered almost impossible that a tumor could metastasize to the thymus. However, in the present study, five cases of thymic metastasis from PTC were identified by final pathology, within the thymus upper poles. Our results are consistent with previously reported studies [15-17], and might be explained because blood-thymus barrier is not as robust in the medulla of the organ as it is in the cortex, when the structure of the thymus is precisely analyzed. The septum of the thymus is comprised of interlobular connective tissue with blood vessels, lymph ducts and nerves, which theoretically does not exclude the possibility of metastasis [14]. And we presumed that because of the lymphatic metastasis behavior of the PTC [18], the mechanism of metastasis by the thyroid cancer to thymic may have been via a lymphatic pathway. However, whether the location of the tumor suggested metastasis via a lymphatic pathway or local venous pathway needs further study.

When CND was performed, the fibrofatty tissue in the midline is incised to expose the trachea down to the level of the brachiocephalic vessels inferiorly, and the medial border of the carotid artery is dissected down to the prevertebral fascia. The superior limit of dissection is at the level of the cricoid cartilage, and the thymus is transected at the level of the brachiocephalic vessels and the specimen is removed [7, 19]. Anatomically both the

inferior parathyroid gland and the thymus upper poles are located in the central compartment of neck. Embryologically, the thymus gland originates from the third pair of branchial pouches high in the neck during early foetal life and starts their descent toward the mediastinum. And the inferior parathyroid gland has the common embryologic origin, which is responsible for the close relationship and the shared blood supply between both glands [20]. In our study, the unilateral group had fewer transient hypocalcemia cases than the bilateral group, suggesting that the increased rate of postoperative hypocalcemia is more related to bilateral thymectomy, with removal or devascularization of the inferior parathyroid glands during a central neck dissection. Furthermore, all of the thymic metastases were found in the side of the tumor, no contralateral thymic metastases were found in either group. Our results are consistent with previously reported studies [17, 21], indicating that the unilateral thymectomy provides enough carcinologic resection. It is necessary to differentiate the thymus upper pole in both side and preserve the thymus contralateral to the cancer with the goal of keeping a better parathyroid function.

The main limitation of the study is represented by the fact that, this is a retrospective observational study. Thus, a large randomized trial with long-term follow-up is needed, however, the low prevalence of PTC combined with its relatively indolent nature has meant that ideal treatment research protocols are difficult to undertake.

In summary, the unilateral thymectomy with total thyroidectomy could be an alternative surgical option for clinically node-negative papillary thyroid carcinomas, because it results in a reduced transient postoperative hypocalcemia and similar carcinologic resection. Further

study with a larger number of patients and long-term follow-up is needed.

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Written informed consent was obtained from the patient for publication of this article and accompanying tables. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure of conflict of interest

None.

Abbreviations

PTC, papillary thyroid cancer; CND, Central lymph node dissection.

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