

## Original Article

# The implement of prophylactic central neck dissection in patients with cNO papillary thyroid carcinoma

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**Abstract:** Background: Central lymph node metastasis of papillary thyroid carcinoma (PTC) is common, however, routine central lymph node dissection (CLND) is still controversial because of the uncertain efficacy and possible increased morbidity. The purpose of this study is to determine when prophylactic central neck dissection should be performed in patients with cNO papillary thyroid carcinoma. Methods: A protocol on the indication for prophylactic CLND in PTC was designed according to our experience combined with international guidelines, and PTC patients during 2005-2006 who qualified for this protocol were included in this study. Patients who underwent prophylactic CLND were designed as CLND group, and patients who underwent thyroidectomy alone were designed as Tx group. The 10-year recurrence rate of two groups was compared. Results: 170 PTC cases were included in this study. CLND group had 119 patients, Tx group had 51 patients. In CLND group, the incidence of involved central neck lymph nodes was 71%. During a follow-up of over 10 years, More patients had recurrences in CLND group than in Tx group (11% vs 3.9%;  $P < 0.01$ ). Conclusion: This protocol was an accurate way to select high risk PTC patients, and at the same time, allow low risk PTC patients to avoid unnecessary CLND, which is helpful for implementing personalized therapy for PTC.

**Keywords:** Papillary thyroid carcinoma (PTC), central lymph node dissection (CLND), personalized therapy

## Introduction

Despite most papillary thyroid carcinoma (PTC) patients has good prognosis, metastasis to lymph nodes is common. Up to 20-90% patients with PTC may have lymph node metastasis detected during the initial surgery [1, 2]. The central neck compartment is the most common site of metastases. Consequently, some surgeons recommend routine prophylactic removal of the central neck lymph nodes at time of the initial operation [3, 4]. However, this was countered with some studies showing no benefit [5, 6]. The purpose of this study is to determine when prophylactic CLND should be performed in patients with cNO PTC.

## Patients and methods

A protocol on the indication of prophylactic CLND in cNO PTC was designed according to our experience combined with international guidelines. The content of the protocol includes:

(1) PTC patients with the maximum tumor size over 1.5 cm; (2) PTC patients over 45 with tumor size between 1.0 cm and 1.5 cm; (3) PTC patients over 45 with multi-focal tumors. Patients qualified for any criteria should receive thyroidectomy plus prophylactic CLND. Patients who disqualified received only thyroidectomy. The database of patients with histologically proven papillary thyroid carcinoma at Peking Union Medical College Hospital from January 2005 to December 2006 was screened and 170 cases of PTC was included in this study. Patients who underwent thyroidectomy alone were designated as group Tx, whereas those undergoing thyroidectomy with prophylactic CLND were designated group CLND. Patients with evident preoperative abnormal lymph nodes, distant metastasis or those who had subtotal thyroidectomy or hemi-thyroidectomy were excluded. CLND is defined as the removal of all level VI and VII nodes [7]. Of the 282 patients treated surgically for PTC from January 2005 to December 2006, 170 patients satis-

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**Table 1.** Patient characteristics

	CLND group (n=119)	Tx group (n=51)	P value
Median age	44	48	NS
Gender			NS
Male	19	11	
Female	100	40	
Pathology			
Multifocal	28% (34)	21% (11)	<0.05
Median tumor size(cm)	1.8	1.1	<0.01
Extrathyroid extension	17% (21)	8% (4)	<0.01
Positive lymph node	71%		
MACIS score	5.8	4.1	<0.01

**Table 2.** Operative complications

	CLND group (n=119)	Tx group (n=51)	P value
Temporary hypocalcemia	29% (35)	8.1% (4)	<0.01
Permanent hypoparathyroidism	2.1% (3)	1.6% (1)	NS
Temporary RLN injure	2.1% (3)	1.6% (1)	NS
Permanent RLN injure	1.4% (2)	1.6% (1)	NS

**Table 3.** Disease recurrence requiring reoperation

	CLND group (%)	Tx group (%)	P value
Reoperation	13 (11%)	2 (3.9%)	<0.01
Central	9 (7.6%)	1 (2.0%)	<0.01
Lateral	11 (9.2%)	2 (3.9%)	<0.01
Central plus lateral	7 (5.9%)	1 (2.0%)	<0.01

fied inclusion criteria. 51 patients underwent thyroidectomy alone and 119 patients underwent thyroidectomy and CLND.

We routinely removed badly blood-supported parathyroid during operation and cut it into 1 mm pieces to implant in the sternocleidomastoid muscle. Patients were monitored postoperatively with serum calcium determination. Temporary hypocalcemia was defined as serum calcium <8 mg/dl anytime during the initial 6-month follow-up. Permanent hypoparathyroidism was defined as a need for continued calcium beyond 6 months after surgery with persistent serum calcium <8 mg/dl. Transient recurrent laryngeal nerve (RLN) palsy was confirmed by fiber optic laryngoscopy between 0 and 6 months after operation, and permanent

RLN palsy was confirmed by fiber optic laryngoscopy beyond 6 months after operation. Recurrence was defined as local regional or disease requiring reoperation or other repeat treatment, as detected by serial cervical ultrasonographics or radioactive thyroid scan.

Patients with positive lymph node underwent radioactive iodine ablative therapy with iodine<sup>131</sup> (<sup>131</sup>I) 3-4 weeks after operation. All patients entered a scheduled clinical follow-up program on an average duration of over 10 years. Follow-up of patients' involved annual examination of neck ultrasonography, <sup>131</sup>I scintigraphy, computed tomography and so on.

Statistical analysis was performed using SPSS13.0 software. Data were compared for statistical analysis using the chi-square tests to evaluate differences between qualitative variables, and using the Student's t test to compare quantitative variables, P<0.05 was considered significant.

### Results

Patient characteristics are summarized and operative results were analyzed between two groups based on operative and surgical pathology reports in **Table 1**. There were no significant differences in the age, gender distribution. The number of patients found to have involved central neck lymph nodes on final pathology was 85 of 119 (71%) in group CLND.

The incidence of operative complications is summarized in **Table 2**. There was a higher rate of temporary postoperative hypocalcemia in group CLND. Permanent hypoparathyroidism was equivalent between the groups. There was no difference in the incidence of temporary and permanent RLN injury between two groups.

During final follow-up, no one died in this study. There was no recurrence in the thyroid bed. Group CLND had a significant higher recurrence rate (P<0.01) compared with group Tx, which did not have CLND (shown in **Table 3**). In group CLND, all 13 recurrences occurred in regional lymph nodes, 9 of whom had central section

lymph nodes recurrences and 7 of whom had both central and lateral section lymph nodes recurrences. 2 recurrent disease occurred in group Tx with 1 in central compartment and 2 in lateral section.

### Discussion

The incidence of PTC has been increasing within recent years [8]. Although it has been accepted that patients with PTC have benign clinical courses [9], cervical lymph node metastases are common [1, 2]. Furthermore, it has been reported regional lymph node metastasis was associated with increased local recurrence rates and reduced survival [3, 10, 11]. However, most of central lymph node metastases are too small to be detected by using sonography [12, 13]. Therefore, there is renewed interest in the operative management of cervical lymph node metastases. Although most surgeons agree that grossly involved lymph nodes in the central neck of patients with PTC should be managed by a selective neck dissection, controversies remain on whether prophylactic should be performed for cN0 PTC patients because of the uncertain efficacy and possible increased morbidity. Zuniga et al reported that prophylactic CLND did not reduce recurrence rate of PTC [14]. The higher complication rates such as temporary hypocalcemia, permanent hypoparathyroidism and RLN palsy are often cited in arguments against prophylactic CLND in the treatment of PTC [15, 16]. Therefore, in order to solve the problem, we have to answer the question which PTC patients could benefit from prophylactic CLND. This retrospective, cohort study was planned to determine when prophylactic CLND should be performed in patients with cN0 PTC.

It has been reported that multiple factors including age, tumor size, extra-thyroid extension, and multi-focal were related with tumor progression and poor prognosis. Based on our experience, we combined the above risk factors to design a protocol on the indication for prophylactic CLND, through which we could select high risk PTC patients. This study showed that patients with PTC selected by our protocol not only had higher lymph node metastasis rate, but also had higher recurrence rate than other PTC patients. They are proper candidates for prophylactic CLND.

In conclusion, our protocol is reasonable and practical, which is helpful for implementing personalized therapy for PTC patients. The limitations of this study include its nonrandomized, retrospective design, leaving the results vulnerable to the selection biases. A large prospective study should be performed to test this protocol further.

### Disclosure of conflict of interest

None.

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