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Lateral lymph node recurrence after total thyroidectomy and central neck dissection in patients with papillary thyroid cancer without clinical evidence of lateral neck metastasis

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ABSTRACT

Background: This study analyzed the incidence, pattern, and predictive factors for lateral lymph node (LN) recurrence in patients with papillary thyroid cancer (PTC) without clinical evidence of lateral LN metastasis.
Methods: A retrospective analysis was performed on 246 patients with PTC who underwent total thyroidectomy and central neck dissection from 2004 to 2010. None of the patients had clinical evidence of lateral LN metastasis at the time of diagnosis. Predictive factors for lateral LN recurrence were evaluated using the chi-square test. Binary logistic regression was used for the multivariate analysis. Recurrence-free survival rates were estimated by the Kaplan–Meier and Cox regression methods.
Results: Of the 246 patients, 11 (4.5%) developed lateral LN recurrence with a median follow-up of 49 months. In the multivariate analysis, tumor size >1 cm (odds ratio [OR], 8.14; 95% confidence interval [CI], 1.01–65.68; $p = 0.049$) and central LN metastasis (OR, 10.59; 95% CI, 1.32–85.17; $p = 0.026$) were independent predictive factors of lateral LN recurrence. Especially, extranodal extension of a metastatic central LN (OR, 38.82; 95% CI, 5.71–264.10; $p < 0.001$) was an independent predictor of lateral LN recurrence.
Conclusions: Tumor size and central LN metastasis were independent predictors of lateral LN recurrence in patients with PTC without initial clinical lateral neck metastasis who underwent total thyroidectomy and central neck dissection. Close surveillance may be necessary for early detection of lateral LN recurrence in PTC patients with tumor size $\geqslant 1$ cm, and central LN metastasis with extranodal extension.

Introduction

Papillary thyroid cancer (PTC) is the most common thyroid malignancy, accounting for 85% of total thyroid cancer cases in iodine-sufficient areas worldwide [1,2]. Most cases of PTC have excellent prognosis and a low mortality rates [3,4]. However, PTC results in metastatic lymph nodes (LNs) in 30–80% of patients [5,6]. Although LN metastasis generally does not affect survival rate in patients with low-risk PTC, it has been associated with a higher rate of locoregional recurrence [7,8]. Cervical LN recurrence is closely related with a patient's quality of life despite having no major effect on the survival of patients with PTC.

Surgeons initially examine the cervical neck and primary tumors of patients with PTC to detect a metastatic LN and determine the extent of surgery required. Ultrasound (US) and computed tomography (CT) are generally used to evaluate cervical LN metastasis. Prophylactic lateral LN dissection is generally not recommended when no suspicious metastatic LN is found in the lateral neck [9]. However, a lateral LN recurrence can occur in patients with PTC without evidence of lateral neck LN metastasis at the initial evaluation despite a total thyroidectomy, central neck dissection, and appropriate postoperative radioactive iodine (RAI) therapy. Although many studies have reported locoregional recurrence in PTC [10–14], few studies have reported lateral LN recurrence after total thyroidectomy and central neck dissection in patients with PTC without clinical evidence of lateral LN metastasis at the time of the initial diagnosis. The present study analyzed the incidence, pattern, and risk factors of lateral LN recurrence in patients with PTC without clinical evidence of lateral LN

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metastasis, who were initially treated with total thyroidectomy and central neck dissection.

Materials and methods

A retrospective analysis was performed on 246 patients with PTC who underwent total thyroidectomy and central neck dissection at the Department of Otolaryngology-Head and Neck Surgery of Chungnam National University Hospital (Daejeon, Korea) from 2004 to 2010. None of the patients had clinically suspicious metastatic LNs in the lateral neck at the time of diagnosis. Preoperative US and CT in all patients were used to identify LNs suspected of metastases in the lateral neck. All patients received bilateral central LN dissection. Patients who received a lobectomy only, did not receive a central neck dissection, or whose medical records were unclear, were excluded from the study. This study was approved by the Institutional Review Board of Chungnam National University Hospital.

All patients received postoperative suppressive levothyroxine treatment. RAI ablation was applied to patients with positive metastatic central LNs, capsular invasion, or extrathyroidal extension on a permanent biopsy. I-131 ablative therapy was administered after levothyroxine withdrawal for at least 4 weeks. A whole body scan (WBS) was performed 7 days after I-131 therapy in order to evaluate whether ablation was successful. During follow-up, routine clinical examinations (every 3 months in the initial year and the at yearly interval) included neck US, whole body scan (WBS), serum-free thyroxine and thyroid stimulating hormone levels, thyroglobulin (Tg), and anti-Tg antibodies. For patients suspected for disease recurrence, we conducted fine needle aspiration cytology or CT scan. Recurrent disease was defined as pathological evidence of disease on excision or US-guided cytology or recurrent disease confirmed by elevated Tg and a WBS. We investigated the pattern and risk factors for lateral LN recurrence according to the clinicopathological features of patients with PTC.

SPSS software (ver. 18.0; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Predictive factors for lateral LN recurrence were evaluated by a univariate analysis using the chi-square or Fisher's exact test. Significant variables in the univariate analysis were included in a multivariate analysis using binary logistic regression. Recurrence-free survival rates were estimated by the Kaplan–Meier and Cox regression methods. A p-value < 0.05 was considered significant.

Results

Patient characteristics

The 246 patients with PTC comprised 210 females and 36 males (median age, 48 years; range: 20–81 years). The mean size of the primary tumor was 1.6 cm (range: 0.4–5.7 cm). Multifocal tumors were detected in 103 (41.9%) patients. Capsular invasion, extrathyroidal extension, and lymphovascular invasion were identified in 168 (68.3%), 152 (61.8%), and 174 (70.7%) patients, respectively. Prophylactic central LN dissection was performed in 212 patients without evidence of metastatic LN on US or CT; 34 patients with evidence of metastatic LN received therapeutic central LN dissection. The overall rate of central LN metastases was 44.7% (110 of 246), and the occult ratio of central LN metastases was 35.8% (76 of 212). RAI therapy was applied to 215 patients (Table 1).

Clinicopathological characteristics of patients with lateral LN recurrence

Table 2 shows the clinicopathological characteristics of 11 patients with lateral LN recurrence after initial total thyroidectomy and central neck dissection. The patients with PTC and lateral LN recurrence consisted of nine females and two males (median age, 49 years; range: 38–78 years). Lateral LN recurrences were ipsilateral to the primary tumor in all cases. Mean size of the primary PTC was 1.9 cm (range: 0.7–3.5 cm). All patients except one showed extrathyroidal extension of the primary tumor. All patients except one had metastatic central LN, with a mean metastatic LN ratio of 0.57 (range: 0–0.8). Six patients had extranodal extension of a metastatic central LN at the time of the initial surgery. Mean follow-up duration was 28.7 months (range: 15–52 months). Five and six cases of lateral LN recurrence were single and multiple levels, respectively. Levels III and IV were the most common neck levels for the lateral LN recurrences. All patients were salvaged through therapeutic lateral neck dissection and RAI therapy for lateral neck recurrence.

Table 1
Patient characteristics and lateral lymph node recurrence according to clinicopathological factor of 246 papillary thyroid cancer patients.

Patients risk factors	Total	Lateral recurrence, No. of cases (%)	p-Value
Sex			0.666
Female	210	9 (4.3)	
Male	36	2 (5.6)	
Age (years)			0.751
<45	88	3 (3.4)	
⩾45	158	8 (5.1)	
Tumor size (cm)			0.010*
<1	123	1 (0.8)	
⩾1	123	10 (8.1)	
Multiplicity			0.126
Solitary	142	9 (6.3)	
Multiple	103	2 (1.9)	
Capsular invasion			1.000
No	78	3 (3.8)	
Yes	168	8 (4.8)	
Extrathyroid extension			0.055
No	94	1 (1.1)	
Yes	152	10 (6.6)	
Lymphovascular invasion			0.183
No	72	1 (1.4)	
Yes	174	10 (5.7)	
Type of central ND			0.653
Prophylactic	212	9 (4.2)	
Therapeutic	34	2 (5.9)	
Central LN metastasis			0.003*
No	136	1 (0.7)	
Yes	110	10 (9.1)	
RAI therapy			0.368
No	31	0 (0)	
Yes	215	11 (5.1)	

ND, Neck dissection; LN, Lymph node; No., Number; RAI, Radioactive iodine.
* $p < 0.05$ between the two categories for a given variable.

Lateral lymph node recurrence according to patient clinicopathological factors

Among the 246 patients, 11 (4.5%) had a recurrence in the lateral neck. In a univariate analysis, the lateral LN recurrence rate was significantly higher in patients with primary tumor size ⩾1 cm ($p = 0.010$) or central LN metastasis ($p = 0.003$). However, no association was found between lateral LN recurrence rate and sex, age, multiplicity, capsular invasion, lymphovascular invasion, type of central neck dissection, or receiving RAI therapy. A borderline significant relationship was detected between lateral LN recurrence and extrathyroidal extension of the primary tumor