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Clinical implications of pathologic factors after thyroid lobectomy in patients with papillary thyroid carcinoma

Young Min Park, Doh Young Lee, Kyung Ho Oh, Jae-Gu Cho, Seung-Kuk Baek, Soon-Young Kwon, Kwang-Yoon Jung, Jeong-Soo Woo*

Department of Otorhinolaryngology-Head and Neck Surgery, Korea University College of Medicine, Seoul, Republic of Korea

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ABSTRACT

Objective: We evaluated the clinical and prognostic significance of pathologic factors by analyzing the treatment results of patients who underwent thyroid lobectomy.
Materials and methods: We retrospectively analyzed data from 734 patients diagnosed with papillary thyroid cancer who underwent thyroid lobectomy at Korea University Hospital from January 2004 to December 2016.
Results: A total of 734 patients were included in the study and their mean age was 44.5 years (range, 15–83). On univariate analysis, tumor size and recurrence-free survival were significantly related. The 10-year recurrence-free survival was 98.3% for tumors ≤1 cm, 77.8% for > 1 cm and ≤2 cm, and 66.7% for > 2 cm ($p = 0.014$). Recurrence-free survival was significantly different between patients with and without microscopic extrathyroidal extension ($p = 0.002$). The 10-year recurrence-free survival rate was 99.2% for patients without extrathyroidal extension and 92.2% for patients with microscopic extrathyroidal extension. Multivariate analysis showed only microscopic extrathyroidal extension was significantly correlated with recurrence-free survival ($p = 0.029$).
Conclusion: In patients undergoing thyroid lobectomy for low-risk papillary thyroid cancer, microscopic extrathyroidal extension was an important prognostic factor associated with recurrence-free survival. However, in cases with microscopic extrathyroidal extension findings on postoperative pathologic examination, appropriate ultrasonographic follow-up of the contralateral thyroid lobe and cervical lymph node to facilitate early detection and prompt treatment of recurrence can control the disease without a deterioration of survival rate.

Introduction

Papillary thyroid carcinoma (PTC) is the most common malignant tumor of the thyroid gland. The disease-specific survival rate for PTC is excellent and the 10-year overall survival rate is over 90% [1,2]. Various clinicopathologic factors such as age, sex, tumor size, extrathyroidal extension (ETE) and distant metastasis are known to be associated with prognosis. For tumor size, Bilimoria et al. reported that total thyroidectomy should be recommended for PTCs larger than 1 cm because of poor overall survival compared with PTCs smaller than 1 cm [3]. On the contrary, contemporary studies suggest no significant difference in overall survival between patients undergoing thyroid lobectomy and total thyroidectomy and they insisted that thyroid lobectomy may be an effective treatment for low-risk PTC [4,5]. Based on these results, the indications for thyroid lobectomy were expanded in the revised American Thyroid Association guidelines (2015). Thyroid lobectomy could be considered in the absence of ETE and clinical cervical lymph node metastases for tumors larger than 1 cm and smaller than 4 cm. However, the proper follow-up methods after thyroid lobectomy and the indications for completion thyroidectomy remain controversial. Therefore, studying the clinical and prognostic significance of pathological factors reported by microscopic examination of surgical specimens after thyroid lobectomy is necessary. In this study, we evaluated the clinical and prognostic significance of various pathologic factors reported by histologic examination of surgical specimen by analyzing the treatment results of patients who underwent thyroid lobectomy.

Materials and methods

We retrospectively analyzed data from 734 patients diagnosed with PTC who underwent thyroid lobectomy at Korea University Hospital from January 2004 to August 2016. The indications for thyroid lobectomy in patients with PTC were: (1) tumor confined to one thyroid

* Corresponding author at: Department of Otorhinolaryngology-Head and Neck Surgery, Korea University Guro Hospital, 148, Gurodong-ro, Guro-gu, Seoul 08308, Republic of Korea.
E-mail address: diakonos@korea.ac.kr (J.-S. Woo).

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lobe, and (2) no suspicious or malignant nodule in the opposite thyroid lobe. Exclusion criteria were: (1) previous surgery or radiotherapy due to other head or neck cancer, (2) preoperative diagnosis of lymph node metastasis or distant metastasis, (3) malignant nodules in the opposite thyroid lobe, and (4) completion thyroidectomy within 6 months after first operation. This study was approved by the Institutional Review Board of Korea University.

Ultrasonography (US) was performed on all patients before surgery. In the case of indeterminate or suspicious nodules in opposite thyroid lobes, US-guided fine needle aspiration cytology was performed and thyroid lobectomy was performed only for confirmed benign nodules. Prophylactic central compartment lymph node dissection was not performed in patients undergoing thyroid lobectomy. The mean follow-up period was 50.4 months (range, 12–152). All patients were followed up at intervals of 6–12 months postoperatively with physical examination and thyroid function test. Neck US was performed for the first 6–12 months after the first operation and every 12–24 months thereafter.

Pathologic factors including tumor size, multifocality, ETE, lymphovascular invasion, surgical margin, and thyroiditis were collected from medical records for surgical specimens and analyzed for association with recurrence of disease. ETE referred to tumor invasion into surrounding tissue beyond the thyroid gland [6–9]. Microscopic ETE (micro-ETE) was defined as ETE not visualized grossly during surgery but with histological ETE findings observed by microscopic examination [10]. Locoregional recurrence was defined as lesions observed in imaging studies and confirmed by pathological or cytological examination. Recurrence-free survival (RFS) was defined as time between the first operation and structural recurrent disease. All patients underwent laryngeal endoscopy before and after surgery to confirm the occurrence of complications such as vocal-fold paralysis.

Chi-square or Fisher's exact tests were used to evaluate differences in categorical variables between two independent groups. Independent two-sample *t*-tests were used to assess differences in continuous variables between two independent groups. Kaplan-Meier curves were used to analyze RFS, and survival outcomes were assessed using log-rank tests. Multivariate analysis was performed to model dichotomous variables using logistic regression models. A p-value < 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS 20 for Windows (SPSS, Chicago, IL).

Results

Patient clinicopathologic information

A total of 734 patients were included. Their mean age was 44.5 years (range, 15–83) and 143 (19.5%) were men and 591 (80.5%) were women. Tumor sizes were as follows: 665 (90.6%) were ≤1 cm, 63 (8.6%) > 1 cm and ≤2 cm, and 6 (0.8%) > 2 cm. Postoperative pathology examinations revealed micro-ETE in 190 (25.9%) patients and no ETE findings in 544 (74.1%). Multifocal lesions were found in 97 (13.2%) patients and not found in 637 (86.8%) patients. Lymphovascular invasion was observed in 1 (0.1%) patient and not seen in 733 (99.9%) patients. Positive surgical margins were reported for 29 (4.0%) patients with 705 (96.0%) showing negative margins. Accompanying thyroiditis occurred in 239 (32.6%) patients and did not occur in 495 (67.4%) patients. No distant metastases or deaths occurred during follow-up. During the follow-up period, 23 (3.1%) recurrences were observed, with 17 in the opposite thyroid lobe, 3 nodal (1 case in the central neck compartment and 2 in the central & lateral neck compartment), and 3 in the contralateral lobe with nodal recurrence (1 case in the lateral neck compartment and 2 in the central & lateral neck compartment). No recurrent disease was observed in the previous thyroid operative bed. Mean time to recurrence after initial treatment was 50.3 months. Other clinical information for patients is presented in Table 1.

Table 1
Clinicopathologic features of patients (n = 734).

Variables (n = 716)	N (%)
Age, years	
< 45	378(51.5)
≥45	356(48.5)
Gender	
Male	143(19.5)
Female	591(80.5)
Tumor size	
≤1 cm	665(90.6)
> 1 cm and ≤2 cm	63(8.6)
> 2 cm	6(0.8)
micro-ETE	
No	544(74.1)
Yes	190(25.9)
Multifocality	
No	637(86.3)
Yes	97(13.2)
Lymphovascular invasion	
No	733(99.9)
Yes	1(0.1)
Margin	
Negative	705(95.9)
Positive	29(4.1)
Thyroiditis	
No	495(67.4)
Yes	239(32.6)
Recurrence	
Contralateral lobe	17
Nodal recurrence	3
Contralateral lobe & nodal recurrence	3
Thyroid (previous op. bed)	0
Average time to recurrence	50.3 months

micro-ETE: microscopic extrathyroidal extension

Table 2
Univariate analysis of clinical variables according to recurrence-free survival.

Clinical variables	No. patients (%)	No. of events	10-year RFS	p-value
Age (years)				0.169
< 45	378(51.5)	15	96.8	
≥45	356(48.5)	8	98.6	
Gender				0.321
Male	143(19.5)	2	97.0	
Female	591(80.5)	21	98.3	
Tumor size				0.014
≤1 cm	665(90.6)	20	98.3	
> 1 cm and ≤2 cm	63(8.6)	2	77.8	
> 2 cm	6(0.8)	1	66.7	
micro-ETE				0.002
No	544(74.1)	13	99.2	
Yes	190(25.9)	10	92.2	
Multifocality				0.967
No	637(86.3)	22	98.4	
Yes	97(13.2)	3	96.3	
Lymphovascular invasion				0.999
No	733(99.9)	23	98.5	
Yes	1(0.1)	0	100.0	
Margin				0.437
Negative	705 (95.9)	23	98.4	
Positive	29 (4.1)	0	100.0	
Thyroiditis				0.095
No	495 (67.4)	12	98.8	
Yes	239 (32.6)	11	96.5	

RFS: recurrence-free survival, micro-ETE: microscopic extrathyroidal extension.

Univariate analysis of clinicopathologic factors and RFS

The relationship between clinicopathologic factors and RFS was analyzed with univariate analysis (Table 2). Age, gender, multifocality, lymphovascular invasion, surgical margin, and presence of