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Risk factors for central neck lymph node metastasis of clinically noninvasive, node-negative papillary thyroid microcarcinoma

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Central neck;
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Abstract

BACKGROUND: To examine predictive factors for subclinical central neck lymph node metastases (LNM) of papillary thyroid microcarcinoma (PTMC).

METHODS: The clinical and pathological findings of 287 patients with clinically noninvasive, node-negative, solitary papillary thyroid carcinoma (PTC), who had undergone thyroidectomy plus central compartment neck dissection and showed pathologically confirmed nodal metastases, were analyzed. Predictive risk factors for central LNM were quantified.

RESULTS: Pathologic LNM was identified in 63 (32.6%) PTMC patients and 48 (51.0%) PTC patients (tumor size >1 cm; $P = .003$). Tumor size (>.7 cm; $P = .011$), multifocality ($P = .010$), and microscopic extracapsular extension ($P = .050$) were significant variables predictive of central LNM from PTMC in univariate analysis. Tumor size (odds ratio 2.28, 95% confidence interval 1.19 to 4.38; $P = .014$) and multifocality (odds ratio 2.38, 95% confidence interval 1.14 to 4.93; $P = .020$) were independent variables predictive of central LNM in multivariate analysis.

CONCLUSIONS: Cervical LNM is highly prevalent in clinically noninvasive, node-negative PTC. Central neck LNM is associated with larger tumor size and multifocality of PTMC.

Papillary thyroid microcarcinoma (PTMC), measuring 1 cm or less in maximal diameter, is generally characterized by indolent clinical behavior.[1] Ultrasonography (US) followed by fine-needle aspiration biopsy (FNA), rather than palpation, is now the preferred method for examination of the thyroid nodule. The use of US and FNA has facilitated increased preoperative detection of malignant nodules, particularly in relation to small thyroid carcinomas.[2,3]

In patients with clinically node-negative PTMC, subclinical lymph node metastasis (LNM) is frequently detected (30% to 65%) in pathologic specimens.[4–6] The rate of locoregional recurrence of PTMC has been reported to be 8% in patients with LNM.[7,8] A large population-based, case–control study reported that differentiated thyroid carcinomas with

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Table 1 Patient characteristics

Variables	Size of unifocal malignant thyroid nodule*		*P* value†
	≤1 cm (*n* = 193)	1.01–1.5 cm (*n* = 94)	
Sex, *n* (%)			
Male	32 (16.6)	19 (20.2)	.784
Female	161 (83.4)	75 (79.8)	
Age (years)			
Mean ± SD	49.2 ± 9.7	50.0 ± 9.7	.513
Size of malignant nodule* (cm)			
Mean ± SD	.61 ± .18	1.23 ± .15	<.001
Surgery, *n* (%)			
Lobectomy plus ipsilateral CLND	65 (33.7)	0	<.001
TT plus bilateral CLND‡	128 (66.3)	94 (100)	
Pathology, *n* (%)			
Multiple malignant nodules	43 (22.3)	26 (27.7)	.377
Extracapsular extension	103 (53.4)	58 (61.7)	.206
Central LN positivity	63 (32.6)	48 (51.0)	.003
Size of metastatic foci >.2 cm	27 (14.0)	21 (22.3)	.092
Metastatic LNs, mean ± SD (range)§	2.8 ± 2.3 (1–15)	2.7 ± 2.1 (1–9)	.709
MACIS score			
Mean ± SD	4.3 ± .8	4.7 ± .9	.002
≥6, *n* (%)	6 (3.1)	9 (9.6)	.043

Patient characteristics comparing 2 groups of 193 papillary thyroid microcarcinoma patients and 94 papillary thyroid carcinoma (>1 cm) patients.
CLND = central neck lymph node dissection; LN = lymph node; MACIS = metastasis, age, completeness, invasiveness, and size; SD = standard deviation; TT = total thyroidectomy.
*The sizes of unifocal malignant nodules localized to the unilateral lobe were measured by preoperative ultrasonography.
†Assessed using Student *t* test (continuous variables) or 2-sided chi-square test (categorical variables).
‡Includes 16 completion thyroidectomies after initial lobectomy.
§The numbers were calculated only in patients with central LN positivity.

LNM resulted in a 3-fold higher disease-related mortality rate.[9] Therefore, therapeutic lymph node dissection has been recommended in patients with clinically node-positive papillary thyroid carcinoma (PTC).

Routine central neck lymph node dissection (CLND) is gaining acceptance for treating PTC because of the high number of patients with cervical LNM that show local recurrence. The revised American Thyroid Association guidelines recommend that prophylactic CLND may be considered in patients with high-risk thyroid cancer.[10] However, the indications for, and efficacy of, prophylactic CLND in patients with PTMC are still controversial.[1,4] Preoperative high-resolution US plays an important role in determining the extent of thyroidectomy and lymph node dissection[11]; however, the sensitivity of US for detecting central LNM in PTC patients has been unacceptable and has been reported to be as low as 10.9% to 30%.[1,12] Therefore, the identification of PTMC patients with aggressive clinical features who may benefit from elective CLND is an emerging goal of PTC management.[6,13–16]

The patient and clinical factors predictive of central LNM in patients with clinically noninvasive, node-negative PTMC remain uncertain. The aim of this study was to examine the frequency and factors predictive of subclinical central LNM in patients with PTMC who underwent elective CLND. A further aim was to investigate which clinical, US, and pathological features were predictive of central LNM in PTMC patients in comparison with those of control patients with PTC measuring 1.01 to 1.5 cm in its greatest dimension by preoperative US.

Patients and Methods

Study patients

A total of 528 patients underwent thyroid surgery for previously untreated PTC in Asan Medical Center from January to December 2010, as part of a study approved by the Institutional Review Board of our hospital. The inclusion criteria were as follows: patients with clinically noninvasive, node-negative PTC; aged 70 or under; and with a tumor size ≤ 1.5 cm on US. The exclusion criteria were as follows: patients with preoperative or intraoperative lymph nodes; those with significant, locally invasive thyroid carcinomas; and those who had undergone prior head and neck irradiation or oncological surgery.[10] Furthermore, an intraoperative finding of significant tumor invasion to surrounding structures, such as the larynx, trachea, esophagus, or recurrent laryngeal nerve, led to patient exclusion. Following application of the inclusion and exclusion criteria, 287 patients were included in this study (Table 1). The patients were divided into 2 groups according to the size of the primary tumor in preoperative US: ≤1 cm (PTMC) - study group (*n* = 193); and 1.01 to 1.5 cm - control group (*n* = 94).