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Using ultrasonographic features to predict the outcomes of patients with small papillary thyroid carcinomas: a retrospective study implementing the 2015 ATA patterns and ACR TI-RADS categories

ORIGINAL ARTICLE

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Background: The aim of this study was to evaluate whether risk stratification systems using ultrasonographic (US) features show associations with the outcomes of patients with small papillary thyroid carcinomas (PTCs).

Methods: This retrospective study received institutional review board approval. From March 2007 to February 2010, 775 patients who underwent surgery for small PTCs (10–20 mm) were included. Based on preoperative US features, PTCs were categorized according to the 2015 American Thyroid Association (ATA) guideline and the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS). The associations of clinicopathological and US features with postoperative patient outcomes were evaluated.

Results: In total, 61 patients had high-volume central lymph node metastasis (CLNM, 7.9%) and 100 patients had lateral lymph node metastasis (LLNM, 12.9%). In univariable analyses, a high number of suspicious US features and higher ACR TI-RADS point totals were significantly associated with both high-volume CLNM (P=0.001, each) and LLNM (P<0.001, each). In multivariable analyses of preoperative features, a higher number of suspicious US features and higher ACR TI-RADS point totals were independently associated with high-volume CLNM (odds ratio [OR], 1.516 and 1.201; P=0.002 and P=0.001, respectively) and LLNM (OR, 1.763 and 1.293; all P<0.001). Individual US features, ATA categories, and ACR TI-RADS point totals were not significantly associated with recurrence or distant metastasis.

Conclusion: The number of suspicious US features and the ACR TI-RADS point total are potential risk factors for cervical lymph node metastasis in patients with small PTCs.

Keywords: Papillary thyroid carcinoma; Ultrasonography; Lymphatic metastasis; Prognosis

Key points: Preoperative ultrasonographic features are associated with cervical lymph node metastasis in patients with small papillary thyroid carcinomas. These features could be considered when estimating the prognosis and deciding the management in patients with small papillary thyroid carcinomas.

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Introduction

To date, thyroid cancer is the most common endocrine malignancy, and its annual incidence rate is steadily increasing [1,2]. Among its various histologic types, papillary thyroid carcinoma (PTC) accounts for the vast majority of cases (85%–95%) [3]. PTC is known to have an indolent clinical course, and patients show an excellent prognosis, with 10-year survival rates of 93%–95% [2,4–7]. However, approximately 14%–26% of PTC patients experience recurrence within 10 years of treatment and require additional treatment [2,8–10]. Ongoing efforts have been made to evaluate preoperative factors that can identify PTC patients at high risk for post-treatment recurrence and a poor prognosis. Well-known clinical and pathological factors associated with PTC recurrence include age, tumor size, histologic subtype, extrathyroidal extension (ETE), and lymph node (LN) metastasis [2,4,11–14]. Although these risk factors are important when deciding upon the surgical extent and perioperative management, with the exception of age, most of these factors can only be determined postoperatively based on a pathological evaluation. If there are reliable preoperative risk factors that can be used to predict the prognosis of PTC patients, they could help clinicians tailor both the surgical extent and postoperative management of the disease for each individual.

Ultrasonography (US) is routinely performed for the preoperative diagnosis and staging of thyroid cancer. Several studies have evaluated the associations of US features with patients' outcomes, and their findings suggest that PTCs with a malignant appearance on preoperative US are more likely to show a poor prognosis than benign-appearing ones [2,8,15,16]. While these studies have provided evidence that US features can be used to predict patient outcomes in PTC, arbitrary US assessments were made by each study group for their research. Several authoritative groups have published risk-stratification systems for thyroid nodules based on US features, including the 2015 American Thyroid Association (ATA) guideline [17] and the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) [18]. These risk stratification systems provide uniform US descriptors and 4- to 5-tiered final assessment categories that can be used for more objective risk prediction. In addition, since PTCs smaller than 10 mm (i.e., papillary thyroid microcarcinoma) have an exceptionally good prognosis, it was hypothesized that if risk stratification categories are confirmed as reliable measures of risk, they would be particularly beneficial for patients diagnosed with small PTCs measuring 10–20 mm, since they could be utilized to guide surgical extent and postoperative management in these patients.

Thus, this study aimed to investigate the usefulness of individual preoperative US features, the 2015 ATA guideline patterns, and the ACR TI-RADS categories as risk factors for the outcomes of patients treated for small PTCs.

Materials and Methods

Compliance with Ethical Standards

The institutional review board of Severance Hospital, Yonsei University College of Medicine. Approved this retrospective study and waived the requirement for informed consent (2021-0545-001). However, written informed consent was obtained from all patients prior to US-guided fine-needle aspiration (FNA) or biopsy as part of daily practice.

Patients

From March 2007 to February 2010, 6,724 patients with 6,860 nodules underwent surgery at the authors' institution. Of the 6,860 nodules, 1,002 thyroid cancers in 882 patients were <20 mm in their largest dimension and the 882 patients had preoperative US results available for analysis. Among these patients, 879 had dominant thyroid cancers ≥10 mm and <20 mm, of which 794 were reported as conventional PTC on pathologic reports. Of the 794 patients with conventional PTC, 19 were excluded because their postoperative follow-up duration was shorter than 12 months. In total, 775 patients who were surgically diagnosed with small PTC were included in this study. The mean patient age was 40.0±12.3 years (range, 15 to 83 years). The mean nodule size was 12.6±2.6 mm (range, 10 to 19 mm). Of the 775 patients, 133 (17.2%) were men and 642 (82.8%) were women.

Preoperative US Examinations and Categorization according to Guidelines

Thyroid US examinations for FNA or preoperative staging were performed with a 5–12 MHz linear array transducer (iU22, Philips Medical Systems, Bothell, WA, USA). Each US examination was performed by one of 14 board-certified radiologists (four faculties and 10 fellows) with 1 to 20 years of experience in thyroid imaging. Subsequent US-guided FNAs were performed by the same radiologist who did the thyroid US examination, if required. The following US features of the PTC nodules were prospectively recorded in the institutional database by the radiologist who performed the US examination [19]. The composition was classified as solid, predominantly solid (cystic portion <50%), predominantly cystic (cystic portion ≥50%), or spongiform. Echogenicity was classified as hyperechoic, isoechoic, hypoechoic, or markedly hypoechoic compared to the echogenicity of the surrounding thyroid parenchyma or adjacent strap muscle. The margin was classified as well-circumscribed, microlobulated, or irregular. Calcifications were classified as no

calcifications, macrocalcifications or eggshell calcifications, or microcalcifications (i.e., microcalcifications or mixed calcifications). The shape was classified as parallel or taller-than-wide (greater in the anteroposterior dimension than the transverse dimension).

The prospectively recorded US features of the PTC nodules were retrospectively classified according to the 2015 ATA guideline [17] and ACR TI-RADS [18] by one radiologist (J.H.Y., 10 years of experience in thyroid imaging) (Supplementary Table 1). Nodules that were not classified into a specific 2015 ATA pattern were categorized as having an "intermediate suspicion" pattern based on the results of a previous publication [20].

Surgical Procedures and Pathologic Diagnosis

The extent of surgery was decided based on clinical and radiological factors. Total or near-total thyroidectomy was performed for patients with multiple or bilateral tumors, suspected ETE, or cervical LN metastasis, and for patients more than 45 years old. All patients underwent central neck node dissection following the routine protocol, while lateral neck node dissection was performed selectively in patients in whom lateral LN metastasis (LLNM) was either cytologically proven or localized on preoperative imaging studies. When metastatic LNs were suspected on preoperative computed tomography or in the operative field, selective frozen sections with subsequent lateral neck node dissection were performed. The histopathologic results were retrospectively reviewed and the size, location, number of PTCs, the presence of ETE, and/or central or lateral LN metastases were recorded. The postoperative surveillance protocol is summarized in Supplementary Data 1.

Data and Statistical Analysis

Marked hypoechogenicity, microlobulated or irregular margins, the presence of microcalcifications, and a taller-than-wide shape were considered as suspicious US features based on previously published criteria [19], and the number of suspicious US features found for each patient was summed. Patient outcomes were categorized as central LN metastasis (CLNM), LLNM, disease recurrence, and distant metastasis. For CLNM, high-volume LN metastasis was defined as the presence of 6 or more metastatic LNs on pathology [17,21,22]. The Student t-test and Wilcoxon rank-sum test were used to compare continuous variables. Either the chi-square test or the Fisher exact test was used to compare categorical variables. Univariable and multivariable logistic regression analyses were used to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for the associations of clinicopathological and US features with patient outcomes.

Statistical analyses were performed using the R programming language (version 3.4.3, The R Foundation for Statistical Computing, Vienna, Austria). P-values less than 0.05 were considered to indicate statistical significance.

Results

Of the 775 patients included in this study, 61 (7.9%) had high-volume CLNM and 100 (12.9%) had LLNM. The mean follow-up duration for the 775 patients after surgery was 87.3 months (range, 13 to 129 months). Twenty-two patients (2.8%) had recurrence; nine with cytologically-proven LLNM and 13 with biochemical recurrence without a gross abnormality detected on imaging studies. Five patients (0.6%) had distant metastasis detected during follow-up; four had lung metastasis and one had bone metastasis. The mean follow-up duration for the 753 patients with no recurrence was 87.5 months (range, 13 to 129 months). The mean follow-up duration for the 22 patients with recurrence was 69.0 months (range, 23 to 110 months), while it was 75 months (range, 39 to 91 months) for the five patients with distant metastasis.

Clinicopathological and US Characteristics according to LN Metastasis or Postoperative Outcomes

The distribution of clinicopathological and US features according to high-volume CLNM or LLNM is summarized in Table 1. Younger patients (40.9 years vs. 47.6 years, P<0.001) and men (31.1% vs. 16.0%, P=0.003) had significantly higher rates of high-volume CLNM. Patients with LLNM had significantly larger tumors (P=0.032).

For individual US features, significantly higher rates of non-circumscribed margins, calcifications, and a taller-than-wide shape were seen in PTC patients with cervical LN metastasis (all P<0.05, respectively). The number of suspicious US features was significantly different between patients with and without high-volume CLNM or LLNM (P=0.011 and P<0.001, respectively). Patients with high-volume CLNM or LLNM had significantly higher ACR TI-RADS point totals (all P<0.05, respectively). As for the ACR TI-RADS categories, significant differences were seen between categories according to the presence of LLNM (P=0.003). No significant differences were seen in the 2015 ATA patterns according to central or lateral LN metastasis.

Patients with high-volume CLNM (P=0.001) or LLNM (P=0.041) had significantly higher incidence rates of recurrence (Supplementary Table 2). Patients with high-volume CLNM had a significantly higher incidence of distant metastasis (P=0.007). No significant differences were seen for individual US features, ACR TI-RADS point totals, ACR TI-RADS categories, or the 2015 ATA patterns according to recurrence or distant metastasis.

Preoperative Factors Associated with CLNM or LLNM

The results of the univariable and multivariable regression analysis for the associations between preoperative factors and high-volume

Table 1. Clinicopathological and US features of the 775 patients with small PTCs according to cervical LN metastasis

Clinical characteristic	High-volume central LN metastasis			Lateral LN metastasis		
	No (n=714)	Yes (n=61)	P-value	No (n=675)	Yes (n=100)	P-value
Age (year)	47.6±12.3	40.9±10.9	<0.001	47.3±12.1	45.5±13.6	0.181
Sex			0.003			0.169
Men	114 (16.0)	19 (31.1)		111 (16.4)	22 (22.0)	
Women	600 (84.0)	42 (68.9)		564 (83.6)	78 (78.0)	
Size (mm)	12.6±2.5	12.8±2.8	0.522	12.5±2.5	13.1±2.7	0.032
US features						
Composition			>0.999			0.671
Solid	658 (92.1)	57 (93.5)		620 (91.9)	95 (95.0)	
Predominantly solid	22 (3.1)	1 (1.6)		21 (3.1)	2 (2.0)	
Predominantly cystic	34 (4.8)	3 (4.9)		34 (5.0)	3 (3.0)	
Echogenicity			0.495			0.436
Hyperechoic or isoechoic	82 (11.5)	4 (6.6)		77 (11.4)	9 (9.0)	
Hypoechoic	505 (70.7)	46 (75.4)		482 (71.4)	69 (69.0)	
Markedly hypoechoic	127 (17.8)	11 (18.0)		116 (17.2)	22 (22.0)	
Margin			0.104			0.003
Circumscribed	129 (18.1)	6 (9.8)		128 (19.0)	7 (7.0)	
Not circumscribed	585 (81.9)	55 (90.2)		547 (81.0)	93 (93.0)	
Calcification			0.107			<0.001
Micro- or mixed calcifications	311 (43.6)	35 (57.4)		285 (42.2)	61 (61.0)	
Macro- or eggshell calcifications	139 (19.4)	8 (13.1)		123 (18.2)	24 (24.0)	
No calcifications	264 (37.0)	18 (29.5)		267 (39.6)	15 (15.0)	
Shape			0.001			<0.001
Parallel	364 (51.0)	17 (27.9)		352 (52.1)	29 (29.0)	
Taller-than-wide	350 (49.0)	44 (72.1)		323 (47.9)	71 (71.0)	
No. of suspicious US features			0.011			<0.001
0	69 (9.7)	2 (3.3)		68 (10.1)	3 (3.0)	
1	168 (23.5)	8 (13.1)		166 (24.6)	10 (10.0)	
2	269 (37.7)	21 (34.4)		252 (37.3)	38 (38.0)	
3	165 (23.1)	25 (41.0)		155 (23.0)	35 (35.0)	
4	43 (6.0)	5 (8.2)		34 (5.0)	14 (14.0)	
ACR TI-RADS point total	9 (7–10)	10 (9–12)	<0.001	9 (6–10)	10 (9–12)	<0.001
ACR TI-RADS			0.067			0.003
TR1	3 (0.4)	0		3 (0.4)	0	
TR2	8 (1.1)	1 (1.6)		9 (1.3)	0	
TR3	16 (2.3)	1 (1.6)		16 (2.4)	1 (1.0)	
TR4	142 (19.9)	4 (6.6)		141 (20.9)	5 (5.0)	
TR5	545 (76.3)	55 (90.2)		506 (75.0)	94 (94.0)	
2015 ATA			0.231			0.231
Very low suspicion	1 (0.1)	0		1 (0.2)	0	
Low suspicion	32 (4.5)	1 (1.6)		32 (4.7)	1 (1.0)	
Intermediate suspicion	96 (13.5)	4 (6.6)		90 (13.3)	10 (10.0)	
High suspicion	585 (81.9)	56 (91.8)		552 (81.8)	89 (89.0)	

Continued

Table 1. Continued

Clinical characteristic	High-volume central LN metastasis			Lateral LN metastasis		
	No (n=714)	Yes (n=61)	P-value	No (n=675)	Yes (n=100)	P-value
Pathologic features						
Extrathyroidal extension			0.003			0.004
No	250 (35.0)	10 (16.4)		239 (35.4)	21 (21.0)	
Yes	464 (65.0)	51 (83.6)		436 (64.6)	79 (79.0)	
Multifocality			<0.001			<0.001
No	437 (61.2)	22 (36.1)		417 (61.8)	42 (42.0)	
Yes	277 (38.8)	39 (63.9)		258 (38.2)	58 (58.0)	
Bilaterality			<0.001			0.003
No	515 (72.1)	31 (50.8)		488 (72.3)	58 (58.0)	
Yes	199 (27.9)	30 (49.2)		187 (27.7)	42 (42.0)	

Values are presented as mean+SD, number (%), or median (interquartile range).

US, ultrasound; PTC, papillary thyroid cancer; LN, lymph node; ACR TI-RADS, American College of Radiology Thyroid Imaging Reporting and Data System; 2015 ATA, 2015 American Thyroid Association.

Table 2. Univariable and multivariable analysis of associations between preoperative US features and high-volume central LN metastasis in patients with small PTCs

	Univariable analysis		Preoperative multivariable analysis							
			No. of suspicious US features		ACR TI-RADS point total		ACR TI-RADS		2015 ATA	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (year)	0.953 (0.931–0.976)	<0.001	0.952 (0.930–0.975)	<0.001	0.951 (0.928–0.974)	<0.001	0.952 (0.929–0.975)	<0.001	0.950 (0.927–0.973)	<0.001
Sex	0.420 (0.236–0.748)	0.003	0.392 (0.215–0.713)	0.002	0.393 (0.216–0.717)	0.002	0.373 (0.204–0.679)	0.001	0.373 (0.205–0.678)	0.001
Size on US (mm)	1.033 (0.935–1.141)	0.521	1.031 (0.930–1.143)	0.565	1.034 (0.932–1.147)	0.532	1.038 (0.936–1.150)	0.482	1.037 (0.936–1.150)	0.485
No. of suspicious US features	1.545 (1.186–2.011)	0.001	1.516 (1.162–1.978)	0.002	–	–	–	–	–	–
ACR TI-RADS point total	1.207 (1.083–1.346)	0.001	–		1.201 (1.078–1.337)	0.001	–	–	–	–
ACR TI-RADS										
TR1-3	1						1			
TR4	0.380 (0.066–2.181)	0.278	–	–	–	–	0.381 (0.064–2.266)	0.289	–	–
TR5	1.362 (0.315–5.883)	0.679	–	–	–	–	1.458 (0.326–6.529)	0.622	–	–
2015 ATA										
Very low to low suspicion	1								1	
Intermediate suspicion	0.504 (0.089–2.866)	0.440	–	–	–	–	–	–	1.338 (0.141–12.744)	0.800
High suspicion	1.716 (0.401–7.334)	0.467	–	–	–	–	–	–	3.535 (0.465–26.892)	0.223

US, ultrasound; LN, lymph node; PTC, papillary thyroid cancer; ACR TI-RADS, American College of Radiology Thyroid Imaging Reporting and Data System; 2015 ATA, 2015 American Thyroid Association; OR, odds ratio; CI, confidence interval.

CLNM are presented in Table 2. In the univariable analysis, younger age, male sex, a higher number of suspicious US features, and a higher ACR TI-RADS point total were significantly associated with high-volume CLNM (all P<0.05, respectively). In the multivariable analysis, a higher number of suspicious US features (OR, 1.516; 95% CI, 1.162 to 1.978; P=0.002), and a higher ACR TI-RADS point total (OR, 1.201; 95% CI, 1.078 to 1.337; P=0.001) were independently associated with high-volume CLNM.

The results of the univariable and multivariable analyses for the associations between preoperative factors and LLNM are summarized in Table 3. Size, a higher number of suspicious US features, and a higher ACR TI-RADS point total were significantly associated with LLNM in the univariable analysis. In the multivariable analysis, a higher number of suspicious US features (OR, 1.763; 95% CI, 1.415 to 2.196; P<0.001), and a higher ACR TI-RADS point total (OR, 1.293; 95% CI, 1.179 to 1.417; P<0.001) were independently associated with LLNM. The ACR TI-RADS categories and the 2015 ATA patterns were not significantly associated with high-volume CLNM or LLNM.

Postoperative Factors Associated with CLNM

In the multivariable model of postoperative factors associated with high-volume CLNM, a higher number of suspicious US features (OR, 1.402; 95% CI, 1.062 to 1.850; P=0.017), a higher ACR TI-RADS point total (OR, 1.172; 95% CI, 1.049 to 1.309; P=0.005), ETE, and multifocality showed significant associations with high-volume CLNM (Supplementary Table 3). In the multivariable model of postoperative variables associated with LLNM, a higher number of suspicious US features (OR, 1.699; 95% CI, 1.354 to 2.132; P<0.001), a higher ACR TI-RADS point total (OR, 1.277; 95% CI, 1.162 to 1.402; P<0.001), ETE, and multifocality showed significant associations with LLNM. The ACR TI-RADS categories and the 2015 ATA patterns were not significantly associated with either high-volume CLNM or LLNM in the postoperative models (all P>0.05, respectively).

Among the individual suspicious US features (Supplementary Table

Table 3. Univariable and multivariable analysis for associations between preoperative US features and lateral LN metastasis in patients with small PTCs

	Univariable analysis		Preoperative multivariable analysis							
			No. of suspicious US features		ACR TI-RADS point total		ACR TI-RADS		2015 ATA	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (year)	0.988 (0.971–1.005)	0.181	0.990 (0.973–1.008)	0.268	0.989 (0.972–1.007)	0.229	0.988 (0.971–1.005)	0.169	0.988 (0.971–1.005)	0.165
Sex	0.698 (0.417–1.168)	0.171	0.674 (0.396–1.148)	0.147	0.673 (0.394–1.150)	0.147	0.648 (0.382–1.099)	0.107	0.666 (0.395–1.123)	0.127
Size on US (mm)	1.089 (1.007–1.177)	0.033	1.092 (1.006–1.185)	0.036	1.094 (1.007–1.188)	0.033	1.103 (1.017–1.197)	0.018	1.096 (1.012–1.187)	0.024
No. of suspicious US features	1.781 (1.429–2.219)	<0.001	1.763 (1.415–2.196)	<0.001	–	–	–	–	–	–
ACR TI-RADS point total	1.299 (1.184–1.425)	<0.001	–	–	1.293 (1.179–1.417)	<0.001	–	–	–	–
ACR TI-RADS										
TR1-3	1						1			
TR4	0.993 (0.112–8.828)	0.995	–	–	–	–	1.035 (0.115–9.317)	0.976	–	–
TR5	5.202 (0.699–38.696)	0.108	–	–	–	–	5.666 (0.752–42.701)	0.092	–	–
2015 ATA										
Very low to low suspicion	1								1	
Intermediate suspicion	0.504 (0.089–2.866)	0.440	–	–	–	–	–	–	3.781 (0.462–30.978)	0.215
High suspicion	3.158 (0.746–13.369)	0.118	–	–	–	–	–	–	5.721 (0.767–42.678)	0.089

US, ultrasound; LN, lymph node; PTC, papillary thyroid cancer; ACR TI-RADS, American College of Radiology Thyroid Imaging Reporting and Data System; 2015 ATA, 2015 American Thyroid Association; OR, odds ratio; CI, confidence interval.

4), a taller-than-wide shape was the single US feature significantly associated with CLNM in the preoperative and postoperative multivariable models (P=0.001 and P=0.002, respectively). The presence of calcifications and a taller-than-wide shape were the individual US features significantly associated with LLNM in the preoperative and postoperative multivariable models (all P<0.001).

Factors Associated with Recurrence and Distant Metastasis

In the univariable analysis for recurrence or distant metastasis (Supplementary Table 5), high-volume CLNM (OR, 4.759; 95% CI, 1.790 to 12.650; P=0.002) and LLNM (OR, 2.629; 95% CI, 1.004 to 6.886; P=0.049) showed significant associations with recurrence. High-volume CLNM (OR, 8.034; 95% CI, 1.316 to 49.031; P=0.024) showed significant associations with distant metastasis. Individual US features and ACR TI-RADS point totals were not significantly associated with recurrence or distant metastasis. The high-suspicion pattern of the 2015 ATA guideline was significantly associated with recurrence in the univariable analysis (OR, 0.263; 95% CI, 0.072 to 0.960; P=0.043), but this association was not significant in the multivariable analysis performed after adjusting for clinicopathologic features (OR, 0.296; 95% CI, 0.058 to 1.520; P=0.145).

Discussion

Although PTC has an excellent overall prognosis, about 7% of PTC cases show aggressive behavior that leads to postoperative locoregional recurrence and morbidity [2,4–7,23]. The preoperative identification of patients likely to have a poor prognosis would help clinicians design tailored management for these at-risk patients. Our study results show that US features may be used as biomarkers associated with cervical LN metastasis or post-treatment outcomes in patients treated for small PTCs. In the present study, the number of suspicious US features and the ACR TI-RADS point total were independent risk factors for cervical LN metastasis in these patients. LN metastasis in PTC has been reported as a poor prognostic factor and to be associated with recurrence or distant metastasis [2,24–27]. Thus, the authors suggest that the number of suspicious US features and the ACR TI-RADS point total both have the potential to identify small PTC patients with poor prognostic factors such as high-volume CLNM or lateral LNM.

In the present study, the likelihood of high-volume CLNM and LLNM increased significantly as the number of suspicious US features on preoperative US increased. Patients with three suspicious US features were more likely to have high-volume CLNM and those with three or more suspicious US features were more likely to have LLNM. Although past publications have associated the presence of suspicious US features with LN metastasis and recurrence in PTC [2,8,28,29], these studies did not specify how to utilize suspicious US features in a clinical setting. By simplifying the combinations of suspicious US features into numeric counts, it was hypothesized that the number of suspicious US features may act as a more practical risk factor associated with patient outcomes, and this hypothesis was supported by the results. Given the absence of consensus regarding the indications for prophylactic cervical LN dissection in small PTCs [17], the results of this study show that the number of suspicious US features may be useful when planning surgical extent and personalizing management for patients with small PTCs.

Along with the number of suspicious US features, the ACR TI-RADS point total was significantly associated with both high-volume CLNM and LLNM. Patients with a higher ACR TI-RADS point total were more likely to have high-volume CLNM and LLNM, with ORs of 1.201 (P=0.001) and 1.293 (P<0.001), respectively. Our results suggest that the ACR TI-RADS point total, as a collective indicator of US morphology for thyroid nodules, can also be an independent risk factor of LN metastasis in patients with small PTCs. Notably, the number of suspicious US features and the ACR TI-RADS point total continued to have significant associations with LN metastasis even after adjusting for postoperative pathologic findings such as ETE, multifocality, and bilaterality (Supplementary Table 3). This further underscores the potential of US features as prognostic factors for patients with small PTCs. To the authors' best knowledge, this is the first study to evaluate the association between the ACR TI-RADS point total and patient outcomes in PTC patients, and future studies are warranted to validate these results.

If suspicious US features are associated with cervical LN metastasis or patient outcomes, it would be reasonable to hypothesize that the final assessment categories or patterns of the 2015 ATA guideline or the ACR TI-RADS would be associated with PTC outcome. However, no significant associations were found between the ACR TI-RADS categories and cervical LN metastasis or between the 2015 ATA patterns and cervical LN metastasis in the present study. Since the 2015 ATA patterns and the ACR TI-RADS categories were developed as sensitive predictors of the malignancy risk of thyroid nodules, these final assessment categories may not be appropriate for the further classification of biopsy-proven malignant nodules [17,18], such as the task of discriminating nodules with poor surgical or postoperative outcomes, as explored in the present study. Furthermore, the individual US features, the number of suspicious US features, ACR TI-RADS point totals, ACR TI-RADS categories, and the 2015 ATA patterns all showed no significant associations with recurrence or distant metastasis in patients with small PTCs, although the small number of patients with recurrence or metastasis may be the reason for this lack of statistical significance.

The present study has several limitations. First, this was a retrospective study conducted at a single institution, making selection bias inevitable. However, the individual US features were prospectively recorded by whoever performed the US examination, thus implying the potential clinical applicability of these features. Second, in each examination, one of 14 radiologists was involved in image acquisition, but variability among radiologists in the US interpretation was not considered. Third, central compartment dissection is routinely performed for thyroid cancer surgery at the authors' institution, and this may have affected the results. In order to overcome this limitation, high-volume CLNM was used as an outcome since the higher number of metastases in this compartment can affect patient outcomes [17,21,22,30,31]. Last, the ACR TI-RADS includes ETE as a suspicious feature in its scoring system, but ETE was not included in the feature analysis. This was because the cancer staging performed during the periods of the US examinations analyzed in this study included both minimal and gross ETE as the presence of ETE; however, the ACR TI-RADS considers only "obvious or clear-cut" invasion as ETE [18,32]. Thus, the ACR TI-RADS point total could have been underestimated in this study compared to studies that included ETE in the feature analysis.

In conclusion, the number of suspicious US features and the ACR TI-RADS point total may be independent risk factors of CLNM or LLNM in patients with small PTCs. As questions still remain regarding the indications for cervical LN dissection, these US features can be considered when deciding on surgical extent or individualizing the postoperative management of small PTCs.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Supplementary Material

Supplementary Table 1. Summary of the 2015 American Thyroid Association (2015 ATA) guideline and the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) (https://doi.org/10.14366/usg.21097).

Supplementary Table 2. Clinicopathological and US features of the 775 PTC patients according to recurrence and distant metastasis (https://doi.org/10.14366/usg.21097).

Supplementary Table 3. Univariable and multivariable analysis of associations between postoperative clinicopathologic features using the number of suspicious US features or the ACR TI-RADS point total and cervical LN metastasis (https://doi.org/10.14366/usg.21097).

Supplementary Table 4. Univariable and multivariable analysis of associations between clinicopathologic features using individual US features and cervical LN metastasis (https://doi.org/10.14366/usg.21097).

Supplementary Table 5. Univariable analysis of the associations of clinicopathologic and US features with recurrence and distant metastasis (https://doi.org/10.14366/usg.21097).

Supplementary Data 1. Postoperative surveillance (https://doi.org/10.14366/usg.21097).

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