

Original Article



Comparison of Diagnostic Values of Ultrasonography and Computed Tomography for Detecting Lateral Lymph Node Metastasis in N1b Papillary Thyroid Carcinoma

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ABSTRACT

Purpose: We focused on the comparison of the diagnostic accuracy of preoperative ultrasonography (US) with that of computed tomography (CT), especially for lateral lymph node metastasis (LLNM) in N1b papillary thyroid carcinoma (PTC).

Methods: We conducted a retrospective cohort study at the Thyroid Cancer Center of Samsung Medical Center, a tertiary referral center in Korea, by analyzing data collected between January 1997 and June 2015. A total of 1,323 patients who met the following inclusion criteria were enrolled.

Results: Diagnostic values were calculated on a “per level” basis by comparing the results of US, CT, and histopathology. Between US and CT, there was no significant difference in the sensitivity (59.3% vs. 61.0%, $P=0.073$), specificity (83.0% vs. 81.1%, $P=0.051$), or accuracy (68.6% vs. 68.9%, $P=0.660$). However, US+CT showed significantly higher sensitivity (74.6% vs. 59.3%, $P<0.001$) and accuracy (74.0% vs. 68.6%, $P<0.001$) compared to US alone.

Conclusion: There was no significant difference in sensitivity, specificity, and diagnostic accuracy for LLNM between US and CT; however, a combination of CT and US had significantly higher sensitivity, specificity, and diagnostic accuracy in detection of LLNM compared to US or CT alone. We conclude that the strategy for the examination of the lateral neck in PTC patients can be effectively determined by the combination of CT and US rather than US or CT only.

Keywords: Papillary thyroid carcinoma; Lymph node, metastasis; CT; Ultrasonography

INTRODUCTION

Ultrasound imaging is commonly used for preoperative evaluation of papillary thyroid carcinoma (PTC). High-resolution ultrasonography (US) can detect even very small lymph node (LN) as small as 5 mm (1), and American Thyroid Association Guidelines suggests that preoperative US imaging is prerequisite for thyroid cancer (2). Although US is useful in the case of the preoperative clinical stage to determine the extent of surgery needed, US has limitations in detecting a deep portion of the neck (3). Some studies suggested that

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Conflict of Interest

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

computed tomography (CT) is superior to US in examining central LN metastasis. There exist only a few studies on lateral lymph node metastasis (LLNM) (3-5). Therefore, in this study, we focused on the comparison of the diagnostic accuracy of preoperative US with that of CT, especially for LLNM in N1b PTC.

METHODS

1. Patient selection

We conducted a retrospective cohort study at the Thyroid Cancer Center of Samsung Medical Center, a tertiary referral center in Korea, by analyzing data collected between January 1997 and June 2015. A total of 1,323 patients who met the following inclusion criteria were enrolled. The inclusion criteria were: pathologically proven N1b PTC, total thyroidectomy with central neck dissection and lateral neck dissection, and preoperative results of both US and CT. The exclusion criteria were: a history of the previous thyroidectomy, non-PTC carcinomas (follicular/medullary/anaplastic), mixed type PTC, lobectomy, or distant metastasis.

2. Preoperative US and CT

US scanners (HDI 5000 or IU22; Philips Medical Systems; Bothell, WT, USA) equipped with commercially available 7 to 12 MHz linear array transducers were used for the primary assessment of cervical LNs. The US criteria for cervical LN metastasis were as follows: focal or diffuse hyperechogenicity, microcalcifications, cystic changes, loss of fatty hilum, round shape (long/transverse diameter ratio <1.5), and abnormal vascular patterns (chaotic or peripheral) (6-8). CT scans were performed preoperatively on patients who showed aggressive features on US scans. Aggressive features included tumor size >1 cm, upper pole-located tumor, multifocality, extrathyroidal extension, and clinically suspicious lymphadenopathy. CT scans were also performed according to the individual clinician's preference at the time of planning a surgery. CT scans were obtained using a 16-detector-row CT scanner (MX8000 Infinite Detector Technology; Philips, Haifa, Israel) with a reconstructed slice thickness of 3 mm for both axial and coronal images. The CT criteria for cervical LN metastasis were as follows: calcification, cystic or necrotic changes, heterogeneous cortical enhancement, and strong enhancement without hilar vessel enhancement (6-8). Two or more experienced radiologists interpreted each US and CT image. Suspicious LNs were defined as LNs meeting at least one of the US and CT criteria listed above. US and CT results were reported on a "per level" basis (7). For patients with multiple follow-up examinations, we selected the result closest to the operation date for analysis.

3. Surgical strategy

At our institution, we perform total thyroidectomy and central neck dissection before lateral neck dissection by following the principles that have been previously described (9). Moreover, we only perform therapeutic lateral neck dissection in patients with clinically suspicious N1b after confirmation based on fine needle aspiration biopsy. We define lateral neck dissection as any excision of lateral neck LNs, including modified radical neck dissection and selective neck dissection (10). Modified radical neck dissection refers to the excision of lateral neck LNs, including levels II–V, with preservation of one or more non-lymphatic structures, such as the spinal accessory nerve, internal jugular vein, or sternocleidomastoid muscle. Level I dissection is not performed unless and otherwise indicated. Selective neck dissection refers to the excision of suspicious lateral neck LNs accompanied by preservation of one or more of the LN groups that are routinely removed in modified radical neck dissection. During

surgery, the cervical LN levels present in the dissected specimens are classified individually with a labeling suture.

4. Histopathological examination of surgical specimens

Surgical specimens were microscopically examined by two or more experienced pathologists. The following histopathologic parameters were assessed: cell type of the main lesion, primary tumor size (longest diameter of the largest lesion), location, multifocality, bilaterality, extrathyroidal extension, lymphovascular invasion, margin involvement, regional LN metastasis, and underlying thyroid conditions, such as chronic lymphocytic thyroiditis. To distinguish bilaterality from multifocality, multifocality was defined as having two or more lesions of conventional PTC in one lobe, regardless of the presence of bilaterality. Of particular note, histopathology results of LN status were reported on a “per level” basis (11) and were indicated by surgeons during operation. Thyroid cancer staging was determined in accordance with the American Joint Committee on Cancer (AJCC) recommendations (12).

5. Statistical analysis

Statistical analysis was performed using SPSS version 21.0 software (SPSS Inc., Chicago, IL, USA) and SAS version 9.4 software (SAS Institute, Cary, NC, USA). The statistically significant differences were defined as those with P values of <0.05. Continuous variables are presented as the mean±standard deviation, and categorical variables are presented as the number of cases and percentages. Preoperative US and CT results were compared with the postoperative histopathology results, and diagnostic values were analyzed based on the “per level” concept in accordance with the AJCC level system (12). McNemar's test was used to compare the statistical difference in sensitivity, specificity, and accuracy between preoperative US and CT. Bennett method was used to compare the statistical difference in positive predictive value and negative predictive value between preoperative US and CT.

RESULTS

1. Clinicopathologic characteristics of 1,323 N1b PTC patients

Of the 1,323 N1b PTC patients, 386 (29.2%) were male and 937 (70.8%) were female (**Table 1**). The mean age of the patients was 44.2 years, and 603 (45.6%) were older than 45 years. Right-sided lateral neck dissection was performed in 573 (43.3%) patients, left-sided lateral neck dissection was performed in 526 (39.8%) patients, and both lateral neck dissection was performed in 224 (16.9%) patients. As *BRAF* mutation analysis was not performed until 2008 in our institution, *BRAF* status was available for only 576 patients. The *BRAF* positivity rate among these patients was 74.0%. The mean tumor size was 1.7 cm and 423 (32.0%) patients had tumors smaller than 1.0 cm. Multiplicity, bilaterality, microscopic extrathyroidal extension, gross extrathyroidal extension, chronic lymphocytic thyroiditis, unilateral central LN metastasis, and bilateral central LN metastasis were seen in 509 (38.5%), 461 (34.8%), 859 (64.9%), 228 (17.3%), 350 (26.5%), 712 (53.8%), and 438 (33.1%) patients, respectively. Skip metastasis, defined as LLNM without central LN metastasis, was found in 173 patients (13.1%).

2. Distribution of LLNM among 5,356 dissected levels in N1b PTC patients

Of the 1,323 N1b PTC patients, a total of 5,356 levels were dissected as follows: 30 in level I, 1,424 in level II, 1,492 in level III, 1,495 in level IV, and 915 in level V (**Table 2**). The overall incidences of level I, II, III, IV, and V metastasis were 46.7%, 56.0%, 75.5%, 77.6%, and 17.2%, respectively.

Table 1. Baseline clinicopathologic characteristics of 1,323 N1b PTC patients

Clinicopathologic characteristics	Values
Male sex	386 (29.2)
Age (yr)	
Mean±SD	44.2±13.2
>45	603 (45.6)
Laterality of neck dissection	
Right	573 (43.3)
Left	526 (39.8)
Both	224 (16.9)
<i>BRAF</i> mutation positivity*	426 (74.0)
Pathologic variants	
Conventional	1,263 (95.4)
Follicular	18 (1.4)
Diffuse sclerosing	40 (3.0)
Tall cell	2 (0.2)
Tumor size (cm)	
Mean±SD	1.7±1.2
≤0.5	96 (7.3)
0.5–1.0	327 (24.7)
1.0–2.0	548 (41.4)
2.0–4.0	289 (21.8)
>4.0	63 (4.8)
Multiplicity	509 (38.5)
Bilaterality	461 (34.8)
Extrathyroidal extension	
Absent	236 (17.8)
Microscopic	859 (64.9)
Gross	228 (17.3)
Chronic lymphocytic thyroiditis	350 (26.5)
Central LN metastasis	
Absent	173 (13.1)
Unilateral	712 (53.8)
Bilateral	438 (33.1)

Data shown are number (%) not otherwise specified.

PTC = papillary thyroid carcinoma; SD = standard deviation; LN = lymph node.

**BRAF* mutation analysis was implemented in 2008 and was performed in 576 patients.

Table 2. Distribution of LLNM among 5,356 dissected levels in N1b PTC patients

Levels	Right			Left			Overall		
	Metastatic levels	Dissected levels	%	Metastatic levels	Dissected levels	%	Metastatic levels	Dissected levels	%
I	6	13	46.2	8	17	47.1	14	30	46.7
II	395	735	53.7	403	689	58.5	798	1,424	56.0
III	587	773	75.9	540	719	75.1	1,127	1,492	75.5
IV	604	771	78.3	556	724	76.8	1,160	1,495	77.6
V	85	480	17.7	72	435	16.6	157	915	17.2
Total	1,677	2,772	60.5	1,579	2,584	61.1	3,256	5,356	60.8

LLNM = lateral lymph node metastasis; PTC = papillary thyroid carcinoma.

3. Diagnostic values of US, CT, and US+CT for detecting LLNM in PTC patients who underwent LND

Diagnostic values were calculated on a “per level” basis by comparing the results of US, CT, and histopathology (**Table 3**). Between US and CT, there was no significant difference in the sensitivity (59.3% vs. 61.0%, $P=0.073$), specificity (83.0% vs. 81.1%, $P=0.051$), or accuracy (68.6% vs. 68.9%, $P=0.660$). However, US + CT showed significantly higher sensitivity (74.6% vs. 59.3%, $P<0.001$) and accuracy (74.0% vs. 68.6%, $P<0.001$) compared to US alone.

Table 3. Diagnostic values of US, CT, and US+CT for detecting LLNM in N1b PTC patients

Values	US	CT	P value*	US+CT	P value†
Sensitivity	1,930/3,256 (59.3)	1,986/3,256 (61.0)	0.073	2,430/3,256 (74.6)	<0.001
Specificity	1,743/2,100 (83.0)	1,704/2,100 (81.1)	0.051	1,534/2,100 (73.0)	<0.001
PPV	1,930/2,287 (84.4)	1,986/2,382 (83.4)	0.165	2,430/2,996 (81.1)	<0.001
NPV	1,743/3,069 (56.8)	1,704/2,974 (57.3)	0.434	1,534/2,360 (65.0)	<0.001
Accuracy	3,673/5,356 (68.6)	3,690/5,356 (68.9)	0.660	3,964/5,356 (74.0)	<0.001

Values are presented as number (%).

US = ultrasonography; CT = computed tomography; LLNM = lateral lymph node metastasis; PTC = papillary thyroid carcinoma; PPV, positive predictive value; NPV = negative predictive value.

*US vs. CT; †US vs. US+CT.

DISCUSSION

In this study, we examined the accuracy of ultrasound, CT, and ultrasound combined with CT in the detection of LLNM. US+CT showed significantly higher sensitivity and accuracy than US alone or CT alone. The previous study reported that CT had higher sensitivity than US in the preoperative evaluation of LLNM (5). On the other hand, many researchers believed that US exhibited higher sensitivity in the detection of the lateral neck metastasis (5,13). We do not generally perform preoperative CT for the routine evaluation of thyroid cancer due to the side effects of contrast agents and radiation exposure (14,15), the unknown sensitivity for detecting LN metastasis from PTC, and high cost. However, US depends on the skill of operators, and assessment of the deep anatomical spaces of the neck compartment is not easy using US (16). CT can compensate for this anatomical disadvantage and operator dependency of US. Our study recommends that both CT and US should be performed to evaluate the lateral neck metastasis.

This study had several limitations. The first is a statistical limitation because it was a non-randomized, retrospective cohort study in a single center, we cannot rule out the possibility of residual confounding variables of some measured or unmeasured factors due to the long-term period involved for data enrollment (between January 1997 and June 2015). The second limitation refers to the possible bias in the accuracy of US and CT due to the improvement in technology for the long-term period. Several CT scans have been used in our center between January 1997 and June 2015, and some equipment have been replaced by new machines. However, there is no significant difference in the performance of the machine and it does not significantly affect the diagnosis of patients. We suppose that the change in the machines, therefore, does not have effect on our results.

CONCLUSION

There was no significant difference in sensitivity, specificity, and diagnostic accuracy for LLNM between US and CT; however, a combination of CT and US had significantly higher sensitivity, specificity, and diagnostic accuracy in detection of LLNM compared to US or CT alone. We conclude that the strategy for the examination of the lateral neck in PTC patients can be effectively determined by the combination of CT and US rather than US or CT only.

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