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### **Main Article**

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# Relevance of level IIb neck dissection in patients with papillary thyroid carcinoma

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### **Abstract**

**Background.** Cervical nodal metastasis is a key prognostic factor in patients with papillary thyroid carcinoma. The role of lymph nodes in papillary thyroid carcinoma management and prognosis remains controversial.

**Methods.** Level IIb lymph nodes obtained from 44 patients with papillary thyroid carcinoma were histopathologically examined retrospectively. Specimens were classified as ipsilateral or contralateral. The number of dissected nodes and prevalence of level IIb metastasis were compared according to pre-operative clinical nodal stage.

**Results.** In the node-negative neck, the prevalence of contralateral and ipsilateral IIb nodes was 0 out of 20 and 0 out of 3, respectively. In the node-positive neck, the prevalence of contralateral and ipsilateral IIb nodes was 1 out of 13 (7.70 per cent) and 3 out of 41 (7.32 per cent), respectively. Clinically determined and pathologically confirmed level IIb node negativity were significantly associated. Thirty-four patients (77.3 per cent) developed accessory nerve complications from level IIb dissection.

**Conclusion.** Level IIb neck dissection for papillary thyroid carcinoma may be required if preoperative examination reveals multilevel, level IIa or suspicious level IIb metastasis.

### Introduction

Regional lymph node spread from papillary thyroid carcinoma can be broadly classified into central neck compartment and lateral neck compartment metastases. The extent of cervical nodal resection is one of the most important prognostic factors, as is the impact of post-operative radioactive iodine. The lymph node regions of the neck are divided into six levels (levels I–VI). The upper jugular lymph node region is classified as level II, which is further divided into two parts by the spinal accessory nerve: levels IIa and IIb. Level IIb is also known as the submuscular recess or supraspinal recess. The extent of neck dissection at the time of initial thyroidectomy has become a topic of contention.

Nerve traction during surgery is the most common cause of injury to the spinal accessory nerve, which subsequently results in shoulder pain and functional impairment following surgery. This dysfunction may be avoided by preserving the level IIb lymph nodes during neck dissection in selected patients.<sup>4</sup> However, some studies have shown a temporary functional deterioration of the spinal accessory nerve even when level IIb is not dissected.<sup>5–8</sup>

This retrospective study aimed to determine whether level IIb neck dissection should be performed or avoided during the surgical treatment of papillary thyroid carcinoma.

### Materials and methods

### **Ethical considerations**

The design of this retrospective observational study was approved by the medical ethics committee of Hamamatsu University Hospital (protocol number: 16-167).

### **Patients**

Patients with pathologically confirmed primary papillary thyroid carcinoma who underwent surgical treatment for primary lesion and therapeutic neck dissection at our institution, between 2013 and 2018, were considered eligible for this study. Factors that potentially affect lymph node metastasis, such as clinical tumour–node (TN) classification, clinical stage, level of lymph node involvement in pathological analysis, age, sex, performance status, cancer history and surgical procedure, were investigated. Patients with metastasis (M) positivity, as per radiographic examinations, were also included. We defined unresectable cases as those with tumour infiltration to the vertebral bone or around the internal carotid artery along with metastatic tumours.

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### Evaluation of lymph node metastasis and level IIb involvement

In all patients, ultrasonography and enhanced neck computed tomography scans were pre-operatively evaluated for neck staging (clinically confirmed node-negative  $(N_0)$  or node-positive  $(N_+)$ ). Contralateral neck dissections were performed for all clinical stage IV carcinoma cases showing involvement of the medial line of the primary tumour with ipsilateral palpable metastases and radiologically suspected contralateral metastases.

Following resection, the neck dissection specimens were separately stored according to the neck level (particularly, level IIa and IIb specimens were separately stored), and sent for histopathological analysis to determine the number and location of nodes containing metastatic disease at levels IIa, IIb, III, IV, V and VI. The pre-operative clinical T and N stages, based on the Union for International Cancer Control system, were confirmed after dissection by evaluating the pathological reports. All specimens were divided into two groups according to the side (ipsilateral or contralateral). The number of dissected lymph nodes and prevalence of level IIb metastasis in each group were then established and compared based on the pre-operative clinical nodal stage of level IIa and/or IIb positivity ( $N_0$  or  $N_+$ ).

### Measurement of shoulder dysfunction

Pre-operatively and at one month post-operatively, we measured shoulder function by assessing the shoulder joint using a goniometer (OG Wellness Technologies, Okayama, Japan) and the Isoforce GT-310 hand-held dynamometer (OG Wellness Technologies).

### Statistical analyses

Fisher's exact test was used to assess intergroup comparisons of the different outcome measures. All statistical analyses were performed using Stata Software, version 12 (Stata, College Station, Texas, USA). A *p*-value of 0.05 or less was considered statistically significant.

### Results and analysis

### **Patients**

Between 2013 and 2018, 44 patients underwent surgical treatment for primary lesion and therapeutic neck dissection at our institution. Sixteen men (36.4 per cent) and 28 women (63.6 per cent), with a median age of 56 years (range, 17–88 years), were included. Neck dissection was bilateral in 33 patients (75.0 per cent) and unilateral in 11 (25.0 per cent). Table 1 describes the demographic and clinical characteristics of the patients with thyroid papillary carcinoma treated surgically.

### Pre-operative tumour-node classification and clinical stage

Pre-operative staging was performed by chest radiography, computed tomography and magnetic resonance imaging of the head and neck. At the initial presentation, the primary tumours were classified, according to the Union for International Cancer Control staging system, as follows:  $T_1$  (n = 7; 15.9 per cent),  $T_2$  (n = 9; 20.5 per cent),  $T_3$  (n = 14; 31.8 per cent) and  $T_{4a}$  (n = 14; 31.8 per cent). Table 1 also

**Table 1.** Demographic and clinical characteristics of papillary thyroid carcinoma patients treated by surgery\*

Characteristic	Value
Sex (n (%))	
- Male	16 (36.4)
- Female	28 (63.6)
Age (range (median); years)	17-88 (56)
Clinical stage (n (%))	
- 1	7 (15.9)
- II	3 (6.8)
- III	3 (6.8)
- IVA	23 (52.3)
- IVC	8 (18.2)
Tumour (T) stage (n (%))	
- T <sub>1</sub>	7 (15.9)
- T <sub>2</sub>	9 (20.5)
- T <sub>3</sub>	14 (31.8)
- T <sub>4a</sub>	14 (31.8)
Performance status (n (%))	
- 0	40 (90.9)
- 1	4 (9.1)
Cancer history? (n (%))	
- No	43 (97.7)
- Yes	1 (2.3)

\*n = 44

shows the clinical N stage for all patients according to the treatment: 7 (15.9 per cent), 3 (6.8 per cent), 3 (6.8 per cent), 23 (52.3 per cent) and 8 (18.2 per cent) patients exhibited stage I, stage II, stage IVA and stage IVC disease, respectively. Eight of the patients had distant metastases.

### Pathologically confirmed lymph node involvement

For the ipsilateral-side group (n = 44), pathological analysis revealed the involvement of levels IIa, IIb, III, IV, V and VI in 26 (59.10 per cent), 3 (6.82 per cent), 36 (81.82 per cent), 33 (75.00 per cent), 4 (9.09 per cent) and 33 (75.00 per cent) cases, respectively. In the contralateral-side group (n = 33), involvement of levels IIa, IIb, III, IV, V and VI was recorded in 5 (15.15 per cent), 1 (3.03 per cent), 6 (18.18 per cent), 7 (21.21 per cent), 0 (0.00 per cent) and 22 (66.67 per cent) cases, respectively (Table 2).

All cases of positive nodes pathologically confirmed at level IIb were suspected clinically (pre-operatively). There were no cases in which level IIb positive nodes were not detected clinically.

Table 3 details the true positive, false negative, true negative and false positive rates that were determined using pathological analysis following neck dissection. Among the 44 neck dissections on the ipsilateral side, 3 cases (7.32 per cent) of clinical level IIb node positivity exhibited pathologically positive nodes. Among the 33 neck dissections on the contralateral side, only 1 case (3.03 per cent) of clinical level IIb node positivity had pathologically positive nodes. Regardless of the side, there was a statistically significant

**Table 2.** Pathologically confirmed lymph node involvement in papillary thyroid carcinoma patients treated by surgery

Lymph node involvement	Cases (n (%))
Ipsilateral side*	
– Level IIa	26 (59.10)
– Level IIb	3 (6.82)
- Level III	36 (81.82)
– Level IV	33 (75.00)
– Level V	4 (9.09)
– Level VI	33 (75.00)
Contralateral side <sup>†</sup>	
– Level IIa	5 (15.15)
- Level IIb	1 (3.03)
- Level III	6 (18.18)
– Level IV	7 (21.21)
– Level V	0 (0.00)
– Level VI	22 (66.67)

<sup>\*</sup>n = 44; †n = 33

association between clinically determined and pathologically confirmed negativity at level IIb (p = 0.022). Over a median follow up of 27.3 months, none of the patients exhibited regional failure at level IIb.

### Complications of level IIb dissection

In total, 34 patients (77.3 per cent) developed shoulder abduction disorder and mitral muscle weakness following level IIb neck dissection. These patients received post-operative rehabilitation involving shoulder joint range-of-motion exercises, pulley exercises, muscle strengthening exercises and neck stretches. In the ipsilateral-side group (n = 44), 10 (22.7 per cent), 24 (54.6 per cent), 7 (15.9 per cent) and 3 (6.8 per cent) patients exhibited complete recovery, good recovery, fair recovery, and no change or deterioration, respectively, at 12 months after surgery.

### **Discussion**

Regarding the applicability of level IIb neck dissection, all patients in the present study exhibited metastases concentrated at levels III, IV and VI, which represent the secondary drainage stage far from these tumours.

In the present study, on the contralateral side, only one case (7.70 per cent) of clinical level IIb node positivity, and no cases (0 per cent) of clinical node negativity, demonstrated pathologically positive nodes. The corresponding values for the ipsilateral side were 7.32 per cent and 0 per cent, respectively. The difference was statistically significant. There were no cases of isolated or contralateral metastasis at level IIb. These findings are similar to those of other studies. 9-11

The incidence of metastasis to the posterior cervical region in patients with papillary thyroid carcinoma is low, and few studies have documented the frequency of metastasis at level IIb. Initial nodal spread from papillary thyroid carcinoma occurs in the central compartment of the ipsilateral neck (level VI). However, Noguchi *et al.* 15 and Gimm *et al.* 16 reported that some patients had posterolateral lymph node

**Table 3.** Diagnostic accuracy confirmed by pathological analysis after neck dissection in papillary thyroid carcinoma patients

	Pathological diagnosis (n (%))		
Parameter	Negative	Positive	<i>P</i> -value
Ipsilateral side*			
Levels II-IV			1.000
- cN- neck dissection	0 (0.00)	3 (100.00)	
- cN+ neck dissection	2 (4.88)	39 (95.12)	
Level IIb			1.000
- cN- neck dissection	3 (100.0)	0 (0.00)	
- cN+ neck dissection	38 (92.68)	3 (7.32)	
Contralateral side <sup>†</sup>			
Levels II-IV			0.394
- cN- neck dissection	10 (50.00)	10 (50.00)	
- cN+ neck dissection	1 (7.69)	12 (92.31)	
Level IIb			0.022
- cN- neck dissection	20 (100.0)	0 (0.00)	
- cN+ neck dissection	12 (92.3)	1 (7.7)	

\*n = 44;  $^{\dagger}n$  = 33. cN— = clinically confirmed node-negative; cN+ = clinically confirmed node-positive

metastasis without involvement of the central compartment. Sivanandan and Soo<sup>17</sup> reported that all patients with postero-lateral lymph node metastases had involvement of the central compartment. With a metastasis in the lymph nodes of the lateral neck, levels II–V are predictably affected, usually with multiple areas of spread in more than one of these levels. Our findings are in accordance with the results of these studies. <sup>15–17</sup>

The removal of level IIb lymph nodes is associated with a high risk of spinal accessory nerve dysfunction as a result of traction injury, which can be inevitable, or due to interruption of the blood supply. This kind of injury results in post-operative shoulder dysfunction. Loss of function of the spinal accessory nerve and the trapezius muscle leads to decreased use of the shoulder complex, which predisposes patients to fibrosis or adhesive capsulitis of the glenohumeral joint capsule. A significant factor of the accessory nerve syndrome could be prevented if the post-operative cycle of disuse and fibrosis is prevented or interrupted. Thus, early-stage rehabilitation for these patients should be encouraged.

- Of contralateral neck dissections, pathologically confirmed level IIb metastasis prevalence was 0 and 7.7 per cent for clinically node-negative  $(N_0)$  and node-positive necks, respectively
- Overall prevalence was 3.03 per cent (p = 0.022)
- Level IIb lymph node removal is associated with high risk of spinal accessory nerve dysfunction
- This is because of traction injury, which can be inevitable, or interruption of blood supply
- Level IIb removal can be avoided in patients with papillary thyroid carcinoma and pre-operative clinical N<sub>0</sub> status, to prevent additional morbidity

The current study aimed to develop an alternative diagnostic tool and therapeutic procedure that can identify the factors contributing to preservation of the function and performance of the spinal accessory nerve. Therefore, we did not address the oncological (i.e. locoregional failure) and survival outcomes.

With therapeutic neck dissection, there is a strong association between clinically positive level IIa metastasis and pathological level IIb involvement; therefore, we recommend the use of level IIb dissection if level IIa shows pre-operative clinical node positivity.

The major limitations of our study included its observational design and the small number of patients. A meta-analysis of the relevance of level IIb neck dissection in patients with papillary thyroid carcinoma is also needed. Further prospective, controlled studies with larger sample sizes are required to assess the correlation between clinically determined and pathologically confirmed level IIb positivity.

The findings of this study suggest that the incidence of level IIb lymph node involvement in clinically node-negative necks is low. Therefore, level IIb removal can be avoided during neck dissection in patients with papillary thyroid carcinoma and a pre-operative clinically confirmed  $N_0$  status, to avoid additional morbidity. Consideration of the individualised surgical extent of lateral neck dissection is important in the treatment of papillary thyroid carcinoma patients with lateral cervical metastasis.

Competing interests. None declared

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