Level V cervical lymph node involvement in patients with stage N1b papillary thyroid carcinoma: a prospective study

Hatem Alwagih[a], Yasser Hamza[a], Alaa Hamza[b], Ahmed Hamed[b], Essam Gabr[a]

[a]Head, Neck and Endocrine Surgery Unit, Department of Surgery, Faculty of Medicine, Alexandria University, Alexandria, Egypt, [b]Department of Surgery, Medical Research Institute, Alexandria University, Alexandria, Egypt

Correspondence to Hatem Alwagih, MD, Faculty of Medicine, Alexandria University, Champollion street, El-Khartoum Square, El Azareeta Medical Campus, Alexandria 21131, Egypt. Tel: 002-03-4862506; E-mail: hatemalwagih@hotmail.com

Received: 12 December 2022
Revised: 29 December 2022
Accepted: 5 January 2023
Published: 28 April 2023

The Egyptian Journal of Surgery 2023, 41:1692–1698

Objective
The aim was to assess involvement of level V cervical lymph nodes (LNs) in patients with stage N1b papillary thyroid carcinoma (PTC) and to determine the clinical risks and benefits of routine level V dissection in these patients.
Patients and methods
The study included 20 patients with papillary thyroid cancer metastasizing to cervical LNs with no evidence clinically or radiologically of lymphadenopathy at level V. All cases were managed by total thyroidectomy and modified radical neck dissection. The study was conducted at the head, neck, and endocrine surgery unit at Main Alexandria University Hospital, Alexandria, Egypt.
Results
Metastatic LNs were distributed in the different cervical levels according to postoperative histopathology as follows: level II LNs were positive for malignancy in 16 neck sides (80%), level III in 17 neck sides (85%), and level IV in 15 neck sides (75%). Level VI LNs were positive in 19 patients (95%). Level V was free of malignancy in all studied patients. Postoperative complications were as follows: shoulder dysfunction was noted in three patients (15%), neck numbness and neuralgia were noted in seven patients (35%), recent hoarseness of voice was noted in one patient (5%), one patient (5%) showed delayed extubation, and ear numbness was noted in five patients (25%). No patients in our study experienced postoperative hematoma, chyle leak, or manifestations of hypoparathyroidism.
Conclusions
Incidence of cervical LN metastasis to level V in patients with N1b PTC is low compared with levels II, III, and IV. Moreover, there is clear evidence of postoperative morbidity from routine level V dissection in these patients. Therefore, level V dissection in patients with N1b PTC may be reserved for patients with clinically or radiologically evident level V metastasis.

Keywords:
level V, neck dissection, papillary thyroid carcinoma

Egyptian J Surgery 41:1692–1698

1110-1121

Introduction

In Egypt, cancer thyroid is the fifth most prevalent cancer in women, accounting for 3.7% of all female patients with cancer, with an incidence that varied from 3.5% in upper Egypt to 3.9% in lower Egypt in 2011 [1]. Papillary thyroid carcinoma (PTC) has an excellent prognosis and a mild biological behavior. Having good management increases survival rates to more than 90%. However, cervical lymph node (LN) metastasis in patients with PTC is frequent, but death owing to PTC is quite uncommon. In 20–50% of cases, cervical LN metastases are identified and in 90% when micrometastases are taken into account [2].

Thyroid carcinoma forms ~1% of all cancers and causes 0.2% of cancer deaths. The majority of these tumors are of the papillary type, which makes up about 80–85% of thyroid cancers [3]. PTC, of all thyroid cancers, has the highest incidence of cervical LN metastasis, which is the most important prognostic factor for locoregional recurrences in patients with PTC [4]. Cervical LN metastasis, however, does not always have a negative effect on overall survival in such patients [5]. The optimal extent of surgery for cervical nodal metastases in patients with papillary carcinoma is still up for debate. Most researchers accept that pathologically negative neck nodes do not require prophylactic neck dissection. However, some physicians recommend modified radical neck dissection (MRND) for neck nodes that are pathologically positive, whereas others advise selective neck dissection with restrictions [6].

In general, therapeutic posterolateral neck dissection means removal of levels II–V. However, routine dissection of level V in patients with PTC with lateral cervical LN metastases is still controversial [7]. According to many recent studies, the incidence of metastasis to level V cervical LNs in PTC is significantly low when compared with the incidence of metastasis to levels II–IV [8].

Aim

The aim of this study was to assess involvement of level V cervical LNs in patients with stage N1b PTC.

Patients and methods

The study included 20 patients with papillary thyroid cancer metastasizing to cervical LNs with no evidence clinically or radiologically of lymphadenopathy at level V. We excluded patients with previous thyroid or cervical LN surgery, patients with other head and neck malignancies, and patients with history of neck irradiation. The study was conducted at the head, neck, and endocrine surgery unit at Main Alexandria University Hospital.

The study was approved by the Research Ethics Committee of Alexandria Faculty of Medicine. An informed consent was obtained from all patients after explaining the benefits and risks involved.

All patients in the study were subjected to the following:

Preoperative assessment: it included thorough history taking, thorough clinical examination, routine laboratory investigations, and thyroid profile. Neck ultrasonography, computed tomography (CT) neck, and ultrasound (US)-guided Fine Needle Aspiration Cytology (FNAC) from suspicious thyroid lesion and suspicious cervical LN were also performed. Operative procedure: All patients in the study were managed by total thyroidectomy and MRND level (II–VI).

Postoperative assessment

Histopathological examination of the specimens acquired and clinical assessment of patients to exclude complications were done.

Statistical analysis

Data gathered from the patients preoperatively, postoperatively, and during the operative procedures were coded and entered to the computer and were statistically analyzed using the IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Statistical Software Package.

Qualitative data were described using number and percentage. Quantitative data were described using range (minimum and maximum), mean, and SD.

Results were tabulated in the form of frequency distributions with percentages from total count and/or from affected count.

Statistical charts were plotted to represent some of the important highlighted results, including Pie and Bar charts.

Results

Age and sex

A total of 20 patients were included, comprising 14 females (70%) and six males (30%). Their mean±SD age was 44.40±15.33 years, ranging from 10 to 74 years.

Complaints of the patients

Overall, 14 patients (70%) complained of midline neck swelling (goiter); 13 patients complained of lateral neck swelling (65%), including six patients (30%) who had right-sided neck swelling and seven patients (35%) who had left-sided neck swelling; and only four patients (20%) complained of compression manifestations (dyspnea and/or dysphagia). No patients in our study complained of voice changes. No patients were asymptomatic at presentation or accidently discovered (Table 1).

Local examination

On local examination, only 14 patients (70%) had palpable thyroid swelling. Six patients (30%) had right-sided palpable cervical LNs and eight patients (40%) had left-sided palpable cervical LNs. This makes a total of 14 neck sides. Six patients were free of palpable LNs clinically. Neck examination showed that palpable LNs were distributed in the different levels of the neck as follows: level II nodes were palpated in six neck sides (30%), level III nodes were palpated in 12 neck sides (60%), level IV nodes were palpated in eight neck sides (40%), and level V nodes could not be palpated in any patient in our study (clinically free) (Table 2).

Table 1 Distribution of the studied patients according to presentation complaints (*n*=20)

Complaint	*N* (%)
Midline neck swelling	14 (70.0)
Lateral neck swelling	13 (65.0)
Compression manifestations	4 (20.0)

Table 2 Distribution of the studied patients according to local examination findings (*n*=20)

Local examination	*N* (%)
Palpable goiter	14 (70.0)
Palpable LN	
Right	6 (30.0)
Left	8 (40.0)
Total	14 (70.0)
LN level	
II	6 (30.0)
III	12 (60.0)
IV	8 (40.0)
V	0

LN, lymph node.

Table 3 Sonographic thyroid examination findings among the studied patients (*n*=20)

US result	*N* (%)
Thyroid gland	
Normal	2 (10.0)
Diffuse goiter	1 (5.0)
Multinodular goiter	12 (60.0)
Right STN	2 (10.0)
Left STN	3 (15.0)

STN, solitary thyroid nodule; US, ultrasound.

US results

US examination of the thyroid gland revealed normal bilateral lobes in two patients (10%), diffuse thyroid enlargement in one patient (5%), multinodular goiter in 12 patients (60%), and solitary thyroid nodule was found in the right lobe in two patients (10%) and in the left lobe in three patients (15%) (Table 3).

US examination of the neck showed that there were suspicious cervical LNs on the right side in nine patients (45%) and on the left side in 11 patients (55%). Suspicious LNs were distributed in the different levels of the neck as follows: level II nodes were enlarged in 10 neck sides (50%), level III nodes in 17 neck sides (85%), level IV in 11 neck sides (55%), and level V was free of malignancy in all studied patients (Table 4).

Computed tomography results

Computed tomography of the neck showed that there were suspicious LNs on the right side of the neck in nine patients (45%) and on the left side in 11 patients (55%). Enlarged LNs were distributed in the different levels of the neck as follows: level II nodes were enlarged in 12 neck sides (60%), level III in 18 neck sides (90%), level IV in 13 neck sides (65%), and level V was free of malignancy in all studied patients (Table 5).

Table 4 Sonographic neck node examination findings among the studied patients (*n*=20)

Affected LNs by US	*N* (%)
Side	
Right	9 (45.0)
Left	11 (55.0)
Level	
II	10 (50.0)
III	17 (85.0)
IV	11 (55.0)
V	0

LN, lymph node; US, ultrasound

Table 5 Computed tomographic neck node examination findings among the studied patients (*n*=20)

CT result	*N* (%)
Affected LN side	
Right	9 (45.0)
Left	11 (55.0)
Affected LN level	
II	12 (60.0)
III	18 (90.0)
IV	13 (65.0)
V	0

CT, computed tomography; LN, lymph node.

Results of preoperative biopsy

US-guided fine-needle aspiration cytology from the thyroid gland and suspicious cervical LN was done in 17 patients (85%); all of them were Bethesda V or VI (suspicious for malignancy or malignant) regarding the thyroid nodule, whereas all LN were positive for malignant cells.

In the two patients presenting with normal thyroid gland (10%), US-guided fine-needle aspiration cytology was done from only suspicious cervical LN, and both showed metastatic papillary carcinoma.

US-guided core biopsy from suspicious LN was done in one patient (5%) and showed metastatic papillary carcinoma.

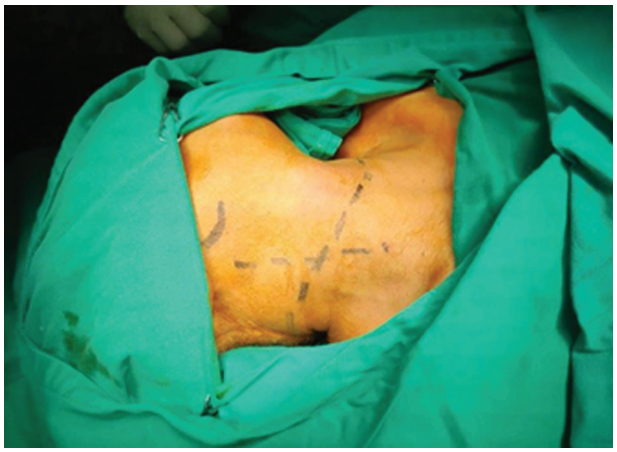
Surgical procedures

All patients in our study were managed by total thyroidectomy and MRND (central neck dissection and lateral neck dissection). Right-side neck dissection was done in nine patients (45%), and left-side neck dissection was done in 11 patients (55%) (Figs 1–5).

Postoperative complications

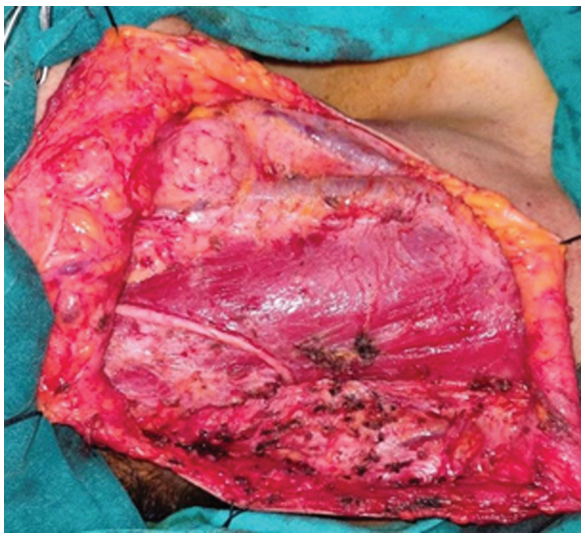
Postoperative shoulder dysfunction was noted in three patients (15%). Neck numbness and neuralgia was noted in seven patients (35%). Postoperative hoarseness of voice was noted in one patient (5%).

Figure 1



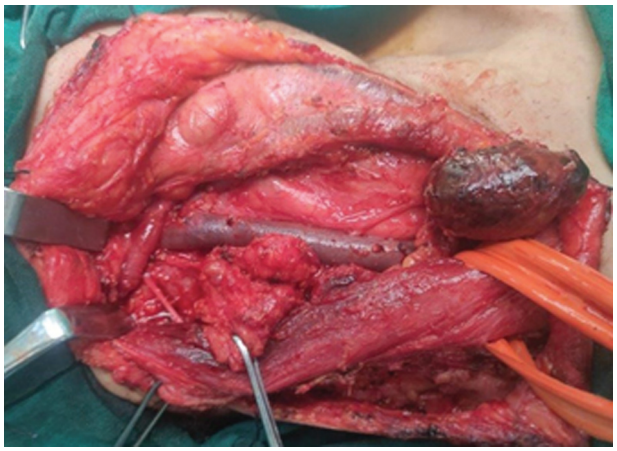
Patient position and marked site of skin incision.

Figure 2



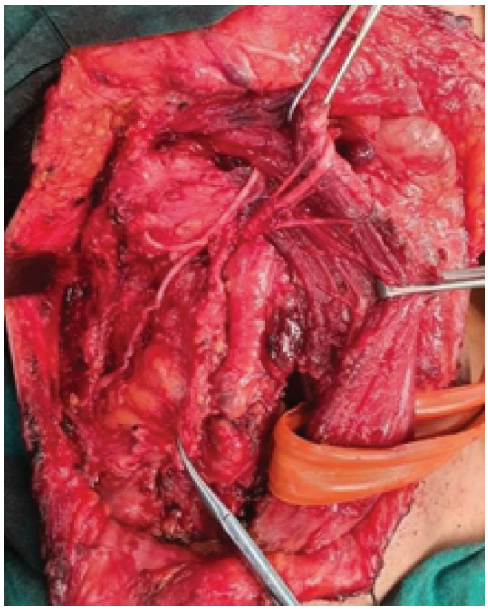
After elevation of skin flaps, showing sternocleidomastoid muscle and overlying great auricular nerve, which emerges at the Erb's point.

Figure 3



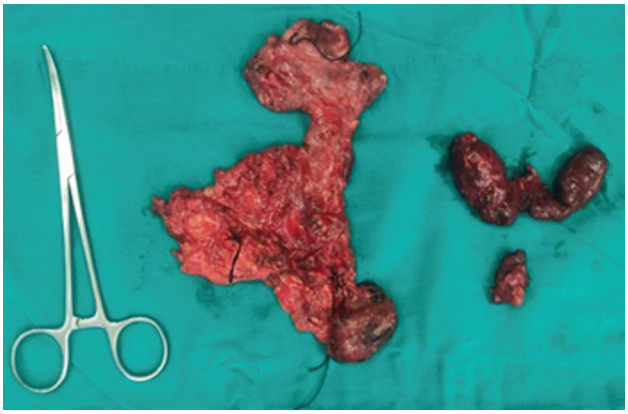
After dissection of level II and preserving the spinal accessory nerve.

Figure 4



Posterior neck triangle showing level V compartment and spinal accessory nerve which has a superficial course from posterior border of sternocleidomastoid muscle (SCM) to trapezius muscle.

Figure 5



Specimens acquired showing thyroid gland and levels II–VI to be sent for histopathological examination.

One patient (5%) showed delayed extubation. After 24 h, this patient was extubated and there was no need for tracheostomy. Ear numbness owing to affection of great auricular nerve was noted in five patients (25%). No patients in our study experienced postoperative hematoma, chyle leak, or manifestations of hypoparathyroidism (Table 6).

Postoperative histopathological results

Histopathological examination of the submitted thyroid specimens showed that PTC was the diagnosis for all of the studied patients with its different histological variants.

Table 6 Postoperative complications among the studied patients (*n*=20)

Postoperative complications	*N* (%)
Spinal accessory nerve affection (shoulder dysfunction)	3 (15.0)
Neck numbness and neuralgia	7 (35.0)
Voice changes	1 (5.0)
Delayed extubation	1 (5.0)
Great auricular nerve affection (ear numbness)	5 (25.0)

Table 7 Distribution of the affected lymph node levels according to postoperative histopathology (*n*=20)

Postoperative histopathology	*N* (%)
Affected lymph nodes (LNs)	
II	16 (80.0)
III	17 (85.0)
IV	15 (75.0)
V	0
VI	19 (95.0)

Histopathological examination of the submitted LN specimens showed that metastatic LNs were distributed in the different levels of the neck as follows: level II LNs were positive for malignancy in 16 neck sides (80%), level III in 17 neck sides (85%), and level IV in 15 neck sides (75%). Level VI LNs were positive in 19 patients (95%). Level V was free of malignancy in all studied patients.

Skip metastasis, which means presence of lateral LN metastasis without central lymph metastasis, was noted in only one patient (5%) (Table 7).

Discussion

Thyroid cancer makes up around 1% of all cancers, but an increasing incidence has been noted worldwide [4]. PTC is the most prevalent type of the Differentiated Thyroid Cancer (DTC), forming more than 90% of DTC and almost 75% of all thyroid cancers [5]. The ideal strategy for management of papillary carcinoma includes complete surgical excision of any evident cervical disease either clinically or radiologically, use of radioactive iodine (when indicated), and postoperative thyroid stimulating hormone suppression [5].

Patients with papillary carcinoma generally have a very good prognosis with a 10-year overall survival rate of more than 90%. However, cervical nodal metastases, including occult metastasis, are discovered in 30–80% of cases at the time of diagnosis [6]. Cervical nodal metastasis in papillary carcinoma was found to be one of the most important risk factors for locoregional recurrence. Therefore, it is essential to perform an effective therapeutic lateral neck dissection [6]. The American Thyroid Association consensus and British Thyroid Association Guidelines recommend therapeutic MRND for stage N1b PTC. MRND includes surgical removal of lateral cervical LN levels II–V, but one or more of the nonlymphatic structures is preserved, such as the sternocleidomastoid muscle, the spinal accessory nerve (SAN), and the internal jugular vein [2].

There is still debate over whether level V should be surgically removed with lateral neck dissection or not because of the relatively low incidence of level V metastases and recurrence. Moreover, although the SAN and branches of the cervical plexus are often grossly preserved during surgery, some operations such blindly extending the range of lateral neck dissection may produce clinically significant postoperative morbidities owing to neuropraxia that results from excessive nerve retraction or ischemia during LN dissection [7]. Therefore, the purpose of our study was to determine the clinical risks and benefits of routine level V dissection in patients with stage N1b papillary carcinoma.

The most presenting symptom in the present study was midline neck swelling (goiter) in 14 patients (70%) followed by lateral neck swelling in 13 patients (65%), and only four patients (20%) complained of compression manifestations. Seven of our patients (35%) were not complaining of lateral neck swelling, and on clinical examination, only one of them had palpable LNs.

Kim *et al*. [8] reported that 8% of patients in their study were asymptomatic and 92% had palpable goiter and 60% of them had compression symptoms. In the present study, no patients complained of preoperative voice changes, whereas Wada *et al*. [9] reported an incidence of 1.5% of their patients presented with hoarseness of voice and had affected vocal cord mobility by indirect laryngoscopy, where 55% of the incidence was due to previous thyroid surgery.

In the present study, side of LN metastases diagnosed by local examination was six patients on the right side (30%) and eight patients on the left side (40%). However, imaging (US and CT) detected nine patients to have LN metastases on the right side (45%) and 11 patients on the left side (55%). Therefore, all of our patients had suspicious lateral neck LNs on imaging. Kouvaraki *et al*. [10] found that preoperative high-quality US-detected LNs or soft-

tissue metastases in cervical compartments believed to be uninvolved by clinical examination in 38% of patients. Wada *et al.* [9] reported LN metastasis in clinically node-negative patients in 50% of their patients.

In the present study, three patients (15%) complained postoperatively from weakness of shoulder elevation (SAN affection). Seven patients (35%) had numbness over the skin of the neck and shoulder. Five patients (25%) suffered from paresthesia of the ear (affected great auricular nerve). One patient (5%) had delayed extubation and was extubated after 24 h postoperatively with no need for tracheostomy, and this patient had some hoarseness of voice early postoperative, but his voice showed marked improvement within few months. None of our patients had postoperative bleeding, hematoma, or chyle leakage. Moreover, no manifestations of hypoparathyroidism were noted.

As shown in many studies, level V dissection, which involves clearance of the posterior triangle of the neck, has the potential to increase the risk of SAN injury, despite gross preservation [11]. R El-Gammal Hammed *et al.* [12] performed a comparative study between two groups of N1b PTC, where the first was managed by MRND (levels II–V) and the second Selective Neck Dissection (SND) (levels II–IV), and found that shoulder syndrome was significantly more frequent in the MRND group than in the SND group (30 vs. 0.0%), and it was also noted that the MRND group had significantly longer operative time and postoperatively more amount of drainage when compared with the SND group. Kim *et al.* [8] also made a similar comparative study and found that shoulder syndrome in the MRND group was significantly more frequent than in the SND group (9.1 vs. 2.7%) and operative time was significantly longer. Wang *et al.* [13] noted that ~10% of the MRND patients experienced shoulder syndrome, and it was only 2.7% in patients with SND. However, Xue *et al.* [14] found that surgical complications related to neck dissection were low among both groups but noted that MRND increased hospital stay and cost.

Regarding the pattern of cervical nodal metastatic spread to the neck node levels, our results were as follows: 80% (16 neck sides from 20) in level II, 85% (17/20) in level III, 75% (15/20) in level IV, 0.0% (0/20) in level V, and 95% (19/20) in level VI. Patients selected for our study had clinically and radiologically free level V preoperatively, and when postoperative histopathological results revealed negative level V in all cases, we concluded that occult LN metastasis in level V was absent (0.0%) for all of our patients. In our study, skip metastasis was noted in one patient (5%).

R El-Gammal Hammed *et al.* [12] stated that incidence of metastatic nodal disease in the patients managed by MRND was as follows: level II was 55% of patients, level III was 80% of patients, level IV was 75% of patients, level V was 5% of patients, and level VI was 90% of patients (skip metastasis 10%). Occult level V metastasis as described by R El-Gammal Hammed *et al.* [12] was 5%.

Kim *et al.* [8] stated that incidence of metastatic nodal disease in the patients managed by MRND was as follows: level II was 54% of patients, level III was 75.1% of patients, level IV was 77.2% of patients, level V was 13.9% of patients, and level VI was 85.9% of patients (skip metastasis 14.1%). Occult level V metastasis as described by Kim *et al.* [8] was 8.6%.

Li *et al.* [15] stated that incidence of metastatic nodal disease in the patients managed by MRND was as follows: level II was 42.8% of patients, level III was 71.2% of patients, level IV was 76.1% of patients, level V was 17.8% of patients, and level VI was 81.3% of patients (skip metastasis 18.7%).

Wang *et al.* [13] stated that incidence of metastatic nodal disease in the patients managed by MRND was as follows: level II was 50.8% of patients, level III was 63.9% of patients, level IV was 72.8% of patients, and level V was 21.3% of patients. However, the results of Xue *et al.* [14] were as follows: level II was 58.7% of patients, level III was 52.3% of patients, level IV was 75.7% of patients, and level V was 21.4% of patients.

The sensitivity of preoperative imaging (US and CT) is particularly not good for detection of level V metastatic spread [16]. Therefore, many studies investigated the factors that predict level V metastases to help establish indications for level V dissection in patients with stage N1b papillary thyroid cancer.

Wang *et al.* [13] described some predictive factors for level V metastases in patients with papillary thyroid cancer with lateral Lymph Node Metastasis (LNM), and these factors were tumor size greater than 2 cm, LN size greater than 2 cm, extranodal extension, unilateral/bilateral central LNM, and involvement of levels II/III/IV. Wang *et al.* [13] concluded that extranodal extension and LN size were most important predictive factors for level V involvement.

Li *et al.* [15] also presented several independent predictive factors for level V metastasis in patients with papillary thyroid cancer such as tumor size greater than 2.5 cm, number of central LNM greater than 3, level II metastasis, and BRAF gene mutation.

From the previous results, we noticed that the incidence of level V involvement is relatively low when compared with levels II–IV in almost all the studies we found. We also noticed low incidence of occult level V metastasis. Because of that in addition to the clear evidence of increased morbidity from level V dissection, we conclude that further studies are required to accurately assess the value of level V dissection in patients with N1b PTC versus its morbidity. The data from the current study suggests that it may be reserved for patients with clinically or radiologically evident metastasis in level V.

Conclusion

Incidence of cervical LN metastasis to level V in patients with N1b PTC is low compared with levels II, III, and IV. Moreover, there is clear evidence of postoperative morbidity from routine level V dissection in these patients. Therefore, level V dissection in patients with N1b PTC may be reserved for patients with clinically or radiologically evident level V metastasis. We recommend that further studies with a larger sample size should be carried out to determine whether level V dissection should be routinely performed in N1b PTC or not and its effect on recurrence and prognosis. Moreover, the predictive factors for level V metastasis in N1b PTC should be well investigated in next studies to help preoperative evaluation of nodal status and to perform tailored therapeutic lateral neck dissection.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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