



## A CLINICAL STUDY TO DETERMINE THE PREVALANCE OF LEVEL IIB METASTASIS IN PATIENTS WITH HEAD AND NECK MALIGNANCIES

### Oncology

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### ABSTRACT

**BACKGROUND:** The purpose of this study was to determine the prevalence of level IIB metastasis in patients with Head and Neck squamous cell carcinomas (HNSCCs).

**MATERIAL AND METHODS:** A prospective analysis of 44 patients with HNSCC who underwent surgical treatment of the primary lesion with simultaneous neck dissection was performed. During neck dissection, level IIB lymphnodes were separately removed and processed. Neck dissection was bilateral in 3 patients and unilateral in 41 patients

**RESULTS:** The mean number of nodes found in the level IIB specimens was 4.7 (range: 0-8nodes). The prevalence of metastasis at level IIB was 0% in pN0 necks and 13% in pN+ necks, with an overall prevalence of 6.8%. A significant association between metastasis to level IIB and type of neck dissection was observed. There were no isolated metastases to level IIB without the involvement of other nodes in the remaining neck specimen.

**Conclusions:** Based on our findings, we suggest that dissection of the level IIB region in patients with HNSCC may be required only in patients with multilevel neck metastasis or if level IIA metastasis is found intra operatively.

### KEYWORDS

Oral squamous cell carcinoma, neck dissection, level IIB, metastasis, spinal accessory nerve.

### INTRODUCTION

The biological aggressiveness of oral carcinoma is reflected by its ability to spread to neck nodes (N+). The work of Weiss *et al.* Established a threshold of a 20% possibility of cervical metastasis as the indication for elective management of the neck in squamous HNC<sup>1</sup>. Although conflicting rational exist regarding the most appropriate therapeutic management of a clinically N0 HNSCC, and based on the observation that lymph node metastasis from carcinoma as of the oral cavity tend to exhibit a typical pattern of spread, most frequently to levels I, II, and III a supraomohioid neck dissection (SOHND) is usually proposed for the treatment of HNSCC in N0 cases. The surgical therapy of patients with HNSCC and clinical N+ neck is less controversial than the treatment of the clinical N0 neck. In present scenario, many surgeons globally still perform standard radical neck dissection (RND) or modified radical neck dissection (MRND) in cases of clinical N+ neck. Unlike RND, MRND preserves important anatomic structures, such as the spinal accessory nerve (SAN), while also maintaining oncologic safety. One of the more technically difficult aspects of ND is the removal of the upper internal jugular vein and the SAN lymphnodes, in the posterior region of level II. This area is known as level IIB, but it also has been called supra retro spinal recess and sub muscular recess (SMR). Level IIB comprises node-bearing tissue that lies superficial to the fascia on the splenius capitis and levator scapulae muscles, and is bordered antero inferiorly by the SAN, supero laterally by the inferior border of the posterior belly of the digastrics muscle, superiorly by the skull base, and posterolaterally by the sternocleidomastoid muscle. Complications that may occur after level IIB dissection include SAN dysfunction, which results in the restriction of shoulder movements and thus has a negative impact on life quality. To overcome this complication, avoiding the dissection of level IIB has been proposed. There still remains a debate about the frequency of metastasis to level IIB, and despite various published works, the question of whether or not to dissect level IIB remains to be answered.

### Objective

Thus, the aim of this study is to determine the frequency of level IIB metastasis in HNSCC by means of a prospective study in order to assess whether dissection of level IIB nodes should be performed or

can be avoided in the treatment of HNSCC.

### MATERIALS AND METHODS

This prospective study involved 44 previously untreated consecutive patients with HNSCC who were treated at the Department of Surgical Oncology at a tertiary level health centre over a period of 18 months. In order to be included in the study, eligible patients had to have undergone surgical resection of a primary HNSCC, in conjunction with a unilateral or bilateral, elective or therapeutic, neck dissection that included sublevel IIB. Exclusion criteria were synchronous head and neck cancers, a history of surgery or radiotherapy of the head and neck, a history of head and neck cancer, and primary treatment with radiotherapy or chemotherapy. Patient and tumor characteristics are provided in **table3**. Tobacco and alcohol consumption history was determined from medical records.

All diagnoses were confirmed histopathologically before treatment, and the disease was staged after the surgical resection of the tumor according to the TNM system of the American Joint Committee on Cancer. The extent of the ND was modulated according to the clinical neck status. The fibro fatty tissue of level IIB was dissected and removed before completing the remainder of the ND, and then labeled and processed in a separate box for histopathological analysis. The ND was subsequently completed and the remaining neck specimen was divided and labeled as Ia, Ib and IIA, III, IV, V level by the surgeon before being submitted for pathological analysis. Postoperative radiotherapy was applied to patients either had pT4 tumors, positive lymphnodes, or margins of less than 4mm.

### RESULTS

Overall, 44 patients were included in the study and 68 neck dissections were performed in total. The number of lymph nodes removed during ND ranged between 9 and 47, with an average of 22 lymph nodes. The mean number of nodes found in the level IIB specimens was 4 (range 0-8nodes). The neck node specimens of 23 (52.82%) patients were pathologically N+; among them, 9 patients had a single positive node, six patients had two positive nodes, 8 patients showed three or more positive nodes. Only three patients had metastases in level IIB, representing 3 out of 44 patients (6.8%) and 3 out of 68 neck dissection

specimens (4.4%), combining pathologically N0 necks and clinically node positive necks. Regarding the tumor site, only one tumor located in the tongue and two tumors at buccal mucosa extending to RMT showed metastasis in the level IIB lymph nodes, while the remaining tongue cancers and oral cavity locations did not show association with level IIB involvement.

Several variables were included in the analysis of potential risk factors for nodal metastasis at level IIB. There was no association between any neck levels with pN+ and the occurrence of pN+ at level IIB. Furthermore, it was not possible to demonstrate the influence of the number of histopathologically positive neck levels over the presence of metastases at level IIB through histopathologic evaluation (Table 4). No statistically significant association between the presence of nodal metastasis at level IIB and advanced pathological N stage was observed, but in no instance were there positive nodes at level IIB without metastatic disease at one other nodal level at least.

## DISCUSSION

The lymph nodal spread of oral carcinoma cells to the neck usually follows a well known pattern. Ninetyone percent of neck node metastases from oral cancers are concentrated in levels I to III, and if level IV is added to the I-III levels in a selective neck dissection, 96% of all nodal metastases from oral cancers would be covered in this dissection. The overall incidence of metastasis from HNSCC to level V is as low as 3.3%. Level IIB lymph node dissection has been performed as part of elective neck dissection since Schuller *et al* observed the high nodal metastasis rate around the SAN<sup>2</sup>. Nevertheless, dissection of level IIB in HNSCC is controversial now a days. It is well known that the oral cavity does not drain directly in to level IIB. The controversy arises from the low reported risk of level IIB nodal metastasis and potential shoulder disability. In patients with selective neck dissections, such as SOHND, shoulder function impairment has been observed in 21% to 60% of cases despite of the preservation of the SAN. Erisen *et al* observed that in all types of neck dissections all patients exhibited electromyographic evidence of denervation when compared with a control group<sup>3</sup>. At about the third postoperative month, the nerve function returns, but reparation of axonal damage can take from 12 to 18 months. Kierner *et al* have reported that the SAN passed dorsally to the internal jugular vein in 44% of cases and ventrally in 56% of cases<sup>4</sup>. Lee *et al* Showed that the SAN courses dorsally to the vein in 57.4% of cases, ventrally in 39.8% of cases, and through the internal jugular vein in 2.8% of cases<sup>5</sup>. The number of lymphnodes at level IIB varies from patient to patient and throughout the course of the nerve. Lee *et al*. noticed that the mean number of lymphodal yeild at level IIB was 6.5 when the SAN crossed ventrally and 6.8 in those cases in which the SAN crossed the internal jugular vein dorsally<sup>5</sup>.

Recent studies that look for the frequency of metastasis at level IIB in N0 HNSCC found figures that ranged from 0% to 22%, with 95% confidence intervals (0% to 44.4%)<sup>6</sup>. Chone *et al*. performed a retrospective analysis of 51 patients with different carcinomas of the upper aero digestive tract and found metastatic lymph nodes in the sub muscular recess in 4 of 62 neck dissections<sup>7</sup>. Three of these patients were having N2 disease and one patient suffered from a T2N0 carcinoma of the floor of the mouth. However, it is well-known that lymphatic metastatic spread patterns from different primary sites can vary greatly<sup>8</sup>, and it is difficult to estimate the prevalence of metastasis in a heterogeneous group of patients with different primary sites despite of only surgically treated cases as initial therapy. Talmi *et al*. reported an incidence of 6% of occult metastasis at level IIB in patients with HNSCC who underwent elective ND<sup>9</sup>. Lim *et al*. reported that level IIB nodal metastasis was present in four (5.4%) of 74 cases of cN0 OSCC in which an SOHND was performed<sup>10</sup>. Elsheikh *et al*.<sup>11</sup> found a prevalence of 10% at level IIB in a molecular study on 48 patients with HNSCC and N0 neck who underwent a SOHND. Villaret *et al* stated that the oral cavity has the highest overall prevalence of level IIB metastasis (10%) among head and neck squamous cell carcinomas, but these metastases are only found in 2% of cN0 cases<sup>12</sup>.

The primary limitation of our study, and all others published to date on this topic, is the sample size, as well as the limited follow-up. However, despite the sample size, we have obtained some usefull results. Lymphnode metastases were detected at level IIB in 3 of 44 patients with HNSCC, which means a prevalence of 8%, lower than in other studies, and the percentage of metastasis at level IIB in N0 cases was 0%. In our study, isolated metastases were not found at level IIB. When

compared with the current literature, this is a low prevalence, and in addition we did not found any association between clinical variables and metastases at level IIB. It would appear that T stage, tumor location and histological grade of differentiation are not reliable indicators of metastasis at level IIB. It may be due to more than 50% of patients had T1 and T2 carcinomas, and 94% of them were well or moderately differentiated. Therefore, a limitation of this study could be the statistical power due to the relatively small number of patients. When an SOHND was performed in cN0 oral cancer patients who had been surgically treated as initial therapy, occult nodal metastasis to level IIB did not occur on either the ipsilateral or contra lateral neck. However, when ipsilateral node metastasis was present, specifically at level II, the cervical metastatic rate to ipsilateral level IIB lymphnodes was 3.4%. In this study, the patient with metastasis at level IIB was also detected to have metastasis at levels IIA. Occult metastases are tumoral lymph node deposits undetected by clinico-radio-graphic examination, and they can be further subdivided into three types: macro metastasis (greater than 2-3 mm in largest dimension), micro metastasis (smaller than 2-3 mm in largest dimension), and isolated tumor cells within the lymphnodes<sup>13</sup>. Elsheikh *et al*. using molecular analysis, found an incidence of occult metastasis to level IIB in 5 of 23 (22%) patients with primary tumors located in the tongue<sup>11</sup>. Thus, they defend that level IIB should be included in the neck dissection in cases of tongue cancer. In our current study, the only level IIB metastasis case found was observed in a patient afflicted with tongue cancer. Level IIB metastases are rarely found in isolation; instead, IIB metastases are most often found combined with occult or gross pathologic nodes at other levels. Maher and Hoffman<sup>14</sup> found cervical sub level IIB lymph node metastases in 4(5.6%) of 71 patients with primary OSCC. Three of these IIB metastases were found in patients with tongue carcinomas, and the other case in a patient afflicted from a cancer located in the retro molar trigone. Pantvaitya *et al*. described similar findings: tongue cancers (5%) and cancers of the retro molar trig-one (6.2%) had the highest incidence of metastasis to level IIB<sup>15</sup>. They also found that metastases at level IIB were associated with metastases at level IIA in 68.1% of dissections; conversely, only 11.3% of all level IIA metastases had positive nodes at level IIB.

Based on our findings, and considering the low incidence of level IIB nodal metastases in HNSCC, we suggest that it may be unnecessary to resect level IIB lymph nodes for most people with HNSCC when performing an elective neck dissection in cN0 cases and, consequently, post operative shoulder disability may be avoided. Thus, dissection of level IIB in patients with OSCC may be required only in patients with multilevel neck metastasis or if level IIA metastasis is found intra operatively. How-ever, because only three patients had sublevel IIB metastasis in this study, our results would require additional validation, and its significance should be interpreted cautiously. The high metastatic rate of patients with clinically positive neck nodes, mainly in patients staged N2b or greater confirms the recommendation given by few authors of need to dissect level IIB in these cases, considering that the optimal time to deal with these nodes is at the time of initial treatment.<sup>7</sup>

## ABBREVIATIONS

CT: Computed tomography; MRI: Magnetic resonance imaging; HNSCC: HEAD AND NECK squamous cell carcinoma; SOHND: supra omohyoid neck dissection, MRND: modified radical neck dissection

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## AVAILABILITY OF DATA AND MATERIALS

The datasets during and/or analyzed during the current study are available from the corresponding authors on reasonable request.

## CONSENT FOR PUBLICATION

Written informed consent was obtained from the patients for publication of clinical data and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval obtained by Intuitional review board in a meeting.

**DISCLOSURE**

There are neither commercial interests nor financial and/or commercial support.

**LEGENDS****TABLE 1 : DEMOGRAPHIC PARAMETERS OF THE STUDY**

characteristics	No of Cases	Percentage
Male	28	63.6%
Female	16	36.3%

**TABLE 2: SHOWING VARIOUS SITE OF DISEASE OCCURRENCE**

Primary site	No of Cases	Percentage
Buccal Mucosa	18	41%
Alveolus	7	16%
Tongue	6	13.6%
Floor of Mouth	2	4.5%
Lower lip	4	9%
Retro Molar Trigone	5	11.3%
Larynx	2	4.5%

**TABLE 3: TUMOR CHARACTERISTICS**

Clinical Tumor Characteristics	No of cases	Percentage
T1	5	11.3%
T2	8	18%
T3	4	9%
T4a	27	61.3%
N0	21	47.7%
N1	19	43%
N2	3	6.8%
N3	1	2.2%

**TABLE 4: RELATIONSHIP BETWEEN PATHOLOGICAL STAGING AND LEVEL IIB INVOLVEMENT**

Pathological stage	No of Cases	Level Iib Involved	Level Iib Uninvolved
T1	7	0	7
T2	4	0	4
T3	9	1	8
T4	24	2	22
N0	21	0	21
N+	23	3	20

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