

## ONCOLOGY

# Status of level IIb lymph nodes of the neck in squamous cell carcinoma of the oral tongue in patients who underwent modified radical neck dissection and lymph node sentinel biopsy

## *Condizione dei linfonodi del livello IIb del collo nel carcinoma squamoso della lingua in pazienti sottoposti a svuotamento linfonodale radicale modificato e a biopsia del linfonodo sentinella*

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## SUMMARY

Status of lymph nodes of level IIb was examined to identify the incidence of nodal metastasis and the lymphatic drainage in squamous cell carcinoma of the oral tongue in patients undergoing modified radical neck dissection (MRND) and sentinel node biopsy (SNB). Overall, 72 patients were divided into two groups; 38 patients (Group A) of any T and N+ or T3-T4- N0 stage underwent MRND. The surgical specimens were sent to the Pathology Department, divided into specific levels (I, IIa, IIb, III, IV, V) and labelled. The remaining 34 patients (Group B) T1-T2 -N0 stage were submitted to SNB. The histological examination of the specimens of the two groups was performed by staining with haematoxylin and eosin several sections from each node at different levels and then using a molecular marker such as cytokeratin and Epithelial Membrane Antigen (EMA). In Group A: In N0 there were no occult metastases at level IIb; in N+ neck, 8 cases (33.3%) showed metastasis at level IIb ( $P = 0.04$ ). Metastases at level IIb were observed only in combination with other levels ( $P = 0.03$ ). In Group B, direct lymphatic drainage was found in 2 patients (5.9%) at level IIb. There were no occult metastases at level IIb. Out of the 54 sentinel nodes harvested, 4 lymph nodes (7.4%) were found to be metastatic; these 4 sentinel nodes were found respectively in 4 patients, 1 at level III, 3 at level IIa with an occult metastasis rate of 11.7%. In conclusion, SNB has prospected a new concept of lymphatic drainage that is variable and individual. SNB has demonstrated that direct lymphatic drainage is possible to level IIb. In our experience with early cancer of the tongue (T1-T2 N0), SNB aided with lympho-scintigraphy seems to be a good technique for staging the neck with minimal morbidity.

KEY WORDS: Oral squamous cell carcinoma • Neck metastasis • Neck dissection • Level IIb • Sentinel node biopsy

## RIASSUNTO

*Il rischio di metastasi linfonodali al livello IIb nei carcinomi della testa e del collo è un argomento ancora molto discusso in letteratura. Nel nostro studio abbiamo esaminato l'incidenza delle metastasi linfonodali, la condizione patologica dei linfonodi del livello IIb, il drenaggio linfatico nei pazienti affetti da carcinoma della lingua sottoposti a svuotamento laterocervicale radicale modificato e biopsia del linfonodo sentinella. Abbiamo trattato 72 pazienti con carcinoma a cellule squamose della lingua dividendoli in 2 gruppi: Gruppo A: 38 pazienti con N+ o T3-T4-N0 sono stati sottoposti a svuotamento radicale modificato del collo. Lo svuotamento laterocervicale ottenuto è stato diviso in livelli (I, IIa, IIb, III, IV e V) ed inviato al dipartimento di anatomia patologica. Gruppo B: 34 pazienti T1-T2 N0 sono stati sottoposti a biopsia del linfonodo sentinella. L'esame istologico dei due gruppi è stato eseguito su numerose sezioni per ogni linfonodo e a più livelli con colorazione ematossilina eosina e usando marcatori molecolari: citocheratina ed EMA (Antigene Epiteliale di Membrana). Nel Gruppo A, nei pazienti con N0, non abbiamo osservato metastasi occulte al livello IIb, nei pazienti N+, in 8 casi (33,3%) abbiamo riscontrato metastasi al livello IIb ( $P = 0,004$ ). Le metastasi al livello IIb sono state osservate solo associate a metastasi in altri livelli ( $P = 0,03$ ). Nel Gruppo B abbiamo osservato un drenaggio linfatico diretto al livello IIb in 2 pazienti (5,9%). Nei 54 linfonodi sentinella prelevati, 4 linfonodi (7,4%) erano metastatici. Dei suddetti linfonodi 1 è stato ritrovato al livello III e 3 al livello IIa con percentuale di metastasi occulta dell'11,7%. Non sono state riscontrate metastasi occulte al livello IIb. La tecnica del linfonodo sentinella ci ha permesso di individuare un diretto drenaggio linfatico ai linfonodi del livello IIb inoltre ci introduce ad un nuovo concetto di drenaggio linfatico del collo variabile ed individuale. Nella nostra esperienza con il carcinoma della lingua nello stadio iniziale (T1-T2-N0), SNB si è dimostrata una buona tecnica per stadiare il collo e ridurre la morbilità di una dissezione elettiva.*

PAROLE CHIAVE: Cancro del cavo orale • Metastasi laterocervicali • Svuotamento laterocervicale • Livello IIb del collo • Tecnica del linfonodo sentinella

## Introduction

Neck dissection is a fundamental part of the treatment of squamous cell carcinoma (SCC) of the tongue due to the high percentage of node metastasis.

The appropriate management of the neck in patients with tongue cancer remains an area under discussion. There is no general agreement on which type of treatment is adequate in patients with a node negative neck, while a positive node in the neck needs a modified radical neck dissection.

Elective dissection of cervical lymph nodes is usually advocated for the treatment of the SCC of the tongue even if cervical metastasis is not present because of the high rate of occult metastasis. Based on the observation that the areas of increased risk of cervical metastasis of SCC of the tongue are on level I-II-III some Authors propose selective neck dissections for patients staged N0<sup>1-3</sup>.

Another technique developed in the past few years in the attempt to avoid unnecessary neck dissection, is the removal of the first draining nodes of the neck after lymphoscintigraphy called "sentinel node biopsy" (SNB) in patients with N0 tongue cancer as a staging procedure<sup>4,7</sup>. All conservative techniques try to improve the quality of life, in fact not eliminating level V and IIb lymph-nodes can lower the incidence of spinal nerve injuries, preserve the roots of the deep cervical plexus, reduce surgical time, and prevent all the complications of modified radical neck dissection.

Level IIb lymph-nodes contained in the sub-muscular recess are the lymph-nodes lying over the fascia of the *splenius capitus* and *levator scapulae*, above the spinal accessory nerve, postero-laterally bordered by the sternocleidomastoid muscle and superiorly by the skull base<sup>8</sup>.

Recently, the incidence of nodal metastasis at level IIb in oro-pharyngeal cancer has been investigated to try to avoid the dissection in this area because the procedure may cause the post-operative shoulder syndrome even in the presence of an integral spinal accessory nerve<sup>8-10</sup>.

The aim of the present study was to analyse the status of lymph nodes of level IIb and to identify the incidence of nodal metastasis and the lymphatic drainage of patients affected by SCC of the oral tongue.

## Materials and methods

This study comprised 72 patients with SCC of the oral tongue. The patients, divided into two groups, were 50 males and 22 females, ranging from 26 to 84 years old (mean 60 years). The diagnoses of SCC were confirmed histopathologically before treatment. None of the patients were treated for any previous SCC of the head and neck. Staging of the primary tumour was established according to the classification of the American Joint Committee on Cancer<sup>11</sup> and the neck was staged by clinical examination and pre-operative Computed Tomography scan.

### Group A

Group A was analysed prospectively and included 38 consecutive patients of any T and N+ stage or T3-T4- N0 stage with SCC of the oral tongue who underwent modified radical neck dissection and the excision of the primary lesion between January 2002 and January 2006.

Modified radical neck dissections were performed in a standard fashion removing lymph nodes groups I-II-III-IV-V (12). The surgical specimens were sent to the Pathology Department, divided into specific levels (I, IIa, IIb, III, IV, V) and labelled. Level IIb was harvested separately during the operation.

### Group B

Group B was analyzed retrospectively and included 34 patients with SCC of the oral tongue staged T1-T2 with clinically and radiographically N0 neck, who underwent sentinel lymph node biopsy and excision of the primary lesion, between January 1999 and January 2007. The technique for SNB has been described elsewhere<sup>4,6</sup>.

Modified radical neck dissection was performed when the node (sentinel) harvested proved to be positive (metastatic); in the case of a negative histological report a strict follow-up routine was applied.

The histological examination of the specimens of the two groups was performed by staining with haematoxylin and eosin several sections from each node at different levels and then using a molecular marker such as cytokeratin and Epithelial Membrane Antigen (EMA). The histological report indicated the number of lymph nodes harvested for each level, as well as the size and the number of metastatic lymph nodes for each level.

### Statistical analysis

The relationships between level IIb and factors such as N+, N0, and the presence of positive lymph nodes at other levels were analyzed by a chi<sup>2</sup> or Fisher exact test. A P value  $\leq 0.05$  was considered statistically positive<sup>13</sup>.

## Results

In Group A patients, the mean number of lymph nodes harvested in MRND (38 ipsilateral and 2 contra-lateral) for each level was outlined in Table I.

**Table I.** Mean numbers of lymph nodes harvested per level during MRND (Group A).

Level	Mean number of lymph nodes harvested
I	4.9 (range 0-12)
IIa	5.5 (range 0-17) (a case of extra lymph node tissue deposit)
IIb	5.3 (range 1-13)
III	12.9 (range 2-32)
IV	8.75 (range 0-16)
VI	11 (range 2-26)

**Table II.** Distribution of positive lymph nodes per node level in cN+.

Level	Number of positive lymph nodes	
	Ipsilateral	Contralateral
I	15	0
Ila	35	0
Ilb	15	0
III	25	0
IV	20	0
V	19	0

There were 16 cN0 and 24 cN + necks in Group A; in cN0 neck, 5 cases showed at the pathologic examination micro metastatic lymph nodes with an occult metastasis rate of 31.25% (1 at level I, 1 at level IV, 2 at level IIa and 1 at level V). There were no occult metastases at level IIb.

In N+ neck, 8 cases (33.3%) showed ipsilateral metastases at level IIb ( $P = 0.04$ ) while no isolated metastasis occurred at level IIb. Metastases at level IIb were observed only in combination with other levels: 7 times with level IIa ( $P = 0.03$ ), 5 times with level IIa and III, twice respectively

**Table III.** Distribution of sentinel node and metastasis per level.

Patients	I	IIa	IIb	III	IV	V	I° contr
1		1 neg		1 neg			
2	1 neg			1 neg			
3				1 neg			
4		1 neg		1 neg			
5				1 pos			
6		1 neg	2 neg				
7		1 neg					
8		1 neg					
9		1 neg					
10				1 neg			
11		2 neg					
12		1 neg					
13	1 neg	3 neg					1 neg
14		1 neg					
15		1 pos					
16				2 neg			
17		1 neg					
18			2 neg				
19		1 neg		1 neg			
20		2 neg					
21				1 neg			
22				2 neg			
23		1 neg					
24		2 neg					
25		1 neg					
26		1 neg					
27				1 neg			
28.		1 neg					
29				1 neg			
30		1 neg					
31		1 pos					
32		3 neg					
33		1 neg		1 neg		1 neg	
34		1 pos					

with levels I, IIa, III, IV, V. The total number of positive lymph nodes found at level IIb was 15 (Table II), in 3 cases 1 lymph node was found, in 3 cases 2 and in 2 cases 3.

In Group B patients, 54 sentinel nodes were found on 35 necks examined (34 ipsilateral, 1 contralateral). Furthermore, 2 sentinel nodes were found at level I, 31 were found at level IIa, 4 were found at level IIb, 15 were found at level III, none at level IV, 1 was found at level V and 1 at level I contra-laterally. A total of 4 sentinel lymph nodes were found in 2 patients at level IIb (5.9%), but these did not contain metastasis. Sentinel nodes were found at level IIb once alone and another once along with level IIa. Out of the 54 sentinel nodes, 4 lymph nodes (7.4%) were found to be metastatic; these 4 sentinel nodes were found, respectively, in 4 patients, 1 at level III, 3 at level IIa with an occult metastasis rate of 11.7%. Double or multiple drainage occurred in 7 cases (20.5%). All data are shown in Table III.

## Discussion

The first part of the study (Group A patients) demonstrates that, in general, the risk of metastasis at level IIb is low, but in the case of N+ (33.3%) ( $P < 0.05$ ) or when level IIa is involved ( $P < 0.05$ ), this is statistically significant. These results, not surprisingly, confirm the studies of other Authors that the nodal spread pattern of SCC of the oral tongue is commonly located at levels II, III and I, while the risk at level IV, V and IIb is low<sup>1-3</sup>.

Various studies have investigated the chances of metastases of SCC of the head and neck at level IIb lymph nodes. Lim et al.<sup>9</sup> reviewed 74 patients with a clinically N0 neck who underwent supra-omohyoid neck dissection (SOHND) for SCC of the oral cavity and found a prevalence of metastases at level IIb of 5% (4 cases). Elsheikh et al.<sup>10</sup> in their molecular study on 48 patients with SCC of the oral cavity and N0 neck who underwent SOHND found an incidence of 10% at level IIb lymph nodes. They stressed that using this method of detecting micro-metastasis could be useful, in fact the incidence rose from 6% to 10% with PCR nested RT-PCR<sup>10</sup>, indeed, for the site of oral tongue the percentage of occult metastasis was higher (22%) than in the whole oral cavity. Talmi et al.<sup>14</sup> reported an incidence of 6% for occult metastasis at level IIb in patients with oral cavity cancer who underwent elective neck dissection<sup>14</sup>. Villaret et al.<sup>15</sup> indicate that the oral cavity has the highest overall incidence of sublevel IIb metastases (10%) among head-neck SCC but with a lower frequency in the cN0 situation (2%).

In our study, the percentage of occult metastases at level IIb alone was 0%, they occur only in combination with other level involvement in N+ neck. The second part of the study, concerning SNB in patients T1-T2-N0, again demonstrates that the risk of metastases at level IIb is low but, at the same time, clearly demonstrates that direct lymphatic drainage to level IIb is possible.

As we know that tongue cancer sooner or later will give rise to metastases and some of these will be found in unexpected levels of the neck including level IIb. The theory of SNB is based on the fact that a limited number of lymph nodes are the recipients of micro-metastases; these nodes are considered sentinel nodes. When lymphatic spread occurs, the first lymph nodes reached are the sentinel nodes, all other lymph nodes are involved thereafter. The closest basin is not the only possible location of metastatic spread. Lymphatic drainage is variable and individual in the neck, even from sites where it was expected.

Shoab et al.<sup>5</sup> in their study on SNB, in mucosal head and neck cancer, found direct lymphatic drainage to level IIb and underlined that lymph nodes in this region have to be removed in the case of a neck dissection.

Kovacs et al.<sup>16</sup> found lymphatic drainage to all levels of the neck; they concluded that, in the future, sentinel node dissection will replace elective neck dissection as a staging procedure. Other Authors hypothesize that the sentinel node technique could be a worthwhile procedure, in the future, in order to avoid unnecessary neck dissections<sup>4 5 16 17</sup>.

The percentage of metastases at level IIb in oral cavity cancer N0 neck looks as if it would appear to range from 0% to 22%; various Authors agree that elective neck dissection is necessary when the risk of nodal involvement exceeds 20%<sup>10 18</sup> and suggest dissecting the IIb lymph nodes, other Authors, on the contrary, believe that this region may be preserved<sup>9</sup>. For other sites (larynx, for example) N0 head and neck SCC, there is general agreement that suggests leaving the cervical IIb lymph nodes undissected, even if some Authors declare that more studies need to be performed to confirm their data<sup>19 20</sup>.

Selective neck dissection is often used as a staging procedure, but recurrence has been found in 4.5% of the cases and this occurred either in the area of neck dissection (57.1%) or beyond (42.9%)<sup>21</sup>.

Discussing the possibility of dissecting level IIb is a false problem, since trying to leave level IIb undissected in selective neck dissection will certainly lead to the discovery, in large series, of the presence of metastases at that level due to the fact that lymphatic drainage is possible to level IIb. Therefore, our efforts must focus on finding micro-metastases.

Sentinel node dissection thus led to a new concept of lymphatic drainage, different from the traditional suggestion. In fact, lymphatic drainage may be unpredictable in patients presenting oral tongue cancer.

In conclusion, we strongly recommend including level IIb in neck dissection in all N+. In early cancer of the tongue (T1-T2 N0), SNB with the aid of lymphoscintigraphy would appear to be a good technique for staging the neck with minimal morbidity. Management of the N0 neck in the T3-T4 lesions is still controversial on account of the high percentage of micro-metastases.

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