



## **Metastatic lymph nodes in the neck of patients with T1 and T2 squamous cell carcinoma of the lower lip detected with lymphoscintigraphy**

Mergime Prekazi Loxha<sup>1</sup>, Idriz Gerqari<sup>2</sup>, Sami Salihu<sup>1</sup>, Zana Agani<sup>3</sup>, Vjosa Hamiti<sup>3</sup>,

<sup>1</sup> *Department of Maxillofacial Surgery, University Clinical Center of Kosova, Kosovo*

<sup>2</sup> *Department of Radiology-Nuclear Medicine, University Clinical Center of Kosova, Kosovo*

<sup>3</sup> *Department of Oral Surgery, Dentistry University Clinical Center of Kosova*

### **Abstract**

#### **Aims and background**

The aim of our research was to use lymphoscintigraphy as a main method to confirm and detect lymph nodes in the neck, in patients with squamous cell carcinoma of lower lip which were clinically T1, T2 and N0, and to justify the use of selective neck dissection in those patients.

#### **Methods**

From April 2010 to January 2011, 31 patients with T1, T2 and N0 SCC of the lower lip were admitted to our center. To detect sentinel lymph nodes, we performed lymphoscintigraphy (LSG). LSG was performed on the day of surgery after intradermal injection of 37 Mbq of Tc99m-Sn-colloid/ml at four peritumoral sites. The sentinel lymph nodes were then extirpated and sent for biopsy.

## **Results**

Among the 31 patients, three (9.7%) were female and 28 (90.3%) were male. LSG detected sentinel nodes in the neck in 21 (67.7%) of the patients. Of these, 10 (47.6%) had a positive sentinel node biopsy. Of all 31 patients enrolled in the study, occult metastases were found in 10 (32.3%).

## **Conclusions**

Our results indicate that, of the methods used to detect positive lymph nodes, the most accurate is LSG. The results also suggest that further study is needed to optimize the treatment protocol in patients with SCC of the lower lip, especially in those with T2 lesions.

## **Introduction**

Squamous cell carcinoma (SCC) of the lower lip is one of the most frequently diagnosed malignant pathologies in the maxillofacial region. After skin cancer, lip cancer is the second most frequent cancer in the maxillofacial region[1,2]. Over 15 years in our department, we have treated 789 patients with SCC of the lower lip, the majority of whom were male (89%). Those with T1 and T2 lesions had a better prognosis [3]. Carcinoma of the lower lip is not an aggressive cancer. Because it grows slowly, it can be diagnosed and treated easily and effectively; however, the early treatment of carcinoma of the lower lip is important because the mortality is still 10–30%. The recommended protocol for the treatment of carcinoma of the lower lip in patients with clinically negative neck lymph nodes is to "wait and see"[4]. Precise diagnosis of malignant pathologies in the maxillofacial region, and the evaluation of susceptible metastatic lymph nodes present in the neck, are of great importance when choosing the best treatment for those patients; it is also critical to predict prognosis [5,6,7]. To date, the most accurate method for finding metastases in the neck is neck dissection with excision of the primary tumor [8].

In cases of T2 lip cancer reported in the literature, occult metastases were present in 15–35% of cases. There is no safe prognosis for which to recommend elective neck dissection [9]. The presence of lymph node metastases is the main prognostic factor. Most methods used to detect susceptible metastases in the neck in patients with malignant pathologies in the maxillofacial region are not completely accurate. CT, MRI and ultrasound can detect lymph nodes, but not metastases. Sentinel node biopsy (SNB) is most advantageous in detecting metastases in neck lymph nodes, and leads to an accurate diagnosis and prognosis, especially in patients with N0[9], and may help in the treatment of these patients[10].

### **Material and Methods**

This prospective clinical study was undertaken in the Department of Maxillofacial Surgery and the Department of Radiology-Nuclear Medicine at the University Clinical Center of Kosova. Ethical approval was issued by the Ethics Committee of the Faculty of Medicine, University Of Prishtina (document Nr.1551, 30.03.2010).

Between April 2010 and January 2011, 31 patients with SCC of the lower lip were admitted to the Maxillofacial Surgery Clinic of the University Clinical Center of Kosova. This study enrolled patients aged 18 years and older, with SCC of the lower lip with TNM classification cT1, cT2 and cN0, with an indication for surgical intervention. Patients excluded from study included those treated with radiotherapy before surgery, with recurrent carcinoma, or with lower lip carcinoma T3 and T4.

In all patients, clinically relevant data (including exposure to sun and tobacco use) were collected, and clinical examination (correct examination of oral cavity and oropharynx) was performed. In suspicious cases, an incision biopsy was done, along with additional examinations such as orthopantomography and dental status. To detect lymph nodes in the neck lymphoscintigraphy (LSG) of the neck was acquired. LSG was performed on the same day as surgery, after intradermal

injection of 37Mbcq Tc99m-Sn-colloid/ml at four peritumoral sites. In patients with positive Lymphoscintigraphy results, sentinel lymph nodes were extracted surgically. The extracted nodes were sent to the Institute for Pathology, University Clinical Center of Kosova, for histopathological analysis.

## Results

Of the 31 patients enrolled in the study, three (9.7%) were female and 28 (90.3%) male. Results are statistically significant by gender ( $\chi^2$ -test = 20.16; P<0.001). More than half of the patients (61.3%) were aged over 60 years. SCC of the lower lip most often occurred in the group of patients aged 60–69 years (Table 1).

**Table 1. Patient population by age group**

Age	No	Gender		%
		Fem	Male	
30–39	-	2	2	6.5
40–49	-	5	5	16.1
50–59	-	5	5	16.1
60–69	1	8	9	29.0
70–79	-	7	7	22.6
80–89	2	1	3	9.7

LSG was more often positive for detection of neck lymph nodes in patients with T2 carcinoma of the lower lip compared with T1 (88.9% vs. 59.1%), although this was not statistically significant ( $P = 0.205$ ; Table 2).

**Table 2. Results of LSG**

LSG	T1		T2		Total	
	Number	%	Number	%	Number	%
Positive	13	59.1	8	88.9	21	67.7
Negative	9	40.9	1	11.1	10	32.3

Sentinel Node Biopsy (SNB) was performed in all 21 patients with a positive LSG finding. Metastases were confirmed in 10 patients (47.6%).

Among these 21 patients, 14 (66.7%) had had the disease for more than 1 year, while in seven (33.3%), the disease was present for less than 1 year ( $P < 0.05$ ; Table 3)

**Table 3. Results of LSG by duration of pathology**

Duration of pathology	%	LSG			
		Negative		Positive	
		N	%	N	%
>1 year	20.0	14	66.7	16	51.6
<1 year	80.0	7	33.3	15	48.4

**P=0.023**

SNB in patients with positive LSG was positive in 10 of the 21 patients (47.6%). Of 14 patients who had the disease for more than 1 year, SNB was positive in nine (64.3%). SNB was more often

positive in cases with pathology present for more than 1 year ( $P < 0.05$ ; Table 4).

**Table 4. Results of SNB by duration of pathology**

Sentinel node		Duration of pathology				
		>1 year		< 1 year		
biopsy	%	N	%	N	%	
Negative	5	35.7	6	85.7	11	52.4
Positive	9	64.3	1	14.3	10	47.6

**P<0.05**

Among all 31 patients enrolled in this study, SNB was positive in 10 patients (32.3%). Occult metastases in this study were present in 32.3% of cases (Table 5).

**Table 5. Positive lymph nodes by SNB in all patients**

SNB	%	Right site		Left site		Medial part		
		N	%	N	%	N	%	
Negative	8	72.7	10	71.4	3	50.0	<b>21</b>	<b>67.7</b>
Positive	3	27.3	4	28.6	3	50.0	<b>10</b>	<b>32.3</b>

## Discussion

In clinical practice, CT and MRI are commonly used to detect neck metastases. It is well known that enlarged lymph nodes do not indicate metastasis, while non-enlarged lymph nodes do not indicate that metastases are present. Therefore, the accuracy of CT, MRI or ultrasound is not sufficiently high for detection of metastatic lymph nodes in the neck[8]. In the literature, FDG-PET

shows a similar frequency of detection of primary tumors as CT and MRI, but is better for the detection of lymph node metastases[11]. Intraoperative lymphatic mapping with different methods such as LSG combined with SNB, however, is the most accurate method in patients with T1, T2 and N0 SCC of the lower lip. LSG in patients with positive SNB can help to determine treatment in patients with radical neck dissection, while those with negative SNB can avoid neck dissection and opt to “wait and see”[12,13].

In patients with SCC in the oral cavity, LSG followed by radio-guided SNB is the best method to confirm the accuracy of SNB in predicting the presence of occult metastases. This method is designed to detect sentinel nodes that are almost always on the neck (levels I and II), thereby limiting the number of nodes examined and the extension of a surgical approach [14]. Dynamic or static LSG is especially beneficial in patients with T2, N0 disease, saving time and costs [15]. The recommended treatment protocol for T3 and T4 carcinoma of the lower lip is tumor excision with neck dissection.

A major problem in T1, T2 and N0 cases lies in the fact that the recommended protocol is to "wait and see", despite the fact that occult metastasis in those cases occurs in 15–35% of patients [16]. Lower-lip SCC is not an aggressive tumor, which is why neck dissection in the early stages generally underestimates the disease; however, the mortality of this pathology remains at 10–30%. Recent studies appear to show that higher rates of clinically positive neck were initially negative[1,17,18]. It should be noted that during this study we admitted five patients (which were not included in study) in our department who were operated before one or half year before our study and in that time they were T1-2,N0. Now, they came with palpable lymph nodes in submental or submandibular region, with positive HP results for metastases.

### **Conclusion:**

These results show that LSG combined with immediate SNB offers very good results for the treatment of T1, T2 and N0 lower-lip carcinoma. Since occult metastasis occurred in 32,3 % of T1

and T2 patients in this study, it would appear to be best to perform selective neck dissection in all patients with lower-lip carcinoma.

## References

1. Baker SR, Krause CJ: Carcinoma of the lip. *Laryngoscope*. 90:19-27, 1980.
2. Medina dos Santos LR, Cernea CR, Kowalski LP, Carneiro PC, Soto MN, Nishio S, Hojaij FC, Dutra A Jr., Silva-Filho GB, Ferraz AR, Medina LR: Squamous cell carcinoma of lower lip: retrospective study of 58 patients. *Sao Paulo Med J*, 114, 1996.
3. S. Salihu ,O.Sejfija, F.Gjinolli,M.Prekazi,N.Heta,S.Berisha,H.Arifi,SH.Uka,N.Baftiul. Ten years survival with squamous cell carcinoma of lower lip. *Proceedings of the XIX Congress of EACMFS, J Craniomaxillofac Surg*, 36:S 130, 2008
4. National Comprehensive Cancer Network, NCCN guidelines, Version 2.2011. [nccn.org](http://nccn.org)
5. Snow GB, Patel P, Leemans CR, Tiwari R. Management of cervical lymph nodes in patients with head and neck cancer. *Eur Arch Otorhinolaryngol*, 249:187-94, 1992.
6. Brown AE, Langdon JD. Management of oral cancer. *Ann R Coll Surg Eng*, 77:404-8, 1995
7. Giovani M, Tartaglione G, Rahimi S, Mafera B, Pagan M. Lymphoscintigraphy and radio guided sentinel node biopsy in oral cavity squamous cell carcinoma: same day protocol. *Eur Arch Otorhinolaryngol Suppl*. 264:163-167, 2007.
8. Ng SH, Ko SF, Toh CH, Chen UL. Imaging of Neck Metastases. *Med J*, 29:119-128, 2006
9. Rapoport A, Ortellado DK, Amar A, Lehn CN, Dedivitis RA, Perez RS, Rodrigues HM. Radical versus supraomohyoid neck dissection in the treatment of squamous cell carcinoma of the inferior level of the mouth, *Rev. Bras. Otorrinolaringol*. 73, 2007.
10. Altinyollar H, Berberoglu U, Celen O. Lymphatic mapping and sentinel lymph node biopsy in squamous cell carcinoma of the lower lip. *Eur J Surg Oncol*, 28:72-4, 2002.
11. Zytoon AA, Murakam K, Hagiwara S. Head and Neck Cancer with Lymph Node metastases: Comparison at CT, MRI, FDG-PET and Validation with Histopathology. *Midd Eastern Journal Age*

and Ageing, 4:7-15, 2007.

12. Altinyollar H, Berberoglu U, Celen O. Lymphatic mapping and sentinel lymph node biopsy in squamous cell carcinoma of lower lip. *Eur J Surg Oncol*, 28:72-4, 2002.

13. Frerich B, Forster M, Schiefke F, Wittekind C, Hemprich A, Sabri O. Sentinel lymph node biopsy in squamous cell carcinomas of the lips and oral cavity-a single center experience. *J Surg Oncol*. 95:97-105, 2007.

14. Vigili MG, Tartaglione G, Rahimi B, Mafera B, Pagan M. Lymphoscintigraphy and radioguided sentinel node biopsy in oral cavity squamous cell carcinoma: Same day protocol. *Eur Arch Otorhinolaryngol*, 264:163-167, 2007.

15. Tartaglione G, Potenza C, Caggiati A, Gabrielli F, Russo A, Pagan M. Sentinel node radiolocalisation and predictive value in lip squamous cell carcinoma. *Radiol Med*. 106:256-61, 2003

16. Yilmaz S, Ercocen AR. Is elective Neck Dissection in T1-2, N0 Patients with lower lip cancer necessary. *Ann Plast Surg* 62:381-383, 2009

17. Bucur A, Stefanescu L. Management of patients with squamous cell carcinoma of the lower lip and N0-neck. *J Craniomaxillofac Surg*. 32:16-18, 2004

18. Kutluhan A, Kiris M, Kaya Z, Kisli E, Yurttas V, Icli M, Kosem M. Squamous cell carcinoma of the Lower Lip and Supra-Omohyoid Neck Dissection. *Acta Chir Belg*. 103:304-308, 2003

