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Long term results of sentinel lymph node biopsy in early oral squamous cell carcinoma

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Abstract: The objective of the study was to evaluate the long term results of the sentinel node (SN) biopsy technique in the management of the clinically negative (N0) neck in patients with early oral squamous cell carcinoma (T1–T2). Patients with positive SN underwent neck dissection. A sentinel lymph node (SLN) biopsy was performed on 31 consecutive patients. Six of the 31 patients were upstaged by the results of the SLN biopsy. The SLN biopsy allowed the identification of node metastasis in 100% of the cases with a sensitivity of 100%, specificity of 100%, and negative predictive value of 100%. There was a mean follow-up of 59 months. The neck control rate was 100% in the SLN negative group and two SLN positive patients developed subsequent neck disease (neck control rate of 88%). One SLN patient presented at the follow-up with a second primary tumor, 18 months later treated successfully by chemoradiotherapy. The overall survival rate was 100% in both groups. The promising reported short-term results have been sustained by long term follow-up. Patients with negative SLN achieved an excellent neck control rate. The neck control rate in SN negative patients was superior to that in SLN positive patients, but not statistically different.
Keywords: sentinel lymph node, characteristics of patients, head and neck cancer

Introduction

Management of the clinically negative (N0) neck in head and neck squamous cell carcinoma is an important issue for the head and neck surgeon. Furthermore, in patients with head and neck squamous cell carcinoma, the presence of lymph node metastases is the most prognostic factor. A number of colleagues worldwide have tried to clarify the sentinel node (SN) concept, subsequently applying it in clinical practice. Articles about SN biopsy in head and neck cancer have been published in relevant journals since the late 1990s.[1–10]

Sentinel lymph node (SLN) biopsy originally was described as a means of identifying lymph node metastases in malignant melanoma and breast carcinoma. The use of SLN biopsy in patients with oral and oropharyngeal squamous cell carcinoma N0 necks was investigated to determine whether the pathology of the SLN reflected that of the neck. Most studies showed that SLN localization is technically feasible in head and neck surgery and is predictive of cervical metastasis with a sensitivity, specificity, and negative predictive value.[1–3] This retrospective report describes the long-term follow-up of T1–T2 oral squamous cell carcinomas patients and clinically negative necks that were candidates for SLN mapping.

Methods

Previously untreated clinically negative neck oral cancer patients were candidates for our study. All the patients enrolled in the study had exclusively T1–T2 head

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and neck squamous cell carcinomas accessible to injection. Focusing on a relation between SN status and long-term results, we excluded eleven patients who were not followed for 24 months or more. The technique of SN biopsy involves the combination of mapping the main lymph node fields of the neck by a radioactive tracer. The tracer passes along the lymphatic channels to accumulate in the SNs, making them radioactive. Prior to surgery (12–24 hours) the patients were injected around the tumor with 10–40 MBq of 99 mTc labeled nanocolloid (Nanocoll; Amersham Health, Little Chalfont, UK) which drained to local nodes. These nodes were usually identified between 15 minutes and 1 hour after injection and marked on the skin to help node localization at surgery. At surgery, the nodes were identified by gamma probe and harvested for histological examination. The nodes were fixed in 10% neutral buffered formalin and after fixation bisected through the hilum, if this was identifiable, or through the long axis of the node. If the thickness of the halves was more than 2.5 mm, the slices were further sectioned to provide additional 2.5 mm thick blocks. Two histological sections were taken from each 2.5 mm slice; one to prepare for hematoxylin and eosin (H&E) staining, the other for cytokeratin antibody, and the remaining four for further evaluation if needed.

Patients revealing multiple lymph node metastases and/or extracapsular spreads proceeded to postoperative radiotherapy with or without chemotherapy to their necks. Patients whose surgical margin was close or positive received postoperative radiotherapy on the tumor bed. After a series of treatments, they were followed-up in our outpatient clinic.

Results

We analyzed 31 patients according to the above-mentioned criteria. Their characteristics are described in Table 1. The patients were predominantly male with a median age

Table 1 Characteristics of patients treated by SLN biopsy

Patients	Age	Tumor site	cT	cN	Stage	SLN (n)	Pos nodes ND	Localization	Type ND
1	56	Tongue	cT1	cN0	I	1	0	II	
2	65	Floor of the mouth	cT2	cN0	II	2	0	II	
3	67	Tongue	cT2	cN0	II	1	1	II	I + II + III + V
4	71	Tongue	cT2	cN0	II	3	3	I + II	I + II + II + V
5	67	Tongue	cT2	cN0	II	3	3	II + III + V	II + III + V
6	51	Tongue	cT2	cN0	II	2	1	II + IV	II + III + IV + V
7	70	Floor of the mouth	cT2	cN0	II	2	0	III	
8	62	Floor of the mouth	cT2	cN0	II	1	0	I	
9	62	Floor of the mouth	cT2	cN0	II	1	0	I	
10	64	Oropharynx	cT1	cN0	I	3	3	II	I + II + III + IV
11	64	Oropharynx	cT2	cN0	II	1	0	V	
12	51	Floor of the mouth	cT2	cN0	II	1	0	II	
13	51	Floor of the mouth	cT1	cN0	II	3	0	II	
14	52	Oropharynx	cT1	cN0	I	1	0	II	
15	73	Oropharynx	cT2	cN0	II	1	0	II	
16	79	Oropharynx	cT1	cN0	I	1	0		
17	66	Tongue	cT2	cN0	II	2	0	II + V	
18	46	Floor of the mouth	cT1	cN0	I	1	0	III	
19	54	Floor of the mouth	cT1	cN0	I	2	0	II	
20	63	Floor of the mouth	cT1	cN0	I	1	0	II	
21	58	Floor of the mouth	cT2	cN0	II	2	0	II	
22	57	Oropharynx	cT1	cN0	I	1	0	III	
23	62	Floor of the mouth	cT2	cN0	II	1	0	II	
24	79	Floor of the mouth	cT2	cN0	II	3	0	II	
25	72	Oropharynx	cT1	cN0	I	1	0	III	
26	73	Oropharynx	cT1	cN0	I	1	1	III	II + III + IV + V
27	68	Oropharynx	cT1	cN0	I	1	0	III	
28	66	Oropharynx	cT2	cN0	II	1	0	III	
29	58	Oropharynx	cT2	cN0	II	1	0	III	
30	62	Tongue	cT2	cN0	II	1	0	II	
31	52	Tongue	cT2	cN0	II	1	0	III	

Abbreviations: cT, clinical T stage; cN, clinical N stage; SLN (n), number of sentinel lymph nodes (SLN) detected; Pos nodes, number of positive nodes detected; Localization, neck level where sentinel positive sentinel lymph node was detected; Type ND, neck levels included in neck dissection.

of 64 years. The median observation period was 59 months and ranged between 28 and 72 months.

An SLN biopsy was performed on 31 patients. Of the 31 patients, five were women and 26 were men. The primary tumor was located on the oral tongue in eight cases, at the floor of the mouth in 12 cases, and at the oropharynx in eleven cases. Twelve primary tumors were stage T1. All other tumors were stage T2. All of the tumors were clinically staged cN0 by palpation and computed tomography (CT) scan or magnetic resonance imaging (MRI). One patient with a midline tumor underwent SLN biopsy on the contralateral side. There was a mean follow-up of 59 months. There were six patients with positive SLN. Neck dissection was done. Two patients showed isolated tumor cells, three patients had micrometastases, and one patient had macrometastases. There were four patients with micrometastases. Three patients had three positive SLNs. There were two neck recurrences in the course of all patients treated. The neck control rate for SLN negative patients was 100%. There were two neck recurrences in SLN positive patients (neck control rate 88%). The difference between the recurrent rate was not statistically significant. One patient with positive SLN presented at the follow-up with a second pulmonary primary 18 months later treated successfully by chemoradiotherapy. The overall survival rate for both groups was 100%.

Discussion

Management of the N0 neck in head and neck squamous cell carcinoma is an important issue for the head and neck surgeon. In patients with head and neck cancer, the presence of lymph nodes metastases is the most important factor. Our study confirmed as most studies that SLN biopsy is an accurate reflector of the status of the regional lymph nodes.[1–9] Furthermore, SLN biopsy is technically feasible and the technique is safe. The SLN biopsy technique offered more accurate staging and mapping for the lymphatic drainage than radiological evaluation. Indeed, early metastases in SNs are very small and occasionally fall beneath the threshold of imaging techniques such as CT, MRI, positron emission tomography (PET), and ultrasound. Consequently, a pathologic analysis of the SN is superior to such indirect diagnostic modalities. SN biopsy is somewhat invasive in terms of its use of radioactive tracers. However, the dose of radioactivity is relatively low in comparison with a PET scan, while the benefit of a direct pathologic evaluation of the SN makes up for its invasiveness. Needless to say, SN biopsy has less impact on patients than routine elective neck dissection.

In our study, six of the 31 patients had positive SNs. Two patients showed isolated tumor cells, three patients had micrometastases, and one patient had macrometastases.

The neck control rate for SLN negative patients was 100%. For SLN positive patients, the neck control rate was 88%. The difference was not statistically significant. The overall survival in both groups was 100%. SLN was not a negative prognostic factor for survival in T1–T2 oral cancer.

In their study, Broglie et all reported their long-term experience in SLN biopsy for oral squamous cell carcinoma.[11] Twenty-nine of 79 patients (37%) had positive SLNs. Six of 29 (21%) showed isolated tumor cells, 14/29 (48%) had micrometastases, and 9/29 (31%) had macrometastases. The neck control rate after 5 years was 96% in SLN negative patients and 74% in SLN positive patients. This difference was statistically significant. Overall survival at 5 years for the entire cohort was 89%.

However, Kovacs et al evaluated the role of SLNs as prognostic factors in T1–T2 oral squamous cell carcinomas.[12] Mean observation time of all patients was 6.7 years. Five-year overall survival of all patients was 92%. The overall survival rate for patients with negative SLN was 85%, for those with positive SLN 38%, respectively. There has been a higher statistical risk for locoregional recurrence for patients with positive SLN. Rates of metachronous second primary tumors developed during follow-up were 10.6% (negative SLN) and 44.4% (positive SLN). In our study, one SLN positive patient developed a second primary.

In their study, Alex and Krag evaluated the application of SLN to solid tumors of the head and neck.[13] His 10-year experience showed no difference in terms of prognostic factors between patients with negative SLN and patients with positive SLN.

Alkureishi et al described the long-term follow-up of a large European multicenter trial.[14] A total of 227 SN biopsy procedures were carried out, of which 134 were performed in clinically T1–T2 N0 patients. There were 79 patients who underwent SLN biopsy. Forty-two patients were upstaged (34%); of these, ten patients harbored only micrometastatic disease. In our study, also, the majority of patients with positive SLN had only micrometastatic disease. No difference in terms of prognosis was mentioned between the patients with negative SLN and patients with positive SLN.

Conclusion

The promising reported short-term results have been sustained by long-term follow-up. Patients with negative SLN achieved an excellent neck control rate. The neck control rate

in SN negative patients was superior to that in SLN positive patients, but not statistically significant.

Disclosure

The authors report no conflicts of interest in this work.

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