

Squamous Cell Carcinoma of the Lower Lip; Is Prophylactic Neck Dissection Required and Evaluating Predictive Factors

Secaattin Gülşen¹ , Saffet Ulutaş² 

¹Clinic of Ear Nose Throat, Private Hatem Hospital, Gaziantep, Turkey

²Clinic of Plastic Reconstructive and Aesthetic Surgery, Deva Hospital, Gaziantep, Turkey

ABSTRACT

Objective: This research introduces a series of 87 cases of squamous cell carcinoma of the lower lip. We aim to evaluate the efficacy of prophylactic neck dissection and assess determinative factors for local recurrence and regional metastasis in lower lip carcinomas. **Methods:** Medical records of 87 consecutive patients who were diagnosed with squamous cell carcinoma (SCC) of the lower lip were retrospectively analyzed for specific parameters at the Ear Nose Throat (ENT) and Plastic & Reconstructive Surgery clinic at the Dr. Ersin Arslan Training and Research Hospital and the ENT clinic at the Gaziantep University School of Medicine between 2011 and 2017. Patients who had been previously operated upon in other centers were excluded from the study. Tumor excision with safe margins confirmed by frozen sections and supraomohyoid neck dissection was performed on all the patients involved in this study. The minimum follow-up was 12 months for all patients. The median follow-up was 23 months (ranging from 12 to 72 months).

Results: The data analysis indicated that local recurrence was significantly related to the tumor size, depth, and proximity of the tumor to surgical margins. Local recurrence was detected in 8 (9.1%) of 87 patients. Time from onset of disease to the diagnosis, size of the tumor, and proximity of the tumor to the lip commissure play an important role in the spread regional metastasis. Overall the regional metastasis rate was found to be 22.9% (20 of the 87 patients). The occult metastasis rate was found to be 9.1% (8 of the 87 patients). The overall survival rate of patients with lower lip carcinoma, who underwent a supraomohyoid neck dissection and excision of the tumor was 96.5% (84 of the 87 patients).

Conclusion: Although lower lip cancers generally have a good prognosis after a proper surgical intervention, it can be life-threatening in case of neck metastasis or local recurrence. Certain factors, such as tumor size, location, and time interval between onset of disease and diagnosis are influencing the prognosis. Prophylactic neck dissection should be performed when the risk of cervical lymph node metastases is high in patients, especially to cases in which the tumor is close to the commissure. Early detection, prophylactic neck dissection, and follow-up with frequent intervals are essential for a good prognosis.

Keywords: Carcinoma, lip reconstruction, lower lip scc, prophylactic neck dissection

INTRODUCTION

Lip cancer is a frequent malignant disease of the oral cavity and is responsible for approximately 30% of malignant tumors of the oral cavity (1, 2). SCC is the most common type of cancer of the lip and rare tumors include adenocarcinomas and melanomas (3, 4). The lower lip is the most frequently involved part and accounts for more than 90% of lip cancer cases. SCC of the lower lip has a favorable prognosis because a lesion of the lower lip can be seen easily and diagnosed early. Nevertheless, mortality due to lower lip SCC may still occur (5). Frequently, lower lip involvement is thought to be more closely related to increased exposure to solar radiation as compared to the upper lip. However, the predisposing factors of lip cancer are not only limited by solar

radiation, but also include tobacco, immunodeficiency, chronic ulcerations, and genetic predisposition (5, 6). Surgery consisting of full-thickness resection of the skin, mucosa, and underlying muscle tissues to ensure a safe surgical margin is the only option for the definitive treatment of lower lip SCC. Although various reconstruction techniques to be performed after safe excision of the tumor have been defined, the reconstruction of the defect is still a challenging issue, especially in large tumors (7). In addition to surgical intervention of the primary lesion site, prophylactic neck dissection should be performed even on clinically N0 neck tumors, to completely cure the occult metastasis to regional lymph nodes, if it is present. Although there is a consensus that therapeutic neck dissection should be performed in patients

How to cite: Gülşen S, Ulutaş S. Squamous Cell Carcinoma of the Lower Lip; Is Prophylactic Neck Dissection Required and Evaluating Predictive Factors Influencing Prognosis. Eur J Ther 2019; 25(4): 259–64.

ORCID IDs of the authors: S.G. 0000-0003-0687-6057; S.U. 0000-0002-8214-4002

Corresponding Author: Secaattin Gülşen E-mail: drsecaattingulsen@gmail.com

Received: 15.09.2018 • **Accepted:** 14.05.2019



with cervical nodal involvement, the indications of prophylactic neck dissection still remain unclear and controversial. The most significant factor that directly affects the survival of a patient with lower lip SCC is the nodal involvement. Even if the tumor is in the T1 stage, if it is located at the lip commissure, the possibility of cervical metastasis should be taken into consideration due to the rich lymphatic network of the lip commissure.

METHODS

Eighty-seven consecutive patients who were diagnosed with lower lip SCC, underwent surgical excision of the tumor, and either had therapeutic or prophylactic neck dissection done as a primary treatment, were retrospectively analyzed. Verbal informed consent was obtained from all the patients prior to the start of the study. Patients who were previously treated at other medical centers and were subsequently referred to our clinic were not included in the study. Medical records were scanned for particular parameters including age, gender, solar radiation exposure, tobacco usage, tumor size, location of tumor, time from onset of disease to diagnosis, clinical and radiological lymph node involvement, and control examination reports. Local ethical committee approval was taken from Gaziantep University (263/2018).

Statistical Analysis

Analysis of the data was performed using the Statistical Package for Social Sciences software version 20.0 (SPSS IBM Corp.; Armonk, NY, USA) and a p-value of <0.05 was considered statistically significant. Descriptive statistics were used to analyze the data (minimum, maximum, mean, and standard deviation). To test the relationship between categorical variables, we used the x² test.

RESULTS

The study consists of a total of 87 patients, 70 (80.4%) males and 17 (19.6%) females, ranging from 34-87 years of age with the av-

erage age being 64 years. The overall male-to-female ratio was 4 to 1. Males were found to have a higher risk for lower lip cancer as compared to females. The distribution of patients according to age is displayed in Table 1. Lower lip cancer was more frequently detected between the ages of 61-70 years (27 of 87, i.e., 31%). Analysis of the medical records revealed that 62 patients (71.2%) were affected by solar radiation exposure as the predisposing factor (farmers, open area workers, rural citizens) and 72 patients (82.7%) smoked more than 20 cigarettes per day. In this study,

Table 1. Patients characteristics and tumor stage

| | Characteristics | (n) | % |
|---------|-----------------|-----|-------|
| Age | <40 | 3 | 3.46 |
| | 41-50 | 14 | 16.09 |
| | 51-60 | 13 | 14.94 |
| | 61-70 | 27 | 31.03 |
| | 71-80 | 13 | 14.94 |
| | >80 | 17 | 19.54 |
| Gender | Male | 70 | 80.4 |
| | Female | 17 | 19.6 |
| Tobacco | Smokers | 72 | 82.75 |
| | Non-smokers | 15 | 17.25 |
| T stage | T1 | 29 | 33.33 |
| | T2 | 38 | 43.67 |
| | T3 | 17 | 19.54 |
| | T4 | 3 | 3.46 |

Figure 1. Distribution of tumors location and lymph node involvement ratio

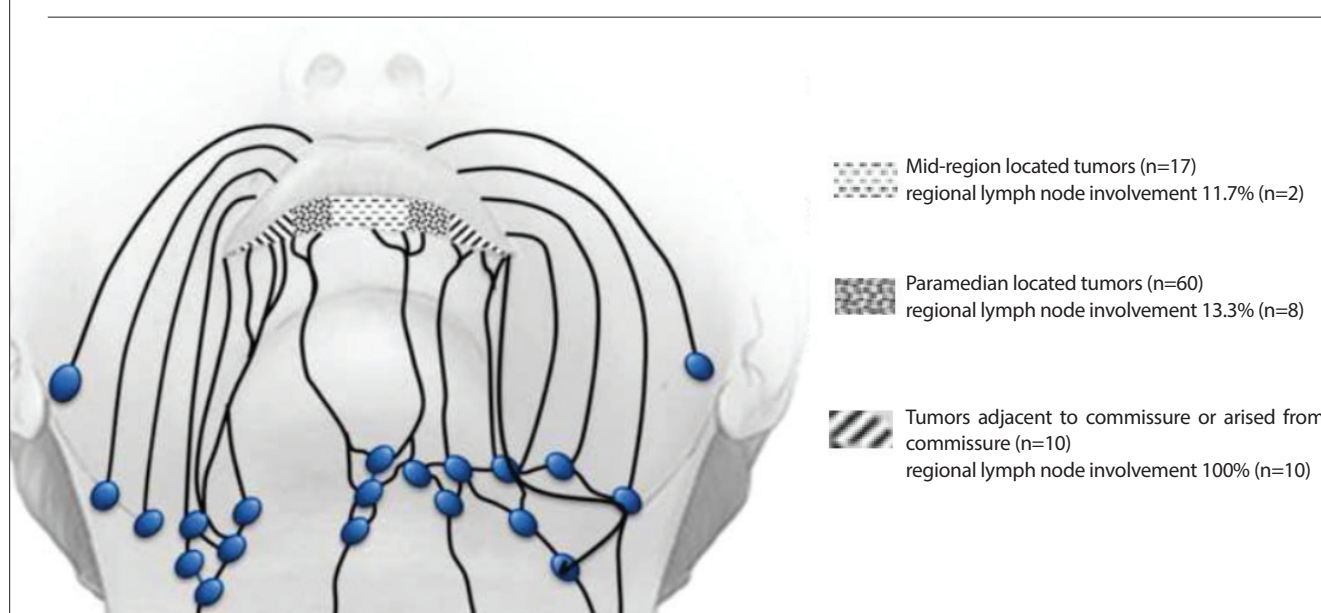


Table 2. Correlation between parameters and recurrence and metastasis

| Parameters | Recurrence | Metastasis |
|--------------------------------------|------------|------------|
| Age | NS | NS |
| Gender | NS | NS |
| Size | p<0.001 | p=0.021 |
| Onset time of disease | NS | p<0.001 |
| The proximity of tumor to commissure | NS | p<0.001 |
| Surgical margin positivity | p=0.017 | p<0.001 |
| Thickness (depth) | p=0.02 | p<0.001 |
| Tobacco | p<0.001 | NS |

NS: stands for not significant

the locations of the tumors were classified in 3 groups: median, paramedian, and adjacent to the commissure. The distributions of the localization of tumor were n=17 (19.6%), n=60 (68.9%) and n=10 (11.5%) respectively (Figure 1). The analysis of cases with neck metastasis showed that there is a significant relationship between lymph node involvement and tumor location (Figure 1). After surgical intervention, metastases to the regional cervical lymph nodes were detected in all of the 10 patients whose tumor had originated from the commissure or close to the commissure. The distribution of the TNM stage is presented in Table 1. There were 29 patients (33.3%) in stage T1, 38 patients (43.7%) in T2, and 17 patients (19.5%) in stage T3. In 3 patients (3.5%), the tumor was in stage T4. Lymph node involvement, as confirmed by fine needle aspiration biopsy, was detected in 12 (13.8%) patients by ultrasonography and physical examination pre-operatively. Histologic evidence revealed that the depth of tumor ranged from 2-10 mm, with the average depth in patients with regional lymph node metastasis being 6 mm (minimum=3 mm, maximum=10 mm). Pathological examination of neck dissection specimen revealed the fact that regional lymph node metastasis was present in 20 (22.9%) patients actually. In 8 patients, there was no detectable clinical lymph node involvement pre-operatively, but after pathological examination, regional lymph node metastasis was found, therefore, the occult metastasis rate was 9.1%. No distant metastasis was identified and all patients were classified as stage M0. We identified a significant relationship between the tumor size at diagnosis and the regional lymph node involvement. Neck dissection, therapeutic in 12 patients and prophylactic in 75 patients, was performed on all patients. Considering the location of the tumor, either unilateral or bilateral neck dissection were performed. We performed unilateral neck dissection in 81 patients with tumors located at the commissure or close to the commissure. In cases where the tumor was located at the midline of the lip and had spread to the contralateral side or had invaded both sides, we performed bilateral neck dissection. Patients having cervical metastases with extracapsular extension and soft tissue invasion were referred to post-opera-

tive radiotherapy. Our follow-up policy stated that patients were to report for examination each month for the first 3 months, then every 3 months for the 1st year, and finally, 2 times per year following the 1st year.

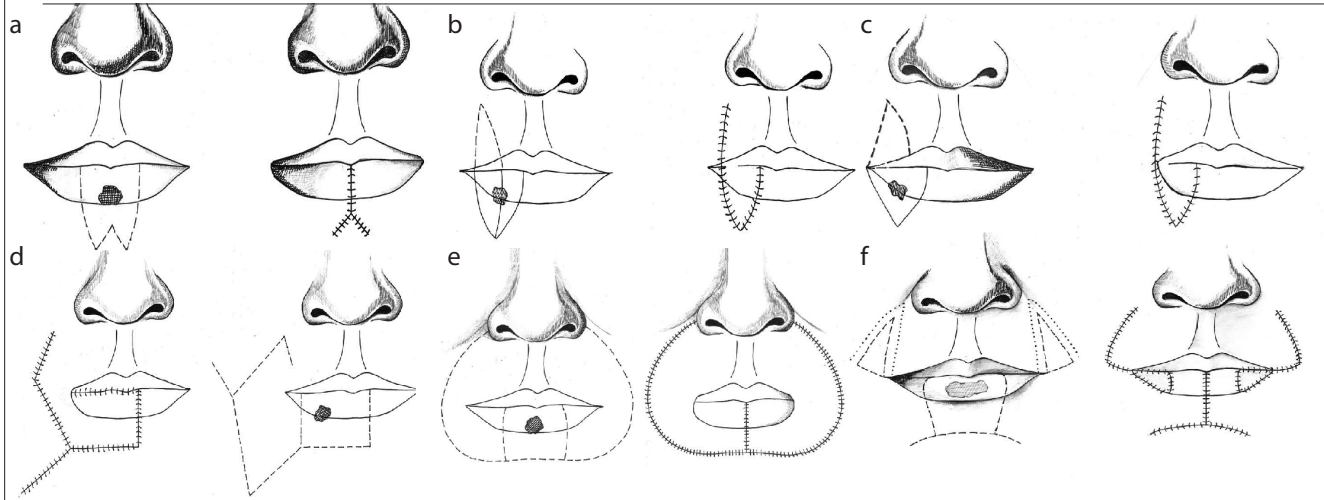
Statistical analyses revealed that parameters such as size and depth of the tumor, time from onset of disease to diagnosis, surgical margin status, and tumor location had a significant effect on the regional recurrence of the tumor and the cervical lymph node involvement (Table 2). Time from the onset of disease to the diagnosis is an another important predictive factor influencing the regional lymph node involvement, which we observed in 20 patients with lymph node metastasis, where the average time from the onset of the disease to the diagnosis was 32 months (ranging from 18-48 months). In 67 patients without lymph node metastases, the average time from the onset of disease to the diagnosis was 6 months (ranging from 3-18 months). For this reason, disregarding the chronic lesions at the lower lip may lead to neck metastasis if they are malignant in nature.

A recurrent case was defined as the growth of tumor at the same location after completion of primary treatment. Local recurrence occurred in 8 (9.1%) patients after a mean follow-up duration of 16 months (ranging from 8-24 months). All the recurrent cases were treated by surgical re-excision, after which surgical intervention adjuvant radiotherapy was advised and these patients were followed-up at more frequent intervals. Various surgical techniques were identified for the reconstruction of lip after tumor excision. For 36 patients (41.3%) with defects spanning less than one-third length of the lower lip, we preferred a U, V, or W- shaped excision and primary suturing for reconstruction. The remaining 51 (58.7%) patients' defects were reconstructed using the Gilles Fan flap, Estlander flap, Abbe flap, Bernard flap, and Karapandzic flap techniques according to the tumor location and defect size (Figure 2). The median follow-up time was 23 months (minimum 12 months, maximum 72 months). Unfortunately, during our follow-up period, 3 patients died, primarily due to lower lip cancer. All 3 patients were living in rural areas, therefore, they neglected to report regular check-ups and disregarded local recurrence of disease and regional lymph node involvement. The overall survival rate of patients with lower lip carcinoma who underwent neck dissection and excision of tumor was 96.5% (84 of the 87 patients).

DISCUSSION

Lip cancer is the common form of malignant oral cavity neoplasms and the frequently involved site in most cases was the lower lip. Moreover, in some studies, it has been advocated that lip cancer is the second most frequent skin cancer in the head and neck region (1, 2). Frequent involvement of the lower lip is attributed to excessive exposure to sunlight, since the lower lip receives considerably more direct sunlight than the upper lip. Solar radiation and smoking are well-known risk factors for the development of lip cancer (3). The gender distribution in our study revealed a considerable tendency toward men, which is consistent with the literature (4). Various treatment options have been defined for the treatment of SCC of the lower lip,

Figure 2. a-f. Lower lip reconstruction techniques. (a) Wedge resection and primary closure for small tumors of the lower lip. (b) Abbe flap for laterally located tumors of the lower lip. (c) Estlander flap for tumors involving oral commissure. (d) Gilles Fan flap for midline located tumors of the lower lip. (e) Karapandzic flap for midline located large tumors of the lower lip. (f) Bernard-Burrow flap for midline located large tumors of the lower lip



including surgery, radiotherapy, chemotherapy, and some combinations of these. Among these options, we preferred surgery that consisted of tumor excision, therapeutic or prophylactic neck dissection, and reconstruction of defects in all patients. We aimed for complete removal of the tumor with a safe surgical margin, and consequently, the surgical treatment involved excision of full-thickness skin, mucosa, and underlying muscle. Adequate resection of the tumor and maintaining a safe surgical margin are contentious issues, since there is no consensus on them. A study advocated that a 3 mm distance seems to be adequate for maintaining a safe surgical margin after excision of early SCC (T 1/T 2) of the lower lip, when a frozen section test was performed for the margins. If a frozen section is not available, at least a 6 mm distant excision to the tumor is recommended (5). Another study has suggested that excision of the tumor should be done at least 6 mm away from the healthy tissue to ensure the maintenance of a safe surgical margin in the surgical treatment of primary squamous cell carcinomas (6). In another study, it was emphasized that the excision should be performed at least 10 mm away from the tumor tissue in order to provide a safe surgical margin (7). In our study, we obtained frozen section for all the cases and resected normal tissue with the tumor to obtain safe surgical margins ranging from 6-10 mm according to the tumor size, depth, and location. We performed additional excisions as long as the frozen test was positive for disease. Nevertheless, even though additional excisions were performed according to frozen section reports, the histologic examination revealed the presence of tumors that were more than 2 mm closer to surgical margins in 9 patients. In various studies, the rate of regional lymph node metastases was reported between 3% to 29% (1, 4). In this study, the lymph node involvement was detected in 12 patients (13.8%) and the initial diagnosis that was made by ultrasonography and physical examination was also

confirmed by fine needle aspiration biopsy. After surgery, the pathological examination of the dissected neck specimen revealed that regional lymph node metastasis was present in 20 patients (22.9%). Therefore, in 8 (9.1%) patients with a clinically N0 neck, occult lymph node metastasis was present at diagnosis. Eight patients with N0 stage with occult metastasis were in T1 (n=1) and T2 (n=7) stages. Neck metastases were detected and treated at an early stage via prophylactic neck dissection in 8 of 87 patients (9.1%). A value of 9.1% is neither too high nor too low as an occult metastasis rate. Authors have reported a poor prognosis for cases that demonstrate nodal involvement during the follow-up period, and for this reason, the surgical approach in clinically N0 patients remains a controversial issue (8). Some other authors, who have adopted the "wait-and-see" policy for N0 necks, advocated that if nodal involvement occurs during the follow-up period, the therapeutic neck dissection combined with radiotherapy should be applied (1). Some studies have supported the use of aggressive surgery, who claimed that a prophylactic neck dissection should be performed in all clinical N0 cases (9-11). Recently, according to some authors, lymphatic mapping and sentinel lymph node biopsy were recommended for deciding whether neck dissection should be performed or not (12). Furthermore, considering that regional metastasis directly affected the patients' survival, it will be a reasonable approach to perform prophylactic neck dissection on patients with lower lip cancer. Based on our experience, the prognosis is poor despite salvage surgery and radiotherapy if there is cervical lymph node metastasis when no prophylactic neck dissection is performed.

Therefore, our surgical approach to lower lip SCC includes excision of the tumor with safe surgical margins confirmed by frozen sections and performing a prophylactic or therapeutic neck dissection regarding the N stage of the neck. The

size, stage, depth, and high histologic grade are found to be related with higher regional lymph node metastasis rates in certain studies (12, 13). On the contrary, some studies claim that the tumor size does not correlate closely with lymph node involvement (14, 15). In our study, we stated that particular factors such as size and depth of tumor, time from onset of disease to diagnosis, surgical margin status, and lesion location has a significant effect on recurrence and regional lymph node involvement (Table 2). We could not find any significant relationship between tobacco usage and regional lymph node metastasis, however, all the recurrent cases were found to be smoking more than one packet cigarette per day. As shown in Figure 1, we found an increase in the rate of regional lymph node metastasis in cases where the tumor was located close to the commissure.

We preferred reconstruction techniques for lip defects after surgery, depending on tumor size, location, and excision width. According to a recent study, combined surgical approaches including Karapandzic, Abbe, Estlander, and Stein flaps may offer excellent aesthetic and functional outcomes in subtotal and total lower lip defects and should be noted as a reliable reconstructive treatment of choice in patients having more than 70% of lower lip defects (16).

Aesthetic and functional expectations should be considered while removing the cancerous tissue, however, the risk of local recurrence and metastasis should not be ignored. Frequent and regular follow-up after surgical treatment is essential for decreasing mortality and morbidity.

Lastly, electrochemotherapy (ECT) is an innovative therapeutic modality based on the application of electrical pulses to the lesion site that increases the permeability of cell membranes to raise the uptake of chemotherapeutic agents, thus enhancing their cytotoxic effects. Additionally, ECT offers a therapeutic treatment option for aged and frail patients who, due to their delicate health condition, are either ill-suited for or refuse surgical interventions (17).

CONCLUSION

We have reported a retrospective study consisting of 87 patients who were treated by excision of tumor and neck dissection in all cases. The tumor size, depth, time from onset of disease to diagnosis, and the location are found to be associated with the recurrences and regional lymph node involvement. According to our experiences and the results of our study, we strongly recommend that prophylactic neck dissection should be performed, not only for accurate clinical staging, but also for treating occult metastases if present. Therefore, our clinical approach is to perform prophylactic neck dissection for lower lip cancer, even if the patient is clinically 0 nodal and involvement-free. Early diagnosis and immediate surgical intervention contribute to decreased morbidity and mortality. Therefore, dentists and general practitioners must remain vigilant about persistent lesions, and suspected patients should be referred to ENT specialists without losing time.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziantep University (263/2018).

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.G., S.U.; Design - S.G.; Supervision - S.G., S.U.; Data Collection and/or Processing - S.G., S.U.; Literature Search - S.G.; Writing Manuscript - S.G., S.U.; Critical Review - S.G.

Acknowledgements: We thank Ersoy Karabay for the statistical analysis of the data. We would like to acknowledge Assoc. Prof. Cengiz Durucu for invaluable contributions to editing the intellectual content of the manuscript.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Vukadinovic M, Jezdic Z, Petrovic M, Medenica LM, Lens M. Surgical management of squamous cell carcinoma of the lip: Analysis of a 10-year experience in 223 patients. *J Oral Maxillofac Surg* 2007; 65: 675-9. [\[CrossRef\]](#)
2. Casal D, Carmo L, Melancia T, Zagalo C, Cid O, Rosa-Santos J. Lip cancer: A 5-year review in a tertiary referral center. *JPRAS* 2010; 63: 2040-5. [\[CrossRef\]](#)
3. Moore SR, Johnson NW, Pierce AM, Wilson DF. The epidemiology of lip cancer: A review of global incidence and etiology. *Oral Dis* 1999; 5: 185-95. [\[CrossRef\]](#)
4. Salgarelli AC, Sartorelli F, Cangiano A, Pagani R, Collini M. Surgical treatment of lip cancer: Our experience with 106 cases. *J Oral Maxillofac Surg* 2009; 67: 840-5. [\[CrossRef\]](#)
5. de Visscher J, Gooris RJJ, Vermey A, Roodenburg JLN. Surgical margins for resection of squamous cell carcinoma of the lower lip. *J Oral Maxillofac Surg* 2002; 31: 154-7. [\[CrossRef\]](#)
6. Brodland DG, Zitelli JA. Surgical margins for excision of primary cutaneous squamous cell carcinoma. *J Am Acad Dermatol* 1992; 27: 241-8. [\[CrossRef\]](#)
7. Lydiatt W. Management of lower lip cancer: A retrospective analysis of 118 patients and review of the literature. *Arch Facial Plast Surg* 2003; 5: 533. [\[CrossRef\]](#)
8. Khalil HH, Elaffandi AH, Afifi A, Alsayed Y, Mahboub T, El Refaie KM. Sentinel lymph node biopsy (slnb) in management of n0 stage t1-t2 tip cancer as a "same day" procedure. *Oral Oncol* 2008; 44: 608-12. [\[CrossRef\]](#)
9. Yilmaz S, Ercocen AR. Is elective neck dissection in t1-2, n0 patients with lower lip cancer necessary? *Ann Plast Surg* 2009; 62: 381-3. [\[CrossRef\]](#)
10. Bucur A, Stefanescu L. Management of patients with squamous cell carcinoma of the lower lip and N0-neck. *J Craniomaxillofac Surg* 2004; 32: 16-8. [\[CrossRef\]](#)
11. Altinyollar H, Bulut H, Berberoglu U. Is suprahyoid dissection a diagnostic operation in lower lip carcinoma? *J Exp Clin Cancer Res* 2002; 21: 29-30.
12. Fukushima S, Masuguchi S, Igata T, Harada M, Aoi J, Miyashita A, et al. Evaluation of sentinel node biopsy for cutaneous squamous cell carcinoma. *J Dermatol* 2014; 41: 539-41. [\[CrossRef\]](#)

13. Luna-Ortiz K, Guemes-Meza A, Villavicencio-Valencia V, Mosqueda-Taylor A. Lip cancer experience in Mexico. An 11-year retrospective study. *Oral Oncol* 2004; 40: 992-9. [\[CrossRef\]](#)
14. Schüller M, Gosau M, Müller S, Gerken M, Rohrmeier C, Legal S, et al. Longterm outcome and subjective quality of life after surgical treatment of lower lip cancer. *Clin Oral Investig* 2015; 19: 1093-9. [\[CrossRef\]](#)
15. Zitsch RP, Lee BW, Smith RB. Cervical lymph node metastases and squamous cell carcinoma of the lip. *Head Neck* 1999; 21: 447-53. [\[CrossRef\]](#)
16. Uglesic V, Amin K, Dediol E, Kosutic D. Combined Karapandzic-Abbé/Estlander/Stein flap for subtotal and total lower lip reconstruction. *J Plast Reconstr Aesthet Surg* 2019; 72: 484-90. [\[CrossRef\]](#)
17. Gargiulo M, Serra Mestre JM, Cortese A, Murphy DC, Parascandolo S, Razzano S. Long term effectiveness of electrochemotherapy for the treatment of lower lip squamous cell carcinoma. *J Craniomaxillofac Surg* 2018; 46: 1968-74. [\[CrossRef\]](#)