Original Article

Role of the Neck Dissection in Early-Stage Lower Lip Cancers

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ABSTRACT

Background: In early-stage lip cancer, spread to cervical lymph nodes is extremely rare. Elective neck treatment options include suprahyoid or supraomohyoid neck dissection, sentinel lymph node biopsy, or close follow-up. **Aim:** In this study, our aim was to investigate the effect of elective surgery on survival in patients operated for early-stage lip cancer. **Methods:** Patients who underwent surgical treatment for lower lip squamous cell carcinoma between 2005 and 2020 were retrospectively analyzed. Age, gender, neck dissection status (yes/no), clinical and pathological T stage of the tumor, grade, and perineural invasion were recorded and 3-year and 5-year overall (OS) and disease-free survival (DFS) rates were estimated. **Results:** Thirty patients were included: 20 patients had pT1 and 10 patients had pT2 tumors. Neck dissection was performed in 13 patients. The 5-year OS rate was 90.9% and 87.8% with and without dissection, respectively. Neck dissection did not appear to affect OS ($P = 0.534$) in these patients. The 5-year DFS rate was 96.4% in the overall group, while it was 91.7% and 100% in patients who did or did not undergo neck dissection, respectively ($P = 0.756$). **Discussion:** Patients with or without neck dissection did not differ significantly in terms of OS and DFS. Watchful waiting with regular ultrasound imaging of the neck in patients with T1 and T2 lip tumors may be an appropriate therapeutic option.

KEYWORDS: *Cancer, lower lip, neck dissection, supraomohyoid, survival*

INTRODUCTION

Lip cancer is the most common tumor of the oral cavity (25%-30%) with an incidence ranging between 1 and 13.5 per 100,000 and occurring more commonly in males aged between 50 and 70 years.[1-3] While 90% of these lesions are located in the lower lip, 6% are seen in the upper lip, and 4% in the oral commissure. Identified risk factors include exposure to solar radiation (as opposed to other oral cavity tumors), smoking, and tobacco use. Among these, squamous cell carcinomas (SCCs) represent the most common histopathological tumor type.[4]

Surgery, the most effective therapeutic modality in this setting, involves the removal of the tumor with a minimum surgical safety margin of 1 cm for both oral cavity and lip cancers. The surgical borders should be checked for the presence of tumor cells with frozen sections after resection, as this approach has been shown to provide better disease control.[5] While 5-year survival rate in surgically treated patients is 75%-80% for stage 1-2 tumors, this figure is reduced to 40%-50% for stage 3-4 lesions.[6]

Despite having a common lymphatic network, spread to the neck lymph nodes in early-stage lip cancer is extremely unlikely. In patients with clinical N0 (cN0) disease, surgery involving the cervical approach is controversial, particularly in case of early-stage lip cancer.[7,8] Possible options include selective suprahyoid or supra-omohyoid neck dissection, sentinel lymph node biopsy, or close follow-up. However, currently there is no consensus regarding the most appropriate approach for specific lesions. Thus, this study aimed to investigate the effect of neck dissection on survival in patients undergoing surgery for early-stage lip cancer.

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MATERIALS AND METHODS

Medical records of patients who underwent surgical treatment for SCC of the lower lip at the Otorhinolaryngology Department of Uludag University Medical Faculty Hospital between 2005 and 2020 were examined. The study was approved by Uludag University Clinical Research Ethics Committee (Number: KAEK-26/442). Thirty patients were included. Exclusion criteria included advanced-stage (T3-T4) disease, tumors located on the upper lip, and tumors with only skin involvement without vermilion and a history of head and neck cancer, Radiotherapy (RT) in the head and neck region, or neck dissection. Age, gender, neck dissection status, clinical and pathological T stage, grade, and presence of perineural invasion were recorded and 3-year and 5-year overall (OS) and disease-free survival (DFS) rates were estimated. T staging was based on The American Joint Committee on Cancer (AJCC) (7th Ed.) definitions. Tumors <2 cm were classified as T1 and tumors with a diameter between 2 and 4 cm as T2. The effect of neck dissection on OS and DFS was investigated in patients with early-stage (T1-T2) lip cancer.

Selective neck dissection was performed when the depth of invasion was >4 mm on frozen sections. If the tumor was located at the midline or extends to the midline, bilateral selective neck dissection was performed. Watchful waiting with ultrasound (USG) was performed for tumors with a depth of invasion ≤4 mm.

Statistical analysis

Study data were analyzed using SPSS v. 22.0 software (IBM SPSS Statistics for Windows, 2013, Version 22.0. Armonk, NY, USA). Normality of the data was tested using Shapiro-Wilk test. Continuous variables were expressed as mean ± standard deviation, and categorical variables as number (n) and percentage (%). The independent samples *t*-test was used to compare the two groups since they showed normal distribution. Fisher's exact Chi-square test was used for the comparison of categorical variables. Differences between groups in OS and DFS rates were examined with Kaplan-Meier analysis and compared using the log-rank test. A value of $P < .05$ was considered statistically significant.

RESULTS

A total of 30 patients' clinical and histopathological characteristics were summarized in Table 1. The mean depth of invasion was 4.62 mm (3.29 mm and 6.35 mm, in groups with or without neck dissection, respectively).

Tumors were excised with V or W resection in all patients. Abbe flap was performed in five patients, Karapandzic flap in one patient, and Webster

Figure 1: (a-c) 'V' resection (a), defect (b) and primarily reconstruction of lower lip squamous cell carcinoma (c)

Table 1: Clinical and histopathological characteristics of the patients

	N: 30 patients	Percentage (%)
Age (years)	67 (min-max: 47-85)	
Gender		
Male	24	80
Female	6	20
T stage		
T1	20	66.6
T2	10	33.4
Neck dissection		
Performed	13	43.4
Not performed	17	56.6
Tumor size (cm)	Average 1,81	
Grade		
Well	16	53.3
Moderate	14	46.7
Perineural invasion		
Present	7	23.3
Absent	23	76.7
Mean follow-up period (months)	74	

modification in one patient. Other lesions were closed primarily in 23 patients [Figures 1 and 2]. Unilateral or bilateral supraomohyoid neck dissection (ND+) with primary tumor resection was carried out in 13 patients, and close follow-up without neck dissection (ND-) was done in 17 patients. Unilateral neck dissection was

performed in six patients and bilateral neck dissection in seven patients. In the ND+ group, the mean age was 69 years and in the ND- group, 65.7 years. No significant differences were found between ND+ and ND- groups with respect to age and gender ($P = 0.428$ and $P = 0.196$, respectively) [Table 2]. The mean tumor size was 1.49 cm (0.3-3.5 cm) in ND- patients and 2.23 cm (0.8-35 cm) in ND+ patients. The average follow-up was 74 months (range, 9-78 months). During the follow-up, a second primary tumor developed in one patient and local lip recurrence was observed in another. No patients had neck metastasis during the watchful waiting period.

Figure 2: (a-d) 'W' resection (a), defect (b), reconstruction with Abbe flap of lower lip (c) and postoperative 3-month view (d)

In the overall group of patients, the 3-year and 5-year OS rate were 89.2% and 89.2%, respectively. The 5-year OS was 90.9% in ND+ group and 87.8% in ND- group. No significant differences were found between the ND+ and ND- patients in terms of OS ($P = 0.534$) [Figure 3a, b and Table 2].

The 5-year DFS rate was 96.4% in the overall study group. Only one patient had local recurrence. The 5-year DFS rate was 91.7% in ND+ group and 100% in ND- group, with no significant differences in terms of DFS ($P = 0.756$) [Figure 4a, b and Table 2].

DISCUSSION

Regional lymph node involvement is the single most important prognostic factor in lip cancers because lymph node involvement is a major determinant of mortality and DFS. Neck lymph node metastasis is rare in early-stage tumors (T1-T2). Vukadinovic *et al.*[9] reported neck involvement in only 12.3% of patients with tumors <2 cm. Metastases in lower lip cancers occur primarily in lymph nodes at level 1 (submental and submandibular). Levels 2 and 3 may also be affected, while Level 4 lymph node involvement is very rare. As per the generally established rule in the treatment of head and neck cancers, an elective lymph node dissection should be performed when the risk of occult metastasis exceeds 20%.[10] As long as early-stage lip cancers are concerned, benefit of elective neck dissection in clinical

Table 2: Survival rates of the neck dissection (+) and (-) groups

	Neck dissection(-)	Neck dissection (+)	*P*
Age (years)	65	69	0.428
Tumor size (cm)	1,49	2,23	0.027
5-year overall survival %	87.8	90.9	0.534
5-year disease-free survival %	100	91.7	0.756
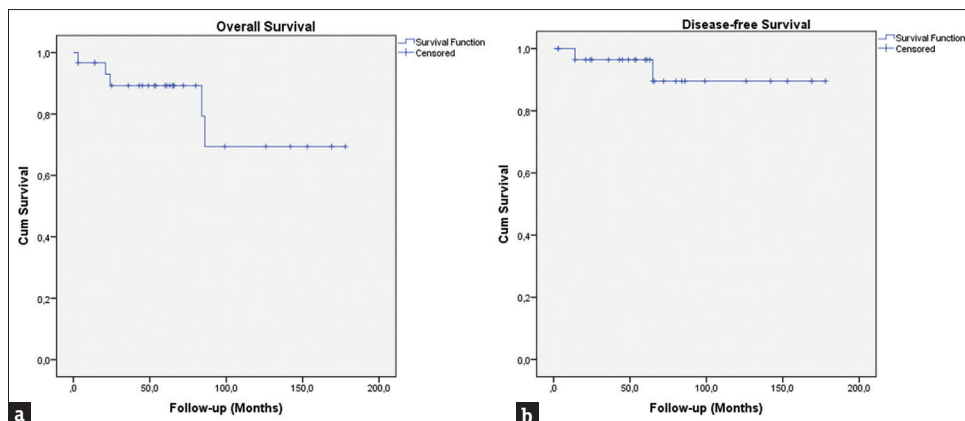
Figure 3: (a and b) Kaplan-Meier curves of overall survival and disease-free survival for the whole study group
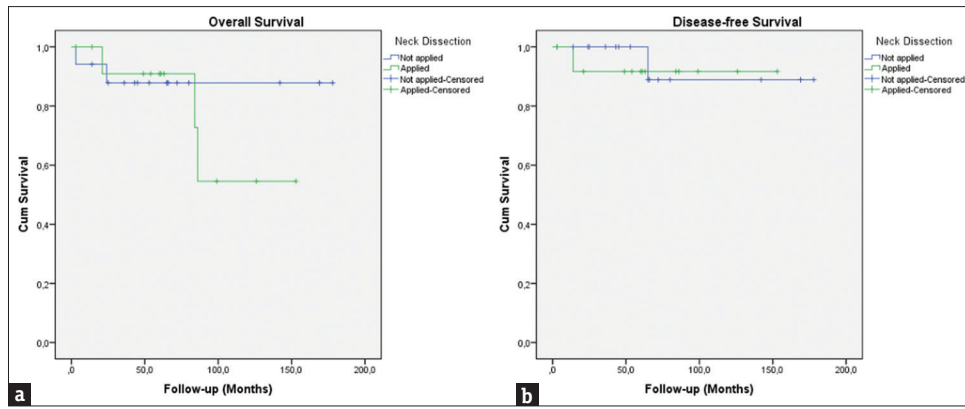
Figure 4: (a and b) Kaplan–Meier curves of overall survival and disease-free survival of the two groups based on neck dissection status

N0 disease and the extent of dissection is controversial. While some authors suggest that close follow-up is sufficient in clinical N0 disease, others recommend the use of elective neck dissection for all lip cancers. Close monitoring of low-risk patients without performing neck dissection reduces morbidity such as shoulder problems and cosmetic deformity.

In a meta-analysis by Bhandari *et al*.,[11] it was concluded that elective neck dissection should not be performed in clinical N0 lip cancers and close follow-up may represent a feasible option. [11] In another study involving 41 early-stage lip cancer patients, close follow-up with neck USG was performed in all cases during which one patient with T1 tumor developed locoregional recurrence and one T2 patient developed both locoregional and distant metastasis. The 5-year OS and DFS rates were 83.2% and 84.1%, respectively.[12] In the present study, OS and DFS rates in the combined T1 and T2 groups were 90.9% and 96.4%, respectively. Watchful waiting with regular neck USG appears to be a feasible, practical, and cost-effective strategy that is associated with decreased morbidity, particularly in early-stage disease.

In a study of 44 patients who underwent therapeutic supraomohyoid neck dissection due to lip tumor, 24 patients had metachronous metastasis and 20 patients had synchronous neck metastasis. In 89% of cases, metastasis occurred within the first 24 months after tumor resection. The time between the initial diagnosis of lip cancer and neck metastasis was approximately 14 months.[1] Therefore, close follow-up of patients for the first 2 years is essential for the detection of potential neck metastases. Serial USG examinations can be performed during the follow-up period. In a study by Morselli *et al*.,[13] no neck metastasis was detected among 57 T1 lip cancer patients at baseline or 32 months after primary surgery. In our study, no synchronous or metachronous neck metastases were detected in any

of the 30 patients. This could be due to the fact that majority of patients had T1 stage disease and the tumor size was <3 cm in most patients with T2 disease.

Level 1 lymph nodes generally represent the initial site of metastasis in lip cancers. Removal of the submandibular gland located at Level 1b in dissections involving this location remains a controversial issue. The following five groups of lymph nodes have been identified by Rouviere at this site with a rich lymphatic network: Preglandular, prevascular, retrovascular, retroglandular, and intracapsular. A therapeutic neck dissection should involve the removal of the lymph nodes in this location. It is important to use USG and computed tomography for early detection of metastases in this area in patients who have not undergone neck dissection. As per Basaran *et al*.,[14] the gland can be preserved in oral cavity cancers in the absence of lymph nodes or primary tumor directly attached to it. In the same study, one (T4) of 12 lip cancer patients had glandular invasion. In our study, the submandibular gland was removed during Level 1 dissection in patients who underwent neck dissection. However, since all cases had stage T1-2 disease, it had been possible to preserve the submandibular gland.

Factors associated with an increased risk of neck metastasis in lip cancers include tumor size, histopathological differentiation, and the presence of perinodal and lymphatic invasion.[15] In a study of 139 surgically treated patients by Vanderlei *et al*.,[16] patients with stage T2 disease were separated into two groups as T2a and T2b, as per a tumor size of <3 cm or ≥3 cm, respectively. Neck metastasis was found in 9%, 9%, 43.7%, and 52.2% of patients with T1, T2a, T2b, and T3 + T4 disease, respectively, leading to the recommendation that prophylactic neck dissection should be performed, particularly in tumors >3 cm. In a study by Casal *et al*.,[17] presence of perinodal and lymphatic invasion has been found to be associated with the risk of cancer-related deaths. In our study, the perinodal

invasion was found only in 23.3% of patients and no poorly differentiated tumors were observed, which could explain the low local and regional recurrence rates.

In a previous study evaluating the risk of lymph node metastasis in lip cancers, the most important predictors of lymph node metastasis included the tumor size, tumor depth, and tumor grade.[18] In that study, patients were separated into three groups as those with a high, medium, and low risk of lymph node metastasis. High risk was defined as a well-differentiated lesion with a tumor depth >5 mm or moderately-poorly differentiated lesion with a tumor depth >2.5 mm, while low risk was defined as a well-differentiated lesion with a tumor depth <5 mm or moderately-poorly differentiated lesion with a tumor depth <2.5 mm. Selective neck dissection or sentinel lymph node biopsy or aggressive close follow-up of Level 1-3 nodes were recommended for high-risk patients. In patients with bilateral tumor extension, bilateral selective neck dissection is required if neck dissection is to be performed. Neck dissection can be performed along with primary tumor resection or within 4 weeks.[18] The rationale for the delayed neck dissection is to allow a time window for the definitive pathology result regarding the depth of invasion.

Currently, there is no consensus on the management of N0 neck in patients with lower lip SCC. We performed neck dissection in our patients if the depth of invasion was >4 mm, as documented by the frozen section. Najim *et al.*[19] reported 87 lower lip and 15 upper lip cancer patients who underwent surgery. Eighty four percent of these patients had T1 tumors. These authors did not perform prophylactic neck dissection. After surgery, 24 patients developed lymph node recurrence, 17 on the lip, and two on both sites. They concluded that tumor thickness (≤4 mm or >4 mm) was a significant determinant of recurrence-free survival. A tumor thickness of more than 4 mm was associated with a three-fold increased risk of lymph node involvement. Similarly, Wemker *et al.*[18] found a higher risk of lymph node recurrence with a tumor depth >5 mm, for which selective neck dissection (level 1-3) or aggressive follow-up of the neck was recommended. Pastuzek *et al.*[20] found a mean tumor thickness of 8.3 mm in patients with lymph node involvement, while the corresponding figure was 3.72 mm in those without lymph node involvement. They showed that median tumor size and median tumor thickness were the predictors of nodal metastasis.

CONCLUSION

Early-stage lip cancers are tumors with favorable prognosis and survival, although the management

of cN0 lesions remains controversial. While close follow-up was found to be effective in some patient series, some experts recommend neck dissection on a selective basis. In our study, no occult metastases were detected in the neck dissection group. In addition, there were no significant differences in terms of OS and DFS rates between the two groups with and without neck dissection. Therefore, watchful waiting appears to be a good therapeutic alternative in patients with T1 and T2 tumors.

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Conflicts of interest
There are no conflicts of interest.

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