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PREVALENCIJA KARCINOMA DONJE USNE U SEVERNOJ MAKEDONIJI: PETOGODIŠNJA RETROSPEKTIVNA STUDIJA

THE PREVALENCE OF LOWER LIP CARCINOMA IN NORTH MACEDONIA: A 5-YEAR RETROSPECTIVE STUDY

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Sažetak

Uvod: *Karcinom donje usne čini približno 5% svih malignih tumora u predelu glave i vrata. Najznačajniji faktori rizika za nastanak karcinoma donje usne su dugotrajno izlaganje sunčevoj svetlosti i pušenje duvana.*
Cilj *ove studije bio je da se analiziraju kliničke i patohistološke karakteristike karcinoma donje usne i ispita njihov uticaj na pojavu metastaza na vratu.*
Materijal i metode: *Ukupno je analizirano 120 pacijenata, od kojih je 76,6% bilo muškog, 23,3% ženskog pola. Najzastupljenija starosna grupa bila je između 60 i 80 godina, pri čemu je više od 90% pacijenata bilo starije od 50 godina. Većinu ispitanika činili su poljoprivrednici i radnici na otvorenom, bez značajnih razlika prema polu i starosnoj strukturi.*
Rezultati: *Tumori su najčešće dijagnostikovani u veličinama T1 i T2, odnosno u stadijumu II bolesti. Lokalni recidivi registrovani su kod 5,8% pacijenata, dok su regionalni recidivi zabeleženi kod 8,3%, najčešće u periodu između prve i druge godine nakon hirurškog lečenja.*
Zaključak: *Recidivi karcinoma donje usne su relativno retki, ali je neophodno redovno i učestalo praćenje pacijenata tokom prve dve godine nakon operacije. S obzirom na to da poljoprivrednici i radnici na otvorenom predstavljaju populaciju sa povećanim rizikom za razvoj ovog karcinoma, preporučuje se sprovođenje skrining pregleda tokom svake stomatološke ili lekarske kontrole radi ranog otkrivanja bolesti.*

Ključne reči: *karcinom donje usne, faktori rizika, retrospektivna studija, lečenje, recidiv*

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Abstract

Introduction: *Carcinoma of the lower lip constitutes approximately 5% of malignant tumors in the head and neck region. Timely treatment may lead to a favorable clinical outcome. Primary risk factors for its occurrence include excessive sun exposure and smoking.*
Aim: *The aim of this study was to analyze the clinical and pathological characteristics of lower lip carcinoma and their impact on the occurrence of neck metastases.*
Materials and Methods: *A total of 120 patients with diagnosed lower lip carcinoma, 92 (76.6%) male and 28 (23.3%) female, were included in the study. The majority of the patients were farmers and outdoor workers, regardless of gender and age. This study employed retrospective analysis for a period of five years. Hospital records of all patients treated for this condition were analyzed. Patient and tumor characteristics: gender, age, occupation, TNM classification, stage, cell differentiation, and occurrence of local and regional recurrences were examined.*
Results: *The most common age affected by lower lip carcinoma was between 60 and 80 years, with over 90% aged above 50. Tumors were most frequently diagnosed at T1, followed by T2 size and Grade II. Local recurrences were detected in 5.8% of patients, while regional recurrences were noted in 8.3% of patients, most commonly in the period between the first and second year post-surgery.*
Conclusion: *Recurrences of lower lip carcinoma are relatively rare, but frequent follow-ups in the first two years post-surgery are necessary. As farmers and outdoor workers represent a high-risk group for lower lip carcinoma development, screening during every dental and general medical visit is essential for early detection.*

Key words: *lower lip carcinoma, risk factors, retrospective study, treatment, recurrence*

Introduction

Lip carcinoma is a malignant neoplasm of the upper or lower lip or the commissure[1] and is coded under the International Classification of Diseases as C00. Some studies consider lip cancer to account for 25% of oral carcinomas[2]. However, lip carcinoma is distinct from other types of oral cancers, often associated with increased exposure to ultraviolet radiation from sunlight. Lower lip carcinoma constitutes less than 5% of malignant tumors in the head and neck region, excluding other nonmelanoma skin cancers[2]. Histologically, 90% of lower lip cancers originate from squamous cells, with the remaining 10% comprising basal cell carcinomas and adenocarcinomas.

Lower lip squamous cell carcinoma may exhibit a slow clinical progression with a favorable prognosis if treated promptly and appropriately. However, in some patients, it can be aggressive, with increased morbidity and mortality, often due to the subsequent appearance of metastases in the cervical lymph nodes[3]. Early identification and treatment of these patients improve the chances of complete recovery.

The commonly used classification of lip carcinoma is based on tumor size, lymph node involvement, and the presence or absence of distant metastases (TNM)[4]. Broder's grading system[5] is the primary system used in studies related to lower lip carcinoma to analyze the histological characteristics of tumor cells. According to this system, lower lip carcinoma is categorized by differentiation as well, moderately and poorly differentiated.

Globally, the incidence by gender is higher in men than in women[6,7], with most patients being over 50 years of age[8,9]. Risk factors for developing lower lip carcinoma can be defined as environmental, pathological, and endogenous factors. Environmental factors include UV exposure, more common among people living in rural areas and those involved in agriculture. Pathological risk factors include smoking (including pipe smoking), occupation, alcohol consumption, socioeconomic status, and viral infections (e.g., HPV). Endogenous factors include familial and genetic predisposition, immunosuppression, and immunodeficiency. Race and cultural characteristics can also be considered risk factors.

The standard treatment for lower lip carcinoma is surgical excision of the lesion, potentially followed by radiotherapy, depending on the stage of carcinoma, its aggressiveness and differentiation, and involvement of neural and vascular structures[10–17]. Postoperative (or adjuvant) radiotherapy is recommended for patients with close or positive excision margins when re-excision is not feasible[18–24].

Therapeutic outcomes in these studies include assessments of locoregional control, recurrence, metastasis, overall survival, cause-specific survival, and disease-free survival[25–30].

This study aimed to analyze the clinical and pathological characteristics of lower lip carcinoma and their impact on the occurrence of cervical metastases in patients who underwent surgical treatment at the University Clinic for Maxillofacial Surgery in Skopje from 2016 to 2021.

Materials and Methods

A retrospective study was conducted for the period 2016–2021. All patients diagnosed with lower lip carcinoma were identified and analyzed in the database of the University Clinic for Maxillofacial Surgery in Skopje. For this purpose, electronic patient records were reviewed in the Hospital Information System, which integrates outpatient visits, hospital records, and all surgical interventions. The search used the International Classification of Diseases (ICD), 10th edition, code C00.4 for lower lip carcinoma. The database was also searched for codes C00, which denotes lip carcinoma in general, and C00.9, to avoid excluding any patients within the scope of interest. Since the preliminary diagnosis code D10.0, indicating benign lip neoplasm, is often used before final pathological confirmation, a review was also conducted of patients under this code, to include those with confirmed squamous cell carcinoma of the lower lip who might not have been subsequently recoded correctly. Additionally, operative logs, outpatient logs, and pathology reports were reviewed for the specified period to double-check data and include patients not entered electronically for any reason.

All identified patients were then thoroughly analyzed by reviewing their complete medical history, including the initial examination, type of surgical intervention, and follow-up visits.

The primary inclusion criteria for the study were as follows: patients must have a confirmed histopathological diagnosis of

squamous cell carcinoma of the lower lip, and have undergone surgical excision of the carcinoma, regardless of the technique used. Additionally, patients needed to have available basic demographic data (age and gender), and a postoperative follow-up, along with properly maintained medical records.

Patients were excluded from the study if they had previously received treatment for lower lip carcinoma outside the study period, had been treated in other institutions before being admitted to the Clinic in Skopje, had undergone neck dissection, or lacked postoperative follow-up and proper medical documentation.

The following data were analyzed in the selected patient group:

• **Age**—Expressed in years and categorized into 10-year age groups: 30–39, 40–49, 50–59, 60–69, 70–79, 80–89 and 90–99; Patients were further categorized into two age groups: under and over 50 years

• **Gender**—Expressed as male or female

• **Profession**—Categorized into three groups (farmer, worker, and other)

• **Tumor classification**—According to the TNM system

• **Definition of clinical stage**—By combining TNM classification parameters

• **Differentiation of tumor cells**—In histopathological analysis, graded from I to III, representing well, moderately, and poorly differentiated cells, respectively

• **Occurrence of local recurrence** (yes, no), as well as the time elapsed from surgery to recurrence in patients with detected local recurrence

• **Occurrence of regional recurrence** (clinically positive cervical lymph nodes).

The study was conducted in compliance with ethical principles and standards for conducting retrospective analyses, following the Ethical Code and the principles of the Declaration of Helsinki. Particular care was taken to protect personal data to ensure that patients could not be identified through the presentation and analysis of findings and results.

Data obtained during the research were statistically analyzed using the SPSS software package, version 22.0 for Windows (SPSS, Chicago, IL, USA). Qualitative variables were analyzed using ratio coefficients, proportions, and rates, presented as absolute and relative numbers. Quantitative variables were analyzed using measures of central tendency and dispersion. The Shapiro–Wilk W test was used to determine the normality of frequency distribution for the variables. Risk factors were quantified using the Odds Ratio (OR) and confidence intervals (CI). A difference test was used for comparing proportions. Pearson's chi-square test, Fisher's exact test, and the Fisher–Freeman–Halton test were used to determine associations between certain dichotomous variables. Spearman's rank correlation coefficient assessed the relationship between numerical variables with non-normal frequency distributions. Non-parametric tests, such as the Mann–Whitney U test for two independent samples and the Kruskal–Wallis H test for multiple independent samples, were used to test the significance of differences between two or more numerical variables with non-normal frequency distributions. All statistical analyses applied a significance level of $p < 0.05$.

Results

Over the five-year period covered by the study (2016–2021), a total of 120 patients of both sexes with squamous cell carcinoma of the lower lip were examined. According to the histopathological findings for each patient in the sample, the distribution was as follows:

• 115 cases (95.83%) of Carcinoma planocellulare Squamous cell carcinoma

• Three cases (2.5%) of Carcinoma planocellulare verrucous

• One case (0.83%) of Carcinoma planocellulare corneum

• One case (0.83%) of Carcinoma planocellulare invasivum

In the sample of 120 patients (100%), 92 (76.67%) were male and 28 (23.33%) were female patients, with a male-to-female ratio of 3.3:1. For $p < 0.05$, the percentage of male patients diagnosed with squamous cell carcinoma of the lower lip was significantly higher compared to female patients.

The average age of participants with squamous cell carcinoma of the lower lip across the entire sample was 67.15 ± 11.16 years, with a minimum/maximum age range of 34–87 years. Fifty percent of these patients were over 67 years of age, with a median interquartile range of 68 (59–75), and 25% were over 75 years. For $p < 0.05$, a significant age difference was observed between genders, with males diagnosed with squamous cell

carcinoma of the lower lip being significantly older than females. Within the sample of patients with squamous cell carcinoma of the lower lip, there were no patients under 30 years of age, and in the 30–40 age group, only one male patient (0.83%) was recorded. The highest proportion of patients was in the 70–79 age group, with 39 cases (32.5%), followed by the 60–69 age group, represented by 35 cases (29.17%). The lowest proportion of squamous cell carcinoma cases during the study period was in the 40–49 age group, with 9 cases (7.5%), followed by the 80–89 age group with 15 cases (12.5%) (Table 1).

Additional analysis of patients with squamous cell carcinoma of the lower lip by age ≤ 50/> 50 years showed that 108 patients (90%) were over 50, while only 12 (10%) were aged ≤ 50. Within the sample from 2016 to 2021, the distribution by age ≤ 50/> 50 showed that 81 male cases (88.04%) were over 50 years. Among female cases, 27 (96.43%) were over 50, with only one case (3.57%) aged ≤ 50, involving a 43-year-old female patient.

The majority of patients in the sample were farmers, totaling 73 (60.83%). Of the male patients, 58 (63.04%) were farmers, while 15 (53.33%) of the female patients had the same occupation. For $p < 0.05$, the percentage of male farmers was significantly higher than that of female farmers. The second most common occupation was general worker, with 34 patients (28.33%) in the total sample. Among male patients, this occupation was recorded for 28 individuals (30.43%), and among female patients, for six individuals (21.43%). For $p < 0.05$, the percentage of male workers was significantly higher compared to female workers. Other occupations were noted in 13 (10.83%) of the total patients, including 6 (6.52%) males and seven (25%) females. In the entire sample, for $p < 0.05$, a significant association was observed between gender and occupation among patients diagnosed with squamous cell carcinoma of the lower lip, as indicated by Pearson's chi-square test (Table 2).

According to the TNM classification for the primary tumor (T), the largest proportion of cases—68 (56.67%)—had a primary tumor classified as T1 (≤ 2 cm in the largest diameter), followed by 39 cases (32.5%) classified as T2 (> 2 cm but ≤ 4 cm in the largest diameter). Eleven cases (9.17%), were classified as T3 (> 4 cm in the largest diameter).

Among the total sample, four cases (3.54%) were identified with clinically positive regional lymph nodes classified as N1 (metastasis in a single unilateral lymph node, ≤ 3 cm), three cases (2.65%) with N2 (metastasis in a single or bilateral lymph node, > 3 cm but ≤ 6 cm), and two cases (1.77%) with N3 (metastasis in a lymph node > 6 cm).

No cases in the sample of patients with squamous cell carcinoma of the lower lip were diagnosed with distant metastasis M1 based on TNM classification.

It was found that the largest proportion of patients with squamous cell carcinoma of the lower lip (2016–2021), 63 (52.5%), had a TNM classification of T1NXMX (tumor ≤ 2 cm in its largest diameter, with regional lymph nodes and distant metastasis unable to be assessed). The second most common classification, found in 18 patients (15%), was T2NXMX (tumor > 2 cm but ≤ 4 cm in its largest diameter, with regional lymph nodes and distant metastasis unable to be assessed). The third most common TNM classification of squamous cell carcinoma of the lower lip was T2N0M0 (tumor > 2 cm but ≤ 4 cm in its largest diameter, without metastasis to regional lymph nodes or distant metastasis), with 15 patients (12.5%) in the sample. Full results of TNM classification by groups are presented in Table 3.

The analysis indicated that the majority of the sample with squamous cell carcinoma of the lower lip were categorized as G2 (moderately differentiated tumor cells), totaling 99 cases (82.5%). Only two patients (1.67%) had G1 differentiation (well-differentiated tumor cells), one from each gender. No cases were identified in the sample with G3 or G4 tumor cell differentiation.

Analysis showed that the majority of patients with squamous cell carcinoma of the lower lip (2016–2021) were classified as Stage I (localized tumor not spread to lymph nodes or other tissues), totaling 54 cases (45%). Stage II (larger tumor not spread) included 25 patients (20.83%). Eleven patients (9.17%) were designated as Stage III (a larger tumor likely spread to lymph nodes or other tissues).

Of the total sample, 97 patients (93.27%) were without local recurrence, with only seven cases (5.83%) experiencing a local recurrence. Regional recurrence was recorded in 10 patients (8.33%) with squamous cell carcinoma of the lower lip. Among those with regional recurrence, three cases (2.5%) experienced it within less than one year post-intervention, and seven cases (5.83%) between one and two year post-intervention.

Table 1. Distribution of patients with carcinoma of the lower lip by age groups and association calculated by Pearson chi-square test

Parameter		Men	Women	Total	p
Age groups					
30 - 39	**N** **%**	1 1,09%	0 0%	1 0,83%	X^2=5,829; df=5; p=0,2122
40 – 49	**N** **%**	8 8,70%	1 3,57%	9 7,50%	
50 – 59	**N** **%**	17 18,48%	4 14,29%	21 17,50%	
60 - 69	**N** **%**	30 32,61%	5 17,86%	35 29,17%	
70 - 79	**N** **%**	26 28,26%	13 46,43%	39 32,50%	
80 - 89	**N** **%**	10 10,87%	5 17,86%	15 12,50%	
≤50	**N** **%**	11 11,96%	1 3,57%	12 10%	X^2=1,677; df=1; p=0,1953
>50	**N** **%**	81 88,04%	27 96,43%	108 90%	
Total	**N** **%**	92 76,67%	28 23,33%	120 100%	
X^2=Pearson Chi-square test;					

Table 2. Differences among patients with lower lip carcinoma according to profession and gender

Profession		Men	Women	Total	Difference test	Pearson Chi-square test
Farmer	**N**	58	15	73	p=0,0001*	X^2=7,697; df=2; p=0,0213*
	%	63,04%	53,57%	60,83%		
General worker	**N**	28	6	34	p=0,0001*	
	%	30,43%	21,43%	28,33%		
Other	**N**	6	7	13	p=0,7768	
	%	6,52%	25%	10,83%		
Total	**N**	92	28	120	p=0,0001*	
	%	76,67%	23,33%	100%		
*significant at p< 0,05						

Table 3. Distribution of pathological parameters according to TNM classification

TNM groups		Gender			Difference test
		Men	Women	Total	
T1 NX MX	**N**	46	17	63	p=0,3224
	%	50%	60,71%	52,50%	
T2	**N**	2	0	2	-
	%	2,17%	0%	1,67%	
T1 N0 M0	**N**	4	1	5	p=0,8571
	%	4,35%	3,57%	4,17%	
T2 NX MX	**N**	14	4	18	p=0,9044
	%	15,22%	14,29%	15%	
T3	**N**	3	0	3	-
	%	3,26%	0%	2,50%	
T3 N1 MX	**N**	0	1	1	-
	%	0%	3,57%	0,83%	
T3 N2 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T3 NX MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N0 M0	**N**	11	4	15	p=0,7452
	%	11,96%	14,29%	12,50%	
T2 N0 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N1 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T3 N1 M0	**N**	2	0	2	-
	%	2,17%	0%	1,67%	
T3 N2 M0	**N**	2	0	2	-
	%	2,17%	0%	1,67%	
T3 N0 M0	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N3 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N3 M0	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
TX	**N**	1	1	2	p=0,3717
	%	1,09%	3,57%	1,67%	
Total	**N**	92	28	120	-
	%	76,67%	23,33%	100%	

Discussion

Cumulative exposure to UV radiation, primarily from the sun, is considered the main risk factor for the development of squamous cell carcinoma of the lower lip[9]. With increasing age, cumulative UV exposure also increases proportionally, which accounts for the higher prevalence of lower lip carcinoma in older populations, particularly in individuals in their seventies and eighties[31,32]. For younger patients with lower lip carcinoma, other systemic factors, such as immunosuppression or immunodeficiency, should be ruled out[33]. In our analysis, the patient with carcinoma in the 30–40 age group did not exhibit immune system impairment. This patient probably had higher cumulative exposure to sunlight, but other molecular and cellular changes, which are beyond the scope of this study, should also be considered as potential contributors to the cellular mechanisms that allow uncontrolled cell division.

In the analysis conducted for this research, the highest proportion of patients was in the 70–79 age group, with 39 cases (32.5%), followed by the 60–69 age group with 35 cases (29.17%). Although age and gender differences in lower lip carcinoma groups were not markedly significant, a noticeably higher percentage of men aged 60–69 had lower lip carcinoma (32.61%) compared to women in the same age group (17.86%), which is consistent with data from the literature[10]. This discrepancy likely reflects the fact that male patients typically experience greater cumulative sun exposure due to occupations requiring outdoor work (e.g., agriculture, construction), as well as generally lower rates of protective measures against UV radiation. This rationale is further supported by the observation that the proportion of male patients with lower lip carcinoma under the age of 50 is slightly higher than that of female patients. Additionally, the accumulation of molecular changes resulting from exposure to risk factors, such as UV radiation, smoking, and other carcinogens, or as a consequence of the biological ageing process, which is associated with DNA damage accumulation, plays a significant role[11,12].

The findings from our study are fully consistent with those from available literature regarding the patients' profession[13,28,34,35]. It is well known that lower lip carcinoma is primarily associated with UVB radiation from sunlight, particularly affecting individuals with prolonged sun exposure, such as farmers and outdoor laborers. The highest proportion of lower lip carcinoma cases in our study was observed among farmers of both sexes, followed by laborers. The significant gender differences in patient proportions are largely attributed to men's generally greater cumulative sun exposure due to prolonged outdoor activity in agricultural and other work settings.

The relatively low rate of cervical lymph node metastasis aligns with the literature[30,36–38]. An 8.33% metastasis rate is neither excessively high nor particularly low. Studies indicate a marked decline in survival rates when nodal involvement is detected during follow-up, thus making neck dissection for patients with clinically negative cervical nodes a controversial issue. The "wait and watch" approach is advocated by some authors, given the low incidence of regional metastasis in lower lip carcinoma. However, when metastasis is detected, neck dissection combined with adjuvant radiotherapy is recommended.

The results obtained in our study align with findings in the literature, where recurrence most often occurs within the first two years following treatment[10,13,17,18,39–42]. Local recurrence, as expected, is observed within the first year post-surgery due to the proximity of tumor cells to resection margins and healthy tissue in the lower lip. In contrast, regional recurrences, represented by metastatic involvement of the cervical lymph nodes, are typically detected between the first and second year post-surgery, which is explained by the time required for malignant cells to disseminate through lymphatic circulation and establish growth within cervical lymph nodes[22,29,38,43–46].

A longer follow-up period for patients (preferably up to five years) is recommended to obtain a more objective picture of the time frame in which recurrences occur post-treatment.

A potential limitation of this study is the shorter follow-up period for patients treated at the Maxillofacial Surgery Clinic in Skopje during the later years of the study period. Nonetheless, all patients in the sample were followed for at least one postoperative year, with those treated in the early years of this study (2016, 2017, and 2018) having longer follow-up periods—six, five, and four years, respectively—compared to three, two, and one year for those treated in the subsequent years of the analysis. There are various weaknesses in many retrospective studies, noting that most studies lack two groups for direct comparison and often only describe the outcome of surgical therapy or radiation therapy as the sole treatment modality (Table 4).

Table 4. Data from retrospective studies about various survival rates and provided treatment for patients with squamos cell carcinoma of the lower lip.

Study	Year	n	OS	DFS	SS	LRC	Bt	Surg	Rad	S+R
de Visscher et al, 1999 (14)	1980-1994	256	+	+	-	-	-	+	+	-
Wilson et al, 2005 (15)	1980-2000	52	-	-	-	+	-	+	-	+
Beauvois et al, 1994 (16)	1972-1991	237	+	-	+	+	+	-	-	-
Tombolini et al, 1998 (17)	1970-1992	57	+	+	-	+	+	-	-	-
Cowen et al, 1990 (18)	1970-1985	299	-	-	-	+	+	-	-	-
Heller et al, 1979 (19)	1955-1969	171	+	-	+	+	-	+	-	-
Petrovich et al, 1979 (20)	1945-1975	250	+	-	-	+	-	-	+	-
Wu et al, 1985 (21)	1958-1974	74	+	-	-	-	-	+	+	-
Giuliani et al, 1989 (22)	1974-1986	121	+	+	-	+	-	+	-	-
Ngan et al, 2005 (23)	1996-2004	13	+	+	+	+	+	-	-	-
Aslay et al, 2005 (24)	1988-2003	41	+	+	-	+	+	-	-	-
Orecchia et al, 1991 (25)	1973-1988	47	+	+	-	+	+	-	-	-
Luna-Ortiz et al, 2004 (26)	1990-2000	113	+	-	-	-	-	+	+	-
Hemprich et al, 1989 (27)	15 years	352	+	-	-	-	-	-	+	-
Califano et al, 1994 (28)	1975-1987	105	+	-	+	-	-	+	-	-
Bilkay et al, 2003 (29)	1983-1999	118	+	-	+	+	-	+	-	-
Jaquet et al, 2005 (30)	1983-2001	24	+	-	+	+	-	+	-	-
van der Wal et al, 1996 (31)	1985-1992	14	-	-	-	+	-	+	-	-
Zitsch et al, 1995 (9)	1940-1987	1252	+	-	+	-	-	+	+	-
Beltrami et al, 1992 (32)		80	+	-	+	-	-	+	-	-
Gooris et al, 1998 (33)	1974-1994	85	-	+	-	+	+	-	+	+
Miltenyi et al, 1980 (34)		170	+	-	+	-	-	-	+	-
de Visscher et al, 1996 (35)	1980-1992	108	+	+	-	-	-	-	+	-
Boddie et al, 1977 (36)	1943-1974	1308	+	-	+	-	-	+	+	-
McCombe et al, 2000 (37)	1979-1988	323	-	-	-	+	-	+	+	-
Cerezo et al, 1993 (38)	1971-1976	117	-	-	-	+	-	+	+	+
Babington et al, 2003 (9)	1980-2000	130	+	+	-	+	-	+	+	+
Holmkvist et al, 1998 (39)	1986-1999	50	-	+	-	+	-	+	-	-
Cruse et al, 1987 (40)	1962-1982	117	+	-	+	-	-	+	-	-
Antoniades et al, 1995 (41)	1979-1989	906	+	-	-	-	-	+	+	+

Kutluhan et al, 2003 (42)	1994-2000	31	+	-	+	+	-	+	-	-
dos Santos et al, 1996 (43)	1980-1999	58	+	+	-	+	-	+	-	-
de Visscher et al, 1998 (44)	1979-1992	184	+	+	-	+	-	+	-	-
Rao et al, 1998 (45)	1987-1989	62	+	-	-	-	-	+	+	+
Blomgren et al, 1988 (46)	25 years	165	+	-	+	+	-	+	-	-

n- number of patients; OS- overall survical; DFS- disease free survival без болест; SS- specific survival; LRC- loco-regional control; Bt- brachitherapy; Surg- surgery; Rad- radiotherapy; S+R, surgery + radiotherapy

Conclusion

Farmers and outdoor workers over the age of 50 are at an increased risk of developing squamous cell carcinoma of the lower lip, and they should regularly undergo screening during visits to their general dentist and primary care physician, regardless of any other health issues they may be facing.

Patients who have undergone surgical intervention for squamous cell carcinoma of the lower lip should be monitored with regular and frequent follow-ups during the first two years, as local and regional recurrences are most likely to occur during this period. Timely monitoring can prevent local recurrence and the metastatic spread of the cancer, thereby increasing survival chances.

Conflict of Interest

All authors confirm that there is no conflict of interest of any form concerning the work presented in this article.

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