REPUBLIC OF AZERBAIJAN

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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

IMPROVEMENT OF SURGICAL AND EPIDEMIOLOGY APPROACHES TO LIP CANCER

Specialty: 3224.01 – "Oncology"

Field of science: Medicine

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GENERAL CHARACTERISTICS OF THE WORK

Relevance of the topic. Lip cancer accounts for 5% of all cancers, except for non-melanomatous skin cancer of the head and neck, and 25-30% of oral cavity cancers[1]. According to the 2018 national assessment of the GLOBOCAN IARC database in 185 countries, lip and oral cavity cancer is the 16th most common malignancy in the world, with 355,000 new diagnoses and 177,000 deaths in 2018[2] Fortunately, lip cancer is included in the list of malignant cancers that can affect more of the head and neck. The 10-year survival rate from this disease is 98%, and the recurrence rate is 90%[3]. Cancer of the lower lip accounts for 88-98% of lip cancers[4]. Pathological processes in the lips are caused by various meteorological factors – sun rays, wind, ionizing effects, sharp temperature changes, various exogenous and endogenous carcinogenic substances, various viral infections (Herpes zoster and chronic HPV infections)[5], immunosuppression, inflammation of the lip, the influence of processes, different types of traumas of the red border of the lip, harmful habits such as smoking and alcohol is undeniable[6].

When evaluating the occupational characteristics of people with lip cancer, it was determined that they mainly belong to farmers, sailors, field workers and other similar occupational groups[6]. Due to lip

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cancer, mainly male and especially between 50 and 60 years of age have a higher risk[4].

Since lip cancer is localized outside, it is detected early and allows for effective treatment. However, although a number of successes have been achieved in solving the problem of lip cancer in recent years, the number of patients initially detected in II-III stages continues to increase, and the long-term results of treatment are not considered completely satisfactory. In this regard, it is necessary to select and optimize reconstructive surgical treatment methods. Clinical-morphological characteristics of the tumor during lip cancer, degree of invasiveness, the impact of metastases on regional and distant lymph nodes on the results of reconstructive surgical operations has not been fully studied, whether performing neck dissections remains controversial[7,8,9,10]. According to the results of the conducted studies, metastatic damage to regional lymph nodes during lip cancer ranges from 2.53-42.3%, and currently there are no clear guidelines for conducting surgical operations in such cases[11]. All these listed justify the goals and objectives of the research work.

The object of study. The research was carried out between 2000 and 2015 at the Department of Otorhinolaryngology and Head and Neck Surgery, Ibn Sina Hospital, Faculty of Medicine, Ankara University, Republic of Turkey (n=59), and between 2010 and 2019, at the Department of Head and Neck Tumors at the National Oncology Center (n=108) patients were included, respectively, who were

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diagnosed with cancer, treated, and whose data were retrospectively analyzed after treatment. A total of 167 patients were included.

The purpose of the research work was to study the epidemiological characteristics of lip cancer in the Republic of Azerbaijan, to optimize diagnostic and treatment methods.

Tasks of the research:

1. Studying the frequency, prevalence and epidemiological characteristics of lip cancer in the Republic of Azerbaijan;
2. Studying the informativeness of radiation diagnostic methods used in lip cancer;
3. Determining the treatment tactics of lip cancer patients depending on the specificity of patient groups and optimizing whether neck lymphodissection is performed in patients and its volume;
4. Determination of 5-year survival rates and recurrence frequency of lip cancer patients after primary treatment. Development of optimal recommendations for practical application according to the results of treatment.

Research methods: magnetic resonance imaging (MRI) of the neck region, computed tomography (CT) of the neck, ultrasound examination of the neck (USM), positron emission tomography. (PET-CT) examination methods, reconstructive and neck dissection surgical methods were used.

The main terms used for the defense of the dissertation work:

1. Its epidemiological characteristics should be taken as a basis for preventive measures of lip cancer.
2. The high incidence of lip cancer and the effectiveness of treatment should be determined based on predictive criteria.
3. In the organization of preventive measures against lip cancer, special oncological precautions are required from health workers for people whose primary ring is 50-59 years old for male and 60-69 years old for female, to people with bad habits and bad oral hygiene.
4. Carrying out neck dissection along with resection of lip cancer leads to an increase in the standard of living and a decrease in the number of recurrences.

Scientific innovation of research. For the first time in the Republic of Azerbaijan, in the National Oncology Center, the detailed clinical features of lip cancer, early detection, age characteristics, regional spread frequency, regional and distant metastases and extracapsular invasion features, selection of treatment tactics, were investigated 5-year survival indicators on clinical material. The social and demographic picture of cancer was studied, a comparative analysis of surgical methods was carried out, the obtained quantitative indicators were analyzed and the main prognostic criteria were developed.

Theoretical-practical significance of research: Based on the results of the study, were given scientifically based recommendations for early diagnosis and treatment of lip cancer in practical oncology These recommendations have made it possible to reduce the frequency of relapses and metastases in patients with lip cancer, improve the overall survival rate and the effectiveness of treatment.

Discussion of dissertation materials. The main terms of the dissertation and the obtained results dedicated National Oncology Mark in the scientific and practical conferences to the birthday of the National leader H.A. Aliyev (Baku, 2017, 2022 and 2023), at the International forum "Innovation oncology" (Moscow, 2021), the XIII meeting of oncologists and radiologists of Eurasian and CIS countries – report and discussion were made at the congress (Kazakhstan, 2022). A report and discussion were held at the international scientific conference dedicated to the 100th anniversary of the national leader H.A. Aliyev on the topic "Actual problems of medicine and prevention" (Baku, 2023).

The main provisions of the dissertation were discussed at the AR SN MOM interdepartmental conference (Baku, October 18, 2023, protocol No2), at the meeting of the FD 1.02 Dissertation Council 3224.01 "oncology" specialty operating under the MOM (Baku, February 21, 2024 protocol № 1).

Implementation of scientific research. The results of the research in the clinical-practical work of the head and neck tumors department of the National Oncology Center of the Ministry of Health of the Republic of Azerbaijan, AR SN AN of H. Aliyev. The teaching

process and lectures is they applied of the oncology department of the Azerbaijan State Physicians Improvement Institute.

Published research works: 15 scientific works on the topic of the dissertation – 3 articles, 2 theses published in foreign journals, 7 articles, 3 theses in the Republic journals.

The name of the organization where the dissertation was conducted. The dissertation work was performed at the Otorhinolaryngology and Head and Neck surgery department of Ibn Sina Hospital of Ankara University Medical Faculty of the Republic of Turkey and the National Oncology Center of the Ministry of Health of the Republic of Azerbaijan.

Volume and structure of the dissertation. Dissertation entry and literature review (62738 marks), study material Chapter II on materials and methods (20 922 characters), Chapter III covering personal studies - 9650, IV chapter – 19 166, chapter V – 38 317, conclusion – 49 698, results - 2139, practical examples (579 signs), including sections. It consists of 203 209 signs. In literature, 201 scientific studies are used (15 of them are Azerbaijan, 5 of them – Turk, 57 – Russian and 124 foreign ones). The dissertation is illustrated with 19 tables, 11 diagrams, 33 pictures, 4 graphs and 1scheme.

MATERIALS AND METHODS OF THE RESEARCH

Clinical characteristics of symptoms. The study was conducted 167 patient, between 2000 and 2015 at the Department of Otorhinolaryngology and Head and Neck Surgery, Ibn Sina Hospital, Faculty of Medicine, Ankara University, Republic of Turkey and Between 2010 and 2019, 59 and 108 patients, who were diagnosed and treated with lip cancer at the SN National Oncology Center of the Republic of Azerbaijan, and whose data were retrospectively examined after treatment, were included, respectively. Patients' anamnesis: age and gender distribution, complaints at the time of application, the period from the onset of complaints to the date of their visit to the doctor, chronic diseases, operations, whether they have any cancer, general physical examinations, as well as ear-nose-throat examination indicators evaluated together. In addition, habits such as smoking, drinking alcohol,

information on the use of dentures were recorded, the oral cavity was examined and the level of hygiene was assessed. 29 (17,4%) of the patients were female and 138 (82,6%) were male. It was 61.3±1,1 years. While there was no statistically significant difference between the age distribution of both genders (p=0.186) (table 1).

Table 1

Demographic characteristics of patients

The groups	Age (year) Mean±SS
Male	60,1±1,1 (n=138)
Female	67,0±0,7 (n=29)
P	0,186
Total	61,3±1,1 (n=167)

When the use of smoking and alcohol, which are among the minor risk factors for the development of lip cancer in patients, is evaluated among the patients it was determined that 46,7% of smoking was used in the whole group (n=78), and the average consumption of smokers was 28,2±1,5 packs/year. The rate of regular alcohol consumption in the patient group was determined as 29,3% (n=49).

When looking at the occupational distribution of patients, it was determined that farmers are the largest group (n=63, 37,7%), after that, pensioners (n=43,25.7%), official (n=33, 19.8%), workers (n=17, 10.2%) and housewives (n=11, 6.6%) was done. When occupation and smoking habits, which are two important factors included in the etiology of lip cancer, are evaluated together, it was determined that 70,6% (n=12) of workers, 66,7% (n=22) officials, 50,8% (n=32) of farmers, 25,6% (n=11) of pensioners and 0,9% (n=1) of housewives use sigarettes. A statistically significant difference was determined according smoking (p=0.010). and to alcohol drinking habits (p=0.012). This shows that the drinking habits of farmers are more, so 42.9% farmers (n=27), 32.6% pensioners (n=14), 23.5% workers (n=4), 12.1% official (n=4). this difference is because housewives smoke and to alcohol less than other professional groups was established (figure 1).

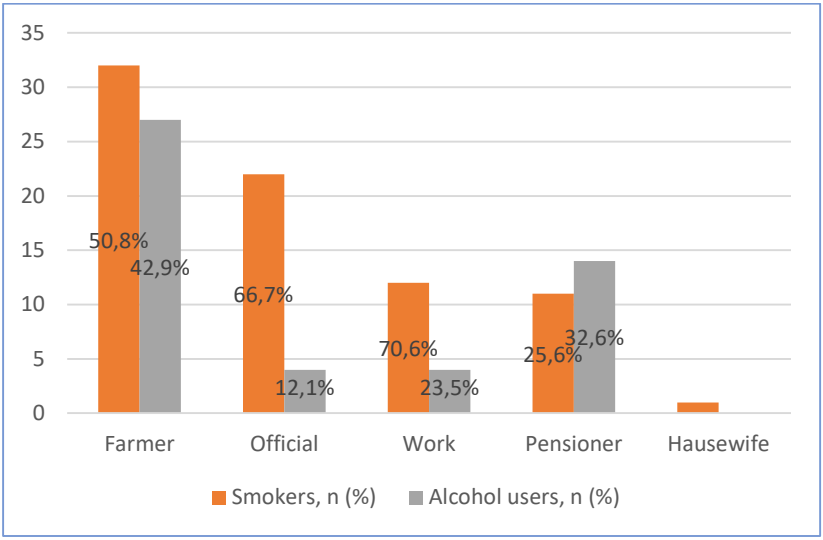


Figure 1. Occupational distribution of patients and smoking and alcohol use habits according to their profession

Oral health assessment, which is another important factor in the etiology of lip cancer, revealed that 38,3% (n=64) of patients had dentures. Oral hygiene of 64,1% (n=104) patients was assessed as bad in oral hygiene examinations of patients.

In terms of the localization of lip lesions, it was determined that 91,0% (n=152) were located in the lower lip and 7,8% (n=13) in the upper lip, 1.9% (n=2) it was determined that it spread to the entire lip. In 34,7% (n=58) of patients in this group, the derivative was localized on the right side, in 26,3% (n=44) on the left side, in 31.7% (n=53) in the midline. 7,2% (n=12) in the patient on both sides, in other words, it covered the entire lip.

Research methods. The diagnosis of lip cancer is based on histopathological analysis of the material taken from the damaged tissue has been approved.

Patients were divided into stages according to the TNM system in two different periods: before surgery and after surgery. The distri-

bution of local tumor (T), regional lymph node (N) and distant metastasis (M) identified in the evaluation is shown. After surgery, T1 – 55,1% (n=93), T2 – 36,5% (n=60) and T3 - 6,6% (n=11). In addition, T4 locally advanced tumor was identified in 2 people (1,2%) (table 2).

Table 2

TNM classification of lip cancer patients

Stages	n (%)
Pathology T	
1	93 (55,1)
2	60 (36,5)
3	11 (6,6)
4	2 (1,2)
is	1 (0,6)
Pathology N	
0	146 (87,4)
1	8 (4,8)
2a	1 (0,6)
2b	6 (3,6)
x	9 (5,4)
Pathology M	
M	-
Mx	3 (1,8)

Distant metastases were not recorded in patients and mainly in only 3 (1.8%) patients (Mx) it was not possible to identify distant metastasis. Among patients prevailed stage 1 (52,7% – n=88) and stage 2 (34,1% – n=57) (figure 2).

According to the results of the biopsies taken from the lesions before the operation and the pathological examination of the material excised after the operation, the majority of patients (n=86, 51,5%) had high-differentiated squamous cell carcinoma.

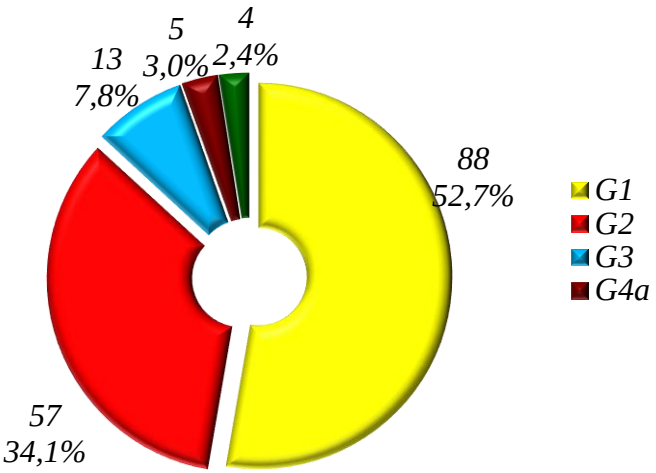


Figure 2. Lip cancer staging

In the postoperative pathological evaluation high differentiated squamous cell carcinoma (n=74; 44,3%), moderately differentiated squamous cell carcinoma (n=55; 32,9%), low differentiated squamous cell carcinoma (n=10; 6,0%), basal cell carcinoma (n=8; 4,8%), verrucous carcinoma (n=4; 2,4%), mucoepidermoid carcinoma (n=1, 0,6%), malignant mesemchymal tumor (n=1, 0.6%), adenocarcinoma (n=2, 1.2%), keratosis (n=2, 1.2%) and chronic inflammation (n=1, 1.7%) forms were identified.

As we mentioned above, USM (Toshiba), CT (Siemens) and PET-CT (Siemens) examinations were performed in addition to the visual method in the examination of lip cancer, in determining metastases to the neck lymph nodes and other organs.

In our research, PET-CT was performed on 21 people, regular CT was performed on 33 people, USM was performed on 140 people, and both CT and PET-CT were performed on 6 people, and both USM and CT were performed on 12 people. In these patients, USM sensitivity – 92.9%, specificity – 90.5%, CT sensitivity – 83.3%, specificity – 88.9%, PET-CT sensitivity – 100.0%, specificity – It was 87.5%. Although the sensitivity of PET-CT is 100.0%, among these examination

methods, USM is more preferred due to both its specificity and financial availability (figure 3).

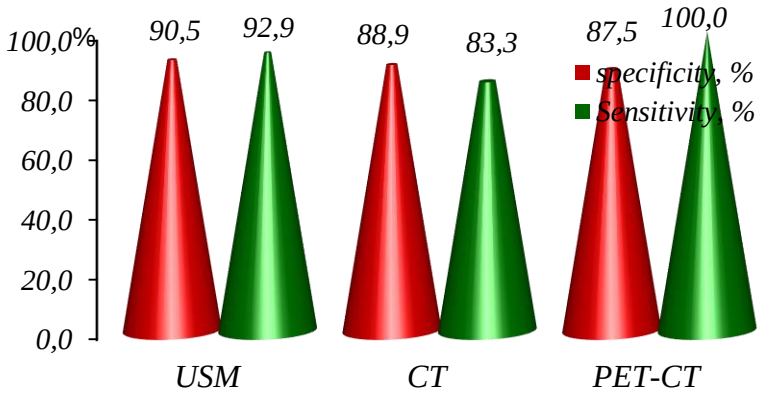


Figure 3. Informativeness of imaging methods in lip cancer patients

Statistical analysis methods. According to the method of research – clinical; by design – analytical; according to volume – selection; by type – scientific; according to the material – prospective; according to duration – width; According to the location, the clinic has been evaluated. For the descriptive statistics of the study, numerical data were presented as means and standard deviations, and categorical data were presented as frequencies and percentages. Non-parametric evaluation was performed with the Mann-Whitney U test for numerical data, and categorical data were compared with the Chi-square test. In the study, The indicators of the patients included in the research group were included in a special statistical card. The Kaplan-Meier (KM) estimator (procedure) was used to compare survival and recurrence indicators on these data in groups separated by different selection (dissection, recurrence) methods. Calculation methods of medical-statistical indicators used in oncology were used for the quantitative assessment of the epidemiological situation. All statistical analyzes were performed two-way using SPSS 21 (IBM Inc, USA) software.

RESULTS OF THE TEST EPIDEMIOLOGICAL CHARACTERISTICS OF LIP CANCER IN THE REPUBLIC OF AZERBAIJAN

In the study, the spread of malignant neoplasms of the lip was studied and the dynamics of morbidity and mortality with this disease in the Republic of Azerbaijan during the years 2010-2019 were evaluated.

The statistical analysis conducted by us showed that during the studied period (2010-2019) in the Republic, lip cancer is in a minor place in the structure of morbidity with malignant neoplasms, and its extensive rate is 0,3% in both male and female. At the same time, the decreasing trend of this indicator was observed both in male (from 0,5% in 2010 to 0,2% in 2019) and in female (from 0,2% in 2010 to 2019 up to 0,6%).

Table 3

Standardization index of lip cancer incidence in the Republic of Azerbaijan in 2019

Age	Intensity indicator (100 min population)		Mean standard		Standardized indictor (100 min population)	
	male	female	male	female	male	female
0-17	–	–	28026,7	24361,1	–	–
18-29	–	–	19362,9	17906,4	–	–
30-39	–	–	17156,8	17525,6	–	–
40-49	0,3	–	12510,8	13105,4	0,04	–
50-59	1,0	0,1	12119,4	13523,3	0,1	0,01
60-69	1,1	0,4	7405,2	8641,2	0,08	0,03
70>	1,2	0,4	3418,2	4937,0	0,04	0,02
∑	0,3	0,08	100000	100000	0,3	0,06

The statistical analysis of the disease intensity factor revealed a slight decrease of this indicator in both male and female. So, in

the studied period, its range among male was $0.4^0/_{0000}$-$0,3^0/_{0000}$, and among female – $0,1^0/_{0000}$-$0,08^0/_{0000}$. The results of the statistical analysis showed that during the studied period, the rate of injury in male decreased. So, if the injury rate in 2010 was $5,8^0/_{0000}$, in 2019 this indicator decreased to $4,1^0/_{0000}$. It remains for the female population, where injury rates tend to increase – from $1,6^0/_{0000}$ in 2010 to $2,0^0/_{0000}$ in 2019. The calculation of mortality rates during the studied period was as follows: its extremely high level in males ($0,3^0/_{00}$), and low mortality rates in females ($0,07^0/_{00}$). Thus, during the studied period, a very obvious decrease of this indicator is observed: both in male ($0,6^0/_{00}$-$0.1^0/_{00}$), and in female ($0,1^0/_{00}$-$0,02^0/_{00}$).

In general, lip cancer occupies a minor place in the structure of morbidity with malignant neoplasms, its extensive rate, regardless of age, is 0,3%.

The analysis of incidence according to the intensity ratio shows a slight decrease in both males ($0,4^0/_{0000}$-$0,3^0/_{0000}$) and females ($0,1^0/_{0000}$-$0,08^0/_{0000}$).

During the studied period, the age-standardized indicator of morbidity does not change in general (in male – $0,3^0/_{0000}$ and in female – $0,1^0/_{0000}$-$0,06^0/_{0000}$). The highest standardized indicator is determined in the 50-59 age group in male ($0,1^0/_{0000}$), in female – in the 60-69 age group ($0,03^0/_{0000}$).

LIP CANCER TREATMENT

Lip cancer is more likely to be diagnosed early and treated successfully. However, patients in the last stage require wide resections and complex reconstruction methods. Successes in the surgical treatment of lip cancer are: complete removal of the tumor, preservation of the anatomical structure and functions of the lip as much as possible, and achieving an aesthetic result.

Patients with lip cancer underwent surgical operations depending on the size and localization of the tumor, including the somatic condition of the patient and metastases to the lymph nodes (table 4).

Table 4

Methods of surgical reconstruction applied to patients

Surgery variations	n (%)
Wedge resection (W)	79 (47,3)
V flap	41 (24,6)
Karapandzic flap	15 (9,0)
Bernard	18 (10,8)
Abbe-Estlander flap	4 (2,4)
Abbe flap	3 (1,8)
Local flap	2 (1,2)
Mucosal incision flap	2 (1,2)
Nakajima flap	3 (1,8)

As can be seen from the results of the study, there is no significant difference between the surgeries performed for lip cancer in both countries. Wedge resection or W resection operations are preferred (47,3%). Was the taken local spread of the disease (T classification) into account in surgical operations performed. The size and location of the tumor are important in choosing the type of operation. In addition, patients with T1 tumors with tumor sizes of 7-18 mm underwent V and W resection. W resection was performed mainly for T2 tumors with a size of 22-38 mm. 2 patients with T2 tumors size 35-38 mm in G3 stage Abbe flap, size 14-20 with T1 tumors size 18-20 mm located in the midline of the lower lip, patients with T2 tumors size 28-35. The Bernard method was performed on the patient with T3 tumors of size 38-42. Patients with T2 tumors 27-38 mm in size, patients with T3 tumors 46-48 mm in size, and patient with T4 tumor 56 mm in size received a Karapandzic fragment, patients with T2 and T4 tumors 36 and 48 mm in size was applied the Nakajima flap method.

COMPARISON OF GROUPS WITH NECK DISSECTION AND NO NECK DISSECTION

In addition to resection and reconstruction operations, radical and selective neck dissection operations were also performed on lip cancer patients.

Neck dissection was applied to 89 (53,3%) of the 167 patients whose data were evaluated in the research conducted. 78 patients (46,7%) did not undergo neck dissection.

Dissection procedures applied to patients undergoing neck dissection shown in the table. 25 patients (15.0%) had left supraomohyoid neck dissection, 4 patients (2.4%) had left selective neck dissection (right level 1A, 1B, 2A, 2B, 3, 4), 19 patients (11.4%) had bilateral supraomohyoid neck dissection, 16 patients (9.6%) had bilateral selective neck dissection (6 (3.6%) patients - bilateral level 1A, 1B, 2,3,4; 4 patients (2.4%) - right level 1 ,2, 3, 4 + left level 1-2A; 3 (1.8%) patients - right level 1A+left level 1B, 2A, 2B, 3; 3 (1.8%) patients - left level 1,2,3 + right level 1,2), right supraomohyoid neck dissection in 9 (5.4%) patients, right supraomohyoid right superfascial paroidectomy in 5 (3.0%) patients, right selective neck dissection (right level 1A, 1B, 2A, 2B, 3, 4) in 3 (1.8%) patients, 3 (1.8%) patients underwent right supraomohyoid + left selective neck dissection (left level 1A, 1B, 2, 3, 4), 3 (1, 8%) patients underwent right supraomohyoid+left selective neck dissection (level 1), 2 (1.2%) patients underwent radical extended neck dissection (table 5).

When examining the reconstruction methods used in patients with and without neck dissection, it was found that there was no statistically significant difference between both groups (p=0.376). Wedge resection or W plasty (n=39; 51.3%) and V flap (n=26; 33.3%) were the primary methods used in the non-dissection group, the same trend in the other group - neck dissection group also recorded: W plasty (n=40; 43.8%) or Wedge resection and V flap (n=15; 16.9%).

As can be seen, V resection is more prevalent in the non-neck dissection group than in the neck dissection group. Unlike the other group, in the neck dissection group, reconstructive surgical methods

such as Karapandzic flap, Bernard, Abbe-Estlander flap, Abbe flap were performed more often (figure 4).

Table 5

Applied neck dissection procedures

Neck dissection procedures	n (%)
Left supraomohyoid neck dissection	25 (15,0)
Left selective neck dissection (right level 1A, 1B, 2A, 2B, 3, 4)	4 (2,4)
Bilateral supraomohyoid neck dissection	19 (11,4)
Bilateral selective neck dissection:	**16 (9,6)**
Bilateral level 1A, 1B, 2,3,4	6 (3,6)
Right level 1 ,2, 3, 4 + left level 1-2A	4 (2,4)
Right level 1A+ left level 1B, 2A, 2B, 3	3 (1,8)
Left level 1,2,3 + right level 1,2	3 (1,8)
Right supraomohyoid neck dissection	9 (5,4)
Right supraomohyoid right superfascial paroidectomy	5 (3,0)
Right selective neck dissection (right level 1A, 1B, 2A, 2B, 3, 4)	3 (1,8)
Right supraomohyoid + left selective neck dissection (left level 1A, 1B, 2, 3, 4)	3 (1,8)
Right supraomohyoid+left selective neck dissection (level 1)	3 (1,8)
Radical extended neck dissection	2 (1,2)

The habits of smoking and alcohol use were investigated between the groups that underwent neck dissection and those that did not. In Turkey, it was found that 41,0% (n=32) of non-dissection patients smoked 19,9±2,4 packs/year on average, and 59,0% (n=46) of the dissection group smoked 33,7±2,0 packs/year on average.

There was no statistically significant difference between the groups according to the smoking percentage of the patients (p=0,168), but when the consumption amounts were compared, it was determined that the patients in the neck dissection group smoked significantly more than the limit (p=0,007). 40 patients (81.6%; p=0.005) who used alcohol were in the neck dissection group (figure 5).

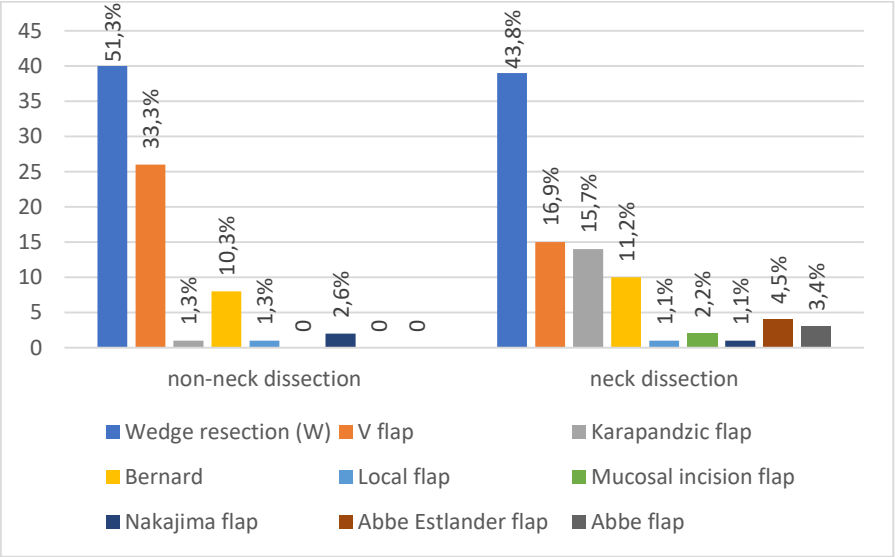


Figure 4. Reconstruction methods in the neck dissection group

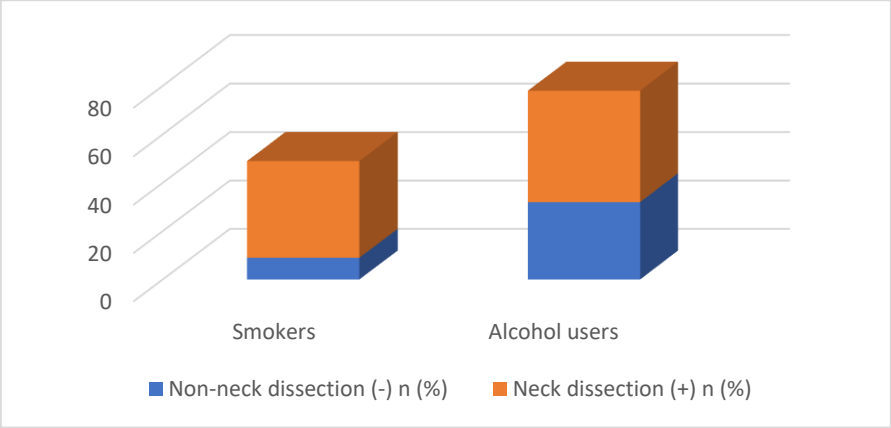


Figure 5. Smoking and alcohol use habits in the neck dissection group

In the dissection group, 39,3% of all professions (n=35) of farmers, 22,5% of offisial (n=20), 9,0% of workers (n=8), 22,5% of pensioners (n=20, 0%), and in the non-dissection group, 35,9% of farmers

(n=28), 14,6% of offisial (n=13), 10,1% of workers (n=9), 22,5% of retirees (n= 20) was established. However, there is no statistically significant difference between both groups in terms of occupational distribution (p=0.471).

Oral hygiene was evaluated worse in patients who neck dissection (74,2%; n=66) than in the non-dissection group (52,6%; n=41).

It was shown that there was no statistically significant difference between both groups according to the percentage of localization of the derivative in the lower or upper lip. A statistically significant difference (p=0,022) was determined between the two groups in terms of which side of the lip the lesion was located on, as 43.6% of injuries in the non-dissection group were located in the midline, while in the dissection group injuries were mainly on the left (32,6 %) were localized on the side, and the amount of lesions located in the middle side was only 21.3% (figure 6).

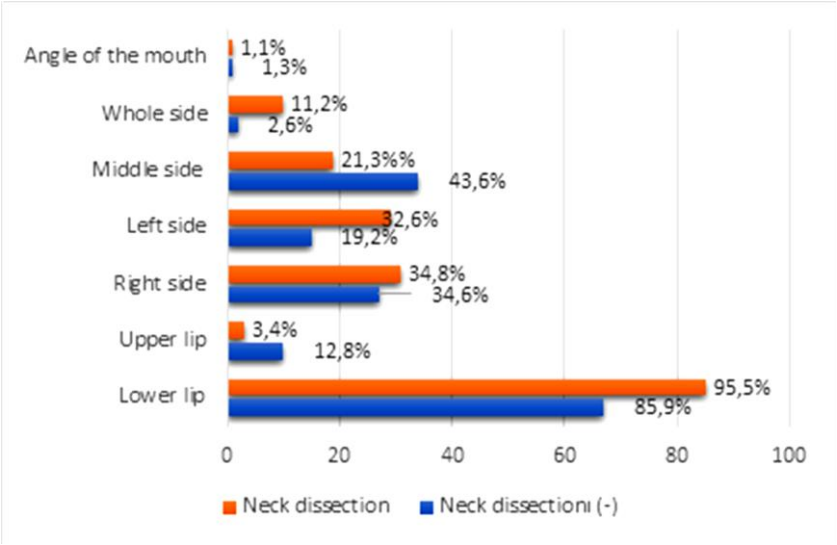


Figure 6. Localization of the derivative in groups according to neck dissection.

İn the group without neck dissection, T1 (n=57; 73.1%) locally diffuse was recorded more often. In the neck dissection group, a higher

percentage of T2 (n=41; 46.1%) and T3 (n=10; 11.2%) locally disseminated tumors were observed compared to the dissection group, but T-No statistically significant difference was found (p=0.122). At the same time, among the patients who underwent dissection, 2 (2.3%) had T4 locally disseminated tumors.

In terms of spread of the regional tumor to the lymph nodes, most of the patients in the non-dissection group (n=76, 97.4%) had N0, while in the dissection group, N1, N2a and N2b metastases were found, respectively 10.1% (n=9), 3.4 (n=3) and 4.5% (n=4).

A statistically significant difference was determined between the stage of the dissection and non-dissection groups (p=0.041). Accordingly, 60.3% (n=47) of the non-dissection group - stage 1, 33.3% (n=26) - stage 2, 3.9% (n=3) - stage 3, 1.1% (n=1) – stage 4a, while in the dissection group, stage 1,2, 3 and 4a disease rate was 46.1% (n=41), respectively; 34.8% (n=31); It was 11.2% (n=10.0%) and 4.5% (n=4). Thus, neck dissection operations were applied mainly in T2, T3 and T4 tumors, as well as in G3 and G4a stage.

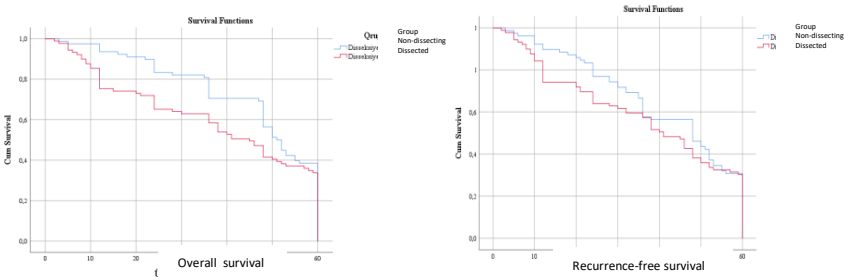
LIP CANCER SURVIVAL RATES

In addition to the treatment of the primary tumor, the diagnosis and treatment of cervical metastases is also an important factor determining the prognosis.

When analyzing the survival of patients after lip cancer, 21 patients (12.6%) died, 4 (2.4%) died from lip cancer, and 17 (n = 10.2%) died from various other causes, mainly heart failure. It is noted that in the group where cervical dissection was used, 4 patients were registered who died from lip cancer; these patients were classified as T4aN0M0, T2N2bM0, T4N1M0 and T3N1M0. Patients were followed for 60 months (5 years) after surgery, 21 of them experienced tumor recurrence, and 3 of these patients underwent bilateral supramohyoid cervical dissection. During the 5-year follow-up period, recurrence was observed in 27% (n=3) of patients with T3-T4 tumors (n=11) who underwent cervical dissection, 3 patients were prescribed CDM for lymph node metastases, 8 patients were diagnosed with

lymph node metastases as a result of neck dissection, the risk was avoided.

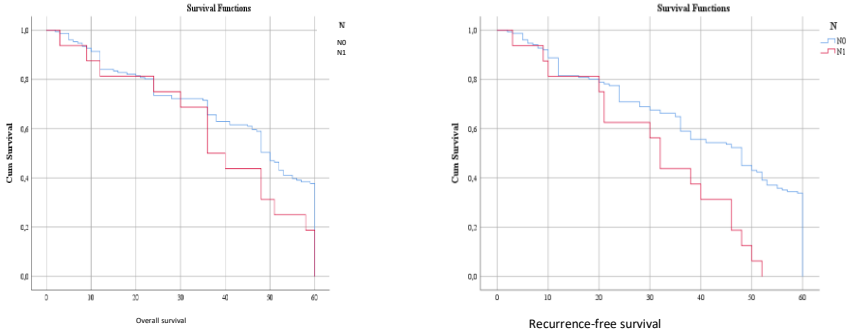
Overall, the mean 5-year survival rate among patients with lip cancer was 42.3 ± 1.5 months and 97.6%. According to the Kaplan-Meier plot, 5-year overall survival in the group without neck dissection was Median in the group with dissection: 51.0 ± 2.0 months (95EI: 47.2-54.8 months), and among patients who underwent dissection, - the median was: 45.0±3.8 months (95EI:37.6-52.4 months). Disease-free survival in the group without neck dissection Median: 48.0±5.3 months (95EI:37.6-58.4 months), and in the group with dissection: Median: 41.0±3.6 months (95EI:33,9-48.1 months). There was no statistically significant difference between both groups in terms of 5-year overall survival (p=0.124) and disease-free survival (p=0.452) (graph 4). There was no statistically significant difference between both groups in terms of 5-year overall survival (p=0.124) and recurrence-free survival (p=0.452) (graph 1).



Graph 1. Overall and recurrence-free survival rate in the dissection groups

Overall survival in patients without regional lymph node metastases (cN0). Median: 50.0±1.3 months (95% CI: 47.5–52.5 months), disease-free survival. Median: 48.0±3.9 months (95% CI: 40.4–55.6 months). In patients with metastases (cN+), overall and disease-free survival was 36.0±5.0 months (95% CI: 26.2-45.8 months) and 32.0±2.0 months (95% CI: 26.2-45.8 months) respectively. 28.1-35.9 months). The recurrence rate was 14.6% (n=13) in the dissection group

and 20.5% (n=16) in the non-dissection group. Although there was no statistically significant difference between the groups in overall survival (p=0.125), there was a statistically significant difference in disease-free survival (p<0.001). As can be seen, patients with cN+ lip cancer have significantly lower disease-free survival compared to patients with cN0 (graph 2).



Graph 2. Five years overall and recurrence-free survival of lip cancer patients according to cN0 and cN+

Thus, if early-stage lip cancer is properly treated, the average 5-year survival rate reaches 97,6%. Cervical lymph node metastasis has a negative impact on the prognosis and the 5-year survival rate decreases to 38,9% compared to cNO. Selective neck dissection (especially supraomohyoid dissection at I-III level) is recommended in patients with T2, T3-T4 cNO neck metastasis risk, and other patients should be monitored dynamically. In modern times, since no tomography method can identify occult metastases 100%, prophylactic neck dissection has been recommended because the prognosis and survival rates are better in N0 necks. Prophylactic dissection can be of great importance in the prevention of hidden metastases and in improving the overall and recurrence-free survival rates of the disease.

The results of the conducted research showed that the recommendation of our clinic is surgical operation, and the treatment method should be determined according to the patient's somatic condition, tumor size and metastasis.

CONCLUSIONS

1. In the Republic of Azerbaijan in 2010-2019, lip cancer is in a minor place in the structure of morbidity with malignant neoplasms, and its extensive indicator is 0.3% among both male and female. In the studied period, the intensity index is $0.4^0/_{0000}$-$0,3^0/_{0000}$ among male, and $0,1^0/_{0000}$-$0.08^0/_{0000}$ among female [8,9, 10,11].
2. The specificity of USM was 90,5% and the sensitivity was 92,9% among the radiation diagnostic methods used in lip cancer. Although the sensitivity of PET-CT is 100,0%, among visualization methods USM is considered more informative due to its specificity [15].
3. The incidence of T1 and T2 locally advanced tumors among lip cancer patients was determined to be 88,0%. After initial treatment, the recurrence rate in patients is 17,4% and is mainly observed in T3 and T4 tumors.
4. In determining the treatment tactics of lip cancer patients stage of the disease, tumor size, localization, bad habits of the patient, level of oral hygiene and metastases to the neck lymph nodes are important and optimizing the volume of lymphodissection in observation groups [4,6].
5. The 5-year overall survival rate is 97,6%.Metastasis to regional lymph nodes led to a decrease in overall ($p=0,125$) and disease-free ($p<0.001$) survival of patients, since in patients with metastases to regional lymph nodes (cN+) overall survival was 36,0±5,0. months, without relapse – 32,0±2,0 months, and in patients without metastases (cN0) – 50,3±1.3 months and 48,0±3,9 months, respectively [4, 3, 14].
6. Dissection of the neck together with resection of lip cancer does not have a statistically significant ($p=0.085$) effect on overall survival, but it leads to a decrease in the risk of recurrence, so that the total frequency of recurrence is 17.4%, while in the group with dissection of the neck - 14, 6%, in the group without neck dissection – 20.5% ($p=0.169$) [13,14].

PRACTICAL RECOMMENDATIONS

1. Special oncological care is required for persons aged 50-59 years for male and 60-69 years for female in the organization of lip cancer prevention measures.
2. In T1 and T2 localized tumors of lip cancer, the use of skin-muscle pieces from anatomically close areas is recommended.
3. Carrying out neck dissection along with resection of lip cancer can allow timely detection of hidden metastases to the neck lymph nodes, increase the survival rate, decrease the number of recurrences and improve the effectiveness of treatment.

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LIST OF ABBREVIATIONS AND TERMS

AJCC – American Joint Committee on Cancer
IJV – internal jugular vein
DNA – Deoxyribonucleic acid
EBV – Epstein-Barr Virus
CI – confidence interval
GRBD – Radical expanding neck dissection
HPV – Human Papilloma Virus
CT – Computed tomography
MRND – Modified Radical Neck Dissection
MRI – Magnetic Resonance Imaging
N – Nervus
OAS – Accessory Nerve
PET – Positron Emission Tomography
END – Radical neck dissection
SCM – sternocleidomastoid
SND – Selective neck dissection
TNM – Primary tumor, zonal lymph nodes, distant metastasis
ISM – Ultrasound examination
SCC – – squamous cell cancer

The defense of the dissertation will be held on 21 june 2024, at 14:00 at the meeting of the Dissertation council FD 1.02 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the National Center of Oncology of the Ministry of Health of the Republic of Azerbaijan.

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